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Review

Plant mutation breeding in agriculture

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Abstract

A mutation is a sudden heritable change in the DNA in a living cell, not caused by genetic segregation or genetic recombination. Mutation breeding is the purposeful application of mutations in plant breeding. Unlike hybridization and selection, mutation breeding has the advantage of improving a defect in an otherwise elite cultivar, without losing its agronomic and quality characteristics. Mutation breeding is the only straightforward alternative for improving seedless crops. Since the first release of mutant cultivars that resulted from basic mutation research in Europe, mutation breeding has found a niche in plant breeding because of these advantages. Methodologies for mutation induction have been improved in main crops for both physical and chemical mutagens, and selection methodologies for mutant populations have been described. New mutagenic agents such as ion-beam radiation and cosmic rays are being investigated and a hitherto undescribed wide spectrum of mutations has been observed. Nevertheless, alkylating agents and ionizing radiation are still popular. The development of robust *in vitro* techniques for many crop species has contributed to improving the efficiency of mutation breeding. The ability to handle large mutagenized populations in a confined space, faster progeny turnover in vegetatively propagated species and the ability to screen for several biotic and abiotic stress factors in the culture environment make *in vitro* approaches very efficient. Mutant screening has undergone revolutionary changes in the past decade with reverse genetic approaches taking precedence. Therefore, integration of mutation techniques with molecular approaches is providing exciting opportunities for modern plant breeding.

Keywords: Radiation, Evolution, Crop, Mutagenesis, Domestication, Reverse genetics, *In vitro* selection

Review Methodology: ISI Web of Knowledge and Google Scholar were searched electronically using appropriate key words for different sections. IAEA publications and databases available online as well as manuals and conference proceedings available through library resources were accessed. Review papers, books and book chapters on different aspects of mutation breeding were also consulted.

Introduction

A mutation is a sudden heritable change in the DNA in a living cell, not caused by genetic segregation or genetic recombination [1]. Mutation breeding can be described as the purposeful application of mutations in plant breeding. Plant breeding can be seen as human-guided evolution of crop plants, and genetic variation is its foundation. When desired variation is available in different cultivars of a crop, its breeding objectives may be achieved through cross-breeding. However, when one or more of the parent cultivars possessing the desired characters used in cross-breeding are poorly adapted, it becomes necessary to implement a back-crossing strategy to recover the elite type. Another problem encountered in conventional crossbreeding is the poor combining ability of some parental genotypes. For example, aromatic rice varieties have poor combining ability, and cross-breeding with non-aromatic varieties will lead to a decrease in aroma and quality [2, 3]. Under such circumstances, mutation induction can be of advantage to produce cultivars with desired traits within defined germplasm pools.

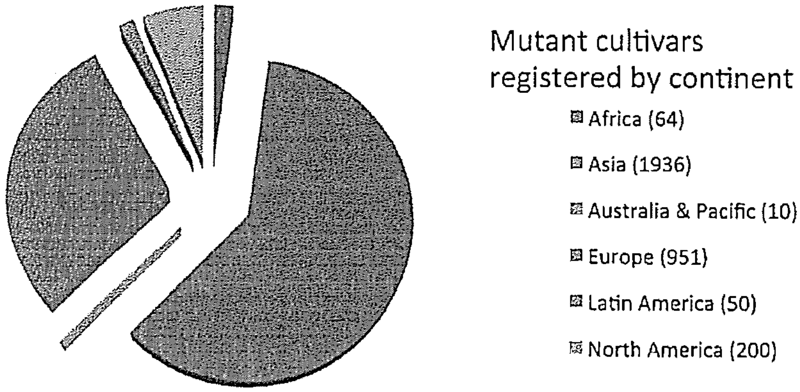

Figure 1 Number and proportion of mutant cultivars released, categorized by continents (based on IAEA mutant database [18])

Sometimes genes conferring undesirable characters are tightly linked to genes controlling desirable traits. In such a situation, mutation induction may result in a crossing-over event or isolation of an independent mutation for the desired trait. In crops that do not produce seeds, such as edible banana or seedless grapes, mutation induction may be the only acceptable way of increasing variability for developing new cultivars [4–7]. This also applies to many root and tuber crops [4, 5, 7, 8], and the development of novel colours and variations in ornamental plant species propagated vegetatively [1, 5, 9, 10]. Cross-breeding in vegetatively propagated perennial crop species, such as many fruit crops, is also subject to constraints of time, growing space and clonal identity, and mutation induction can be a valuable breeding strategy [5, 8, 11].

Induced mutations have a history of 83 years since the first publications by Muller [12] and Stadler [13, 14]. Plant mutation breeding has been applied actively for over a half century, with the Joint FAO/IAEA Division based in Vienna assisting developing countries to quickly adopt advances in the technology [15–17]. This approach helped widespread use of mutation technology and the release of 3211 registered mutant varieties (Figures 1 and 2) in more than 170 different plant species to date [18]. Some of these mutant cultivars have revolutionized agriculture not only in densely populated developing countries but also in agriculturally advanced countries.

Types of mutations

Descriptions of different types of mutations, their classification and effects have been reviewed in the literature [1, 7, 19, 20]. Mutations can be broadly divided into intragenic or point mutations (occurring within a gene in the DNA sequence), intergenic or structural mutations within chromosomes (inversions, translocations, duplications and deletions) and mutations leading to changes in the chromosome number (polyploidy, aneuploidy and haploidy). In addition, it is important to distinguish between nuclear and extranuclear or plasmone (mainly chloroplast and mitochondrial) mutations, which are of considerable interest to agriculture.

Intragenic mutations

Loss or gain of one or more base pairs is referred to as deletions and insertions, respectively, and if they do not occur in multiples of three nucleotides in the sequence, it results in a frame-shift mutation (within exons of coding regions). Therefore, deletion or insertion of a single base pair or two may result in a substantial effect, including the loss of function through a shift within the reading code. However, the effect of such a mutation can depend also on the location where the change happens. Thus, a frame-shift mutation near the $3'$ end of the gene will result in only a change in the terminal part of the polypeptide chain as translation takes place only in a $5' \rightarrow 3'$ direction. Under such circumstances, even a frame-shift mutation can result in a functionally similar protein.

The other type of gene mutation is base-pair substitution, common with chemical mutagens such as alkylating agents. They result in the incorporation of alternate bases during replication. For example, A-T base pair can be switched to G-C, C-G or T-A. Thus, one base of a triplet codon is substituted by another, resulting in a changed codon. Where that change leads to an altered amino acid sequence, the result is a mutated protein. If a purine base is replaced by another purine base (G by A or A by G) or a pyrimidine by another pyrimidine (T by C or C by T) the substitution is called a transition. Transitions are by far the most common types of mutations and C to T transitions occur more frequently than any other base pair substitutions [21, 22]. If a purine base is substituted by a pyrimidine, or *vice versa*, the substitution is called a transversion. McCallum *et al.* [23] calculated that in *Arabidopsis*, about 5% of mutations caused by alkylating agent ethylmethane sulfonate (EMS) will introduce a stop codon (non-sense mutation), 65% will be missense

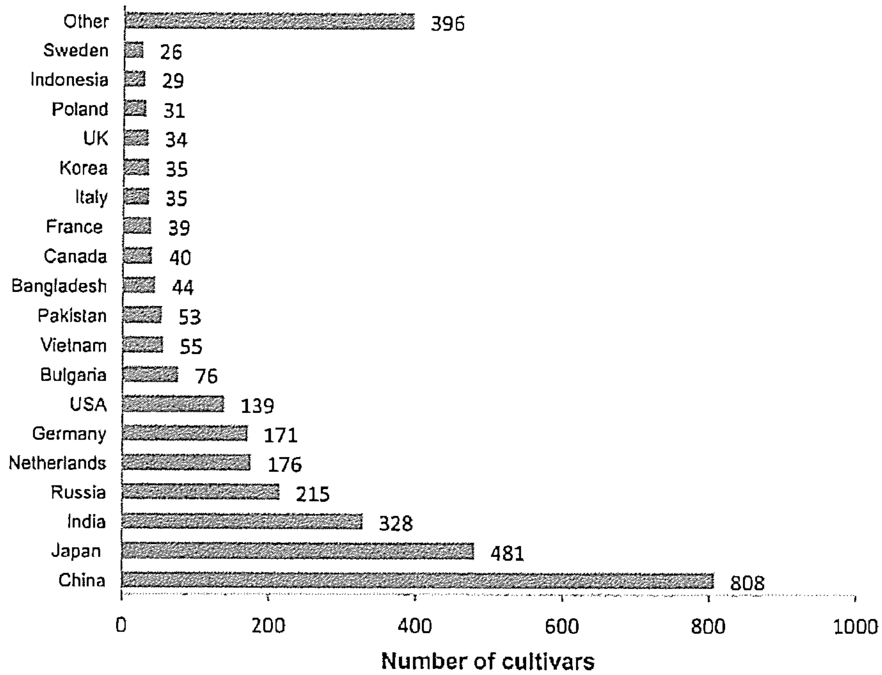

Figure 2 Number of mutant cultivars released in different countries (based on IAEA mutant database [18])

mutations (a codon coding for one amino acid is converted to a codon coding for another amino acid), and 30% will be silent changes, where the final protein product remains unchanged.

Chromosome rearrangements or structural mutations

Structural mutations are the result of chromosome breaks and their rearrangements. Ionizing radiation results mostly in such changes [1, 19, 24]. Four categories of such rearrangements can be distinguished: deletions or deficiencies, duplications, inversions and translocations. About 90% of the chromosome aberrations brought about by ionizing radiation are deletions and often are lethal [1]. However, some deletions can block biochemical pathways and, for example, if this happens in a pathway leading to the synthesis of a toxic metabolite, such a deletion may result in a useful non-toxic plant product. Duplications have been a cornerstone in crop evolution, particularly at diploid level. For example, the smallest known plant genome, that of *Arabidopsis*, carries three major duplications that have taken place between 14.5 and 300 million years ago [25]. Similar evolutionary patterns have been unravelled for sunflower as well [26]. Such studies lead us to the conclusion that most, if not all, angiosperms are palaeopolyploids.

Inversions (180° rotation of blocks of nucleotides) and translocations are also common in evolution of crop plants. For example, by comparative mapping, Heesacker *et al.* [27] identified five translocations and two inversions in cultivated sunflower during its evolution. Emerging evidence of the role of chromosomal rearrangements in crop evolution suggests that crop improvement can be quickened through the combination of distant hybridization coupled with radiation breeding. The first example of this application was demonstrated by Sears by transferring a small section of an *Aegilops umbellulata* chromosome containing a gene for resistance to brown rust (*Puccinia triticina*) to hexaploid wheat through a bridging cross employing *Triticum dicoccoides* and irradiation [28].

Changes in chromosome number – genome mutations

Mutations at the genome level, leading to changes in chromosome number are also of utmost importance in crop evolution and plant breeding [29]. These mutations are broadly divided into allopolyploidy, autopolyploidy and aneuploidy. It is estimated that 50–70% of the ornamental flower crops are polyploids [1]. Allopolyploidy is the result of a combination of genomes of two or more species and commonly arises through interspecific or intergeneric hybridization followed by the doubling of chromosomes. Evolution of many crops, such as wheat, soybean, cotton and *Brassica* species, has taken this path [29, 30]. Mutant selection is often complicated by the presence of duplicated homoeologous allele pairs in allopolyploids, but targeting induced local lesions in genomes (TILLING) populations are helpful in identifying and targeting these alleles for breeding. There are examples of crop evolution at a diploid level, and rice, maize, barley, sesame and tomato belong to this group [30].

Autopolyploidy is the result of multiplication of chromosome number within the species and the nucleus contains more than two homologous chromosomes. Cultivated and tuber producing wild potatoes have a polyploidy series of 24, 36, 48, 60 and 72 chromosomes [31, 32]. Edible banana evolved at a triploid level through polyploidization at a single-genome level as well as through allopolyploidy as a result of interspecific hybridization of the two wild species *Musa acuminata* and *Musa balbisiana* [33]. The great diversity of banana germplasm, comprising fruits suitable for cooking through to soft and sweet desert types, can be attributed to this divergence at a genome level. Modern breeding of sugar beet is based on hybridization of diploids with tetraploids to produce hybrid triploids. Sugar beet produces the highest yield and sugar content at a triploid level [34]. Autopolyploidy can be induced by the use of compounds that inhibit spindle fibre formation during mitosis, thus the divided chromosomes are retained in the same cell. Homozygous lines for heterosis breeding can also be obtained using these chemicals on haploid plants produced through anther, microspore or ovule culture [35]. Colchicine and oryzalin are the most widely used chemicals for artificial polyploidization [1].

Extranuclear or plasmone mutations

In higher plants, two extranuclear genetic systems can be distinguished, those of chloroplast and mitochondria. Mutations in these genomes have been shown to be of value in agriculture. Many authors have shown that nitroso compounds produce a high frequency of plasmone mutations. Using nitroso compounds, chloroplast mutations for antibiotic resistance have been induced in *Nicotiana* [36, 37]. Chlorophyll mutations observed already in the first generation after treatment with mutagens are also the result of such mutations. These mutations can be used to an advantage in breeding ornamental crops with various leaf or fruit characters as they often occur as chimaeras [38, 39]. As plastid mutations are carried through the cytoplasm, they are maternally inherited and do not behave in a Mendelian fashion. Resistance to some fungal diseases and cytoplasmic male sterility are other important characters inherited through plasmonic genes and discussed in detail by van Harten [1].

Mutagenic agents and their use in mutation breeding

Physical mutagens

Ionizing radiation was used exclusively in mutation research until the effects of certain chemicals on the DNA were published in the mid-1940s [40, 41]. In the beginning, X-rays were used, but γ-rays from radioactive sources such as ^{60}Co and ^{137}Cs became popular as they were made available to many developing countries through the IAEA. Fast neutrons from nuclear reactors can also be used, particularly as this irradiation service is available through the Joint FAO/IAEA Division in Vienna. Ionizing radiation results in chromosomal breakages, allowing cross-linking of DNA strands. More deleterious effects, therefore, can be expected than from chemical mutagens that result in minor changes in the DNA such as base-pair substitution. Among physical mutagens, ultraviolet (UV) rays are non-ionizing. They therefore have low penetration and are effective in producing purine or pyrimidine dimers, resulting in point mutations. UV rays can be effectively used to irradiate pollen in the late or early uninucleate stages [1, 19, 42]. Radiation doses and conditions for irradiating seeds and buds have been optimized and published for main crop species [1, 7, 8, 19, 20]. Treatment conditions and doses need to be experimentally derived for new or minor crop species as information may not be readily available. A suitable dose for irradiation has often been recommended as the one that reduces growth and morphogenic performance to 50% (GR 50) of untreated controls [19, 20, 43], but for seeds it is recommended to use 2–3 doses [19]. The main external factors affecting irradiation are oxygen and moisture contents, temperature and post-irradiation storage conditions [1, 19].

Chemical mutagens

High rates of chromosome aberrations resulting from ionizing radiation and the accompanied detrimental effects made researchers look for alternate sources for inducing mutations. As a result an array of chemical mutagens has been discovered. A wide variety of chemical mutagens, however, makes it difficult to establish common rules and conditions for treatment. Classification of chemical mutagens, methods of treatment, post-treatment handling and selection after treatment has been discussed for main crop species in the literature [1, 7, 19, 20]. Since the reporting of mutagenic effects of sodium azide [44], no new chemical mutagens of widespread use in plant breeding have been discovered. The most widely used chemical mutagens are alkylating agents, with EMS being the most popular because of its effectiveness and ease of handling, especially its detoxification through hydrolysis for disposal. Nitroso compounds are the other alkylating

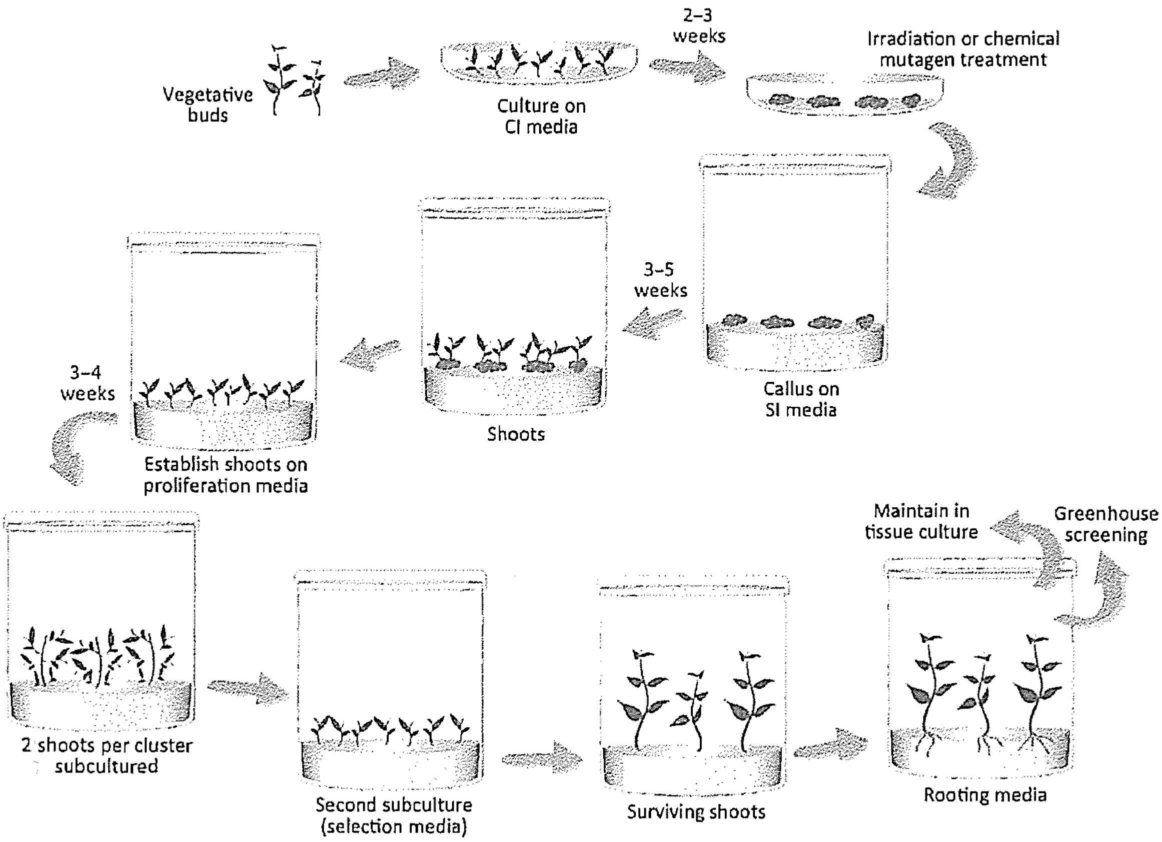

Figure 3 A hypothetical scheme for mutation induction and selection *in vitro.* CI media – callus induction media, SI media – shoot induction media

agents widely used, but they are light-sensitive and more precautions need to be taken because of their higher volatility [19]. Chemical mutagens are also popular in *in vitro* mutation induction, although irradiation can also be applied at low doses [7, 8, 17, 43, 45–47]. EMS has become the mutagen of choice for developing mutant populations for high throughput screening such as in developing TILLING populations [21, 23, 48–51].

New methods for mutation induction

Since a large proportion of basic research on plant mutations has been accomplished for temperate cereals, most of the straightforward recommendations relate to them. However, this research has been successfully adapted to rice and other tropical cereals, legumes, oilseeds and vegetables as demonstrated by the growing numbers of released cultivars – 3211 registered in over 170 species [18].

Fast development of *in vitro* based methods in the past two decades has helped plant breeders to develop more efficient induction and screening processes using plant cell and tissue cultures. This has been particularly useful in developing novel variation in vegetatively propagated crops such as banana [6, 43, 52–55], cassava [16], sweet potato [4, 52], ulluco [56], sugarcane [45, 46, 57–59], *Citrus* sp. [8, 60], Indiangrass [61] and many ornamental species [7, 17, 52]. *In vitro* cultures have the advantage of producing large mutant populations in a limited space, and the possibility of screening for some useful characters such as tolerance to salt [57–59], toxic elements [47] or fungal toxins [62] in the laboratory environment. This allows the transfer of only putative mutants for field screening, and in the case of vegetatively propagated crops, removal of chimaera through several subcultures. *In vitro* mutation induction and screening methods have been established for widely cultivated crops such as banana, potato, cassava, sweet potato, grapevine and sugar cane [5–8, 16, 17, 43, 46, 52, 55, 62–64] and a hypothetical scheme for *in vitro* mutation induction and selection is given in Figure 3. Callus cultures are treated with the mutagen and individual shoots are regenerated in shoot induction media. Selection presure can be applied at this stage. Regenerated shoots are then subcultured to remove chimeras in selection media and surviving shoots can be rooted and further tested in the greenhouse before field evaluation.

In recent years, plant mutations have been obtained using high-energy (220 MeV) ion beam implantations in Japan [10, 65–68], and in China using low-energy (30 keV) ion beams [69]. Resistance to bacterial leaf blight and blast in rice [70], yellow mosaic virus in barley [66], potato virus Y in tobacco [63] and black sigatoka disease in banana [71] are a few examples of useful mutants in field crops developed through ion beam irradiation. Many ornamental crop cultivars with unique colour characteristics have been developed as well [66, 72]. Tanaka *et al.* [66] recently summarized the results of 19 years of work in different crops and concluded that the spectrum of mutations induced by ion beam radiation is different from that of gamma rays, and novel mutant types hitherto not produced have been isolated in ornamental plants. However, in rice the spectrum of different ion beams (C and He) was similar to that of gamma rays, but frequency was higher [67]. Additional information on the use of ion beam mutagenesis can be found in a recent review by Magori *et al.* [72].

Cosmic radiation is another novel source for mutation breeding and a term 'space breeding' has been coined to describe it. Spacecraft, recoverable satellites and high-altitude balloons have been used and more than 60 cultivars have been released as a result of this programme. Both genomic and epigenetic changes have been detected in plants derived from seeds exposed to space flight [73–75]. Molecular and segregation analysis of three blast-resistant rice mutants induced by space flight revealed that one or two dominant mutations were responsible for resistance to different isolates of the pathogen [70]. Discovery of dominant mutations from space flight is noteworthy and may be indicative of a different spectrum from other mutagenic agents.

Insertional mutagenesis is a useful method for producing mutants to investigate gene function because those mutations are tagged with DNA fragments of known sequence. There are two methods to construct such mutants: T-DNA insertions and transposon tagging. T-DNA insertions are considered genetically modified, carrying T-DNA sequence from *Agrobacterium tumefaciens* [76] and thus pose difficulties associated with regulatory barriers to GM crops in an agricultural environment. On the other hand, transposable elements are an internal genetic factor that has been harnessed recently for mutation breeding through their transcriptional activation. These elements can get incorporated into various regions of the plant genome (insertion mutations) and their position can be identified by PCR-based methods or *in silico* screens of databases that contain the DNA sequences flanking all insertions [77–79]. Transgenic copies of the maize Activator/Dissociation (Ac/Ds) transposon system has become a very popular tool for gene tagging and functional genomics in various plant species and thus for 'targeted mutations'. Within the last decade populations carrying such insertional mutations have been developed not only for the model plants *Arabidopsis* [80, 81] and *Lotus japonicus* [82] but also for economically important food crops such as rice [78, 83], barley [84], maize [85, 86] and soybean [87]. High density of mutations in these populations has helped researchers to move beyond functional genomics and use them in crop improvement programmes [83, 88]. Jiang and Ramachandran [88] have reviewed the different mutant rice populations available for genetic analysis and estimated that the rice genome encodes about 32 000 protein coding genes.

Restriction endonucleases have been successfully used to induce double-strand breaks, resulting in mutations [89, 90]. Further perfection of technology has now seen the use of zinc finger nucleases (zinc finger DNA-binding proteins) for inducing site-specific mutations [91, 92].

Mutation rates and detection of mutations

Mutation rates

The random nature of mutational events applies not only to natural mutations but also to those induced. Thus, there is little control over the magnitude or kind of genetic change expected. However, there are reasonable estimates on the frequency of mutations. Provided an effective treatment is given, a particular gene could be expected to mutate once in about 10 000 treated cells [93]. Molecular-based methods, particularly reverse genetic approaches, have enabled more accurate estimation of mutation rates in recent years. Thus, TILLING of an EMS-generated *Arabidopsis* mutant population of 3000 plants revealed that 14 base mutations per 1.5 kb fragment length can be discovered [94]. Mutation rates for hexaploid wheat has been estimated at 1 per 25 kb [95], in *Brassica rapa* 1 per 60 kb [96], but for maize [97] and barley [98] the rates were as low as 1 per 500 kb. In peanut, the mutation rate for the major allergen gene *Ara h 1* in an EMS population was estimated to be 1 per 967 kb [99]. Both EMS and a combined treatment of sodium azide and *N*-nitroso-*N*-methylurea (NMU) produced about one mutation per <300 kb length in rice [51]. In two EMS-derived mutant populations of tobacco, Julio *et al.* [100] estimated mutation rates from 1/30 to 1/83 kb for two genes controlling nornicotine biosynthesis. These mutation rates are average figures and estimates, and can vary depending on the gene, kind of mutagen used, plant part used for mutagen treatment, conditions of treatment, post-treatment handling and even the location of cells, for example whether dormant or actively dividing meristematic cells [1, 7, 19]. For example, Cooper *et al.* [101] compared mutation rates in four soybean TILLING populations derived from EMS and NMU. In the NMU and one of the EMS populations the rate was estimated at 1 per 140 kb. In the other two EMS populations the rates were 1 per 250 and 1 per 550 kb. These different mutation rates can serve as guidelines to estimate the number of mutagenized plants that need to be screened in a practical mutation breeding programme.

Detection of mutations

For practical plant breeding, mutations occurring in those cells that give rise to the progeny are relevant. In the early phases of mutation breeding, most of the selected mutants that led to released cultivars resulted from easily recognizable characters such as early flowering and maturity, changed plant architecture and height, fruit and seed characteristics or resistance to diseases that can be screened easily due to their epiphytotic nature [1, 7, 19]. Development of low-cost, high throughput screening methods resulted in the development and release of mutant cultivars with improved or changed quality, as in the development of linola or the black spot disease resistant mutants of Japanese pear described in the section on the application of mutation breeding and impact of mutant cultivars. *In vitro* screening methods can be applied for traits that can be mimicked in culture such as drought [102, 103], salinity [45, 57–59, 64, 104, 105], toxic elements [47, 106] and for disease resistance, for example using culture filtrates from toxin-producing pathogenic micro-organisms, fungal or bacterial toxins or their analogues [62, 107–114]. Detection of mutants in haploids is faster (can be detected in the first generation) and easier, and will be directly applicable if the breeding programme is based on doubled haploids as demonstrated by Carlson [108].

In the last decade new molecular biological tools have been developed that can screen mutants at the gene level. Although genome sequencing is considered the 'gold standard' for mutation detection as it can reveal the exact location of a mutation and its type, applying this to large populations is costly and is rarely used in practical mutation breeding. Moreover, direct sequencing may not readily detect heterozygous alleles. Therefore, several methods to scan amplicons in mutant populations for the presence of sequence polymorphisms have been developed. Among the novel techniques, TILLING has emerged as a robust, high-throughput method that can be applied to many species. The potential of this method in plant agriculture has been reviewed in this series [48]. Since that review, TILLING populations for oat [115], sorghum [116], soybean [101], pea [117], *B. rapa* [96], *Brassica napus* [118], tomato [119] and rice [51, 120] including one of the 'green revolution' cultivars 'IR 64' [121] have been developed and many more populations are in the pipeline. TILLING is a reverse genetics approach and relies on the detection of sequence alterations in target genes to identify allelic variations among mutant populations. TILLING populations are developed by chemical mutagenesis covering the entire genome and then using an enzymatic detection method in combination with gel electrophoresis or denaturing high-performance liquid chromatography [21, 23, 122, 123]. It relies on the detection of single-base mismatches in heteroduplexes using endonucleases. Many TILLING populations have been developed based on a method described by Colbert *et al.* [122], which relies on a mismatch-specific endonuclease found in celery. The method used by Till *et al.* [51] to develop a high-density TILLING population in rice is given in Figure 4. Seeds are treated with the mutagens and M_1 plants are allowed to self-pollinate and a single seed strategy is followed to M_2. M_2 plant is grown to provide DNA for mutation discovery and seed for banking. DNAs are pooled eightfold and arrayed in a two-dimensional format on 96-well plates. After PCR amplification of target genes, heteroduplexes are formed upon heating and annealing, and then digested using crude celery juice extract containing the CEL I nuclease. Cut strands are separated by denaturing polyacrylamide gel electrophoresis, and visualized by fluorescence detection using a Li-Cor DNA analyzer. The presence of cut products in two pools identifies the individual harboring the polymorphism. TILLING has worked well in a wide variety of plant species and until recently, has been one of the only available techniques for identifying *de novo* single nucleotide polymorphisms (SNPs) or point mutations in genomes for which the entire sequence is not available [124]. In allotetraploid species such as peanut, TILLING is being used to improve selected characters such as the removal of allergens or improving quality traits [99]. While the attempts to develop TILLING populations using mutagenized populations in allopolyploid annual species such as wheat [95], *B. napus* [118], soybean [101] and peanut [99] have been successful, researchers tend to use heteroduplex analysis by enzymatic cleavage to assess natural variation (EcoTILLING) for cross-pollinating annuals such as melon and sunflower [125, 126] and for forest tree species [127, 128]. Banana is the first perennial fruit species to be assessed by EcoTILLING [129].

One disadvantage of TILLING arises from relatively poor cleavage efficiency and exonuclease activity [130]. Endonuclease digestion reactions and electrophoresis in classical TILLING are time-consuming and costly. Another disadvantage is its low sensitivity when screening genes with multiple small exons separated by larger introns as they rarely affect gene function [130]. Also, a mutagenized population arrayed for TILLING is required, and for many species, establishment of such populations is time-consuming and expensive [119, 124] or can be complicated, for example when the desired cultivar is heterozygous and vegetatively propagated. To overcome these shortcomings, more robust technologies are being developed.

High-resolution melt analysis (HRM) distinguishes different PCR products by their thermal denaturation profiles. The melting temperature (T_m) of a PCR product depends on the GC content, length and sequence of the duplex. Small changes in the melting curve are indications of the heterogeneity in the sequence. Therefore, high resolution scanning and genotyping, enabled by new classes of saturation dyes coupled with high-throughput

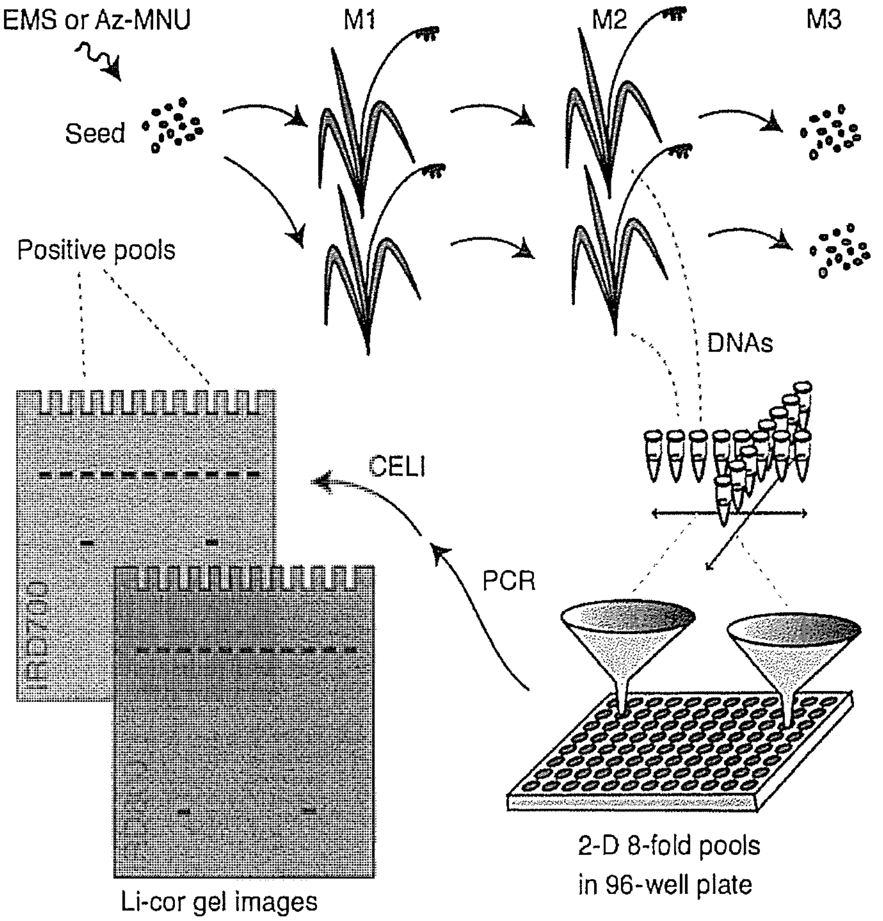

Figure 4 TILLING strategy for rice using endonuclease digestion (Figure courtesy of Dr Bradley J. Till and published in [113])

instrumentation, have contributed to the wider applicability of the technique, including plant mutation screening. HRM has been applied to cultivar identification of grape and olive by characterizing high-resolution melting of dinucleotide microsatellite repeats [131]. Since then the method has been extended to capsicum [132, 133], melon [134], tomato [135], wheat [136], potato [137] and almond [138]. Primers are being designed for amplification of sex markers in triploid hops [139]. Li *et al.* [140] developed a cost-effective dye (EvaGreen) for use in HRM analyses and successfully applied it for mutation screening of an EMS mutagenized maize population and mapped rice using SNP markers. The method has also been successfully applied for mutant screening in barley [141]. Conserved regions of a gene often represent functional domains and have high sequence similarity between homoeologous loci, presenting difficulties in classical TILLING. Dong *et al.* [136] demonstrated the usefulness of HRM as an alternative for screening mutations in conserved functional domains of homoeologous genes using an EMS mutagenized wheat TILLING population by screening mutations in the carboxyl terminal domain of the starch synthase II (*SSII*) gene. This method can also be used for SNP marker development and eco-TILLING in polyploid species [136].

Another novel high-throughput, but low-cost mutant detection method based on capillary electrophoresis-single strand confirmation polymorphism (CE-SSCP) analysis was proposed by Julio *et al.* [100]. They applied it to a practical mutation breeding effort to produce nicotine-free tobacco, targeting two genes in the nornicotine biosynthetic pathway, *ADC1* and *NtabCYP82E4*. CE-SSCP was used to identify wild-type, heterozygous and homozygous plants in the M_2 progeny of EMS mutagenized tobacco for both genes. Homozygous plants for a truncated mutant of *NtabCYP82E4* displayed near-null nornicotine contents while the heterozygous mutant showed an intermediate level. Several other truncation and missense mutants of the same gene displayed very low-level nicotine-converter phenotype [100]. The authors concluded that because the *NtabCYP82E4* nicotine *N*-demethylase mutated alleles are stably inactivated by point mutation, introgressed elite tobacco lines display a stable non-converter phenotype, whereas genetically modified tobacco through RNAi

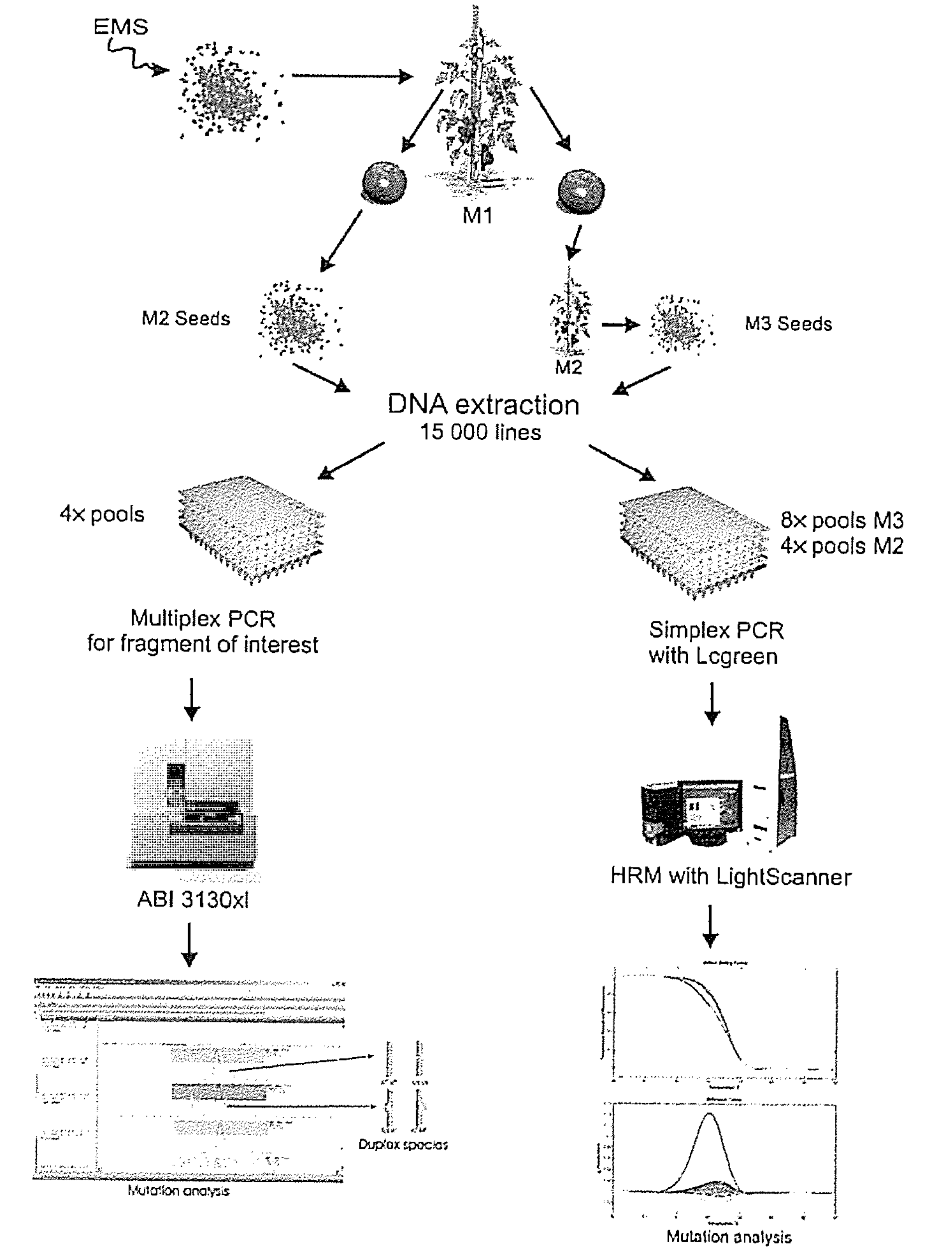

Figure 5 TILLING strategy for tomato using two non-enzymatic methods (Figure was reproduced from [119])

targeting may be silenced in some of the transgenic plants, thus reverting back to the wild-type [100]. In tomato, Gady *et al.* [119] used two non-enzymatic high-throughput screening techniques for TILLING; conformation sensitive capillary electrophoresis (CSCE) and HRM (Figure 5). This scheme simplifies TILLING as it avoids the time consuming endonuclease digestion reactions as well as gel electrophoresis but achieves an average mutation detection rate of 1.36 mutations per kb. For M_2 and M_3 populations, DNA was pooled 4 or 8 fold. For CSCE, after multiplex PCR amplification with fluorescent labeled primers, samples were directly pooled and loaded on capillaries filled with CAP polymer. Pools containing mutations were identified using Applied Maths' HDA peak analyser software. For HRM, pools were analysed for their product melting temperatures after PCR amplification in the presence of LC-Green+^{TM}.

With the continuous development of novel mutation detection techniques, targeted mutation breeding will become more practical in the future. In this respect, TILLING and HRM allow sample pooling to reduce costs. A major constraint with polymerase chain reaction

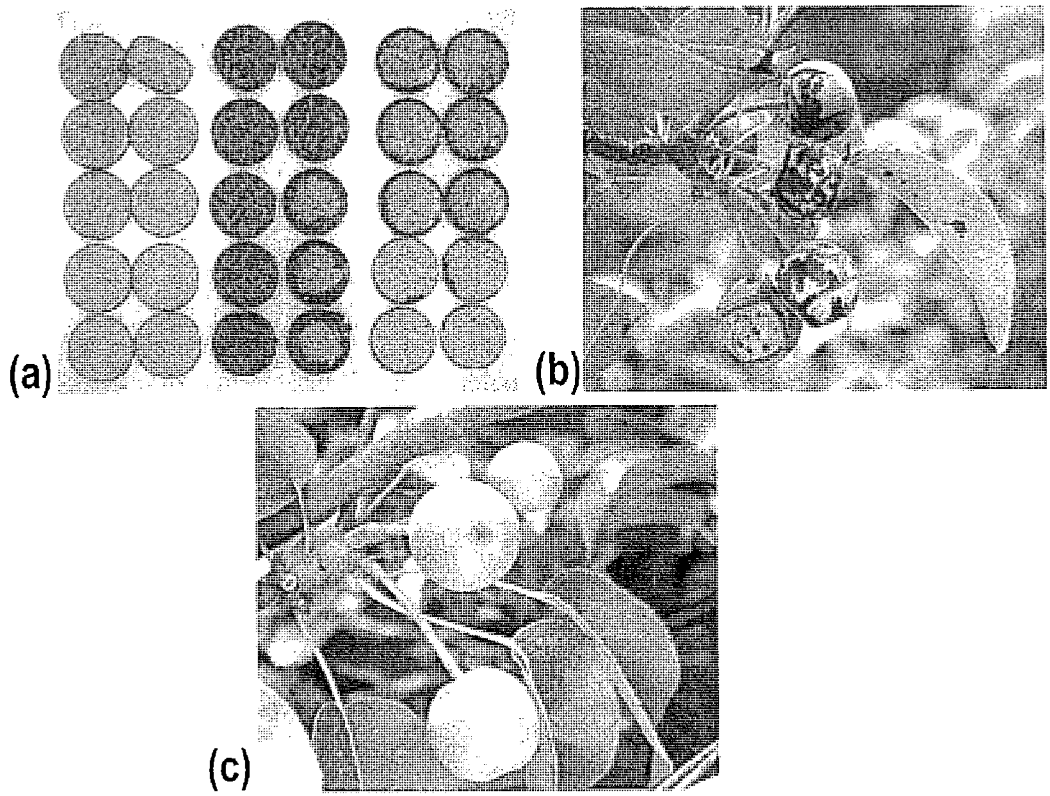

Figure 6 Development of Japanese pear mutants resistant to black spot disease using chronic gamma irradiation coupled with screening for colour change in leaf discs treated with AK toxin [55, 56]. (a) The disease susceptible leaves change to black and resistant material stay green when incubated with AK toxin; (b) diseased fruit; (c) fruit from a resistant cultivar. Courtesy of Dr Terutaka Yoshioka, Head of Mutation Breeding Laboratory, Institute of Radiation Breeding (IRB), National Institute of Agrobiological Science, Japan

(PCR)-based techniques for mutation screening is their inability to selectively amplify low levels of mutations in a wild-type background [142]. Li *et al.* [142] demonstrated that replacing regular PCR with CO-amplification at Lower Denaturation temperature PCR (COLD-PCR) increases the mutation detection sensitivity up to 100-fold. By incorporating a synthetic reference sequence during COLD-PCR, Milbury *et al.* [143] could enhance amplification of unknown mutant sequences even further. With next-generation sequencing (NGS) technology it is now conceivable to sequence candidate amplicons in multiple parallel reactions (SCAMPR), and the costs are comparable to TILLING [124].

Applications of mutation breeding and impact of mutant cultivars

Crop domestication and adaptation to new environments

Mutations have played an important role in plant domestication. Natural mutations and selection by man has been the driving force in the evolution of crop plants [29, 144]. Recent molecular studies show that duplications [25, 145] and polyploidization [26, 33, 146] in particular are responsible for the evolution of many crop species. Crop yield increases attributed to changed plant architecture to suit modern agronomic practices such as dwarfing in cereals [147–150], bushy mutants of legumes [151–154], cotton [15, 153], sunflower [15, 155, 156] and castor [157] are also the result of inducing and incorporating mutant genes into old cultivars. The reduction or complete removal of toxic substances such as alkaloids in lupins [158] and glucosides in *Melilotus* species [159, 160] helped the introduction of these crops into agriculture.

Changing the product quality through mutation breeding also resulted either in new products from existing crops, such as the development of a new edible oil, linola [161–167], utilizing two induced mutants of flax isolated in Australia [168, 169], or the overall improvement of product quality that resulted in the widespread use of a crop, such as in the case of a high oleic acid sunflower mutant that was bred in Russia [170] and used extensively in the breeding programmes in North

Table 1 Some examples of disease-resistant mutants developed directly through gamma irradiation

Crop	Disease	Parent	Mutant	Country	Reference
Rice	Rice blast	Simei No. 2	Zhefu 802	China	[147]
Rice	Rice blast	Maratelli	Marathon	France	[18]
Rice	Rice yellow mottle virus	Supa	Mwangaza	Tanzania	[182]
Rice	Bacterial leaf blight and bacterial leaf stripe	Mutant line 627/10-3/PsJ	Atomita 3	Indonesia	[18]
Wheat	Stripe rust	F_1 (Zaoyang× Dongfenhong 3)	Yuandong 1	China	[18]
Durum wheat	Black stem rust	Castelporziano	Sredetz	Bulgaria	[18]
Mungbean	Yellow mosaic virus	F_1 (Mutant MB55-4× AVRDC line V1560D)	Binamoong-5	Bangladesh	[18]
Mungbean	Yellow mosaic virus	K851	MUM2	India	[15]
Mungbean	Yellow mosaic virus	BINA Acc B.10	Binamash-1	Bangladesh	[18]
Chickpea	*Ascochyta* blight and *Fusarium* wilt	C 727	CM 88	Pakistan	[183]
Chickpea	*Ascochyta* blight and *Fusarium* wilt	K 850	CM 98	Pakistan	[184]
Soybean	Multiple (myrothecium leaf spot and yellow mosaic virus)	JS 80-21	TAMS 98-21	India	[18]
Soybean	Rust (*Phakopsora pachyrhizi* Syd.)	Chiang Mai 60	Chiang Mai 5	Thailand	[18]
Cotton	Bacterial blight	F_1(AC134×Deltapine)	NIAB78	Pakistan	[185]
Cotton	Cotton Leaf curl virus	F_1 (NIAB313×CIM 1100)	NIAB 111	Pakistan	[153]
Japanese pear	Black spot	Nijisseiki	Gold Nijisseiki	Japan	[15,176]
Japanese pear	Black spot	Shinsui	Kotobuki Shinsui	Japan	[8,15]
Sugarcane	Red rot	Co 449	Co 6608 mutant	India	[18]
Sugarcane	Red rot	Co 997	Co 997 mutant	India	[18]
Sesame	*Phytophthora nicotiana* var. *parasitica*	MI 1	ANK-S2	Sri Lanka	[179,180]
Apple	Powdery mildew (*Podosphaera leucotricha*) & *Venturia inaequalis*	McIntosh	McIntosh 8F-2-32	Canada	[5,18]
Rapeseed	Stem rot (*Sclerotinia sclerotiorum*)	Huashuang 3	9 resistant lines	China	[111]
Mentha	*Verticillium* wilt	Mitcham	Murray Mitcham	USA	[174,175]
Tomato	Bacterial wilt (*Ralstonia solanacearum*)	Manik	M-127	Sri Lanka	[186]
Sweet pepper	Powdery mildew	Kurtovska Kapia	Pirin	Bulgaria	[18]

America and Europe to produce high oleic acid sunflower hybrids [15, 171].

Biotic stress resistance

Through mutation breeding it has been possible to save some crops from diseases that had been devastating for growers. Powdery mildew resistance in barley was one of the first examples. At least 32 independent mutations in the *mlo* locus have been reported and, of these, most have been induced by chemical mutagens, five with radiation and one (*mlo*11) occurs naturally [172]. Resistance to *Verticillium*-wilt in peppermint, a sterile allohexploid (*Mentha*×*piperita*), was induced in 1959 by irradiation, and the resistance of newly bred cultivars was still effective after 30 years [173–175]. Resistance to black spot disease (*Alternaria alternata* pv. Japanese pear), considered to be the most serious disease in Japanese pear (*Pyrus serotina* var. *culta*), was induced in Japan in the 1960s through chronic irradiation of the cultivar 'Nijisseiki' and a resistant cultivar 'Gold- Nijisseiki' was released [15, 176]. The success of this programme led to radiation breeding of susceptible 'Shinsui' and 'Osa-Nijisseiki' cultivars resulting in resistant cultivars 'Kotobuki-Shinsui' and 'Osa-Gold' [8, 15, 177, 178]. The 'Osa-Gold' mutant has the added advantage of being self-compatible, eliminating the need to grow pollinators [15]. The selection for disease resistance using AK toxin and a comparison of diseased and resistant Japanese pear cultivars is given in Figure 6. The development and introduction of phytophthora-resistant sesame mutants through radiation breeding resulted in stabilizing the declining sesame yields in Sri Lanka [179, 180].

There are many other examples of disease-resistant mutants developed either through direct selection after mutation induction (Table 1) or through cross-breeding with mutants [1, 18]. A good example of induced virus resistance is the cultivar 'NIAB Karishma', a cotton hybrid of the mutant cultivar 'NIAB 86', released in 1996 and resistant to cotton leaf curl virus [18]. During the period 1997–2005, it brought additional income amounting to US$294.4 million to farmers in Pakistan [153]. A number of pulse crop mutants with disease resistance have contributed to sustainable farming in India. Among these, bacterial pustule resistance in 'TAMS 38' soybean; powdery mildew resistance in mungbean mutants 'TARM 1', 'TARM 2', 'TARM 18' and 'TM 96-2'; yellow mosaic virus resistance in mungbean mutants 'TMB 37' and 'TJM 3'; and yellow mosaic virus resistance in urdbean mutant 'TU 94-2' are noteworthy [151]. Combination of targeted mutation breeding techniques including the use of TILLING populations or HRC and the recently proposed strategy of disabling plant disease susceptibility genes (S-genes) [181] will result in many more durably resistant cultivars developed through mutation induction.

Abiotic stress tolerance and adaptability traits

Mutants with tolerance to abiotic stresses such as salinity, acid soils, drought and toxic soil conditions have enabled breeders to develop crop cultivars adapted to adverse soil environments. Adaptability traits such as photoperiod [187] and temperature response, changes in breeding systems of crops affecting cross- or self-incompatibility and male sterility [1, 188] are among many other characters that have been changed to produce new cultivars through mutation breeding. The gamma ray-induced 'Zhefu 802' rice cultivar with a shorter growing season, tolerance to cold and rice blast disease and high yield potential under low-input conditions was the most widely planted variety in China in 1986–1994. During this period its cumulative planted area reached 10.6 million ha [147]. A concerted effort in mutation breeding of rice in Vietnam has resulted in a total area of 2.54 million ha of mutant varieties cultivated in the period 2000–2008 in the Mekong Delta Region, with eight rice mutant varieties adding an estimated return of US$374 million. These mutant varieties have early maturity allowing cultivation of three rice crops annually, lodging resistance, acid sulphate soil tolerance and resistance to major pests requiring two- to three-fold less pesticide sprays during the growing period [189–192]. Similar successes with mutant varieties of rice have been reported from Australia, Thailand, Japan, India, Costa Rica and Myanmar [15, 147, 178].

As the *indica* type semi-dwarf donors did not have an acceptable grain quality, rice breeders in California successfully used induced mutations to produce semi-dwarf mutants in *Japonica* and *Javonica* backgrounds; 'Calrose 76' was the first direct release semi-dwarf cultivar produced through seed irradiation with gamma rays, released in 1976 [193]. Already in the early 1980s, the added value to rice farmers in California from the induced semi-dwarf mutant was US$20 million per year, as a result of a yield advantage of 14% over the tall *Japonica* types [148, 149]. Genetic evaluation showed that the semi-dwarfing gene in 'Calrose 76' was allelic to *sd1* in the indica 'green revolution' varieties derived from Dee Geo Woo Gen [194]. Cross-breeding has resulted in 25 semi-dwarf varieties bred and released in the USA, Australia and Egypt that trace their ancestry to 'Calrose 76' [149]. Mutation breeding has also contributed other semi-dwarf mutants non-allelic to *sd1*, waxy endosperm, early maturity and Basmati-type aromatic semi-dwarf mutants to the California breeding programme [148, 149].

In cotton, a mutant cultivar 'NIAB 78' released for cultivation in Pakistan with high adaptability traits and better fibre quality recorded an additional cumulative income of US$612.4 million from 1983 to 2005 [153]. Although the economic analyses have not been published, sunflower became an intensive crop as a result of the many dwarf mutants developed in the early years of its cultivation [156]. Radiation breeding is one way of adapting crops to new environments. When cross-breeding is not an option such as in the case of aromatic rice, mutation induction and screening in the new environment may enable quick adaptation of the crop [3, 148, 150].

Improvement of crop quality and nutritional traits

In the section on crop domestication and adaptation to new environments, the development of linola and high oleic sunflower through mutation breeding was mentioned. Similar improvements to oil quality in soybean [195, 196], canola [197] and peanut [147, 151, 198] have also been achieved in subsequent years. Sequencing has revealed that a G to A transition was responsible in one such peanut mutant [198]. Increased seed size in the TG series of peanut mutants in India has contributed immensely to the confectionery industry [147, 151]. The mutant barley cultivars 'Golden Promise' and 'Diamant' have added billions of dollars to the value of the brewing and malting industries in Europe. For its high malting quality, 'Golden Promise' was in wide cultivation in the UK and Ireland in the 1960s and 1970s. Even 30 years after release, it is still popular in Scotland and is estimated to have contributed US$417 million to Scotland's industry alone [15].

High-quality durum wheat mutants in Italy and bread wheat in India and Pakistan have contributed immensely to the grain industry of those countries [15, 147]. Using high performance thin layer chromatography to screen low glycoalkaloid mutants in a population derived from gamma ray irradiated bud eye pieces of potato, Love *et al.* [199] isolated three mutant lines with high potential for the potato chip industry. A high-amylose cassava mutant has been isolated by seed irradiation followed by screening in the M_2 population and subsequent clonal multiplication and evaluation [200].

Oilseed meals low in phytic acid is desirable in poultry and swine feed and is also environmentally friendly by reducing phosphate loads to agricultural lands and ground water. An EMS-induced low-phytate mutation in a non-commercial genotype of soybean has now been transferred to a commercial cultivar through a marker-assisted back-crossing programme [201]. Similarly, the two-row barley cultivar 'Clearwater' has low phytate (40–50%) and derives from 'Pmut640', a sodium azide-generated mutant. Inorganic P content in the seed has increased by 400% as a result [202]. Studies have shown that these changes are associated with improved feed quality and reduced environmental impacts when fed to non-ruminant animals, based on increased P digestibility and reduced fecal P content [202]. Similar work in rice is also underway [203]. Work towards reduction of allergens from peanut and improving oleic to linoleic acid ratio using a TILLING approach is underway [99].

As a result of mutation breeding coupled with other biotechnological methods, wheat and barley cultivars suited for celiac patients are also being developed [204]. This is achieved by inhibition of demethylation of gene promoters that control the production of gliadin-type proteins during endosperm development by mutation, without affecting the high molecular weight glutenin formation as the latter is sufficient to produce the molecular structure of elastic fibrils that form dityrosine cross-links during dough formation and baking [204]. Celiac patients are sensitive to epitopes of gliadin-type prolamins which are of no importance to baking because high molecular weight glutenin alone is sufficient to produce high-quality bread. A viable mutant of barley with such a mutation has already been obtained [204]. For hexaploid wheat, the current strategy is to use TILLING populations to discover mutations in the 5-methylcytosine DNA deglycosylase genes in the three homoeologous genomes [49, 95, 204].

Conclusions

For half a century, induced mutations have played an important role in plant breeding, contributing to increased food production in both developed and developing economies. Classical mutation breeding continues to be used for the benefit of communities in parallel with application of modern genomic tools for mutation induction and discovery in advanced laboratories. With 3211 registered mutant varieties in more than 170 different plant species, mutation breeding has proven flexible, workable and ready to use on any crop if objectives and selection methods are clearly identified. A range of mutagens are at our disposal to induce mutations from the single nucleotide level to the genome level. Induced mutations have not only played an unprecedented role in developing new crop cultivars and novel products from existing crops, but also increasingly contribute to our understanding of gene function and biochemical pathways. Along with newly emerged 'omics' techniques, induced mutations are contributing to the development of newly emerging subject of systems biology.

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Cleancrop™ Brassica System: The development of herbicide resistant brassica crops for New Zealand farming systems

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Abstract
This paper presents results from a breeding program which, using seed mutagenesis combined with traditional plant breeding techniques, has resulted in the development of the Cleancrop™ Brassica system. Seedlings of *Brassica napus* with increased chlorsulfuron resistance were identified following seed mutagenesis with ethyl methanesulfonate (EMS) and *in vitro* screening of seedlings in the presence of the herbicide. Surviving herbicide resistant seedlings were used in a traditional breeding program to introgress resistance into leafy turnip, bulb turnip, rape and swede. Acceptable herbicide resistance to at least a double application of chlorsulfuron from either a pre-emergence or a 4-leaf post emergence timing has now been produced in all these crops. Results from trials sown at Lincoln, Canterbury and Knapdale, Southland with chlorsulfuron herbicide application at both these timings with HT-S57 swede showed excellent weed control and no noticeable crop phytotoxicity. The pre-emergence herbicide application produced significantly more total dry matter per hectare than the untreated control. This weed management system represents a new tool for New Zealand farmers which will expand the use of forage brassica crops into more marginal areas which historically have had difficult to control weed problems.

Keywords: Seed mutagenesis, chlorsulfuron, acetolactate synthase, field plant breeding, Cleancrop™ Brassica System, HT Brassica™

Introduction

Forage brassica crops are needed to fill periods of feed shortages in winter, when pasture growth is restricted due to low temperatures, and in summer due to drought, and to improve the nutritive value of the total diet at times when pasture quality is low (White & Hodgson 1999). Forage brassica crops occupy the largest area of cultivated land in New Zealand, with over 300 000 hectares grown annually. About 30–40% of the area is grown for the dairy industry, with much of this crop used as winter feed (kale, swedes and turnips) in the South Island and summer milking feed in the North Island (bulb turnips and to a lesser extent rape). The other 60–70% of the area consists of winter, summer and autumn feed crops (kale, swedes, rape, bulb turnip and leafy turnip) for the sheep, beef and deer industries (PGG Wrightson Seeds pers. comm.).

The aim of forage brassica crops is to achieve high dry matter (DM) yields which can be utilised efficiently by grazing animals. The DM yield and forage quality of forage brassicas can both be significantly reduced through competition by weeds. Cultivation to kill young weeds prior to sowing and the use of chemical weed control in the early growth stages of the crop is usually essential for a successful crop (White & Hodgson 1999).

Currently in New Zealand there are only a few herbicides registered for use in forage brassicas, and none provide an ideal solution to weed control. Drawbacks include only partial control of the targeted weed spectrum, poor performance in dry conditions, undesirable levels of phytotoxic effects on the brassica crop, and high levels of residual toxicity in the soil affecting species such as clover and lucerne. Internationally, plants with improved herbicide resistance have been developed using traditional plant breeding and selection, as well as through transgenic methods (Conner & Meredith 1989; Field *et al.* 1993). The development of plants with resistance to sulfonylurea herbicides by seed mutagenesis has been successful in a number of plant species (Conner *et al.* 1994) and is recognised as being developed through non-transgenic technology by the Environmental Risk Management Authority (ERMA).

Sulfonylurea herbicides are more environmentally acceptable than many conventional herbicides because of their low usage rates (application rate of chlorsulfuron (DuPont™ Telar®) is 20 g product/ha) and low mammalian toxicity (Beyer *et al.* 1988; Stidham 1991). The sulfonylurea group of herbicides kill weeds by inhibiting the activity of acetolactate synthase (ALS), the first enzyme in the biosynthetic pathway of branched chain amino acids (Ray 1984). Chlorsulfuron resistance is due to point mutations resulting in amino acid changes that reduce herbicide binding to the ALS enzyme (Yu 2003). A single primary site of action makes it easier to develop crop cultivars with greater resistance to a chosen herbicide in the sulfonylurea group (Dastgheib & Field 1995).

This paper reports the use of seed mutagenesis and traditional plant breeding for the development of forage brassicas with resistance to DuPont™ Telar® (75% chlorsulfuron), a sulfonylurea herbicide.

Seed Mutagenesis

A population of rapid cycling rape was obtained from the Crucifer Genetics Cooperative, and two lines of *Brassica napus* with resistance to chlorsulfuron were developed through seed mutagenesis. Seeds were soaked overnight (16 hours) in 0.3% ethyl methanesulfonate (EMS), washed in running water for 2–3 hours, then dried on absorbent paper for 2 days. Seeds were sown in a greenhouse and transplanted out as 33 first generation (M1) populations of 100 plants each, which were allowed to self-pollinate and set seed. The seed from each M1 population was harvested together to give 33 second generation (M2) populations of 180–2580 seeds, resulting in a total M2 population size of 30 609 seeds; this process was continued until the M4 generation, with each generation screened for chlorsulfuron resistance (Conner *et al.* 1994).

The M3 progeny of rape plants 19 and 30 showed clear segregation for seedlings that were chlorsulfuron resistant or susceptible (Table 1). As expected, resistant plants were either homozygous, true breeding plants or heterozygotes that segregated 3:1 for resistance. The observed number of homozygous and heterozygous plants was consistent with the 1:2 ratio expected for a single dominant mutation conferring resistance (Conner *et al.* 1994). The growth of lines 19c and 30a was compared to the original wild type under glasshouse conditions. All lines showed similar growth when untreated with herbicide. The wild type plants showed severe damage with all chlorsulfuron rates (Table 2). In contrast, lines 19c and 30a showed herbicide tolerance, with all plants maintaining active growth following chlorsulfuron application as high as 30 g product/ha (Conner *et al.* 1994). Some phytotoxicity was observed in both chlorsulfuron resistant lines, but was more evident in line 19c (Conner *et al.* 1994). The better of the two lines, line 30a, was chosen for use in a conventional breeding and selection programme.

Table 1. Segregation of chlorsulfuron resistance among the progeny of the rape mutants (Conner *et al.*1994)

	Number of seedlings resistant	Number of seedlings sensitive
M3 Generation		
Wild type	0	151
19	53	23
30	56	28
M4 Generation		
Wild type	0	166
19a	37	16
19b	26	10
19c	149	0
19d	80	35
30a	150	0
30b	93	0
30c	55	14
30d	54	16

Table 2. Visual assessment scores of rape lines 4 weeks after spraying with different rates of chlorsulfuron, 1 = dead, 10 = healthy (Conner *et al.*, 1994)

Assessment	Line	Chlorsulfuron Concentration (g product/ha)					
		5	10	15	20	25	30
Visual Score	Wild type	2.8	2.0	1.4	1.6	1.4	1.8
SEM =0.5	19c	6.4	7.2	5.0	5.8	5.2	5.0
	30a	9.8	8.8	6.8	6.2	6.8	5.6

Plant Breeding

The plant breeding process involved several generations of backcrossing and single plant selection to introgress chlorsulfuron resistance into leafy turnip (*Brassica rapa)*, bulb turnip (*B. rapa* var. *rapa)*, forage rape (*B. napus* var. *biennis*) and swede (*B. napus* var. *napobrassica*) with enhanced forage agronomic characteristics (increased forage yield, multiple regrowth, palatability, insect and disease tolerance).

The transfer of chlorsulfuron resistance from rape (*B. napus*) to kale (*B. oleracea* var. *acephala*) is a technical challenge in breeding. This is partly due to the normally incompatible cross between these two species requiring embryo rescue to produce interspecific hybrid plants. Embryo rescue involved removing intact ovules from the plant and culturing them on a plant culture medium designed to promote growth. Plants which were successfully produced tended to revert back to more of a rape-type plant, resulting in unusable progeny. Rape is an allotetraploid species derived from a cross between the turnip and kale groups. Therefore, even if rape × kale hybrids were successfully backcrossed to kale, they would still need a recombination event between genomes to transfer the resistance to kale. The success of this cross seems very unlikely, so work is on-going with EMS seed treatment to produce mutants in an elite kale.

Between 2002 and 2009 a series of screening trials was carried out each year to test potential chlorsulfuron resistant breeding lines against a range of application rates at three growth stages (pre-emergence, 2-leaf stage and 4+-leaf stage). The aims of these trials was to ensure that all breeding material was resistant to at least twice the standard herbicide application, to ensure crop safety during spray overlaps.

From this work it was shown that chlorsulfuron application to 'Pasja' leafy turnip, 'Green Globe' bulb turnip, 'Goliath' rape and 'Aparima Gold' swede at all application rates resulted in complete crop death. In contrast, the phytotoxicity seen on 'HT-LT46' leafy

Table 3. Plant health visual scores for HT-S57 swede sown at Lincoln, Canterbury on the 10 February 2012 with 20 or 40 g product/ha of chlorsulfuron applied pre-emergence and post-emergence at the 2- or 4-leaf growth stage compared to the untreated control

Clorsulfuron Treatment	Date of Scoring 03 March 2012	 12 April 2012	 03 May 2012
Untreated	9.0	9.0	9.0
Pre emergence 20g/ha	9.0	9.0	9.0
Pre emergence 40g/ha	9.0	9.0	9.0
Post 20g/ha 2-leaf stage	5.8	5.8	9.0
Post 40g/ha 2-leaf stage	4.0	4.3	8.0
Post 20g/ha 4-leaf stage	8.8	8.8	9.0
Post 40g/ha 4-leaf stage	8.3	8.0	8.3
Mean	7.5	7.7	8.8
LSD (5%)	0.71	0.80	0.28
CV%	6.4	7.1	2.2

Scores are on a 1 to 9 basis (1= severe phytotoxicity, 9 = no phytotoxic symptoms)

Table 4. Leaf yield, dry matter (DM) content and plant weight of HT-S57 swede sown at Lincoln, Canterbury on the 10 February 2012 with 20 or 40 g product/ha of chlorsulfuron applied pre-emergent or post-emergent at the 2- & 4-leaf stage compared to the untreated control, harvested on the 24 April 2012 (74 days after sowing).

Chlorsulfuron Treatment	Leaf Yield (kg DM/ha)	Plant Dry Matter (% DM)	Average Plant dry matter (g DM/plant)
Untreated	4446	10.0	77.5
Pre-emergence 20g/ha	4202	10.4	89.0
Pre-emergence 40g/ha	4657	9.7	109.0
Post 20g/ha 2-leaf stage	4044	9.9	69.0
Post 40g/ha 2-leaf stage	3086	9.7	60.2
Post 20g/ha 4-leaf stage	4399	10.2	65.5
Post 40g/ha 4-leaf stage	4276	9.8	85.9
Mean	4159	10.0	79.4
LSD (5%)	1004	1.22	38.0
CV%	13.6	6.9	26.9

turnip after a double application rate was acceptable for a commercially grown crop. This trial result provided the confidence to enter 'HT-LT46' into commercial seed production during 2006.

The phytotoxicity from a double rate of chlorsulfuron applied to 'HT-R24' rape was of concern however. Even though plants did recover to a certain extent over time, there was too much phytotoxicity and some plant death, which was considered to be commercially unacceptable. Plants surviving after a double dose of chlorsulfuron were reselected for increased herbicide resistance, successfully retested and entered into commercial seed production in 2007. This type of plant breeding and agronomy was also carried out prior to commercial seed production for the 'HT-BT35' bulb turnip (commercial seed production in 2008) and the 'HT-S57' swede (commercial seed production 2011). Acceptable resistance to a double application rate of the herbicide chlorsulfuron has now been produced in all these crops.

Product Development

'HT-S57' swede was the focus of the product development programme over the 2011/12 summer growing season. This was due to the high value of the crop as a winter forage source and corresponding weed infestation problems currently experienced by swede growers.

Two trials were established, the first trial examined the effect of chlorsulfuron applications at different growth stages on 'HT-S57' swede from a late planting (10 February 2012) at Lincoln, Canterbury to determine the relationship between increased crop phytotoxicity and herbicide applications during a period of reducing soil temperatures. This trial also explored the effect of chlorsulfuron on 'HT-S57' at different growth stages (pre-emergence, 2- and 4-leaf stage). Plant health scores were taken and leaf yield was measured 74 days after sowing (half the recommended growing period of 150 days).

The trial was sown after peas; plots were 1.5 × 8.0 m and drilled in 150 mm drill rows at a depth of <10 mm using a Øyjord cone seeder at 1 kg/ha. Leaf yield was assessed with two randomly selected, 1 square metre quadrat cuts per plot, and total wet weight and plant number per quadrate recorded. DM was assessed by taking one bulked sample of leaf material per plot and drying at 95°C for 24 hours.

Chlorsulfuron applied at the 2-leaf stage at both the 20 and 40 g product/ha rate significantly reduced the

Table 5. Plant health and weed control visual scores of HT-S57 swede sown at Knapdale, Southland on the 1 December 2011.

	Plant Health Scores		Weed Control	
Chlorsulfuron Treatment (20 g product/ha)	16 February 2012	28 March 2012	16 February 2012	28 March 2012
Pre-emergent only	9.0	8.8	7.3	7.8
Post-emergent only	7.5	8.3	8.0	7.8
Pre- & post-emergent	6.8	6.5	8.8	8.5
Untreated	9.0	9.0	1.8	1.3
Mean	8.0	8.0	6.4	6.3
LSD (5%)	1.13	0.8	0.7	0.9
CV%	8.8	6.2	6.5	9.2

Scores 1= severe phytotoxicity/poor weed control, 9= no phytotoxic symptoms/complete weed control
Pre-emergent applied on 6/12/2011, post-emergent applied on 16/2/2012, pre-emergent + post-emergent applied on 6 December 2011 and 16 February 2012 respectively

Table 6. Yield of HT–S57 swede sown at Knapdale, Southland on the 1 December 2012, with 20 g product/ha of chlorsulfuron applied at either the pre-emergent, post-emergent (fourth leaf stage), or both stages, harvested on the 14 June 2012.

Chlorsulfuron Treatment (20 g product/ha)	Bulb Yield (kg DM/ha)	Leaf Yield (kg DM/ha)	Total Yield (kg DM/ha)	Plant Density (plants/m^2)
Pre-emergent only	11995	3508	15503	7.6
Post-emergent only	9673	2926	12599	7.1
Pre- & post-emergent	9486	3210	12696	7.7
Untreated	8520	2827	11347	7.3
Mean	9918	3118	13036	7.0
LSD (5%)	3595	965	3979	2.4
CV%	22.7	19.3	19.1	20.4

kg DM/ha = kilograms of dry matter per hectare plant health score on the 3 and 12 April 2012, but plant health score increased by the 3 May 2012 score. Only the 40 g product/ha post-emergence application at both the 2- and 4-leaf stage resulted in a reduced plant health score on the 3 May 2012 (Table 3). No phytotoxicity was observed in any of the pre-emergence applications, which were identical to the untreated control (Table 3).

Chlorsulfuron applied at 40 g product/ha at the 2-leaf stage significantly reduced 'HT-S57' leaf yield at 74 days after planting (Table 4). Pre-emergence and post-emergence application at the 4-leaf stage at both 20 and 40 g product/ha had no significant effect on 'HT-S57' leaf yield or average plant weight.

A second trial, sown on the 1 December 2011 at Knapdale, Southland, measured the effect of chlorsulfuron applied to 'HT-S57' swede at the recommended rate (20 g product/ha), at pre-emergence and post-emergence at the 4-leaf stage, or at both pre- and post-emergent application. The trial was sown at 650 g/ha after pasture, using a traditional ridger. Ridge spacings were 600 mm apart and plots were 2.4 × 8 m. DM yield was assessed on 14 June 2012 by harvesting 2.2 m^2 of the middle two ridges from each plot and splitting the sample into leaf and bulb. Bulb percentage DM was assessed by taking a core sample from 15 swede bulbs from each plot, and leaf percentage DM was assessed by taking one bulk sample of leaf material per plot; both leaf and bulb samples were dried at 95°C for 24 hours.

Dry conditions in Southland affected crop establishment; germination was highly staggered and this resulted in a wide variation in plant growth stages in the trial. Due to this staggered germination the post-emergent chlorsulfuron applications were delayed until the 16 February 2012. On this date a number of plants had not yet reached the 4-leaf stage when the herbicide was applied, and this may have increased the phytotoxic effect of the post-emergence application.

Chlorsulfuron applied from pre-emergence or post-emergence (4-leaf stage) had no effect on 'HT-S57' compared to the untreated control (Table 5). The only phytotoxicity observed was in the combined pre- and post-emergence treatment, which may have been due to the variation in growth stages due to the dry conditions experienced. Control of wild turnip, californian thistle, dandelions, chickweed, fathen, shepherd's purse, dock, willow weed, white clover, twin cress and spurrey (yarr) was complete in the combined pre- and post-emergent treatment and only nightshade was unaffected by the application of chlorsulfuron at both timings.

To assess the effect of chlorsulfuron on total DM yield, bulb and leaf yields were assessed at crop maturity on 14 June 2012. The pre-emergent application produced significantly more total DM per hectare than the untreated control (Table 6).

Both trials showed positive results for 'HT-S57' swede when used in conjunction with chlorsulfuron herbicide within the Cleancrop™ Brassica system.

Cultivars available with Cleancrop™ technology: The Cleancrop™ Brassica system is available in a package that includes three components: seed of selected HT Brassica™ cultivar, chlorsulfuron herbicide, and a best practice and stewardship plan. These are designed to maximise the on-farm performance with responsible weed management to minimise unintended build-up of resistant weeds. Four cultivars are currently available:

HT Swede ('HT-S57') is a high yielding, white fleshed, purple skin, main crop swede with similar clubroot and dryrot tolerance to 'Aparima Gold' and improved leaf disease tolerance (PGG Wrightson Seeds 2012).

HT Rape ('HT-R24') is a high yielding 'Goliath' type rape with improved leaf percentage and crop utilisation. Crop maturity is 90–110 days after planting and it has good regrowth ability combined with excellent winter keeping ability (PGG Wrightson Seeds 2012).

HT Bulb Turnip ('HT-BT35') is a high yielding 'Green Globe' type bulb turnip with a maturity of between 90–110 days after planting and can be used for summer, autumn or winter feeding (PGG Wrightson Seeds 2012).

HT Leafy Turnip ('HT-LT46') is a multiple graze 'Pasja' type with a maturity of between 50–70 days after planting which provides a flexible grazing option for all stock types over summer, autumn and early winter (PGG Wrightson Seeds 2012).

Conclusions

The Cleancrop™ Brassica System was developed through seed mutagenesis, combined with traditional plant breeding techniques; this is internationally recognised as non-transgenic technology.

The Cleancrop™ Brassica System provides a simple, selective control of mixed weed populations, with control of wild turnip and shepherd's purse, excellent performance in dry weather, combined with reduced crop phytotoxicity and soil herbicide residue.

Chlorsulfuron (Telar®) applied at 20 g product/ha, showed excellent weed control from either a pre-emergence or a post-emergent 4-leaf application in HT-S57 swede and had no noticeable crop phytotoxicity effect, whilst having excellent level of weed control across a range of species which are economically important to control in a forage brassica crop.

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Voices and Views: Why Biotech?

Edited by
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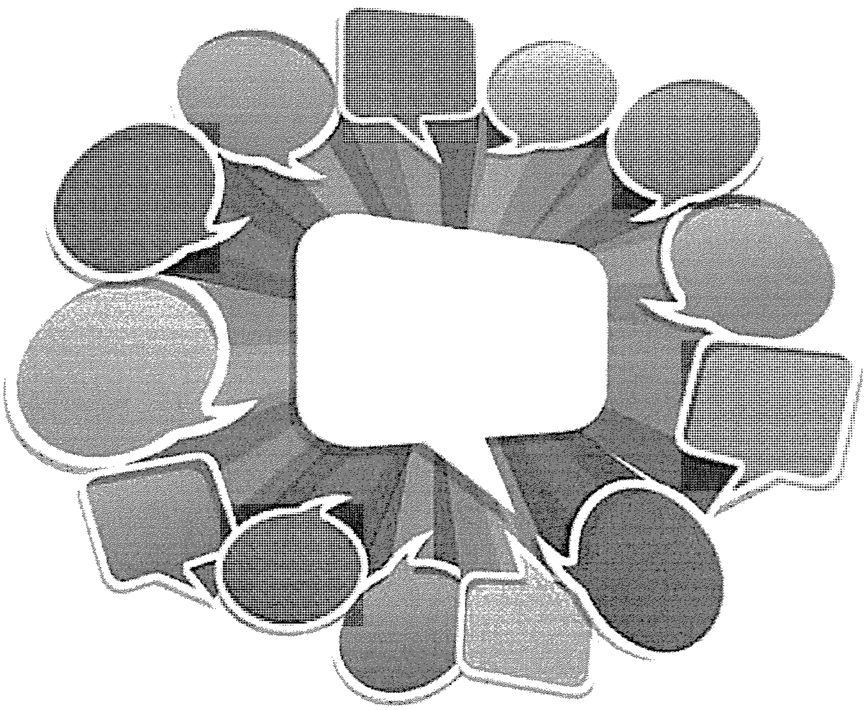
Director, Global Knowledge Center on Crop Biotechnology



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> "We need to hear the voices of those who think technology has something to offer so that these can resonate to others and be part of a chorus that is able to make informed opinions and produce sustained action."

Preface

Nothing in life is to be feared,
it is only to be understood.

-Marie Curie

Public discourse or conversations on the process and products of science and technology need to be dynamic and sustained. This is important as society needs to be fully aware about the whats, hows, and whys of technology to enable it to make decisions on its use or adoption. Public support for such technology in turn is critical once we enter the realm of policy formulation and implementation.

Voices and Views: Why Biotech? is a collection of personal essays on individuals from all over the world who have followed the development of biotechnology and are convinced that it has a significant role to play in improving the quality of life. It is a compilation of different key stakeholders' viewpoints, which are meant to generate interest in the field, inspire, and inform decision makers and to contribute to a better understanding of why the technology deserves attention. In the same manner, the essays pose challenges that the technology faces with the intent to bring opportunities to the surface as well as identify potential avenues for development.

Thirty-two experts from Africa, Asia, Europe, and North America were interviewed face-to-face or through email by members of the biotech information network of the International Service for the Acquisition of Agri-biotech Applications (ISAAA). These stakeholders represent policy makers, scientists, academics, media practitioners, and farmers who are willing to have their voices heard amidst the cacophony of divergent opinions. The list includes a former science and technology adviser to U.S. Secretaries of State, a World Food Prize awardee, noted scientists, economists, journalists, and farmers from Burkina Faso, China, Egypt, India, Indonesia, Kenya, Malaysia, Pakistan, Philippines, Switzerland, Thailand, Uganda, the U.S., and Zambia. They answered these basic questions: How did you get into biotech? Is there a place or future for biotech in your country/the world? What is its impact? What are the prospects and challenges?

Respondents with technical background and exposure to biotechnology enumerate many benefits of the technology — from improving yield, reducing use of pesticides and toxic chemicals, decreasing soil erosion, and diminishing agriculture's carbon footprint; while increasing the nutritive value of major crops and generally playing a vital role in improving the quality of human life. They note many studies and peer-reviewed papers documenting these benefits that will contribute to meeting the food and agricultural needs of the future. One scientist, in fact, was able to get almost 4,000 scientists to sign an online declaration in support of agricultural biotechnology, of which 25 were Nobel laureates.

Unfortunately, there are challenges that the field is faced with as recognized by the experts. One is the small but committed group of critics who have instilled fear among consumers, policy makers, and governments through misinformation and widespread campaigns using scare tactics and unproven claims. The other challenge involves the strict regulations that have made development and approval of new biotech crops a very rigorous and expensive process. The experts likewise caution that, although benefits have been considerable, if products fail to meet certain criteria, such as safety and efficiency, then there is no basis for supporting them. Likewise, the technology is to be regarded as merely one of other possibilities in the quest for better agricultural productivity.

Journalists, economists, and non-technical stakeholders all went through a process of discernment in their search for evidence-based answers. In seeking balance in their writing or analysis of information, they were guided by peer-reviewed articles, interviews with experts, exposure to farmers through field visits, and rejection of sensational and exaggerated claims not characterized by scientific rigor. They got into media reporting or the socioeconomic study of biotechnology only when they felt that the literature or actual field exposure supported the claimed benefits. Similarly, farmers' experiences with the use of the technology speak for themselves. Words fail them while they share the changes that the technology made in their lives.

We thank the 32 individuals, all experts in their respective fields, for being part of this project. Twenty-three authors and contributors made it possible to capture the experts' voices and views. Eric John Azucena provided the innovative layout and cover design while Ms. Teresita Rola did the final editing. The ISAAA staff led by Dr. Randy Hautea supported and gave various forms of assistance. In particular, Rhodora Aldemita, Kristine Tome, Ian Reaño, and Clement Dionglay reviewed and proofread the drafts.

This publication, to be made available in print and online versions, will be widely disseminated worldwide, particularly to policy makers in developing countries where the technology stands to benefit stakeholders the most. It is being released in time for the anniversary of the Millennium Development Goals which were formulated in 2000 to address issues of poverty and hunger.

We need to hear the voices of those who think technology has something to offer so that these can resonate to others and be part of a chorus that is able to make informed opinions and produce sustained action. The initial chords that this publication will make will hopefully contribute to a more dynamic exchange of narratives and encourage public engagement.

Mariechel J. Navarro

Technology for Humanity

Nina V. Fedoroff

- Eva Pugh Professor at the Pennsylvania State University (USA) and Distinguished Professor Emerita, King Abdullah University of Science and Technology (Saudi Arabia)
- Former Science and Technology Adviser to U.S. Secretary of State
- Former President of the American Association for the Advancement of Science
- National Medal of Science laureate in the field of biological sciences (USA)

"...molecular modification is the safest and most powerful technology we've ever developed for the daunting task of continuing to increase the amount of food for a growing population and doing it more sustainably."

Can We Feed 10 Billion People?

Mariechel J. Navarro

Science and technology have completely transformed agriculture in the last two centuries. Three key innovations proved critical: synthetic fertilizer, combustion engine, and genetics. First, the development of a method for converting atmospheric nitrogen into forms that plants can use (fertilizer) enabled man to produce more food for a growing population. Second, the invention of tractors powered by fossil fuels allowed machines to replace a lot of manual labor, thus allowing people to do things beyond just producing food. However, it is the exciting and amazing technology of genetic modification (GM) that has the potential to help feed an estimated 10 billion people in the not too distant future.

"The irony," however, says Dr. Nina V. Fedoroff, a professor of life sciences and biotechnology, and former Science and Technology Adviser to U.S. Secretaries of State Condoleezza Rice and Hillary Clinton from 2007 to 2010, "is that fear of the technology is drowning out its potential benefits."

Contrary to popular belief, almost all the food we consume is genetically modified. "Genetic modification is the basis of all evolution," Dr. Fedoroff explains, "and we have devised ways to accelerate the process."

Vast Literature on Biotech

Like most other plant scientists, Dr. Fedoroff has used molecular techniques for more than three decades and knows the vast literature on the technology. "There's plenty of evidence that using molecular methods to add, silence, and modify genes is less disruptive of both the genetics and epigenetics of plants than the methods used in the 20th century and before, be it controlled cross-breeding, tissue culture, or chemical and radiation mutagenesis. These are better and less disruptive methods than the ones we used before. That, combined with the astonishing growth of knowledge about plant physiology, biochemistry, and genetics, gives me confidence that molecular modification is the safest and most powerful technology we've ever developed for the daunting task of continuing to increase the amount of food for a growing population and doing it more sustainably."

> "Genetic modification is the basis of all evolution and we have devised ways to accelerate the process."

Genetic modification is the basis of all evolution and we have devised ways to accelerate the process.

Unfortunately, "contemporary GM crops are being blamed for farm suicides in India, tumors in rats, autism, obesity, and even infertility — even after 25 years of government research and a European Union report stressing that crop modification by GM techniques is no more dangerous than conventional products. The fear is being fuelled by electronic gossip and organizations that exploit GM fears for profit," Dr. Fedoroff says. In a TEDx event in October 2014, she challenged the audience with the query: "Will we continue to ignore facts and cling to fear-based belief systems?"

The scientist and science adviser had earlier echoed this sentiment in a 2013 article in the journal *Trends in Genetics*. Similarly, she asked the question, "Will our interconnected civilization with its globalized food supply so readily available to anyone who can afford it really discard an essential technology based on electronic hearsay?" And, in *ScienceFocus*, she raised the issue of why people were "willing to be frightened by nonsense and so reluctant to be persuaded, even by mountains of evidence?"

Transposons and Evolution

Dr. Fedoroff walks the talk, having pioneered on plant transposons, particularly doing groundbreaking work on molecular characterization of maize transposable elements or jumping genes. "I cloned one of the first plant genes ever cloned, figuring out how to adapt the molecular methods that had been worked out in microbial and animal systems to plants. I became a plant biologist after I met Barbara McClintock and read all of her work. I decided it would be fascinating to understand her genetic observations at the molecular level, both the genetic and the epigenetic aspects." Barbara McClintock was the 1983 Nobel laureate in physiology or medicine for her discovery of mobile genetic elements. In 2013, Dr. Fedoroff edited the book *Plant Transposons and Genome Dynamics in Evolution,* which gives an overview of plant transposons from McClintock's time to today. The book analyzes the research literature on plant transposable elements and how transposons shape gene structure and regulation, as well as their role in evolution.

> "If we throw away these important tools, we'll find it very difficult to improve sustainability while continuing to increase production."

President George W. Bush awarded Dr. Fedoroff a National Medal of Science in the field of biological sciences in 2006, the highest award for lifetime achievement in scientific research in the U.S. Her research sought to understand and strengthen the mechanism that allows plants to withstand the environmental challenges of a changing climate.

She served as President of the American Association for the Advancement of Science in 2012 and is a member of the United States National Academy of Sciences, the American Academy of Arts and Sciences, the European Academy of Sciences, and the American Academy of Microbiology.

Dr. Fedoroff graduated *summa cum laude* in 1966 from Syracuse University with a dual major in biology and chemistry. She received her PhD in molecular biology from the Rockefeller University. At the Pennsylvania State University, she was appointed as a Willaman Professor of Life Sciences and as an Evan Pugh Professor, the university's highest academic honor. She is a Distinguished Professor Emerita at the King Abdullah University of Science and Technology in Saudi Arabia. Among other prestigious awards, she received the Outstanding Contemporary Women Scientist Award from the New York Academy of Sciences and the John P. McGovern Science and Society Medal from Sigma Xi.

Keys to Meeting Food Challenges

Dr. Fedoroff says the deepening physiological understanding of plants and animals and increasing availability of molecular tools provide the keys to meeting the challenges of food for a still growing population sustainably in the face of a warming climate. "If we throw away these important tools, we'll find it very difficult to improve sustainability while continuing to increase production. Genetic modification of plants and animals using molecular methods can decrease the use of toxic chemicals, decrease soil erosion, decrease food waste and spoilage, and decrease agriculture's carbon footprint, while increasing the nutritive value of major calorie crops. There's just no other way."

This won't happen, Dr. Fedoroff warns, if fear-mongering and vilification of molecular approaches continue. "That's what stands in the way of politicians and regulators doing the hard work of reexamining the stringent biotechnology regulations in the light of the decades of research that have accumulated since their establishment. The pipeline of innovation will open up only if the regulatory regime changes, making it possible for scientists in both public and private sectors to work on all the different agricultural plants and animals used in the world. Today, that's both too expensive and too slow for anyone, except the big biotech companies working on the major commodity crops." Widespread public hostility to GM crops has led to the development of more complex regulations and, in many countries, has completely blocked GM crop introduction.

Challenges to Address

The author of *Mendel in the Kitchen: A Scientist's View of Genetically Modified Foods* says, "the science is quite clear, but major challenges need to be addressed: 1) make regulation blind to the modification method (there is no evidence that molecular modification is dangerous) and based solely on the nature of the crop and the modification, 2) change peoples' belief systems about modern molecular modification, 3) fund the kinds of research necessary to address problems and challenges earlier mentioned, and 4) set a government-subsidized facilities to test those crops developed by both public and private sectors deemed in need of testing."

To the question Can the world feed its growing populace?, Dr. Fedoroff is optimistic that "we can, if we think and act differently." She proposes the need to invest in technological innovations so that "we can give everyone a livelihood, enough food to eat, and a seat at the table."

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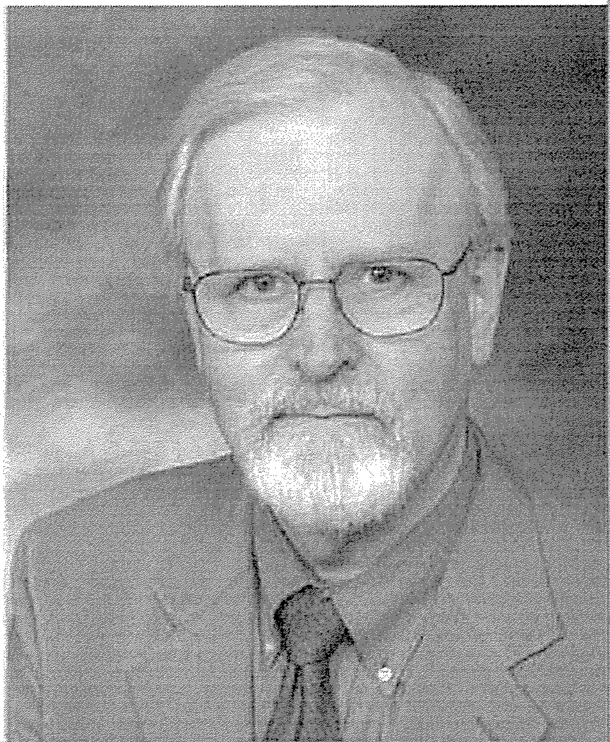

Per Pinstrup-Andersen

- Graduate School Professor and Professor Emeritus of Cornell University (USA)
- World Food Prize laureate
- Former Director General of the International Food Policy Research Institute

> "There is an important place for genetic engineering in efforts to promote agricultural development, reduce rural poverty, improve nutrition and ensure sustainable management of natural resources."

A Matter of Choice

Mariechel J. Navarro

"How, in all conscience, can the well-fed of the world, by turning what should be a choice into a global dictate, opt out of the new technologies that could provide the opportunity for all the world's people to be well-fed? "

In their book *Seeds of Contention* Dr. Per Pinstrup-Andersen and Ebbe Schioler pose this question. They forward the thought that hunger is not just about the lack of food or capital but more of a powerlessness or lack of ability to choose what food to eat, what agricultural products to use, and what technologies to adopt. "The poor should be given the opportunity to decide for themselves." The authors encourage a progressive approach of using scientific innovations such as biotechnology that have the potential to end hunger not as the sole solution but as part of the system where free choice reigns.

In 2001, Dr. Pinstrup-Andersen received the World Food Prize (WFP) for his contribution to agricultural research, food policy, and uplifting the status of the poor in the world. The WFP, given in honor of Nobel Peace Prize laureate Norman Borlaug, recognizes the achievements of individuals who have advanced human development by improving the quality, quantity, or availability of food in the world. The awarding committee noted that Dr. Pinstrup-Andersen's " major accomplishment has not been technical or scientific in nature; instead, it has been the recognition that true food security will come as much from reliable policy research and exchange and thorough policy implementation as it will from technological and scientific advances." Dr. Borlaug, in fact, noted Dr. Pinstrup-Andersen to be "one of the most influential economists and policy makers today" and "an outstanding spokesperson for effective economic policies for transforming agricultural production of food-deficit nations."

Dr. Pinstrup-Andersen has worked on the economics of technological change in developing-country agriculture, including the Green Revolution technologies, most of his professional life. He became interested in the opportunities for promoting agricultural development and improved food and nutrition security presented by the development of improved crop varieties through genetic engineering back in the 1990s, when he was director general of the International Food Policy Research Institute (IFPRI). It was through his leadership that IFPRI became the world's leading think-tank on hunger issues.

In fact, as early as 1993, Dr. Pinstrup-Andersen launched the 2020 Vision Initiative, the most comprehensive and ambitious research and dissemination program on global food security. 2020 Vision alerted the world to potential food security crises in the 21st century.

Checking on the Evidence

"What really interested me," Dr. Pinstrup-Andersen recollects, "was why something as promising as this was met with opposition by certain advocacy groups. I spent a great deal of time trying to understand both what genetic engineering had to offer small farmers and poor consumers and what was driving the opposition. The evidence that most of the advocacy groups that opposed genetically modified organisms (GMO) forwarded were reasons other than their concerns for health and the environment. This made me even more interested in trying to contribute to a more evidence-based debate and decision making. I believed then and I believe now that the misinformation and the resulting action (or lack of action) were and are harmful to low-income people's incomes, food security, and nutrition. While most civil service organizations are helping poor people, some multinational non-government organizations (NGOs) are doing more harm to poor people than the multinational corporations they criticize."

Currently Graduate School professor and professor emeritus of Cornell University, Dr. Pinstrup-Andersen states that all potential solutions to the problems confronting poor people and natural resources must be considered and assessed for their potential benefits, costs, and risks. Some of these problems are best solved by means of molecular biology, including genetic engineering. He says that there are plenty of examples of gains from the application of genetic engineering in agriculture, food, and health.

The agricultural economist who pursued his degrees at the Danish Agricultural University and Oklahoma State University notes that the impact of genetically engineered varieties for cotton, maize, soybean, and some fruits and vegetables has been documented. "There is an important place for genetic engineering in efforts to promote agricultural development, reduce rural poverty, improve nutrition and ensure sustainable management of natural resources."

Challenges Ahead

"The prospects are excellent to further move science toward solutions needed to achieve and maintain sustainable food and agricultural systems and alleviate most food and nutrition insecurity," Dr. Pinstrup-Andersen opines. The main challenge is to overcome opposition among those groups who do not have to take the consequences of their action. National and international agreements to penalize irresponsible behavior by multinational organizations would be an important step. He cites the case of African governments who were told about the alleged risks of biotechnology by many European governments and transnational NGOs. They listened and did not permit their farmers to grow GM maize even if their counterparts in South Africa as well as smallholders in Argentina, Brazil, China, India, and other countries are already doing so.

Another challenge is to streamline and reduce the time used for testing, approval, and satisfying biosafety systems, without sacrificing the quality of the process and outcome.

The man's outspoken advocacy for the hungry people in the developing world resonates to this day. Having been raised on a farm in Denmark and having worked for several years as a farm worker, Dr. Pinstrup-Andersen knows what he is talking about. "I am a believer in the use of modern science to solve problems confronting people and the environment in which we live because I believe it is essential to achieve and maintain the world we would like for current and future generations." He says he is not aware of any evidence-based reason why genetic engineering is promoted for use in the health sector but opposed in the food, agriculture, and natural resource sectors.

Failure to use the best that science can offer will make it difficult and possibly impossible, he says, to deal effectively with existing and new plant and animal diseases and pests, including "those likely to develop in the slipstream of climate change and the doomsday predictions that the world cannot feed future generations may actually materialize." Dr. Pinstrup-Andersen warns that "if that happens, it will be due to our failure to behave rationally."

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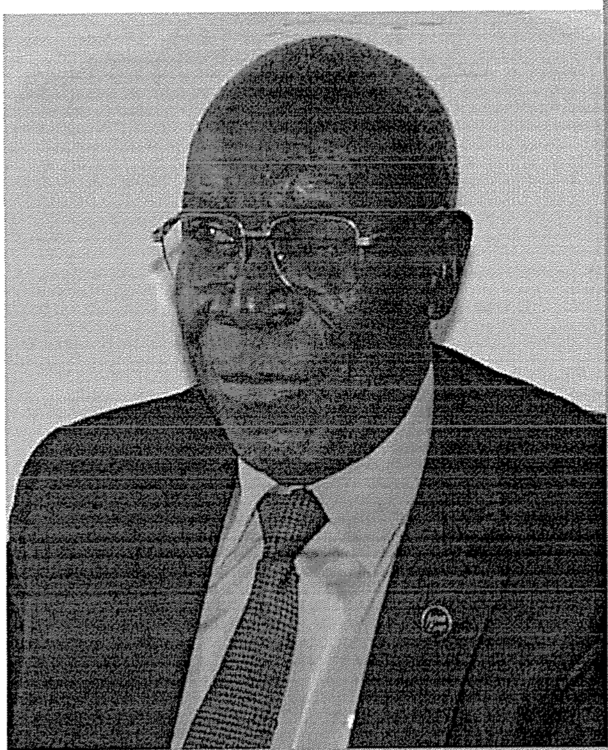


Zerubabel Mijumbi Nyiira

- State Minister for Agriculture and elected Member of Parliament (Uganda)
- Founding Executive Secretary of the National Council for Science and Technology
- Presidential Awardee for Outstanding Leadership in Agricultural Sciences

"GM technology is not the preserve of the western world and so [our people] must come to understand that we are not passive recipients of technology but that we are, indeed, capable of defining our own biotechnology research and development agenda to solve uniquely Ugandan and African problems."

Biotechnology is New Knowledge to Advance and not Retrogress Humanity

Gilbert Gumisiriza

As the founding executive secretary of the Uganda National Council for Science and Technology, Prof. Zerubabel Mijumbi Nyiira had the privilege of having an early opportunity to recognize and appreciate the potential of modern biotechnology toward contributing to the country's priority sectors — health, agriculture, manufacturing industry, and environment. He championed the integration of modern biotechnology into the country's research agenda and led efforts to establish mechanisms for the safe application of biotechnology in the early 1990s.

Currently the state minister for agriculture and also an elected member of parliament for Buruli County, Masindi District, Prof. Nyiira still holds the deep conviction now, as then, that modern biotechnology bears great potential for revolutionizing agriculture. In a confident tone, he asserts, "There is no doubt that modern biotechnology represents the future as far as plant breeding is concerned; it is part of the knowledge continuum in the field of crop genetic improvement."

Responding to New Knowledge

He points out that, throughout history, agricultural enterprise has been characterized by progress. "From the work of Gregor Mendel in the 19th century — which laid the foundation for modern classical breeding, to the unravelling of DNA in the 20th century — that ushered in the era of genetic engineering, agriculture has always progressed in tandem with advances in our understanding of biology. That is to be expected because new knowledge should take us forward rather than backward!"

To secure a comfortable place in an increasingly knowledge-based global economy, Prof. Nyiira emphasizes the importance of embracing opportunities that bring new knowledge to shape a brighter future for humanity. In stern admonition, he affirms, "we can only shun new knowledge at our own peril," and adds that with the recent advances and convergences in fields such as biotechnology, genomics, and nanotechnology, "we should expect to see new knowledge translated into practical solutions that are brought to bear on some of the most pressing challenges of the time for the betterment of the livelihoods of our people."

Prof. Nyiira's experience spans over four decades in agricultural research, science administration and management, public policy, academia, and political leadership, both locally and internationally. His debut to this long and illustrious career was in November 1968, at the age of 28, when he was appointed head of the Kawanda Agricultural Research Station, making him the first African to hold the position under British colonial rule.

He has subsequently held the positions of director of agricultural research, chief agricultural research officer and head of Uganda's agricultural research before joining the International Service for National Agricultural Research (ISNAR) as senior research fellow; the International Centre of Insect Physiology and Ecology (ICIPE) as senior principal research scientist and director of international cooperation and training; director of the Agro-technology Resource Centre (ARC), and consultant advisor on science economy and international science policy at the UN.

For his outstanding accomplishments, Prof. Nyiira received the 2006 Presidential Award for Outstanding Leadership in Agricultural Sciences, and two national medals in 2013 for Outstanding

Scientist and Outstanding Science and Technology Administrator in Uganda.

As a member of parliament, Prof. Nyiira has been notable for championing an aggressive approach to wealth creation in his constituency through agriculture. He pioneered the establishment of community-based and parish-based seed banks and seedling nurseries with over 3.5 million coffee seedlings from which beneficiaries have planted in excess of 1500 acres of coffee and earned millions of shillings.

Technological Refinement

The science of biotechnology remains generally shrouded in controversy, but Prof. Nyiira notes that biotechnology is broad and we have been exploiting it for millennia, in its most rudimentary forms, through processes such as brewing beer and making yoghurt. Modern biotechnology only represents a technological refinement in the application of knowledge that has been with us for a very long time. He remarked that knowledge has advanced to the level where it is now technically feasible to identify a particular gene determining a beneficial plant characteristic and transferring that beneficial factor into a plant of choice — something that man has been doing for thousands of years, albeit in more rudimentary ways. "Using this new knowledge," he notes, "plant breeders can accelerate the rate of achieving genetic gain in crops with unprecedented pace and precision. This is particularly useful in Africa where most of our staples are difficult to cross-breed due to narrow gene pools."

He believes that one of the biggest challenges regarding modern biotechnology is how to explain this sophisticated science and precision technology to the masses, most of whom still have trouble visualizing the abstract. "In democratizing science and technology, we must take a deliberate and purposive approach to enlighten our people and elevate them to the point where their understanding of science is in the positive sense of what it can do for them," he posits. His conviction is that education, more than anything else, will drive the paradigm shift in how people view modern biotechnologies, such as genetic engineering, as tools for positive transformation. He adds that this process will be gradual and must take into account the peoples' cultural sensibilities and contextual realities. "It must build upon the indigenous knowledge and cast it into a modern perspective that can be better appreciated over time. That is the hope and vision that we must build."

Prof. Nyiira, however, cautions that biotechnology and genetically modified (GM) crops in particular should not be viewed in isolation but in the context of broadening the options available to farmers to address a wide range of agricultural challenges. GM crops would work best as only one part in an array of different but well-integrated enabling technologies available to farmers in different situations.

> “If you want to call the tune, you must be ready to pay the piper; we ought to be able to define our own priorities and engage with new technologies on our terms rather than being influenced from outside.”

On the public controversy and apparent confusion surrounding agricultural biotechnologies, he says, "Unfortunately, our people have been manipulated and misinformed by anti-science activists and have been led to believe that nothing good can come out of biotechnology. This is shortchanging the many people who need the technology and disarming the fight against poverty and development."

He goes on to explain that there is nothing inherently bad about any particular technology — including biotechnology — beyond the context in which it is applied and it is therefore unfortunate that the dialogue on GM technology has been very polarized and driven by fear and myths rather than by reason and facts. He stresses that, "We must not forget that every new technology has concerns and adoption does not imply zero risk. If we want to be assured of absolute safety in life, we would be doing nothing — including riding in motor vehicles or walking the streets. The important thing is to minimize the risks through improving technology and put in place the necessary safety mechanisms in the way of regulatory systems, good monitoring and evaluation systems, which, in the case of GM technology— is the focus of biosafety."

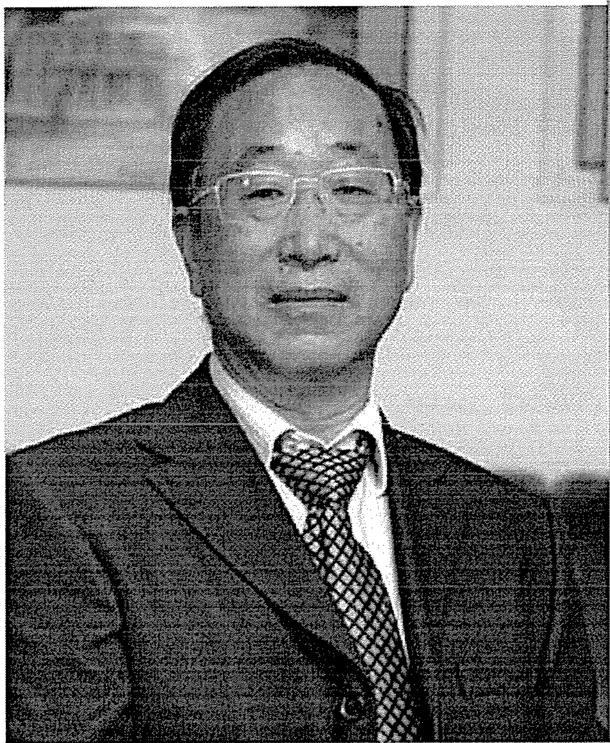
> The more our scientists are exposed, the more they are moved to innovate. At the end of the day, what is important is to remain competitive in an increasingly knowledge-based global economy.

Develop Own Markets

A common argument against adoption of biotechnologies such as GMOs is that it would result in the loss of European markets. However, Prof. Nyiira views this as simplistic and rather paternalistic. He argues that, with the move toward regional integration, the focus ought to be on developing our own markets as Africa and increasing our bargaining power. "If you want to call the tune, you must be ready to pay the piper; we ought to be able to define our own priorities and engage with new technologies on our terms rather than being influenced from outside." However, in a reassuring tone, he remarks that, "It is better to follow the right direction even if you are behind everybody else."

Prof. Nyiira also dismisses as simplistic the argument that GM technology will make local farmers dependent on multinational corporations. "GM technology is not the preserve of the western world and so [our people] must come to understand that we are not passive recipients of technology but that we are, indeed, capable of defining our own biotechnology research and development agenda to solve uniquely Ugandan and African problems."

He, however, remarks that building this technological independence will be dependent on two key factors: the first is developing our own human and infrastructural capacity in biotechnology by investing heavily in knowledge-generating systems. The second is supporting these knowledge systems through deliberate policy interventions that positively impact on science and technology. He adds that it is also important to establish strategic collaborative linkages globally to leverage comparative advantages, because knowledge is exchangeable and exposure also mentors individuals. He intimates, "The more our scientists are exposed, the more they are moved to innovate. At the end of the day, what is important is to remain competitive in an increasingly knowledge-based global economy."



Guo Sandui

- Scientist, Biotechnology Research Institute, Chinese Academy of Agricultural Sciences (China)
- Recognized as Father of China's insect-resistant cotton
- One of the top 10 meritorious figures in China's seed industry

"...biotechnology not only unveils the mystery of life, but also transforms nature and promotes human progress and development."

Biotechnology Promotes Human Progress and Development

Tian Zhang

In the early 1990s, there was a large outbreak of cotton bollworm in northern China. The consequent decrease in cotton production caused serious economic losses and resulted in cotton shortage across the country in 1992, pushing the textile industry to the brink of collapse. Pesticides that were originally sprayed two or three times during the planting season did not work, even when sprayed more than 20 times, as pests had developed resistance. Farmers in many cotton growing areas were often poisoned when spraying pesticides on cotton, sometimes even with lethal consequences. The soil was greatly contaminated due to excessive use of pesticides, rendering cotton fields untillable. Cotton farmers "turned pale at the mention of pests."

While conducting an investigation in a cotton-growing area one day, Prof. Guo Sandui from the Biotech Research Institute, Chinese Academy of Agricultural Sciences (CAAS), met an old man in his seventies spraying pesticide on cotton, his little grandson with him. The old man, upon learning that he was an expert on insect-resistant cotton, came up to him asking. "Are you here to save us?" Thereupon, the old man became tearful, speechless with a lump in his throat. Upon inquiry, he learned that the old man's son and daughter-in-law both died from poisoning after spraying pesticide on cotton two years ago. At that moment, Guo Sandui felt deeply saddened. As an agricultural researcher, he was really ashamed that he was unable to alleviate the suffering of farmers.

Bt Cotton in China

At the end of 1992, the research team headed by Prof. Guo Sandui synthesized insecticidal protein genes derived from *Bacillus thuringiensis* (Bt) for the first time in China. At that point, there were some people in China who were in favor of importing technologies directly from the United States. As the leader of a major project aimed at developing key technologies for the "development of insect-resistant transgenic cotton" under the National "863" High-tech Program, Prof. Guo Sandui was adamantly opposed to the idea. He said, "The ultimate solution lies in independent innovations in the nation and the establishment of a system for the production of insect-resistant cotton on an industrial scale."

> "China puts great importance to research and application of biotechnology."

In 1994, Prof. Guo Sandui and his research team successfully developed monovalent insect-resistance genes with Chinese intellectual property rights using biotechnology and introduced such genes into cotton to create a new genetically stable insect-resistant variety of cotton. They were able to develop the first transgenic cotton plant in China and provide an excellent germplasm for domestic breeders to cultivate insect-resistant varieties of cotton. Later, he successfully developed a bivalent insect-resistant cotton (*Cry1A/CpTI* double-gene transgenic cotton).

But the Chinese scientist did not stop innovating. His goal was to develop new varieties suitable for different cotton-growing areas of China. He cooperated with entrepreneurs in the Chinese seed industry to bring about industrial-scale production of insect-resistant cotton, increasing production and reducing labor costs. In addition, he sought to promote the development of the cotton industry and related industries such as the textile industry while reducing the use of pesticides to protect the environment and farmers' health. This goal gave him the motivation to successfully create a new system of molecular breeding techniques that resulted in high yielding, high quality and highly efficient three-line cotton hybrids. In 2005, he successfully developed the GM insect-resistant three-line hybrid cotton variety for the first time in the world and used it in production.

> "The general public must be able to understand, touch, and use biotechnology products."

Prof. Guo Sandui has made China the second country to have insect-resistant cotton with independent intellectual property rights after the U.S. By 2012, the acreage of domestically developed insect-resistant cotton had accounted for more than 95% of the total area devoted to insect-resistant cotton throughout the country. For this reason, Guo Sandui was honored as the "Father of China's insect-resistant cotton" and "One of the Top 10 Meritorious Figures in China's Seed Industry." The latter was granted by the Ministry of Agriculture, China National Seed Association, and *Farmer's Daily.* A media practitioner first referred to him as 'Father' of the technology and other journalists eventually used this tagline.

Fortunate Events

Giving an account of how he embarked on insect-resistant cotton research and development, Guo Sandui used several "fortunate enough's" to describe his experience: "I was fortunate enough to get admitted into the Department of Biology of Peking University to study biochemistry, since then I have been introduced to the booming field of biotechnology. After graduation, I was fortunate enough to be assigned to the genetics laboratory of the Institute of Microbiology, Chinese Academy of Sciences, which fostered in me a strong interest in using biotechnology to study the genetics of microorganisms such as *Bacillus subtilis* and *Bacillus thuringiensis*. Later, I was fortunate enough to be transferred to the Biotechnology Research Institute, Chinese Academy of Agricultural Sciences, which gave me the desire and the opportunity to use biotechnology to solve major challenges in key technologies in the field of agriculture. I was fortunate enough to be sent to the world-famous Pasteur Institute in France to study the structure and function of insecticidal proteins from *Bacillus thuringiensis*, which gave me the confidence and responsibility to use this tool after returning home. I have been lucky all my life — and to top this, I owe my being able to do something for the country and to convince farmers to choose biotechnology. I believe that biotechnology not only unveils the mystery of life but also transforms nature and promotes human progress and development."

Prof. Guo Sandui has complete confidence in the prospect of using technology to transform China's traditional agriculture, increase farmers' income, and promote industrial development because he sees the great importance that the country attaches to biotechnology: "China puts great importance to research and application of biotechnology. For example, the purpose of the major project aimed at developing technologies for the breeding of new varieties by China is to use biotechnology to cultivate high-yielding, high-quality, disease and insect-resistant, weed-resistant, salinity-tolerant and drought-tolerant new varieties, thereby boosting the capability and competitiveness of China's agricultural sector. So, it has been proven that biotechnology not only has a place in China and even the whole world; it also faces a very bright future."

Assuring Future for Biotech

How can we assure the future of biotechnology? Prof. Guo Sandui says, "We must launch a publicity and promotion campaign for the many biotechnology products in the fields of agriculture, industry, medicine, health, energy, and environmental protection. The general public must be able to understand, touch, and use biotechnology products. These products must be able to improve the quality of life and the health of consumers. With this, the enormous impact of biotechnology will be demonstrated and its bright future is assured."

As a researcher at the Biotechnology Research Institute, Prof. Guo Sandui has been encouraging the application of biotechnology. He has successfully developed a new insect-resistant and herbicide-tolerant transgenic variety of cotton with Chinese intellectual property rights. He explains, "My career goal remains to be the use of biotechnology to breed more new insect-resistant, disease-resistant, and herbicide-tolerant varieties to provide safer food for the public. I want to continue to breed more drought-tolerant and salinity-tolerant varieties to turn arid and saline wastelands into fertile farmland and oases to improve environmental quality. I am convinced that biotechnology plays a vital role in improving the quality of human life."

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Charity Kawira Mutegi

- East Africa Aflasafe coordinator of the Aflatoxin Policy and Program for East Africa project for the International Institute of Tropical Agriculture (Kenya)
- Norman Borlaug awardee for Field Research and Application

> "We haven't seen or been given credible information to show that there has been a safety concern on genetically engineered food because we depend on knowledge that is generated by scientists."

Biotechnology, not a Silver Bullet but a Key Tool for Attaining Food Security

Margaret Karembu, Faith Nguthi, and Brigitte Britta

Growing up in Chuka, a small rural town located on the eastern slopes of Mt. Kenya, Dr. Charity Mutegi was, at a very early age, introduced to crop farming as a way of life. She must have lived around typical rural subsistence Kenyan households that shared typical challenges: poor harvest, failed crop, insect- infested and contaminated stored grain, and lack of market for farm produce. No doubt these experiences consciously, perhaps even unconsciously, influenced her future career choices. Years later, Dr. Mutegi, now a widely respected scientist and the holder of the 2013 Norman Borlaug Award for Field Research and Application, endowed by the Rockefeller Foundation, is a strong believer in the use of science in enhancing agriculture and in improving lives.

Early Interest in Science

As a young school girl, Dr. Mutegi was not one to shy away from science. "From the time I started doing science in primary school, I just found it easier and more interesting than the arts." While many young people struggled with the pure sciences (biology, chemistry, physics), in high school, she excelled in these subjects thus setting the stage for a career in science. She went on to obtain a bachelor's degree in food science and post harvest technology, saying of the degree, "I did not consider it an abstract science; it was something that you live on, on a daily basis." She also clearly understood that the quantity and quality of food that people ate directly affected them. "If you give your body little food, then it's going to show... if you give your body poor-quality food, you are going to compromise your well-being... those are food security aspects. Of course, at that time, "food security" did not exist in my vocabulary but that is where my interest was."

It was this simple interest in how food affects human beings that propelled Charity into the field of biotechnology. She now champions the use of bio-control, a pro-environmental and effective way of managing pests by combating them with their natural enemies. She has been involved in efforts of managing aflatoxin, a natural mold that occurs in stored grain. Dr. Mutegi spearheaded efforts to identify the cause of, and solution to, a deadly outbreak of aflatoxicosis in 2004 to 2005, which proved fatal to 125 people in eastern Kenya who consumed contaminated grain. According to the World Food Prize award body, it was her work in this case that won her the coveted Norman Borlaug Award for Field Research and Application. This award is presented to individuals under the age of 40 who emulate the scientific innovation and dedication to food security demonstrated by Nobel Peace Prize Laureate, Dr. Norman Borlaug. "Her diligent research has led to innovative solutions that will avert future outbreaks and safeguard Kenya's staple crop of maize" (World Food Prize, 2013).

Managing Aflatoxin

Dr. Mutegi currently serves as the East Africa Aflasafe coordinator of the Aflatoxin Policy and Program for East Africa (APPEAR) project for the International Institute of Tropical Agriculture (IITA). She is leading further research into developing a product that can be used to manage aflatoxin at the pre-harvest stage. The project has developed a microbial pesticide "Aflasafe KE01", which is currently undergoing registration through the Pest Control Products Board of Kenya. Once in use, the pesticide will offer a natural, environmentally safe, and affordable way to smallholder farmers — many like those in her home area of Chuka — to protect their maize crop from aflatoxin contamination and exposure.

Dr. Mutegi believes that the current state of food insecurity in the world warrants the use of biotechnology in efforts to provide safe, sufficient, and nutritious food to the global citizenry. In 1961, the world population was about 3.5 billion people and we were feeding that by cultivating about 1.4 billion hectares of land. Fifty years down the line, in 2011, that population had doubled, and we have only increased the cultivated land by 12%. She notes that challenges, including the unavailability of adequate land for cultivation, coupled with a strong reliance on rainfed agriculture and the presence of heavily degraded soils, will not allow countries in sub-Saharan Africa to continue relying on traditional methods of agriculture.

> "Genetic modification (GM) is one of the tools in a basket of many being used to address the issue of food insecurity."

Of the more popular and to many, controversial form of biotechnology, genetic modification (GM), Dr. Mutegi says that it is "one of the tools in a basket of many" being used to address the issue of food insecurity. However, she does point out that, although a useful tool, GM is "not the proverbial silver bullet," a failsafe solution to the problem. Like all forms of technology, it does have its challenges, most certainly, the ever present concern about the safety of GM foods. But is the fear justifiable? Dr. Mutegi believes it is not. She points out that GM foods have been in existence for nearly 20 years now, yet "... we haven't seen or been given credible information to show that there has been a safety concern on genetically engineered food because we depend on knowledge that is generated by scientists." She also notes that GM foods, just like any other foods, undergo the same rigorous safety checks, based on set standards and through well founded protocols across the globe. She believes that the general public is misinformed about GM technology and its application and wishes that "the voices of experts were as loud as those of the antagonists." And, on the issue that GM crops cause cancer, she says, "I prefer to rely on fool-proof evidence that GM foods cause cancer; personally, I have not come across such proof."

As efforts toward sharing knowledge on biotechnology are heightened, it does seem like the right time for countries such as Kenya to fully understand and harness GM technology. After endorsing the National Biotechnology Policy in 2006, supporting the enactment of the National Biosafety Act in 2009, and helping create institutions such as the National Biosafety Authority, Dr. Mutegi believes that Kenya now has the necessary mechanisms to deal with issues of "research, containment, and commercialization" of GM crops. In addition, she is certain that institutions like the Kenya Agricultural and Livestock Research Organization and local universities can provide the infrastructure as well as the capacity to undertake research and offer advice on GM technology.

Advice to Public

Her advice to the general public, those living in fear of GM technology or in blissful ignorance, is to question their sources of information. "I have absolutely no problem about anybody making a decision to, or not, use GM commodities from an informed perspective... You and I must be willing to question the motive and the source; we must be willing to authenticate that information."

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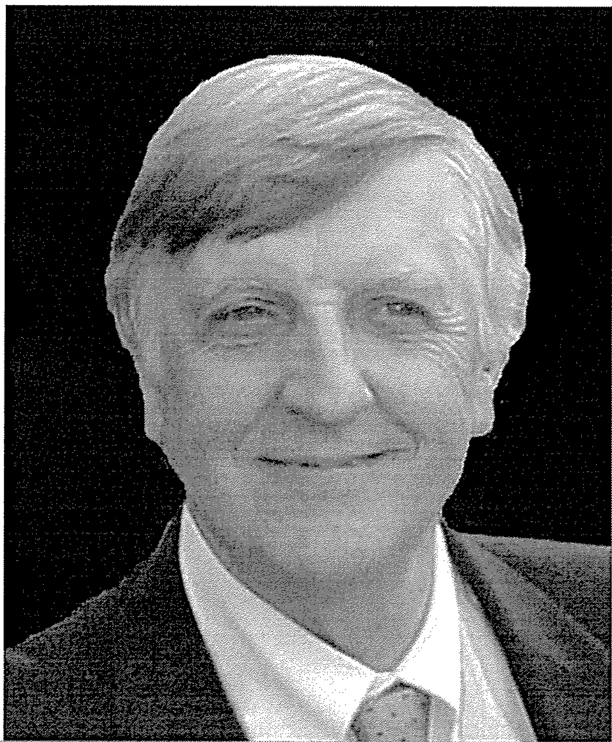


Claude M. Fauquet

- Director of the Global Cassava Partnership for the 21st Century – GCP21
- Awardee of the Order of Academic Palms (France)

"We will have to feed more people in better ways by 2050, while facing global climatic changes. To achieve this goal, all technologies, including biotech, will be required. If we do not succeed, the world will have to face tremendous instability..."

Improved Cassava through Biotechnology

Ian Mari E. Reano

"There is an obvious place and need for biotechnology in the world to feed the global population by 2050. Biotech is safe and technically relatively easy to implement in genotypes that have many acceptable properties by farmers. Biotechnology is ecologically-friendly — we can save chemicals, fertilizer, water, and we can still produce more."

Dr. Claude M. Fauquet, director of the Global Cassava Partnership for the 21st Century (GCP21), is a staunch supporter of biotechnology. He has spent most of his career doing virology and biotechnology research. This story began about three decades ago involving a crop that he dedicated most of his time on: cassava. This is a vital source of food and income for smallholder farmers in Africa and is threatened by several bacterial and viral diseases.

After receiving his doctorate in biochemistry from the University Louis Pasteur in France in 1974, he joined the Office de la Recherche Scientifique et Technique d'Outre-Mer (ORSTOM) in West Africa, later known as the Institute of Research for Development. Here, he worked as a plant virologist for 14 years. In Africa, he worked on different viral diseases that affect food crops, vegetables, and industrial crops.

Work on Cassava

While in ORSTOM, Dr. Fauquet obtained one of the first research grants awarded by the European Community and led a project that tackled the epidemiology of cassava mosaic disease (CMD), a viral disease considered the most severe and most important limiting factor in cassava production in sub-Saharan Africa. It causes about 30% yield loss on the African continent. His project paved the way for a comprehensive study of the viral disease. It was around this time when he first worked on biotech. "I got into biotech when I read about Dr. Roger Beachy, a professor at Washington University, St. Louis, and his work demonstrating that virus resistance could be engineered in plants. I was working with CMD in Africa and I immediately had the vision of rendering cassava-preferred landraces resistant to CMD!"

In 1991, Dr. Fauquet and Dr. Beachy founded the International Laboratory for Tropical Agricultural Biotechnology (ILTAB) at The Scripps Research Institute in California with assistance from several supporters, including the Rockefeller Foundation and IRD. ILTAB focused on biotechnology for virus diseases of tomato, cassava, and rice, and was among the first to develop a rice transformation system. They were also responsible for the production of the first transgenic cassava in 1995. Then in 1999, Dr. Fauquet moved ILTAB to the newly created Danforth Plant Science Center in St. Louis, Missouri, where he directed the studies on cassava genetic transformation for virus resistance and molecular plant virology of geminiviruses and ipomoviruses.

Dr. Fauquet continued his support of the cassava crop when he co-founded the Global Cassava Partnership for the 21st Century in 2003, with Dr. Joe Tohme, from the International Center for Tropical Agriculture (CIAT), to fill gaps in research and development on this very important crop for the world. The partnership aims to unlock the potential of cassava to improve the food security and increase income of poor farmers by developing industrial products. He also initiated the Virus Resistance Cassava in Africa project in 2005, wanting to confer resistance to viral diseases in cassava using pathogen-derived RNAi technology and eventually to deliver products to small farmers.

Although majority of his research on biotechnology has been dedicated to cassava, he would also like to see the technology used on other food crops.

Beyond Cash Crops

"The impact of biotech so far has been on cash crops such as cotton, corn and soybean, and it is a pity that it has not been used on major food crops such as rice, cassava, plantain, sorghum, cowpea, and peanut. Fortunately, some dedicated scientists belonging to the public sector, supported by humanitarian foundations and aid agencies, are persevering and I am hopeful that we will see a number of these products being commercialized in the next few years."

In 2007, Dr. Fauquet was knighted with the Order of Academic Palms by the French Ministry of Higher Education and Research and the president of the French Academy of Sciences for his contributions to the development of improved tropical crops, through education and research, and the application of biotechnology for use in agriculture.

> "I am a strong believer of biotech because it is a fantastic technology, simple, clean, and safe..."

Dr. Fauquet considers biotechnology as a huge factor in the struggle to feed the global population and that all tools and technologies, present and future, could be harnessed in solving mankind's problems.

"I am a strong believer of biotech because it is a fantastic technology, simple, clean, and safe and because we can change the morphology and physiology of plants to make them drought-tolerant and disease-resistant and, at the same time, have very important and acceptable characteristics in agronomy, productivity, and processing. We will have to feed more people in better ways by 2050, while facing global climatic changes. To achieve this goal, all technologies, including biotech, will be required. If we do not succeed, the world will have to face tremendous instability, unrest, and wars and the ecological equilibrium of our planet will be in jeopardy!"

Hala Eissa

- Senior Scientist at the Agricultural Genetic Engineering Research Institute, Agricultural Research Center (Egypt)

"Our duty as biotech proponents is to deliver the right information about the safety and benefits of biotech crops to the public, to the media as well as to the decision makers. They should know that biotech crops are as safe as their traditional counterparts."

Arresting Wheat Problems through Biotechnology

Naglaa Abdallah

"Our dream is to feed all Egyptians from agriculture developed by Egyptians" — this vision is what guides Dr. Hala Eissa, a senior scientist at the Agricultural Genetic Engineering Research Institute (AGERI), Agricultural Research Center, Egypt, in her work.

"I believe that the 21st century is the time for those who believe in science and for those who will have the courage to apply its findings. I am sure that Egypt will be one of the countries that understand the importance and the potential of modern science in solving today's agricultural problems," she says. "I hope to develop our techniques and address biosafety issues in order to commercialize transgenic wheat seeds in the Egyptian market."

Dr. Eissa, who got her PhD from the Department of Genetics, Faculty of Agriculture, Ain-Shams University, was successful in developing a drought-tolerant wheat plant. She believes that Egypt is facing many agricultural problems, including climatic changes due to global warming. "This will affect the availability of water needed for agriculture, as well as cause new plant diseases. Another challenge is the decrease in Egypt's water supply because of plans to erect dams on the Nile. Egypt, therefore, has to adopt new technologies that would help fight hunger," she stresses. Egypt needs to develop plant genotypes that can cope with unfavorable environmental conditions — i.e., drought, heat, and salinity. The country must likewise focus on farmers' health by reducing herbicide and insecticide usage since most of them do not follow safety regulations when they apply these chemicals.

Dr. Eissa and her research group at AGERI have produced drought-tolerant wheat by transferring a gene from barley into wheat. They claimed that their technique reduces the number of irrigations needed from eight to one, and that wheat could be cultivated with rainfall alone in some desert areas. They published their research in the journal *Physiologia Plantarum* in 2005.

Addressing the Drought Problem

Drought stress is a serious problem that limits plant growth and crop productivity worldwide. The research team reported that by transferring a gene called *HVA1* from barley to wheat, the plants could tolerate low water levels more than the control without leaves wilting. Also, they were taller and had higher yields.

The team evaluated the genetically modified (GM) wheat in the greenhouse and in the field. The field trials were conducted for seven seasons, from 1998 to 2004. The experiments using GM wheat and a local variety were carried out under normal rainfall conditions, without irrigation. In addition, improving plants' ability to cope with water stress might mitigate other environmental stresses such as salinity or high temperature.

Dr. Eissa and her team have also developed rust-resistant wheat. Wheat rust is a devastating fungal disease of wheat worldwide. Transgenic wheat (*Triticum aestivum* L.) that expresses the *chitinase* gene was developed and tested for resistance to fungal infection under greenhouse and field conditions. The resistance to rust was confirmed over 4 consecutive years in the field. Increased yield was recorded for transgenic plants compared with controls, indicating the ability of *chitinase* to confer rust resistance in wheat.

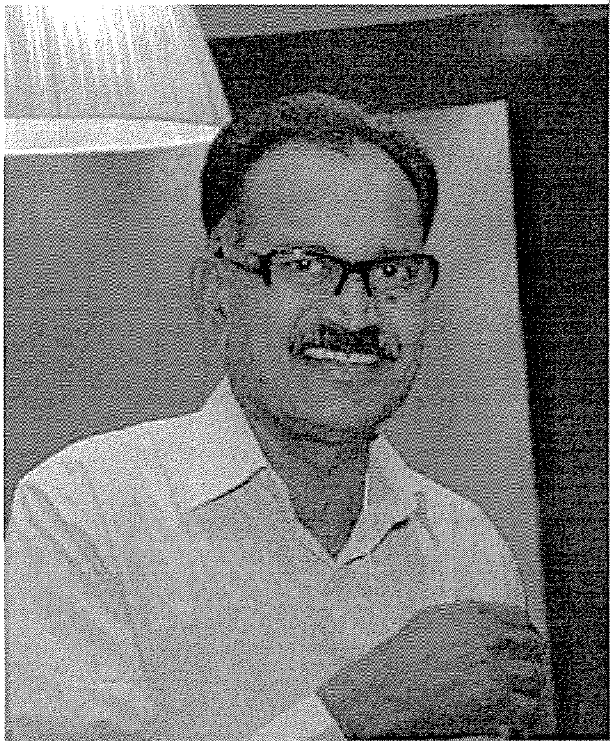
Currently also the vice dean of the College of Biotechnology, Misr University for Science and Technology, Dr. Eissa and her colleagues are paving the way to make their dream come true.

Egypt faces a gap that would reach 45% in wheat consumption because the country's lack of water limits the land area that can be cultivated. They realize that the only solution is to take wheat cultivation outside the Delta, and use genetic engineering to develop several wheat varieties that are tolerant of drought, salt stresses, and rust infection.

> **"I believe that the 21st century is the time for those who believe in science and for those who will have the courage to apply its findings. I am sure that Egypt will be one of the countries that understand the importance and the potential of modern science in solving today's agricultural problems."**

"Our duty as biotech proponents is to deliver the right information about the safety and benefits of biotech crops to the public, to the media, as well as to the decision makers. They should know that biotech crops are as safe as their traditional counterparts. This will contribute to the acceptance of such products by the general public," she notes.

Now, more than ever, "Egypt has a golden chance to benefit from biotechnology, with the new political regime open to new ideas and innovations. A new biosafety law is being established; at the same time, there are a number of biotech crops in the pipeline waiting for approval," Dr. Eissa smiles with optimism.



Vijay Atmaram Ingle

- Farmer leader from Vidarbha, Maharastra, India
- Best Yield awardee, Mahyco and East India Cotton Association
- Best Farmer awardee, East India Cotton Association

> "I shall continue to adopt new technologies as long as I live. Bt cotton is not only my life partner but the thread of my life."

Cotton is my Partner and Thread of Life

Vijay Atmaram Ingle

The cotton plant is the thread that binds my life. I make money from cotton fiber. It is a source of light as the wick in my lamp is from cotton. Cottonseed oil is used as vegetable oil in cooking many Indian cuisine while domestic animals, particularly ruminants, rely on cottonseed meal, a by-product of oil extracted from seeds. Nothing is left as waste as even the stalk is a source of fuel.

Love Affair with Cotton

It is not surprising, therefore, that I have had a love story with cotton for quite a while. I am a third-generation farmer from Vidarbha, Maharastra, India, having engaged in this profession for 40 years. In addition to cotton, we also plant pigeon pea, fruits and vegetables, mainly papaya and banana. I never got to finish school because our family did not have enough money.

In 1976, I owned a 14-acre land which I inherited from my ancestors. I could only harvest 2.5 quintals of cotton per acre as a traditional grower. Water was a problem in my land so I consulted with experts on how to efficiently use the limited water in my farm. Through irrigation, I was able to increase production and I bought an additional 28 acres of land. Although cotton was 'white gold,' attempts to increase yield through the years proved futile inspite of using drip irrigation and nutrient technology management.

A second revolution was brought by Bt cotton when I agreed to be the first to conduct Mahyco's field trials from 1997 to 1999. There was opposition to its use, but I took the chance. I tried the new cotton hybrids, first on 2 acres and then on 10 acres. I was motivated by what the private seed company told me about potential benefits: higher yield, less bollworm damage, and better response to irrigation and nutrients.

> “Achieving the highest yield per acre, my income (from Bt cotton) tripled in the last 10 years.”

Achieving the highest yield per acre, my income (from Bt cotton) tripled in the last 10 years.

Bt Technology Package

I adopted the full package of Bt technology and also improved farm practices based on my experience. Being the first to plant Bt cotton, my farm received wide media publicity, including local newspapers and farm magazines. Support was given by seed company officials and, later, by government officials, university personnel, and an irrigation company. Crop loans were availed of yearly from cooperative banks and organizations.

Achieving the highest yield per acre, my income tripled in the last 10 years. On average, for the last 3 years, our family's farm income is Rs 3,050,000 (US$50,000) per annum. Income from cotton alone is Rs 1,260,000 (US$21,000) by harvesting 28 quintals/acre for 14 acres. When I was planting traditional cotton, I was only getting 2.5 quintals of cotton per acre.

Farmer Vijay Atmaram Ingle shared his experiences during the International Conference on Adoption of Biotech Crops in the Developing World: Case Studies of Farmers in China, India, and the Philippines held on April 2-3, 2013 in Manila, Philippines. His talk in Maharati was translated into English by Dr. Charudatta Mayee, President of the Indian Society for Cotton Improvement in Mumbai.

1 Quintal = 100 kg

> My social status improved and I became popular. I received several awards for being an outstanding Bt cotton farmer.

With my higher income, I am able to give my children good education, an opportunity I was not able to get. My daughter has a degree in education while my son studies agricultural biotechnology in the university. With the additional money, I have been able to build a *pucca* or cement house, expand the drip irrigation facilities for my fruit crop garden, and establish a dairy farm with 100 animals. In 2010, I was able to purchase an additional 8 acres of land. My farm is now 14.08 ha, while my brother owns 18.15 ha. Six members of our family work in the farms for 7-8 hours daily and we hire people as needed. To top it all, I am able to pay my loans regularly and I have time to spare for my hobby, writing poetry.

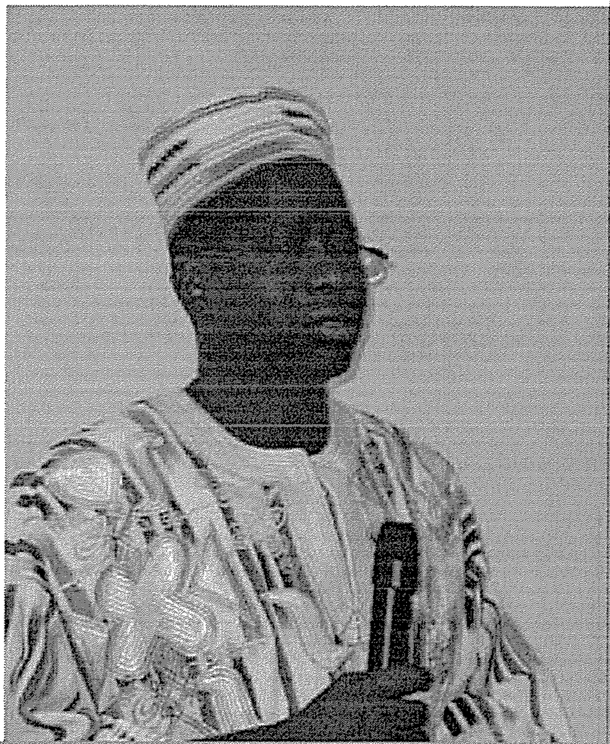
My social status improved and I became popular. I received several awards for being an outstanding Bt cotton farmer. These include Mahyco's highest yield award in 2003, the East India Cotton Association Award for best yield in 2005, and the Best Farmer Award in 2006. The newspaper *Lokmat*, a popular reading fare in Marathi, gave me a certificate of merit for best exhibition in 2012 while *Fertilizer Hemphus* honored me that same year. I received invitations from various organizations to share my story of Bt cotton in India.

Model Village

My village in Chitawaldi became a model for rural development in the Vidarbha region of Maharashtra. Farmers share information on cultivars, fertilizers, spraying, farming costs, irrigation, and market prices. To convince other farmers in the village, we conducted feeding trials during farm demonstrations and had visits by university scientists to disprove toxicity concerns. Farmers who do not make sincere efforts to grow the crop will not experience higher yields and prosperity. But we appreciate technical guidance from experts and the marketing provisions. Discussion with professionals on Bt cotton production is likewise helpful.

In May 2012, we celebrated the 10th birthday of Bt cotton on a grand scale in the village. I invited top executives from Mahyco and a drip irrigation company to witness a rally attended by 1,000 farmers from my village and surrounding ones. To honor the emergence of this technology which has changed my life, I thought the best way was to celebrate its birth in my farm. I did this with the same affection as I did for my children.

I shall continue to adopt new technologies as long as I live. Bt cotton is not only my life partner but the thread of my life.



Karim Traore

- Bt cotton farmer leader (Burkina Faso)
- Chairman, Union of Burkinabe Cotton Farmers

> “I can tell my fellow African cotton growers that this technology is necessary and we must move with the changing times.”

GM Cotton is a Social Safety Net in Burkina Faso

Margaret Karembu, Faith Nguthi, and Brigitte Bitta

The history of cotton production in Burkina Faso dates back as far as the 1900s when it was introduced during the years that the country was under French colonial rule. After 1960, when the country gained its independence, cotton production picked up with greater momentum. This was largely as a result of the formation of SOFITEX (Burkinabe Society of Textile Fibers), a company that saw the state's involvement in the production of cotton, in research and extension services as well as in marketing of the crop. During those years, cotton thrived, leading many farmers in the region to regard the crop as their newfound 'white gold'.

More recently, cotton has found its place as one of the cornerstones of Burkina Faso's economy, accounting for 3.5% of the Gross Domestic Product (GDP), and supporting a large percentage of the rural workforce. The World Bank estimates that between 15 to 20 percent of the labor force derives its income directly from cotton. Aptly put, "cotton plays the role of the social safety net in Burkina Faso". [1]

Cotton Growing through Generations

It is possibly for these reasons that cotton farmers in Burkina Faso take their crop very seriously. Take the case of Mr. Karim Traore, a 48-year old cotton farmer from the region of Boucle du Mouhoun. His people have grown cotton for as far back as he can recall. "My forefathers grew it, my father planted it, and I began to accompany my father to the cotton fields when I was 7 years old. At 20, I became a land owner — I had no doubt in my mind what I wanted to do." So much so that he skipped high school education to pursue his interest in cotton farming. And so evident was his passion that, in 1988, members of his local farmers' group based in Dankuy Village, assigned him the responsibility of weighing all the farmers' cotton during harvest. In the years that followed, he was elected to various positions of responsibility in cotton producers' unions and other types of farmers' organizations at country and regional levels.

The risk of having given up his education for cotton production seems to have paid off because Mr. Traore now stands as one of the country's better known cotton farmers. He owns a 95-ha farm, a third of which he uses to grow genetically modified (GM) or Bt cotton. He is also the chairman of the Union of Burkinabè Cotton Farmers. As chairman of that Union, he represents 350,000 farmers. He is therefore well versed with the production of GM cotton and the issues surrounding its adoption.

> "I believe that Bt cotton is a good seed. The main advantage is that we spray less. With conventional cotton, we sprayed 6 to 8 times thus, polluting the country side, but with the reduction in pesticide spraying of two times only, our health is preserved — after all, one's health is priceless."

While the greater part of Africa has lagged behind in embracing agricultural biotechnology and in particular GM products, not so for Burkina Faso. In 2003, the National Agricultural Research Institute in collaboration with the seed production company Monsanto, commenced field testing of the biotech cotton seed, Bollgard®II. Bollgard®II is a revolutionary seed that was created by taking two genes from the soil bacteria, *Bacillus thuringiensis* and inserting them into the cotton plant, resulting in what some consider a 'super cotton crop'.

By the time Burkina Faso began these field tests, cotton farmers had already started to experience effects of overuse of the pesticides they were using to control pests. Because of cotton's vulnerability to pests such as the cotton bollworm, cotton stainers and red spider mites, all of which attack it at various stages of growth, the crop requires intensive pesticide use.

Mr. Traore remembers that "At that time, although cotton was occupying a smaller portion of the farm than it is now, we used a lot of pesticides. The chemical pesticides were very dangerous and we used to close the chicken house all day during spray days. We noticed that reptiles in the field would die after the sprays." He also vividly recalls a year when his cotton crop was severely ravaged by the cotton bollworm, and instead of harvesting between 500 and 700 kg of cotton per ha as expected, he only managed about 100 kg of cotton per ha.

> "Bt cotton has changed my life. I am able to send all my children to school, meet my medical bills, and allow me to afford better accommodation for me and my family."

Steady Cotton Production Growth

In 2008, Burkina Faso became the second country in Africa, next to South Africa, to commercialize Bt cotton. Shortly after, Mr. Traore joined the group of pioneer farmers who had quickly developed an interest in the new cotton 'super crop.' He says, "I began cultivating Bt cotton in 2008 and have been growing it for 7 years now. Currently, I have a 95 ha farm, where 30 ha is occupied by cotton." From an initial 8,500 ha planted in 2008, the national hectarage for biotech cotton grown in Burkina Faso has risen steadily. In 2014, Mr. Traore, together with thousands of other risk-averse Burkinabe farmers, planted close to 500,000 hectares of biotech cotton.[2] " Mr. Traore notes that "GM cotton production is experiencing growth every year."

The most obvious advantage of the biotech cotton is a remarkable reduction in pesticide use. Mr. Traore says, "I believe that Bt cotton is a good seed. The main advantage is that we spray less. With conventional cotton, we sprayed 6 to 8 times thus, polluting the country side, but with the reduction in pesticide spraying of two times only, our health is preserved — after all, one's health is priceless." He also cites reduced labor involved in the production of Bt cotton production. With fewer pesticide spraying sessions required, less distance is covered and less time is used to cover the cotton fields.

Economic Gains

But perhaps the greatest benefit to farmers such as Mr. Traore, has been the economic gains gotten from the crop. The yield per hectare of Bt cotton as compared with conventional cotton is very high. Traore explains that "In previous years, the yields from conventional cotton were between 500 and 700 kg per ha. With Bt cotton, I get between 1,800 to 2,000 kg. There was even a time my farm yielded 3 tons (3,000 kg) of Bt cotton per hectare." In one season, Mr. Traore can earn anything from 6 million to 7 million CFA Franc (US$12,000 to US$14,000). After spending an average of 3 million CFA Franc (around US$6,000) on farm inputs, he is left with a profit of a similar amount.

Although some farmers have cited the higher cost of Bt cotton seed compared to conventional cotton as being one of the reasons they are not so keen on the crop, Mr. Traore thinks this is a misconception. He notes that "When you look at the number of pesticide sprays we save on, that cost is what makes Bt cotton seed 5 times more expensive than conventional seed. But when you take the cost of doing the 4 to 5 extra pesticide sprays and then consider that you will not need them, you realize that, in terms of the money spent, the difference between the cost of purchasing Bt cottonseed against the conventional cotton seed is only 6,000 CFA Franc (US$10)." He believes that this cost is nothing compared to the benefits accrued to one's health, mainly as a result of using less pesticides.

Mr. Traore is certainly not one of the naysayers of biotechnology. He says that, "Bt cotton has changed my life. I am able to send all my children to school, meet my medical bills, and allow me to afford better accommodation for me and my family." He adds, "I can tell my fellow African cotton growers that this technology is necessary and we must move with the changing times. Even though there are laws governing the introduction of biotech crops in some countries and others are waiting for these laws to be ratified, I can, nonetheless, reassure my fellow cotton growers that producing Bt cotton is very beneficial, is much easier, and less tedious to plant compared with conventional cotton."

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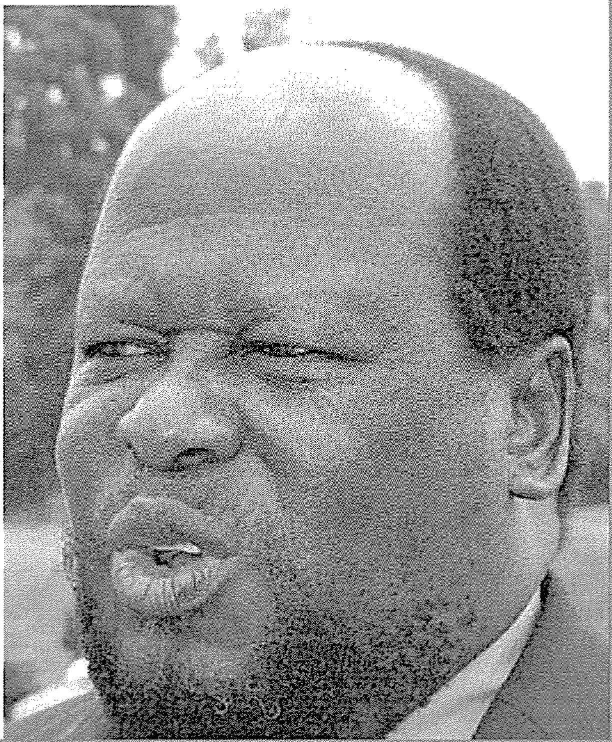
Harnessing Benefits and Potentials



Morris Ogenga-Latigo

- Former Member of Parliament and Vice Chairman of the Forum for Democratic Change Party (Uganda)
- Former Professor of entomology and ecology at Makerere University
- Former Chair of the National Biosafety Committee

"It is absolutely unfair to expect that technology will make up for institutional inadequacies; it will still require the professional extension services, the right policies and strategic investments. At the end of the day, technology cannot be expected to work like a magic wand!"

Embrace Knowledge; Do not Stifle Progress

Gilbert Gumisiriza

"Modern agri-biotechnologies hold enormous potential for revolutionizing African agriculture toward driving economic transformation, so our governments need to facilitate science and not stifle progress." This stern counsel comes from Professor Morris Ogenga-Latigo, an accomplished statesman and former professor of entomology and ecology at Makerere University, Kampala, Uganda.

Pointing to the fact that Uganda is transitioning from a subsistence economy to an increasingly industrialized one that is likely to render prevalent methods of farming obsolete, he wonders, "Do we want to empower our farmers to remain competitive or to remain stuck in the subsistence trap? How are we supposed to feed a burgeoning population and face up to the emerging effects of global climate change with inefficient and outmoded farming practices? We must take an earnest and critical look at what we want the future to look like for us!"

Notable Voice in Uganda

As a key personality in the local scientific and political echelons, Professor Ogenga-Latigo has been one of the most notable voices for science in the country. In 1996, he was chair of the then nascent National Biosafety Committee (NBC), a technical committee of eminent scientists that represents the cornerstone of regulatory oversight in genetically modified organism (GMO) research. He was instrumental in the development of the national guidelines for GMO research which laid the foundation for a biosafety regulatory system in Uganda. During his tenure, the NBC also supervised the successful conduct of the maiden GMO research projects in the country, including confined field trials of GM cotton and clinical trials of a recombinant DNA candidate vaccine for AIDS, the first of their kind in the world.

In 2001, Professor Ogenga-Latigo forayed into politics and was elected member of parliament for Agago County, Pader District. He served from 2001 to 2011. He was also the vice chairman of the Forum for Democratic Change (FDC) political party and leader of opposition in the 8th Parliament. This impressive political record belies an accomplished academician who has authored more than 100 publications and mentored scores of scientists in Uganda and beyond. During his stint as professor at Makerere, he played a key role in establishing the biotechnology training program under the Faculty of Agriculture. This program was the first capacity-building initiative to provide targeted training in modern biotechnology in the region, produced the first crop of biotech professionals in Uganda.

> "I understand the science of GM and can see the promise it holds of transforming agricultural productivity. Nevertheless, if there are any plausible risks that science can identify, it is important that we approach these from a scientific premise rather than an emotive one."

Professor Ogenga-Latigo believes that the current controversy on genetically modified organisms (GMO) is overly simplistic and largely misses the point. He laments that the discussion on GM technology has deteriorated into an ideological impasse that has derailed objective and nuanced discussion about opportunities presented by scientific advances. "Farmers' ability to access new and improved technologies like GM crops is *sine qua non* to improving agricultural productivity yet skeptics are clinging to ideology and ignoring the potential of GM crops." He argues that this has largely served to stifle rather than facilitate progress and that the unfortunate causalities are the resource-poor farmers who stand to benefit the most from advances in agricultural technology.

Shift in GMO Debate

It is time to shift the GMO discussion to a more rational and constructive direction by eschewing ideology and focusing, as much as possible, on what is best for people to become food-secure and self-sufficient. Such a constructive debate has to acknowledge the opportunities offered by GM technologies and address reasonable concerns that the current controversy does not.

"As a scientist with a breadth of experience in biotechnology and biosafety, I understand the science of GM and can see the promise it holds of transforming agricultural productivity. Nevertheless, if there are any plausible risks that science can identify, it is important that we approach these from a scientific premise rather than an emotive one," says Professor Ogenga-Latigo, whose postdoctoral research involved pioneering work on the use of DNA biotyping for the molecular classification aphids.

As a seasoned lawmaker, Professor Ogenga-Latigo is intimately familiar with the nature of discussions around the regulation of GMOs and a proposed biotechnology and biosafety bill currently before the Ugandan Parliament. He notes that, while it is unfortunate that the debate has proven so divisive in the public, it would be even more unfortunate if policy makers ignore scientific consensus and allow emotions and ideology to triumph.

He decries the irresponsible scaremongering by the anti-science activists that has served to perpetuate fear and misinformation about biotechnology, noting that "the anti-GM skeptics will not be swayed by science because they have embraced an ideology that is fundamentally at odds with that science." Most of the arguments against biotechnology are sentimental and unjustified attacks on technology that have nothing to do with science, such as the claim that we will lose the market for our exports. "If we grow GM banana and export non-GM sugarcane, how could we possibly lose access to foreign markets?," ponders Professor Ogenga-Latigo.

> "Farmers' ability to access new and improved technologies like GM crops is *sine qua non* to improving agricultural productivity yet skeptics are clinging to ideology and ignoring the potential of GM crops."

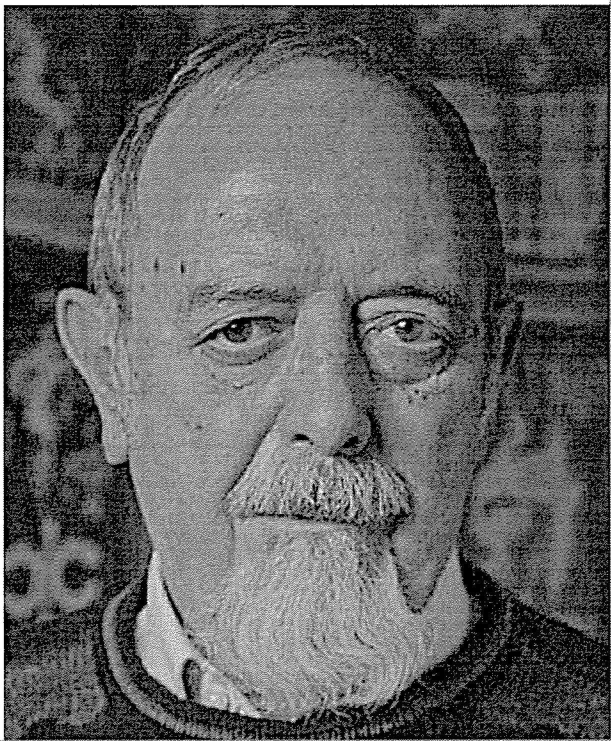
He concedes that the highly technical nature of the science of modern biotechnology has not been adequately simplified to the public, leading to widespread myths and public aversion. "As soon as people start talking about genetic engineering in Uganda, there is a cultural blank because there is nothing to relate to in the everyday experiences of the layman. This gives fertile ground for the propagation of all sorts of falsehoods and misconceptions."

He is, however, optimistic that, as people begin to understand in simplified ways, that DNA is a universal medium for genetic information and that genes are analogous to computer programs that can be exploited to achieve desired outcomes, perhaps they will appreciate the fact that GM technology is just a tool that extends our capabilities to address emerging challenges such as climate change, pests, and diseases.

Option for Innovation

He hastens to caution that GM technology, like all technologies, is not a panacea to all agricultural challenges that beset the resource-poor farmers in Uganda, but rather a complementary tool in the ballpark of options for innovation toward a more sustainable world. "It is absolutely unfair to expect that technology will make up for institutional inadequacies; it will still require the professional extension services, the right policies and strategic investments. At the end of the day, technology cannot be expected to work like a magic wand!"

Above all, Professor Ogenga-Latigo, emphasizes the need for more voices speaking up for science and reason, especially within the political leadership; we must sensitize our leaders and put science in a language that our politicians and the public understand.



Ingo Potrykus

- Scientist and co-inventor of Golden Rice
- One of Top Living Contributors to Biotechnology by the peers of *Scientist* (2005)
- Most Influential Scientist (1995-2005) by the peers of *Nature Biotechnology*

"As soon as GM technology will be freed from automatic, excessive, precautionary regulation, hundreds of public sector projects for the public good would win the minds and hearts of the citizens around the world and this will end the unprecedented hysteria on GMOs."

Use of Biotechnology is a Social Responsibility

Rhodora R. Aldemita

Known as the co-inventor of Golden Rice (GR), a genetically modified rice that contains high beta carotene, Ingo Potrykus was first a biotechnologist and now an advocate of the technology.

His interest in biotechnology was spurred by the phenomenon of totipotency of plant cells — the ability of plant cells to regenerate into whole plants. Dr. Potrykus' fascination was nurtured during his graduate studies at the Max-Planck Institute for Plant Breeding Research in Koln, Germany, in the 1960s.

"Back then, I was dreaming of creating nearly unlimited genetic variation via genetic modifications of those cells and explored somatic hybridization, asymmetric hybridization, transfer of organelles, and transfer of isolated genes," Dr. Potrykus says.

Indeed, the pioneering years of biotechnology in the early 1970s, after the Green Revolution, was the period when scientists were exploring the possible use of recombinant DNA to speed up development of new varieties. The successes in conventional breeding of new varieties of staple crops were instrumental in attaining food security in developing countries during those times.

However, an anticipated increase in population needs more drastic agricultural technologies. Dr. Potrykus, one of the pioneering scientists on biotechnology, was already thinking "big" as he was contemplating on "complementing traditional plant breeding technology with the potential of large populations of totipotent somatic cells to create novel variations in crops."

For Dr. Potrykus, his "academic career was more influenced by the attitude of an engineer (with the desire to solve concrete problems) instead of a scientist (working towards scientific novelty). Contributing to and making use of the progress in tissue culture, molecular biology and genetics, and genetic engineering technology was the most natural way for scientists to follow his social responsibility and contribute to humanity."

With this motivation, Dr. Potrykus' work focused on research that would contribute to food security in developing countries. These include studies on the development and application of genetic engineering technology for "food security" crops such as rice, wheat, sorghum, and cassava; for disease and pest resistance; improved quality and yield; and efficient use of natural resources and improved biosafety.

Golden Rice

His most impressive work was the development of GR with co-inventor Prof. Dr. Peter Beyer of Albert-Ludwigs University in Freiburg, Germany. GR, a genetically modified rice with enhanced beta carotene content, was developed in his laboratory at the Swiss Federal Institute of Technology, Zurich in the late 1990s. The team developed GR by genetically engineering rice cells to contain genes coding for phytoene synthase (*psy* gene) from daffodil and phytoene desaturase (*crtI*) from *Erwinia carotovora*, the two important enzymes that allow the production of beta carotene in the rice endosperm. The prototype Golden Rice in Taipei 309 (japonica subspecies) background developed by the team was able to produce 1.2-1.8 µg/g beta carotene in the grain, using a constitutive promoter (Ye et al. 2000). This research is one of the pioneering works on metabolic engineering and proof that rice has the capacity to produce beta carotene when given the necessary genetic machinery. This research work was the cover and featured research article of *Time* magazine in July 2000.

To improve beta carotene content, the two genes *psy* and *crytl* were placed after an endosperm- specific promoter *gt1* in a Cocodrie background, which produced around 8 µg/g beta carotene (Golden Rice Project website), hence the development of GR 1. A few more years of experimenting various sources of *psy* genes identified corn *psy* to be the most appropriate and the use of another endosperm-specific promoter (*Glul1*). Designated GR 2, some transgenic lines were able to produce up to 37 µg/g beta carotene in the endosperm (Paine et al. 2005).

Distribution and utilization of GR 1 and GR 2 in developing countries affected by Vitamin A deficiency was monitored by the Humanitarian Board composed of scientists and socio-economists and chaired by Dr. Potrykus.

International Recognition

Dr. Potrykus' scientific career spans more than three decades with about 340 publications in peer-reviewed journals and 30 patents. He has garnered international recognition from professional societies; honorary doctorates in two European universities; elected member of science academies of Europe, the Pontifical Academy, Hungary, and Switzerland; and earned prestigious titles such as the "Top Living Contributors to Biotechnology" by the peers of the journal *Scientist* in 2005 and "The Most Influential Scientist" for the decade 1995-2005 by the peers of the journal *Nature Biotechnology* in 2006.

Looking forward, he thinks that the future of biotechnology in many countries and in the world will depend on whether 'reason' and 'logic' can win the minds of the people. Speaking in the midst of countries critical of biotechnology, he opines that "farmers, media and the whole citizenry should understand that "integrated" not "organic" farming and food production is the most sensible way for both food production and protection of the environment. Large-scale intensive farming is essential for survival of the majority of the world population." He also observed that in the EU, "the mind is set on a romantic view of medieval farming practices, and in this mental environment, biotechnology is seen as the enemy and not as the friend."

He is also of the impression that "the 'European March of Unreason' is colonizing effectively, even those countries which do not have problems with the acceptance of plant biotechnology."

> "I believe in science, in the social responsibility of scientists, and in the use of progress in science for humanity. It has been established beyond any reasonable doubt that plant biotechnology does not carry any technology-inherent risk."

Dr. Potrykus, however, is optimistic that, with the many scientific documentation prepared annually by ISAAA and similar agencies indicating increasing adoption and positive impact of biotech crops, many countries will get to accept the technology and reap its immense benefits. And that the targeted benefits for agbiotech industry and farmers in the West are very welcome 'spin-off' benefits from private sector developments for farmers in developing countries.

Public Sector Contribution

Most of the deregulated products on the market so far were developed by a few private agbiotech companies, with almost zero contribution from the public sector. Dr. Potrykus is of the opinion that "this is because of political reasons: an anti-GMO war of eco-ideologists and anti-science populists, and regulation which does not prevent harm to the consumer or the environment, but instead prevents the use of the technology by public institutions for public good."

Dr. Potrykus is primarily interested in the use of biotechnology to contribute to food security, especially for nutrition security in developing countries. "The development of GR," he says, "is an illustration of both the potential and challenges. There is the potential for provitamin A in genetically improved rice endosperm to save millions from blindness and death. And the fact is that the technology is ready since 1999, and will not be deployed — if at all — before 2018, with nearly 20 years of delay because of regulation. There are many projects in the pipeline with potential for nutrition and food security, at or close to proof-of-concept, which will suffer at least the same delay, and if not, they are blocked completely because of shortage of funding."

Regulatory Hurdles

The challenge therefore in this delay and slow progress is regulation. And according to Dr. Potrykus, there is scientific consensus that GMO-specific regulation has no justification and does not make any sense at all. He adds, "if regulation is meant to prevent harm, it must focus on products, not on the technology applied to produce that product." He is hopeful though that, "as soon as GM technology will be freed from automatic, excessive, precautionary regulation, hundreds of public sector projects for the public good would win the minds and hearts of the citizens around the world and this will end the unprecedented hysteria on GMOs."

Social Responsibility

Finally, Dr. Potrykus expressed his belief and social responsibility in the following lines.

"I am not a specific believer of biotech. I believe in science, in the social responsibility of scientists, and in the use of progress in science for humanity. It has been established beyond any reasonable doubt that plant biotechnology does not carry any technology-inherent risk. It is a fact that the technology has the safest track record compared with any other technology in history. There is not a single documented case of harm since its use! It is, therefore, insane not to use it efficiently and prudently. It is immoral to prevent its use for public good. And it is criminal to prevent it from contributing to food- and nutrition security."

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Gregory Conko

- Executive Director of Competitive Enterprise Institute (USA)
- Co-author, *The Frankenfood Myth: How Protest and Politics Threaten the Biotech Revolution*

"And because it will be important to produce more food in coming decades while lightening agriculture's environmental footprint, biotechnology will be one of the tools farmers and plant breeders can use to promote long-term food security and environmental stewardship."

Advocating for More Rational Biotech Regulation

Mariechel J. Navarro

The book *The Frankenfood Myth: How Protest and Politics Threaten the Biotech Revolution* was named by Barron's as one of the 25 best books of 2004. In the foreword, Nobel Peace Prize winner Norman Borlaug said that Henry Miller and Gregory Conko had written a "brilliant account of the way self-interest, bad science, and excessive government regulation have profoundly compromised the potential of the new biotechnology." The political process, the book points out, prevents enormous potential benefits to accrue to consumers.

Mr. Gregory Conko is executive director of Competitive Enterprise Institute, a non-profit public policy organization based in Washington, D.C. His work focuses on the regulation of food and pharmaceuticals to ensure that regulatory policy is based on sound science and is no more restrictive than necessary to protect human health and the environment.

Reading on the Literature

In Mr. Conko's work, he found that many regulatory policies that restrict choice and innovation are based on scientifically unjustified concerns about new products and technologies. "It was in that context that I first took an interest in agricultural applications of biotechnology in the mid-1990s, when the first genetically engineered crops were being introduced for commercial-scale cultivation in the United States. I knew that biotechnology had been used with great success in medical technology, so I was immediately interested in learning whether the allegations of health and environmental risk levied against biotech crops were true. I began to read as much of the scientific literature on the testing of biotech crops as possible. And I talked to dozens of scientists and plant breeders about the process of genetically engineering plants and how the risks compared to those associated with classical breeding."

Mr. Conko discovered that some of the criticisms of plant genetic engineering were valid, but that identical risks were also present in conventional breeding. He saw that many of the criticisms were simply unwarranted. "I also found the innovative nature of the field to be fascinating and was convinced that the technology had much to offer farmers, consumers, and the environment. And I was alarmed to find that the regulatory restrictions breeders faced when testing and commercializing biotech applications were quite strict and that they were impeding the development of many promising crop and livestock products. Armed with that knowledge, I thought it was important to begin advocating on behalf of more rational biotech regulation."

As a regulatory policy expert and legal scholar, Mr. Conko's primary contributions to the biotechnology debate have been in three areas: helping scientists, agronomists, and farmers better understand the legal and regulatory systems that affect biotech research, development, and commercialization; advocating on behalf of more rational, science-based regulatory policy; and helping agriculture experts become more effective advocates.

> "I'd like to think that our efforts are responsible for raising awareness of biotechnology's benefits and debunking myths spread by its critics."

International Collaboration

"Over the years, I've collaborated with a broad range of scientists and agronomists from North and South America, Europe, Africa, and Asia on writing and doing research projects, explaining to them the ins and outs of regulatory policy and how legal and regulatory barriers impact their work, both directly and indirectly. I have, in turn, learned a considerable amount from them about the science of biotechnology and real-world agricultural practices. And together, we have become more effective in communicating the benefits of biotechnology to consumers, as well as governments and their constituents, and better able to address their concerns," Mr. Conko explains. "I'd like to think that our efforts are responsible for raising awareness of biotechnology's benefits and debunking myths spread by its critics."

Benefits for Farmers

The legal expert asserts that biotech crops on the market today have shown significant benefits for farmers in a number of countries — from large-scale commercial growers in wealthy industrialized countries to small-scale, resource-poor farmers in less developed countries, and everyone in between.

"Most have also shown important environmental benefits, such as reduced insecticide spraying, a shift to more environment-friendly herbicides, reduced soil erosion, and lower motor fuel use and engine emissions. At the same time, no environmental harms or human health risks have been identified nor is there any scientific reason to expect that they would. In short, even the relatively limited range of biotech crop traits now available have been all gain and no pain. And because it will be important to produce more food in coming decades while lightening agriculture's environmental footprint, biotechnology will be one of the tools farmers and plant breeders can use to promote long-term food security and environmental stewardship."

A *magna cum laude* from the George Mason University School of Law, Mr. Conko explains that the current biggest benefits from biotech crop adoption accrue to growers. "In wealthy countries, where insects and weeds in conventional farming are managed well with agricultural chemicals, biotech crops reduce the cost of crop production and increase profitability. In less developed countries, insect-resistant biotech crops have not only increased profitability but also increased yields and, in some circumstances, have helped to protect against catastrophic losses from insect predation. So, the benefits of biotech crops have been greatest for poor farmers."

"But the environmental benefits of reduced insecticide spraying, improved soil management, and higher yields should not be underestimated," says Mr. Conko. "Topsoil and ag chemical runoff from farms, for example, are among the worst pollution problems in wealthy industrialized countries, affecting lakes, streams, rivers and other waterways. By accelerating the on-going shift toward no-till and low-till farming, biotech herbicide-tolerant crops have substantially reduced this runoff problem. And, especially in less developed countries, the substitution of biotech insect-resistant crops for insecticide spraying has even resulted in improved farm worker health."

> "Biotechnology is simply a breeding tool, like many others, which gives humans the ability to add, remove, or amplify specific traits to a plant, animal, or microorganism."

Mr. Conko forwards the thought that most consumers have yet to notice these important benefits, noting that environmental improvements delivered by biotech crops help everyone. "To be sure, lower production costs and higher yields have undoubtedly also had positive impacts on the price of food in the marketplace. And if regulatory impediments do not prevent the next generation of biotech crops from reaching the market, consumers will soon notice the availability of foods with improved nutritional value and other direct consumer benefits."

Excessive Government Regulation

"Consumer resistance remains an impediment to broader adoption in some countries, and this affects growers in countries that rely on exporting to markets where consumer resistance remains strong. But the biggest current hurdle to broader biotech crop adoption remains excessive government regulation of biotech crops and foods derived from them. Biotech crop adoption will continue, albeit slowly." Mr. Conko adds that as a new generation of biotech traits begins to deliver perceptible consumer benefits — such as nutritionally enhanced foods — he anticipates consumer acceptance growing more robust over time.

Although public acceptance of biotech foods is generally thought to be the biggest challenge in the biotech world, it is actually the hurdles erected by scientifically unjustified regulation. Mr. Conko elaborates that government restrictions have kept biotech crops off the market entirely in some countries. And, even in a country such as the US, which has approved more biotech traits than any other, the financial cost and time delays associated with seeking and securing regulatory approval make the use of genetic engineering economically impractical for all but very high-value commodity crops and have concentrated commercial development in the hands of a few large multinational corporations.

The regulatory cost alone of bringing a new biotech crop variety to market in a country like the United States can total millions of dollars, says Mr. Conko. He cites Redenbaugh and McHugen (2004), who state that these regulatory costs typically exceed the entire market value of small horticulture crops, such as beans, peas, and lettuce.

Prohibitive Field Testing

Breeders of non-biotech crops, Mr. Conko explains, will often test thousands of unique genetic variants in the field each year in order to select a single cultivar for commercialization. "But regulators treat each transformation event of a biotech crop to be a unique regulated product. So, a single gene inserted into a dozen plants of the identical cultivar results, not in 12 copies of one regulated product, but one copy each of 12 different regulated products. Thus, the normal field-testing process is made prohibitively expensive for biotech crops, and even well-financed breeders must select only a handful of transgenic events for field testing. When small start-up firms, non-profit research centers, and public-sector breeders can afford to field-trial a biotech crop at all, they are generally limited to testing just one or two transformation events, thereby inhibiting the R&D process."

"And if regulatory impediments do not prevent the next generation of biotech crops from reaching the market, consumers will soon notice the availability of foods with improved nutritional value and other direct consumer benefits."

"But many of the most interesting and potentially beneficial biotech crop traits have been or are being developed in public sector and non-profit research institutions. These include crops with added nutritional value, crops modified to address abiotic environmental stresses or to grow well in poor soils common in the tropics, and varieties of crop species grown primarily as staples in less developed countries such as cassava, millet, and sweet potato. Merely testing these crop varieties in field trials is often prohibitively expensive. And, even when one or more varieties performs well in field trials, the cost and political hurdles inherent in seeking full commercial approval too often keep these promising crops out of the hands of the farmers and consumers who could use them most," Mr. Conko notes.

Powerful Technology

Despite the political barriers to commercialization, however, biotechnology needs to be at the radar screen of innovation. Mr. Conko stresses that "biotechnology is simply a breeding tool, like many others, which gives humans the ability to add, remove, or amplify specific traits to a plant, animal, or microorganism. But unlike other breeding methods, biotechnology gives breeders the ability to move single, well-characterized genes rather than rely on the hit-or-miss approaches of classical breeding in which many, typically uncharacterized genes must be moved or altered at the same time. This more precise nature gives breeders a far greater ability to predict the genotype and phenotype that will result from any given breeding experiment.

Biotechnology is therefore far more powerful than other breeding methods. But it is that very power that makes biotechnology safer than classical breeding. Biotechnology cannot solve most of agriculture's problems. However, it has already addressed many once-intractable problems, and it has the potential to address many, many more."

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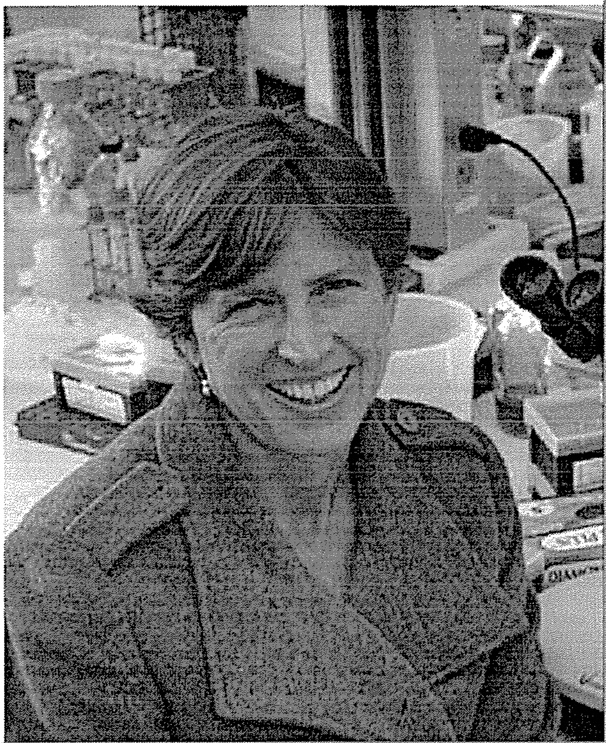

Pamela Ronald

- Professor at the Department of Plant Pathology and the Genome Center at the University of California, Davis and faculty director of the UC Davis Institute for Food and Agricultural Literacy (USA)
- Louis Malassis International Scientific Prize awardee for agriculture and food
- Co-author, *Tomorrow's Table: Organic Farming, Genetics, and the Future of Food*

"To maximize the benefit of GE plants, they would best be integrated into an organic farming system. In this way, there is a complementation of practices and technology — the organic practices protect the environment and the GE technology helps reduce crop losses to disease or environmental stress."

Setting the Table for Tomorrow

Kristine Grace N. Tome

Geneticist Pamela Ronald provides balanced information on genetic engineering. In fact, she hopes to see that future tabletops will have food grown in an ecologically-based manner and advocates for such a future.

Dr. Ronald is a professor at the Department of Plant Pathology and the Genome Center at the University of California, Davis. She is also the faculty director of the UC Davis Institute for Food and Agricultural Literacy.

Dr. Ronald's laboratory is known for the isolation of the rice *XA21* immune receptor and working with colleagues to discover the rice *Sub1A* submergence tolerance transcription factor, which has been used by breeders to develop flood tolerant rice varieties. Because of these breakthroughs, Dr. Ronald and her colleagues received the USDA 2008 National Research Initiative Discovery Award. She also received other prestigious awards such as a Guggenheim Fellowship, the Fulbright-Tocqueville Distinguished Chair, and the National Association of Science Writers in Society Journalism Award. She is an elected fellow of the American Association for the Advancement of Science (AAAS). In 2012, Dr. Ronald received the Louis Malassis International Scientific Prize for Agriculture and Food and Tech Award 2012 for innovative use of technology to benefit humanity.

Aside from her scientific involvement, Dr. Ronald is also active in public engagement. She co-founded Biology Fortified, Inc., a non-profit organization focused on providing factual information and fostering dialogues on issues in biology, especially on plant genetics and agricultural biotechnology. She actively supports science through articles, some of which were published in *The New York Times*, *The Economist*, and *Boston Globe*. In 2008, Dr. Ronald and her husband, Raoul Adamchak, an organic farmer, released the book *Tomorrow's Table: Organic Farming, Genetics, and the Future of Food*.

Impact of Genetic Research

In her interview with *Beacon Reader*, Dr. Ronald narrated the impact of her genetic research to farmers. "Every year, millions of small rice farmers lose their entire crops to flooding. Even though rice plants grow in water, most varieties will die after 3 days of being submerged. Breeders knew of an ancient variety that could withstand 2 weeks of submergence. But every time they tried to introduce this flood tolerance trait using conventional breeding, other genes would be introduced as well, resulting in varieties that the farmers rejected because the seed did not adapt well to their farming practices."

"Together with my colleagues, David Mackill and Kenong Xu, we isolated a gene in the ancient variety, called *SUB1*, that conferred the flood tolerance trait. Then, using that genetic information and a technique called marker-assisted breeding, breeders at the International Rice Research Institute (IRRI) were able to introduce the *SUB1* gene precisely into varieties preferred by farmers without destroying the other important plant characteristics," she said.

Since then, IRRI has developed several flood-tolerant rice varieties that have been rapidly adopted by farmers. Their yields increased by 300% more than what they used to get in planting conventional rice varieties following a flood. Thus, Dr. Ronald stresses that, "For 70 million people who live on less than US$1/day, these types of advances are crucial to food security."

Aside from her own research, she also discussed the impact of other biotech applications in agriculture. "Genetic techniques, such as introducing a bacterial gene into a crop, have helped reduce insecticide use. Bt stands for *Bacillus thuringiensis*; it's a naturally occurring bacteria that is toxic to specific insect pests that attack corn and cotton. Bt has been used by organic farmers for over 50 years to control insect pests. Geneticists have introduced the same trait into corn, called Bt corn. A recent US Department of Agriculture report noted that farmers have been able to reduce the amount of insecticides sprayed on corn tenfold due to planting of the Bt corn seed. This is a huge positive improvement to the sustainability of our farms. The adoption of herbicide-tolerant crops has enabled farmers to substitute glyphosate (classified as non-toxic by the EPA; less toxic than Bt sprayed by organic farmers) for more toxic and persistent herbicides. Still despite these advances, it is clear that farmers cannot rely on seed alone. As we have seen with herbicide tolerant crops, overreliance on a single herbicide has led to the evolution of resistant weeds. "

> **“ I am not a believer in biotech any more than any other breeding technology. I am a believer in enhancing sustainable agriculture and food security for the world's poorest. This will require many technologies and ecologically based farming practices. ”**

In an article about Dr. Ronald in *The New York Times*, the writer asked a significant question — "But how do you retain that productivity without the negative impact?" The answer to this question is found in their book, *Tomorrow's Table*.

"Is genetic engineering (GE) simply a new tool for farmers that in some cases will be the right one? Although genetic modification by conventional breeding and genetic engineering methods are distinct processes, they ultimately have the same end — to alter and improve the genetic makeup of the plant. Whether GE crops fit into a framework of ecological farming gets back to the first thing I tell my students: Organic farming is about health — health of the soil, the plants and animals, the farmer, the consumer, and the environment. A marriage of farming with biological science has always been an important strand of the organic approach. Plants that have been genetically modified using older methods have given rise to nearly every food we eat. Such crops are resistant to diseases, insects, or nematodes; fit in well with organic production; and it seems to me that there is a role there for the right GE crops as well, " her husband Raoul Adamchak wrote.

Biotech and Organic Farming

"At the same time, I think that much of the potential of GE plants is lost in conventional systems that continue to use pesticides and synthetic fertilizers. To maximize the benefit of GE plants, they would best be integrated into an organic farming system. In this way, there is a complementation of practices and technology — the organic practices protect the environment and the GE technology helps reduce crop losses to disease or environmental stress."

Their book surprised people from the scientific sphere and the organic farming sector. Organic farming and GE are perceived to be two distinctly different worlds. Thus, when individuals encounter the book and discover that a believer of biotechnology and a practitioner of organic farming are actually married, they start to question, "Is it really possible for GE and organic agriculture to move towards the same direction?" Their union is a statement that both fields have the same target: food security and sustainability.

In their book, she explained why she thinks that biotechnology can play an important role in the future of food production. During one season, her husband lost half of his tomato crops due to frost. However, they are fortunate that the loss is not a very dreadful situation for them because they still had food on their table.

According to Dr. Ronald, "As Raoul knows, this of course is not the case for the vast majority of farmers on the Earth, where tolerance for environmental fluctuations such as cold, salt, or submergence can mean a difference between eating or not. Traits such as these are the most difficult to address using standard breeding approaches. In the future, this is where genetic engineering will likely have the most significant human impact."

Complementary Technologies

When asked if she is a believer of biotechnology, Dr. Ronald said, "I am not a believer in biotech any more than any other breeding technology. I am a believer in enhancing sustainable agriculture and food security for the world's poorest. This will require many technologies and ecologically based farming practices."

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Photo credit: John Stumbos, University of California, Davis

Inez Slamet-Loedin

- Senior Scientist and Head of the Genetic Transformation Laboratory at the International Rice Research Institute
- LIPI Young Scientist awardee and National Food Security awardee (Indonesia)

“We need to continue the discussion and share with the general public, especially the youth, the real nature of biotech products. Scientists have to speak out because, if not, who else will?”

From Fascination to Fulfillment

Mariechel J. Navarro

As a young child, Inez Slamet-Loedin would tag along with her anthropologist-mother who worked months at a time doing research work in a village in Klaten, Java, Indonesia. "I had a touch of early exposure to rural life despite being raised in the city", Inez intimates. "I saw how simple life was and the problems that plagued residents in rural and urban communities. I grew up being influenced by what I saw and felt, and my mother is my living example about compassion for others and caring for our surroundings."

By the time Inez was in middle school, she developed a fascination with nature, being awed by the simplicity and, at the same time, complexity of living things. Eventually, she took a natural science major in high school and was accepted at Bogor Agricultural Institute where she specialized in agronomy. During her undergraduate years, she volunteered to work with the Indonesia Green Foundation where she taught ecology to high school students every Saturday. "I would hike with students along the forest reservation near Ciapus, Bogor and share my amazement about the wonders of plants and their role in the environment," Inez recalls.

Excitement for Science

In 1988, she passed the selection for a World Bank postgraduate scholarship program, initiated by then Minister of Science and Technology B.J. Habibie, for major areas in the new sciences. Inez decided to take plant biotechnology at the University of Nottingham in the United Kingdom. "At that time, biotech was relatively new. I had been fascinated with the genetics of inheritance way back in high school, so the idea of discovering new techniques at the molecular level was something that excited me and was worth pursuing."

After a Rockefeller Foundation postdoctoral stint in Leiden, Netherlands, also brewing was Dr. Slamet-Loedin's desire to work on improving rice so that it can grow in the drought-prone areas in Indonesia. She initiated the rice research group at the *Lembaga Ilmu Pengetahuan Indonesia* (LIPI) or the Indonesian Institute of Sciences where the team worked on drought tolerance and insect resistance. The group expanded from, initially, only herself and three fresh graduates to, currently, more than 25 young scientists holding doctoral, masters, and bachelors degrees.

> "The challenge is not just to feed billions of people who depend mostly on rice, but ensure that they are getting proper nutrition."

She spent about 15 years at the Research Centre for Biotechnology, LIPI where she eventually became the head of its molecular biology division. She received the LIPI Young Scientist Award in 2002 and the National Food Security Award for her scientific contributions in the field of biotechnology in 2004. She also became a consultant for an UNEP program for biosafety in ASEAN countries.

Next came an opportunity to become a shuttle scientist between the International Rice Research Institute (IRRI) and LIPI in 2006, where she came to the realization that nutritional concerns had a great impact on the well-being and capacity of women and children. She saw that biotechnology was indeed opening opportunities to address abiotic factors and nutritional issues.

Currently a senior scientist and head of the Genetic Transformation Laboratory at IRRI based in Los Baños, Laguna, Philippines since 2008, Dr. Slamet-Loedin is the lead person in projects on genetically modified (GM) rice. The technology has been used at IRRI to identify useful low phosphorus and drought tolerance genes to allow rice to grow under harsh conditions and potential genes to increase rice yield.

Biofortified Rice

Her team is also developing biofortified rice. According to Dr. Slamet-Loedin, "the challenge is not just to feed billions of people who depend mostly on rice, but ensure that they are getting proper nutrition." She cites the prevalence of "hidden hunger" that affects over two billion people around the world. It is a condition with often no visible warning signs, due to chronic lack of vitamins and minerals from the diet, such as iron, zinc, and vitamin A. Many people in Asia rely heavily on rice for most or their entire calorie needs because they cannot afford or do not have access to a full range of nutritious foods. As a result, hidden hunger has become prevalent in rice-consuming countries.[1]

Iron-rich rice, in particular, has the potential to prevent iron-deficiency anemia that affects more than 1 billion people worldwide. Iron deficiency contributes to increased maternal mortality, stifles children's cognitive and physical development, and reduces people's energy. Zinc deficiency, on the other hand, causes stunting in children, affects cognitive development, and compromises the immune system.

Dr. Slamet-Loedin says the iron content in polished rice of the most commonly consumed rice varieties have very low iron concentrations (only 2 to 3 milligrams per kilogram or parts per million), while mining thousands of rice germplasm have resulted in only a maximum of 5-6 ppm iron content. The recommended minimum iron concentration is 13-14 ppm to supply 30% of a person's daily need. Confined field trials of high iron rice in the Philippines and Colombia have shown that this minimum level can be achieved in popular varieties by adding a rice iron transporter and iron-rich soy genes through genetic modification. As a bonus, this GM rice not only reaches the iron biofortification target but also the zinc biofortification target in polished grain.

Misinformation on Biotech

Inspite of the exciting possibilities that biotechnology offers, "there is strong misinformation and hate campaigns being waged by certain groups with strong sentiments against genetic engineering. We have done studies on toxicity, allergenicity, and other concerns for our potential products, and we strive to ensure that the development of any GM rice is done in full compliance with national and international biosafety regulations. Unfortunately, the speculative negative side continues to predominate. I have learned the painful lesson that spreading fear is often easier than spreading good news."

The lady scientist recalls that she had agreed to be a co-supervisor of a PhD student with a university professor who held a negative view of the technology. She shared peer-reviewed journals and other documents and discussed research parameters with the student. She said that the student followed the scientific process recommended and empirical evidence disproved her main supervisor's contentions. "The important thing was that my student learned the scientific evidence herself, and even my colleague became more open to GM." Dr. Slamet-Loedin adds that she

[1] IRRI is currently developing healthier rice varieties as a potential way to help address hidden hunger and improve the nutrition of rice consumers. These varieties have the potential to reach many people because rice is eaten by half of humanity. IRRI and its partners are developing rice varieties that have higher levels of iron, zinc and beta-carotene (a source of vitamin A, also known as Golden Rice). These healthier rice varieties can complement current strategies to reduce micronutrient deficiencies.

has remained good friends with some members of civil society groups, some of them just totally misinformed that biotech products will inevitably lead to an oligopoly of a handful of private firms.

> Regulation is certainly needed for the safe and responsible use of modern biotechnology, but we must determine what information is really needed versus information that might be nice to know.

She believes that it is important to maintain credibility as a scientist. While some media interviews result in articles that highlight imagined negative consequences of a safe technology, her opinions are included nevertheless to provide a scientific perspective. "We have to show that, as scientists, we do not have hidden motivations," says the lady scientist. "We are doing our work to help contribute to the betterment of mankind."

Regulation Concerns

Dr. Slamet-Loedin also worries about the cost of stewardship and deregulation in nurturing a GM technology from the lab to the field, particularly the costs associated with deregulation processes. "Regulation is certainly needed for the safe and responsible use of modern biotechnology, but we must determine what information is really needed versus information that might be nice to know. For any agriculture product, it is difficult, if not impossible, to prove with absolute certainty the absence of risk; reasonable consensus is needed to agree when accumulated evidence is sufficient to show that certain GM products are as safe as their non-GM counterparts".

Dr. Slamet-Loedin says that many scientists are not well-informed about commercialization processes and many eventually believe that only major private sector actors can bear the costs of the release of GM products. Many barriers to the commercialization of GM products do not reside in the technology itself, but in the process that it undergoes to be approved for commercialization. "If we can prove that changes in the genome of a product is far less than when mutation technology is utilized, why should the former be regulated more heavily than the latter? "

The lady scientist believes that the next generation will determine the future of biotech. "We need to continue the discussion and share with the general public, especially the youth, the real nature of biotech products," she says. "Scientists have to speak out because, if not, who else will?"

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Wayne Parrott

- Professor of the Institute of Plant Breeding, Genetics and Genomics at the University of Georgia (USA)
- Member, Editorial Boards of *Plant Cell Reports, Plant Cell Tissue and Organ Culture,* and *Crop Science*
- Former Chair of the biotechnology section of the Crop Science Society of America and of the plant section of the Society for In Vitro Biology

> “As long as there is malnutrition in the world, there is a place for biotech. As long as there are farmers who cannot progress past subsistence, there is a place for biotech. As long as agriculture uses too much water, fertilizers, and pesticides, and causes too much erosion, there will be a place for biotech.”

There's Always a Place for Biotechnology

Kristine Grace N. Tome

A scientist knows science, does science, and fights for science. This is the kind of scientist you will find in Dr. Wayne Parrott. He does research and instruction on biotechnology and also devotes time fulfilling his role of engaging the public into science. His zeal in fighting for science is immeasurable.

It all started when he was studying agronomy at the University of Kentucky with much interest in plant breeding. "When I saw my first plant in a test tube I was hooked. It was also the time when scientists reported the first expression of foreign genes in plant cells, which made it evident it would be an exciting way to complement plant breeding." Since then, he held on to the promise of genetic engineering.

Research Focus

After finishing his undergraduate degree, he pursued MS and PhD degrees in plant breeding and plant genetics from the University of Wisconsin-Madison. Then in 1988, he joined the faculty of the Department of Agronomy, which is currently the Institute of Plant Breeding, Genetics and Genomics at the University of Georgia. His research is focused on developing tissue culture and gene transfer systems to introduce value-added traits for legumes such as soybean, alfalfa, and peanut. His research team is also geared toward developing techniques for multiple gene transformation, alternative selection systems, early analysis of transgenes, investigation on the specific role of centromere in maize, and transposon mutagenesis for gene discovery in soybean. Aside from doing research, he is also actively mentoring graduate students and postdoctoral fellows and teaching graduate-level courses in genetics and undergraduate courses in agroecology and sustainable agriculture.

Prof. Parrott has released a guide for environmental risk assessment of genetically modified organisms (GMO), with a second edition to be released soon, together with more than 90 journal articles in refereed publications and 14 book chapters. He has been part of the editorial boards of *Plant Cell Reports, Plant Cell Tissue and Organ Culture,* and *Crop Science*. He also served as chair of the biotechnology section of the Crop Science Society of America and of the plant section of the Society for In Vitro Biology, and is a fellow of both of these societies.

> "As a minimum, biotechnology in all its forms contributes to make breeding more efficient. At its best, biotechnology extends the reach of plant breeding to produce crops we could only dream about a generation ago."

Debunking Junk Science

Aside from his laboratory work, he also came up with the website *The GMO Crop (mis)Information Page*, which features links to information resources on GM crops for public use. He featured research articles on GMO that he considers "junk science" and gave the authors failing grades because of misleading methodology or results. For instance, he failed the article reporting that 93% of pregnant women and 69% of non-pregnant women tested had GMO-Bt protein in the blood. It got a failing mark because the detection test used is known not to work on blood samples. Because of Prof. Parrott's fervor in debunking junk science, he has been invited to give talks on biotechnology in various countries.

When he was in Honduras, he talked to a farmer and saw first-hand the impact of what scientists like him do. "The farmer was not getting enough income from his land, so he got a part-time job in town. However, without his full attention, his land yielded even less. Then, he was given his first biotech maize. The labor savings meant he could still work in town, and yet provide all the labor needed by his farm without compromising yield. With the extra income, he was able to send his daughter to school and buy seed for the following season. He never wants to go back to his old varieties. Multiply his experience by 18 million smallholder farmers, and the impact is self-evident."

> "There are still millions of smallholder farmers being condemned to perpetual poverty by Western-financed NGOs who deny them the right to use improved seeds under the pretense of protecting their health, livelihood, traditions, or culture."

Daunting Challenges

Prof. Parrott views that the most daunting challenges of biotechnology may not be climate change or pests but fear and emotion which are not technical issues that can be addressed methodologically through science. "The challenges are based on fear and emotion, and do not respond to reason and logic; fear is propagated by various non-government organizations (NGOs) who profit richly from their activities. I do not think any of us saw that the rise of these groups was on the horizon in the early days of biotech. Now, they have chased away capital and talent, and erected unsurmountable regulatory systems with no foundation in science. The tragedy in this picture is that there are still millions of smallholder farmers being condemned to perpetual poverty by Western-financed NGOs who deny them the right to use improved seeds under the pretense of protecting their health, livelihood, traditions, or culture."

Because of this challenge, Prof. Parrott has reached out to legislators and regulators throughout his native Latin America and other countries to equip them with knowledge on making a functional regulatory system that ensures safety of biotechnology products. He also did volunteer work as scientific advisor to the Biotechnology Committee of the International Life Sciences Institute, which serves to bring the best science available to help guide those who formulate regulatory policies.

> "Biotech remains the most powerful and flexible set of technologies we have when deployed within the context of a comprehensive rural development strategy that includes education, infrastructure, and advanced agronomic practices."

Impact of Biotech

Prof. Parrott views the benefits of biotechnology as a dream come true. "Sadly, almost no one is aware of the huge impact that plant breeding has had on their lives. Most are clueless what living with yields from 1900 would be like, and do not realize the impact it would have on prices, land use, and the agricultural footprint in general. Ultimately, the wealth of mankind starts with agricultural productivity. So, first and foremost, I am a believer in plant breeding. As a minimum, biotechnology in all its forms contributes to make breeding more efficient. At its best, biotechnology extends the reach of plant breeding to produce crops we could only dream about a generation ago."

Despite opposition and other challenges of biotechnology, Prof. Parrott stands by his belief that there will always be a place for it. "As long as there is malnutrition in the world, there is a place for biotech. As long as there are farmers who cannot progress past subsistence, there is a place for biotech. As long as there are crop failures, there is a place for biotech. As long as agriculture uses too much water, fertilizers, and pesticides, and causes too much erosion, there will be a place for biotech. Biotech remains the most powerful and flexible set of technologies we have when deployed within the context of a comprehensive rural development strategy that includes education, infrastructure, and advanced agronomic practices."

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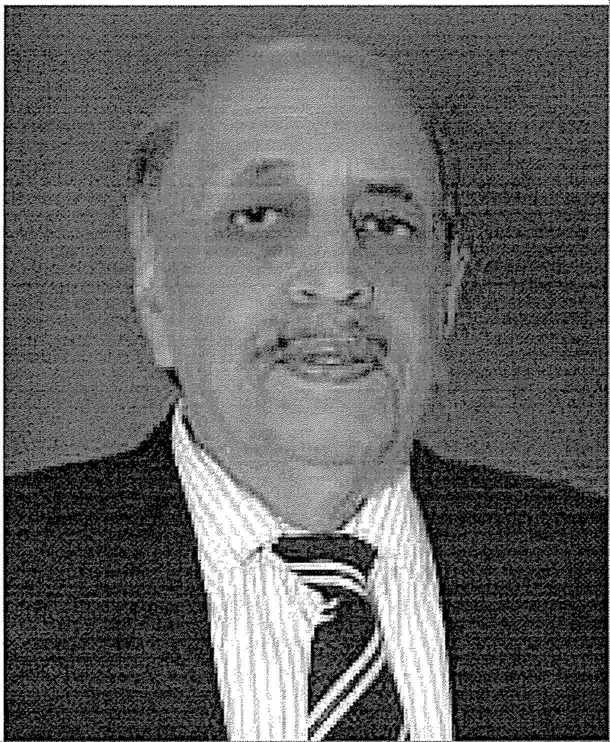
Photo credit: *Columns*, University of Georgia Online Newsletter

Championing the Cause



Anwar Nasim

- Secretary General of the Pakistan Academy of Sciences
- Father of Biotechnology in Pakistan
- Presidential Awardee: Pride of Performance and *Sitara-i-imtiaz*

"I strongly believe that use of agricultural biotechnology has enormous potential to provide food and feed to all, not only increasing production but by reducing farm inputs such as pesticide, fertilizers, herbicides and water."

A Non-Government Individual Leads Biotech Efforts

M. Iqbal Choudhary, Saifullah Khan, and Sammer Yousuf

In a developing world, things move in a slightly different manner. The paradigm of development has different dynamics. Systems often do not exist. Individuals play key roles. They are the champions of change, good or bad. Changes are made "despite the government." These individuals are called non-government individuals (NGIs), a term coined by Dr. Anwar Nasim, in parallel to the well known non-government organizations (NGOs). NGIs are towering personalities who catalyze change, contribute toward the betterment of society, and redefine the future of nations. They emerge out of nowhere and leave profound marks behind them.

One such NGI is Dr. Anwar Nasim S.I., the Father of Biotechnology in Pakistan. In the book *Biotechnology in Developing Countries: Prospects and Challenges* which Dr. Nasim co-authored, the vision and mission statements for biotechnology are well elucidated:

> **Vision**: Attaining new heights in biotechnology research, and shaping it into a tool, to act as an engine of socio-economic development;
> **Mission**: Realizing biotechnology is an intellectual enterprise of mankind to provide impetus that fulfills this potential and utilizing it to the advantage of humanity and technological empowerment of the developing world.

Dr. Nasim is a big name in the field of science, especially in biotechnology, in Pakistan. Currently the secretary general of the Pakistan Academy of Sciences, Dr. Nasim is actively engaged in the promotion of science. His main areas of interest include molecular biology, biotechnology, and genetic engineering.

In 1995 and 1999, he received two national awards from the President of Pakistan: the Pride of Performance and *Sitara-i-imtiaz*. These prestigious awards are given to eminent personalities for their most valuable contributions in their respective fields.

> "Effective and judicious applications of modern agricultural biotechnology can play an important role in the sustainable agriculture development and economy of Pakistan as well as in improving the livelihood of poor farmers."

He was awarded a gold medal by the University of the Punjab, Lahore, in 1957 for securing first position in his pursuit of an MS in Botany degree. Soon after, Dr. Nasim then went to Edinburgh University (UK) and completed his PhD in biochemical genetics in 1966, the first Pakistani who specialized in this field. He started as a researcher/scientist at the Biology and Health Physics Division of the Chalk River Nuclear Laboratories (Canada) and later became a member of the National Research Council of Canada.

Biotech for Pakistan

During his research engagement in Canada, he remained in close touch with his motherland, Pakistan, through numerous short visits and extensive dialogues with researchers. As an active scientist of international stature, he witnessed the great progress in the field of biotechnology the world over. He could see the benefits that biotechnology could bring to the world.

"Pakistan's growing population requires careful planning and coordinated efforts to cater to the country's present and future needs. The most important of these human needs are food, fodder, and fiber. These all come from the agriculture sector; it is, and will remain the most important sector in the economy," Dr. Nasim explains. The imbalance in food intake and crop production ratio is a big challenge for developing countries such as Pakistan. In addition to the heavy use of pest/ insect controls, low crop yields are contributing to the poverty of farmers. "Effective and judicious applications of modern agricultural biotechnology can thus play an important role in the sustainable agriculture development and economy of Pakistan as well as in improving the livelihood of poor farmers. However, it demands national commitment for increased production of food, fodder, and medicine," he asserts.

Dr. Nasim was concerned about the poor state of scientific research, particularly in biotechnology, in Pakistan. The impediments include lack of trained manpower, poor institutional infrastructure, sustainable financial support, and lack of commitment by the national government. Dr. Nasim worked in getting government officials to understand the importance of biotechnology in increasing production, decreasing production cost, and improving the living standards of people.

Establishment of Biotech Centers

The turning point in the status of agri-biotechnology in Pakistan was in 1981 when Dr. Nasim visited his home country. He organized the first course on biotechnology in Faisalabad and trained a large number of young scientists, who are now among the most prominent scientists in the country. He proposed the establishment of a national biotechnology institution in Pakistan. During this historical visit, he met with the chairmen of the Pakistan Atomic Energy Commission and the University Grant Commission and emphasized the need to act quickly. He told them, "The National Institute of Genetic Engineering is imperative for the country within the shortest possible time to bring Pakistan at par with the developed world. Unlike electronics where Pakistan is far behind, genetic engineering is a field where the West is only a few years ahead. There is no apparent reason, therefore, to let this gap widen."

During his subsequent visits, he also proposed the establishment of an institution of genetic engineering in Pakistan. As a result, two premier institutions, the Centre of Excellence in Molecular Biology in Lahore and National Institute of Biotechnology and Genetic Engineering in Faisalabad were set up, thus, opening the doors to applied and basic research in biotechnology.

His valuable and continuous efforts were also recognized internationally and he was awarded by the Overseas Pakistani's Institute for his role in promoting science in Pakistan.

"Unlike electronics where Pakistan is far behind, genetic engineering is a field where the West is only a few years ahead. There is no apparent reason, therefore, to let this gap widen."

Making a Choice

Dr. Nasim says the introduction of modern technologies always plays a major role in the development of the agriculture sector. He noted that traditional methods in agriculture were not sufficient to feed millions of additional mouths every year. He challenged higher authorities, saying that "Traditional plant breeding has limited potential as most of it has already been exploited under the Green Revolution and no major breakthrough in food production looks feasible. Under these circumstances, we have only one choice of using technology for the benefit of our own people. We need to explore non-traditional methods of increasing farm production."

He continues: "I strongly believe that use of agricultural biotechnology has enormous potential to provide food and feed to all, not only by increasing production but also by reducing farm inputs such as pesticides, fertilizers, herbicides, and water. An improvement of our environment will result if we use zero tillage and less fertilizers because there would be less contamination of the aquifer's water tables."

As the science advisor at COMSTECH (OIC's Standing Committee on Scientific and Technology Cooperation) in 2010, he was actively involved along with Dr. Atta-ur-Rahman FRS, coordinator general of COMSTECH, in the development of science and technology in the 57 OIC member countries. He strongly advocated the role of biotechnology application to improve the economy in the Muslim world.

Biotech and Islamic Nations

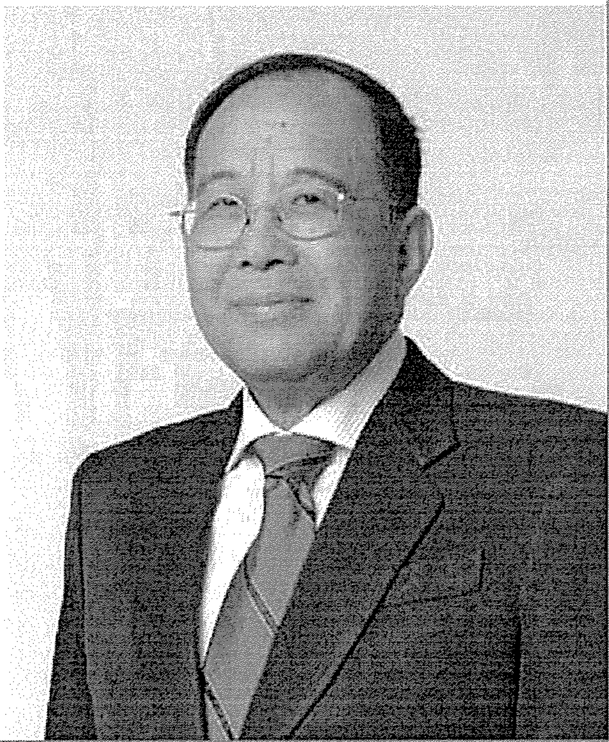
"For Pakistan, as in other countries of the world, especially the Islamic nations, where the main economic activity is based on agriculture, biotechnological application such as genetic engineering can be utilized to improve production both quantitatively and qualitatively by transferring more precisely and efficiently the genes of interest. Molecular markers can be utilized to make plant breeding more precise and efficient by marker assisted selection. This may result in saving time and resources by early selection and roughing out undesirable genotypes at an early stage. Similarly, this technology may play a vital role in the sustainability of the environment," Dr. Nasim explains.

In the same vein, tissue culture techniques are being utilized for mass multiplication of true-to-type and disease-free plants of a required quality throughout the year. This is very important for crops where large-scale replacement of clean planting material is required due to viral infection. Example of major crops that can benefit from these techniques are citrus, pineapple, banana, and many more. Moreover, biotechnology in developing countries can influence the human health by transferring health beneficial traits into food plants. These include lower saturated fat, increased omega-3 fatty acid, and increased isoflavone content. Consumers can be rest assured that agricultural biotechnology is safe," Dr. Nasim elaborates.

In 2006, Dr. Nasim proposed the establishment of the Pakistan Biotechnology Information Center located at the LEJ National Science Information Center, International Center for Chemical and Biological Sciences in the University of Karachi. He remains as patron of the center.

"Biotechnology remains to be my passion. I am always available to attend almost each and every event where biotechnology is the subject of discussion. The existence of people who oppose the technology is nothing new. In human history, there were always groups who oppose change. There is a great potential to serve humanity. Biotechnology is based on deep knowledge, it is not black magic. People who oppose it lack the data to support their arguments," he explains.

Dr. Nasim is a genuine champion of agri-biotechnology as a vehicle for the betterment of mankind. "We must advance our knowledge of biotechnology and make its applications our mission for the sake of humanity, not only in Pakistan, but the world over."



Emil Q. Javier

- Former Minister of Science and Technology (Philippines)
- Former President, University of the Philippines System
- Former President, National Academy of Science and Technology
- Chairman of the Coalition for Modern Agriculture Modernization in the Philippines

"I know enough of the science to understand that it has many potential useful applications. There are enough safeguards. The benefits outweigh the risks, which are speculative and exaggerated."

Biotech Visionary

Clement Dionglay

Scientists play a number of roles in society. Influential and respected, they can be supporters and advocates for different causes, in addition to their research engagement. Some also see the need to inform the public and help them understand science better. Such is the case of Dr. Emil Q. Javier, who has held four leadership positions: chancellor of the University of the Philippines (UP) Los Baños, president of the National Academy of Science and Technology (NAST), minister of science and technology, and president of the UP System.

Dr. Javier is a strong supporter of science particularly crop biotechnology. "I know enough of the science to understand that it has many potential useful applications. There are enough safeguards. The benefits outweigh the risks, which are speculative and exaggerated."

He states that the country's current regulatory protocols are very rigid and science-based, and crops developed through genetic engineering technologies are equivalent, or maybe even safer, than those bred through conventional plant breeding.

"There is nothing to fear nor wonder about the transfer of DNA across widely unrelated forms of life, e.g. DNA from bacteria to plants and animals. These merely confirm the theory of evolution — that all living things have a common genetic blueprint (our DNA) because all life originated from single-celled organisms billions of years ago."

It was 1962 when Dr. Javier, then a young graduate student of agronomy at the University of Illinois, realized that the future of agriculture will revolve around the DNA and the manipulation of genes not at the level of populations and individuals but at the sub-cellular level. The DNA helix had been deciphered a decade earlier, and he anticipated that agriculture would take a different path in the future.

"I realized that the new ballgame will have to be in genetics and biochemistry. So, in Illinois, I spent more time in the arts and sciences faculty than in agriculture. I studied basic biochemistry, microbiology, genetics, and physiology, trying to understand where this new world of plant breeding was going into."

Institutional Efforts

Years later, Dr. Javier took the initiative to strengthen plant breeding activities in the country and proposed a new institute to President Ferdinand Marcos who issued Presidential Decree No. 729 in 1975, establishing the Institute of Plant Breeding (IPB) in the University of the Philippines Los Baños (UPLB), appointing Dr. Javier as the Institute's first director.

Dr. Javier recalls, "President Marcos was very supportive of agriculture as well as of science and technology. It did not take much convincing to persuade him to establish an institute of plant breeding. When we started IPB, we organized strong laboratories for biochemistry, genetics, virology, analytical chemistry, and tissue culture."

An advocate of interdisciplinary and multidisciplinary approach to collaboration, Dr. Javier brought into the Institute a strong mix of experts from across disciplines and lines of work. "From the beginning, while we were preoccupied with conventional plant breeding, we were anticipating work on DNA manipulation. We were preparing for genetic engineering."

But he recognized that the new trend in agriculture has more applications beyond plant breeding. When Dr. Javier became the chancellor of UPLB, he made sure that the modern tools were also applied in forestry, food technology, veterinary science, and the rest of agriculture. He then proposed the establishment of the National Institutes of Biotechnology and Applied Microbiology for which he was likewise appointed as founding director.

In 1981, President Marcos brought Dr. Javier to his cabinet as minister of science and technology and director general of the National Science and Technology Authority (now Department of Science and Technology). As science minister, he formed sectoral councils, established regional offices, promoted a dedicated science career service in government, and developed the concept of science communities. Dr. Javier also co-founded the Crop Science Society of the Philippines to foster sharing of scientific human resources, information, and materials for crop improvement.

When he became the UP president in 1993, Dr. Javier created three more biotechnology research institutes with specific niches in pharmaceutical applications, industry and energy, and marine industry in the UP campuses in Manila, Diliman, and the Visayas.

As NAST president, Dr. Javier was principal author of *Philippine Agriculture 2020 (PA 2020): A Strategy for Poverty Reduction, Food Security, Competitiveness, Sustainability, and Justice and Peace* in 2011. PA 2020 is a medium-term strategic plan for the development of the agricultural and natural resource sectors of the country, conceived from NAST-organized consultations and workshops with scientists, farmers, entrepreneurs, and other stakeholders. Biotechnology is identified in PA 2020 as a tool to increase agricultural productivity through the development of quality seeds and crops and livestock with beneficial traits.

A practicing farmer himself, Dr. Javier emphasized that biotechnology has transformed the Philippine corn industry from being highly import-dependent into an almost self-sufficient one. "The Philippines has a long history of biotech crop adoption. Our own corn farmers had been planting Bt corn for more than a decade, and they have benefited through increased yields and reduced pesticide use. The technology is so practical and profitable that small Filipino farmers purchase the expensive GMO corn hybrid seeds without subsidy from the government."

Corn's Competitive Edge

Dr. Javier notes that "the country's yellow corn feed sector has found a new competitive edge due to the large-scale adoption of Filipino corn farmers of high yielding genetically modified (GM) corn hybrids. Corn farmers in the Philippines planted 813,000 ha of GM corn in 2014, or 57% of the total area planted to corn in the country. Farmers who planted GM corn harvested 7–8 tons per hectare, compared with the 4.4-4.9 tons per hectare from conventional hybrids."

"In theory, we can compete in the world trade for corn feed. However, since we have yet to fully satisfy the domestic demand for animal feed and industrial uses, the more realistic immediate objective is to further increase supply of competitively priced quality feed corn to strengthen the competitiveness of our poultry and swine industries. This will bring down the cost of chicken and pork for domestic consumption as well as for export," Dr. Javier explains.

> " The technology is so practical and profitable that small Filipino farmers purchase the expensive GMO corn hybrid seeds without subsidy from the government. "

Despite the success of biotech corn adoption in the Philippines, Dr. Javier voices the concern of many Filipino scientists today. The rapid progress made all over the world in the development of new products and processes using genetic engineering have profound impacts on farm productivity, farmers' incomes, health and nutrition, integrity of the environment, and economic competitiveness. Yet, he says, the application of the *Writ of Kalikasan*[1] on agricultural biotechnology research has tied their hands. "We are very close to commercializing our first GMO crop developed by Filipino scientists, but that is now on hold." There is currently a Court of Appeals order to stop field trials of Bt eggplant and an appeal by the proponents is with the Supreme Court.

Their frustration is even more aggravated due to recent developments in modern biotechnology, which can help the country become more food secure and economically competitive. Aside from Bt eggplant, Dr. Javier cites opportunities such as the need to develop drought-tolerant sugarcane to help the country's sugar industry, which is facing heavy competition from other Southeast Asian countries as well as from Australia and Brazil.

Eroding Gains

"We have the training and expertise to exploit these opportunities to advance our national interests. We were so much ahead among developing countries in training people, establishing institutions, and instituting a regulatory framework so much so that our neighbors like Thailand, Indonesia, and Vietnam and several countries in Africa have sent their own regulators to study and observe how the Philippine biosafety system works. These gains are now slowly eroding before our eyes."

Dr. Javier continues to support science and technology and agriculture. He is involved in efforts to educate the public about science and their potential to improve people's access to food and health and to emphasize the need for modern biotechnological innovations for a food-secure Philippines.

He is the chairman of the Coalition for Agriculture Modernization in the Philippines (CAMP, Inc.), a non-stock, non-profit organization of volunteers from business and industry — academe, government, professional groups, and international organizations — driven by a patriotic call to contribute their expertise and resources to help raise productivity, competitiveness and incomes of farmers in the country.

The scientist also writes a weekly column "*Why Not?*" in the Manila Bulletin, the second oldest newspaper in the Philippines. He starts his articles with a Robert Kennedy quote, "*There are those who look at things the way they are, and ask why... I dream of things that never were, and ask why not?*" His column covers topics in agriculture and, science, particularly modern biotechnology. It is widely read and followed not only by members of the science community but also by the general public. Asked what compelled him to write a column, his answer is simple. "As a Filipino and as an academic, it is my obligation to make our leadership and our people aware of the potential of modern science to advance our national purposes."

[1] Writ of Nature, a legal remedy in Philippine law for persons whose constitutional right to "a balanced and healthful ecology" is violated by an unlawful act or omission of a public official, employee, or private individual or entity.

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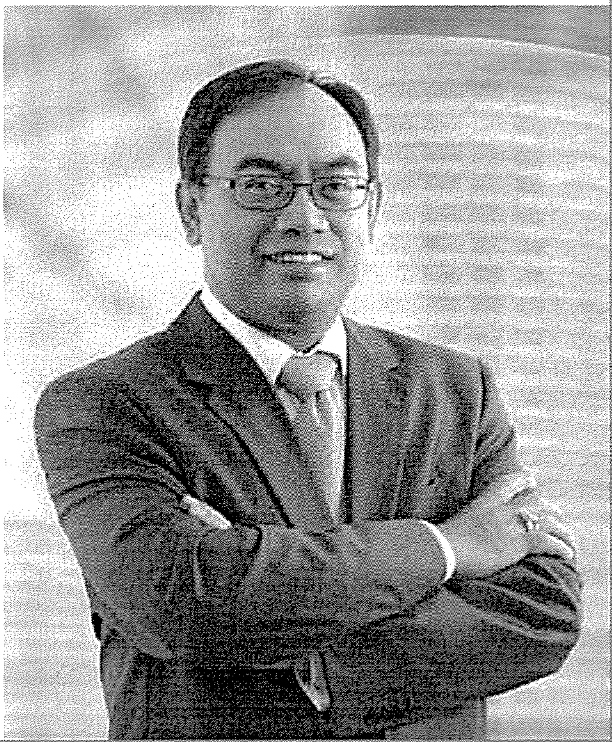


Mohd Nazlee Kamal

- CEO, BiotechCorp (Malaysia)
- Former Professor at the University Technology Malaysia

> "Biotechnology and bio-based applications offer a technological platform with immense potential to deliver advancements in the fields of healthcare, agriculture and industry. In Malaysia, our challenge is to develop an ecosystem that is conducive to the growth, development and adoption of these technologies."

Championing Biotech and Bioeconomy Initiatives in Malaysia

Mahaletchumy Arujanan and Brian Chow

Malaysia is one of the few countries in Asia to have a national policy dedicated to biotechnology. The National Biotechnology Policy (NBP) was formulated in 2005 and the Malaysian Biotechnology Corporation or BiotechCorp is the lead development agency for the biotechnology industry in the country. Dr. Mohd Nazlee Kamal, a chemical engineer by training and former professor at the University Technology Malaysia for 10 years, is CEO of BiotechCorp. He occupies the hot seat of biotech in the country as it has an investment target of RM15 billion (USD4.3 billion) by 2020.

"I am proud to be involved in formulating the National Biotechnology Policy (NBP) and the Bioeconomy Transformation Programme (BTP)," says Dr. Kamal who spearheads and implements both policies. As BiotechCorp enters its 10th year, Malaysia has witnessed encouraging development in terms of investment and industry growth.

"Biotechnology and the bio-based domain is an exciting and rapidly expanding area. Leading the sole economic developer for the bio-based sector in Malaysia is a huge responsibility to shoulder, however, with it also comes a sense of fulfillment as well."

"Biotechnology and bio-based applications offer a technological platform with immense potential to deliver advancements in the fields of healthcare, agriculture and industry. In Malaysia, our challenge is to develop an ecosystem that is conducive to the growth, development and adoption of these technologies. It is an exciting challenge. Our companies need to increase technological content in their products and encourage more innovation," adds the BiotechCorp CEO.

"Through biotechnological advancements, we can create new and less invasive medical solutions to save lives as well as reduce unwanted side effects in patients. Bioprinting for instance is an exciting breakthrough. In the future, we might be able to print 3D organs for transplantation! It does not stop there. We are now able to provide cheaper, more reliable methods of cultivating agricultural products by creating better plant cultivars that require less land usage and less pesticides. We can make better quality food and feed with these improved plant characteristics. And finally, we can also develop cleaner and more sustainable forms of energy and fuel by utilizing environmental-friendly options such as biomass. Though these may all sound far-fetch, the fact is, it is happening right now as we speak. Truly, when it comes to biotechnology, the only limit is our imagination. The prospects of what we could further achieve in the coming years get me excited," Dr. Kamal notes.

The Biotech Aspiration for Malaysia

The ultimate objective of the NBP is to transform the biotechnology sector into one of the key economic pillars of Malaysia. With its pro-business and pro-science policies, Malaysia is an excellent destination for biotechnology companies and investors.

"Through NBP, biotechnology will not only contribute to economic gains of the country but would produce significant benefits to the society," says Dr. Kamal who envisages the country to join the ranks of other developed countries and major biotechnology and/or bioeconomy players such as Canada, the United States and South Africa in the foreseeable future.

Dr. Kamal sees adapting the best of the U.S. and its initiatives might be the game changing plan for Malaysia. The education system that produces innovative and productive students, research at universities, funded and driven by industry and tertiary education reflect the current needs of the industry, which is up to date and relevant. As a result, the American education system produces a pool of talented and innovative workforce. These are the main ingredients needed for growing the biotechnology industry.

> “Truly, when it comes to biotechnology, the only limit is our imagination. The prospects of what we could further achieve in the coming years get me excited.”

Dr. Kamal envisions putting in place similar initiatives to encourage relevant biotechnology companies to work closely with local universities and to provide sufficient funding platform for our researchers. BiotechCorp has already implemented programs to encourage more collaborations between universities and industry through public-private partnerships. A key component for building the biotechnology industry and strengthening the funding ecosystem in the country is the need for experience and technical expertise. To address the issue, BiotechCorp aims to partner with key institutions in creating University-Industry Centre of Excellences (CoEs) for the bio-based sector.

BiotechCorp has also forged strategic partnership with international partners such the University of California Institute for Quantitative Biosciences (QB3) and the Larta Institute — two prominent organizations that are vital in advocating entrepreneurship and public private partnership for training of local scientists, entrepreneurs and start-ups". In the long run, it is hoped that all strategies will help achieve the objective of making Malaysia a global biotech player," Dr. Kamal says.

Thoughts on Emerging Technologies

Dr. Kamal feels genetically modified (GM) crops, cloning of tissues, gene therapy and synthetic biology are controversial and complex with many concerns surrounding them, largely due to ethical concerns raised by various parties, be they scientists, academics, activists, industry, religious representatives or consumer bodies. "The ethical debate is very subjective itself, in the way that values or standards that people use to determine whether the actions are good or bad differ."

Being an old hat in this field, he understands that biotechnology is not spared from this global science debate, citing genetic modification as an example which is one of the core components in modern day biotech technique. "Many see it as human intervention in altering the blueprint of life itself and hence, an unnatural act. Others may believe that biotechnology disrupts the natural order and violates the limits of what humans are ethically permitted to do. But on the other end, some may also share the view that life sciences/ biotechnology are merely tools for progress designed to benefit mankind," stresses Dr. Kamal.

Responsible Use of Biotech

He further explains that there are pros and cons to the argument. "Not limiting to biotechnology, what is more important is these knowledge and/or technologies are being used responsibly. It is true that there will be some universal ethical concerns that we must consider and to address accordingly. However, these technologies present opportunities for progress faster than what nature can offer."

"If done responsibly, these are all very promising technologies, yielding enhanced products to provide social and economic benefits, without compromising health, safety and the environment. Because of these reasons, I strongly support these emerging technologies," proclaims the CEO.

Fighting Pseudoscience

Dr. Kamal sees the internet as a double-edged sword. He says it is disheartening to see all the misconception revolving around biotechnology. Most people in general, without a basic understanding of biotechnology, are vulnerable to misleading information found on the internet. He urges everyone to bear in mind that not all information is reliable information and some basic understanding of biotechnology may enable readers to distinguish between trustworthy from misleading ones. Practitioners of pseudoscience and scaremongers spread inaccurate and false information through the exploitation of the general population's lack of understanding, not only in biotechnology but perhaps any other topic you can think of.

"People tend to fear what they don't understand. And biotechnology is something a lot of people assume is too technical or too complicated to comprehend. Truly, this is not the case," laments Dr. Kamal. He does not underestimate the need to promote biotechnology awareness and education with a goal to spread scientific awareness to the public and other important stakeholders relating to modern day biotechnology.

"We have similar initiatives in Malaysia. For example, the Malaysian Biotechnology Information Centre (MABIC) is a non-profit organization dedicated to building the public's understanding and awareness of biotechnology. For the past 10 years, MABIC has conducted various outreach programs targeting a broad spectrum of audiences," explains Dr. Kamal.

Vandalism on GM Field Trials

Dr. Kamal's one word to describe this act is "wrong". "I wonder whether those responsible for the vandalism realize the consequences of the action. They may have a different point of view with regard to GMOs, however field trials are also the culmination of years of research and are equally the hard work done based on the different views held by well-intentioned scientists and researchers. Vandalism of GM crops will definitely put academic and research freedom at risk, not to mention the act of vandalism itself is against the law in civic societies."

If any good can come out of vandalizing or destroying field trials, those who are responsible will put themselves under greater scrutiny in the future. Each person's opinion is valid as long as it is based on accurate information and any action taken should abide by the law," the BiotechCorp CEO opines.

Benigno D. Peczon

- Former Vice President of United Laboratories (Philippines)
- First President of the Biotechnology Association of the Philippines, Inc.

"Technological advances change cultures and the development of nations. In the same manner that cellular phones and communication devices and networks have opened up a whole new range of possibilities, biotechnology will affect nations."

Biotechnology, a Tool to Help Humanity

Rhodora R. Aldemita

"I am not so much a believer of biotechnology per se as I am a person who believes that each and every individual on earth should be part of the solution and not be part of the problem. I see biotechnology as a tool. Since I consider myself to be a scientist, I seek the best solutions based on demonstrable data. As passengers of Spaceship Earth, we must collectively seek the best solutions that redound to the common good."

A chemist, Dr. Benigno D. Peczon or Doc Ben as friends fondly call him, got interested in biotechnology while doing basic work on diabetes in the 1980s. The production of human insulin in 1978 at Genentech through biotechnology caught his attention. Prior to 1978, insulin was isolated from porcine and bovine pancreas in limited amounts at a high cost and with some adverse effects on a significant percentage of diabetics. That biotechnology breakthrough catalyzed his interest to know more.

"I endeavored to read about biotechnology and attend as many biotechnology conferences as were available to a pharmaceutical researcher residing in the Philippines," Dr. Peczon revealed. His formal education at the University of the Philippines Los Baños and Purdue University and his research work at Oklahoma State University, Harvard Medical School, Schepens Eye Research Institute in Boston, and University of Kansas School of Medicine facilitated his understanding of biotechnology. His publications on enzyme kinetics, membranes, nature of tissues, and analytical chemical methods helped him better understand biotechnology.

Fellow Purdue University alumnus Dr. Kin-Ping Wong, one-time California State University at Fresno dean of graduate studies, kept him informed about products such as a glycoprotein that enhances production of red blood cells, growth hormones, and medical diagnostic kits, all of which came from biotechnology.

When he returned in 1983 as a "balik-scientist" (scientist returnee) to the Philippines, Dr. Peczon was already well-prepared for the big challenges explaining the benefits of biotechnology. Thus, during and after serving as a department manager, senior scientist, and later vice president of the Chemistry and Quality Assurance Division from 1983 to 2002 at the largest pharmaceutical company, United Laboratories (UNILAB), based in the Philippines, Dr. Peczon became an advocate of biotechnology.

Identified as Biotech Champion

In the 1990s, then secretary of the Philippine Department of Trade and Industry (DTI) Cesar Bautista identified biotechnology as a 'sunrise' industry. DTI identified Dr. Peczon as a biotechnology champion. With the help of DTI, the Biotechnology Association of the Philippines, Inc., (BAPI) was created, with Dr. Peczon serving as its founding president. After a DTI-funded mission to Singapore, Dr. Peczon became more convinced of the potential of biotechnology. He says, "The Singaporean government embraced biotechnology through awarding of significant grants to attract the best and brightest scientists from all over the world, including Sir Ian Wilmut, a member of the team that cloned the first mammal, Dolly the Sheep."

Dr. Peczon became involved in biotechnology education activities, especially for the youth. He recounts that, "Dr. Delfin B. Samson, Jr., then president and CEO of UNILAB, cognizant of the promise of biotechnology, asked me to create the UNILAB Mobile Biotechnology Education Program (UMBEP) in the late 1990s. The program was intended to introduce high school students to biotechnology." And so, "with a generous financial outlay from UNILAB and help from National Scientist Lourdes J. Cruz and toxicologist Dr. Flerida A. Cariño (a member of the Philippine Committee on Biosafety), we created the program. With equipment unique to biotechnology transported in a van, the UMBEP was deployed in over 100 high schools in the country. Wherever the van went, invariably, the group was invited back, indicating openness to this game-changing tool."

In 2001, Dr. Peczon already perceived that "biotechnology would have a major impact not only on the health sector but also on agriculture." By 2002, with the addition of agriculture to its scope, BAPI morphed into the Biotechnology Coalition of the Philippines (BCP). Under his leadership, BCP organized many symposia and used print media, radio, and television to address biotechnology issues. His passion as a biotech advocate never faltered, even while encountering naysayers, drawing inspiration from Albert Einstein who once said, "Great spirits have always encountered violent opposition from mediocre minds."

> "...as more people shed the shackles of ignorance, safe and responsible use of biotechnology will be widespread."

In early 2002, the Department of Agriculture Policy and Planning Department under Undersecretary Segfredo Serrano completed the draft of Administrative Order No. 8, the guidance document covering the import for direct use, confined field tests, multilocational trials, and commercialization of genetically modified (GM) crops. Dr. Peczon recounts, "BCP, together with noted academicians, scientists, civic leaders, and farmers, worked in concert to lend their names and integrity to vouch for the safe and responsible use of biotechnology throughout the country. The naysayers were Greenpeace and locally based organizations that mirrored the viewpoints of Greenpeace. They simply repeated the mantra, 'Are GM foods safe?' without ever having shown science-validated data that, indeed, biotech food was not substantially equivalent to the genetically unaltered food."

Dr. Peczon's leadership of BCP included a well-attended hosting of the Third Asian Biotechnology Meeting in Manila in 2006. More than 100 hundred participants gathered to discuss biotechnology issues, including policies governing its acceptance and adoption and future biotech crops for Asia.

Struggle for Biotech Acceptance

He observed that, after the Philippine Government approved commercialization of biotech corn in 2002, the crop was readily accepted by farmers. Since that year, an ever increasing number of farmers have planted GM corn, with a corresponding increase in hectarage. There was also a substantial increase in public acceptance of biotechnology, attributed in part to its embrace by opinion leaders such as philanthropist extraordinaire Bill Gates and former U.S. Secretary of State Hillary Clinton. Nonetheless, Dr. Peczon remarks, "The struggle for acceptance is far from over because in 2013, through a court ruling based on a *Writ of Kalikasan*, Philippine scientists are currently prevented from performing tests aimed in fact to answer the very questions raised by opponents to the utilization of modern biotechnology."

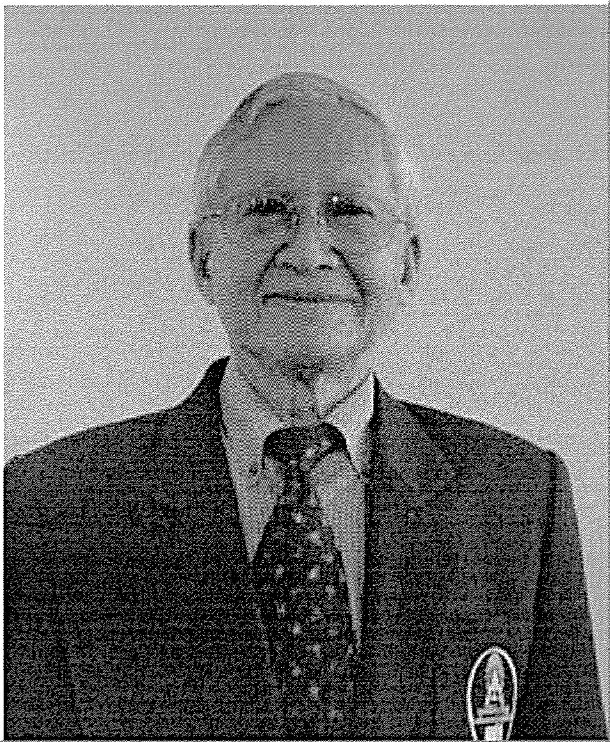
With the turn of events in the Philippines, Dr. Peczon is not relenting. He opines, "Technological advances change cultures and the development of nations. In the same manner that cellular phones and communication devices and networks have opened up a whole new range of possibilities, biotechnology will affect nations."

He adds that "The unprecedented adoption by millions of resource-poor farmers has become a 'game changer' in the sense that proper utilization of modified seeds produces so much more: increased yield, reduced need for pesticides, and adoption of no-till land preparation that reduces soil erosion. As more research for better versions of rice, cassava, sweet potato, millet, and other crops — in terms of increased yield and drought, pest and disease tolerance and other desirable characteristics, — and for greater capacity to address pollution and climate change are completed, thinking men everywhere cannot help but realize what a boon biotechnology has to offer."

Potential for Corn Export

Dr. Peczon pointed out that "prior to 2002 and for a few years thereafter, the Philippines purchased corn from abroad to meet the local feed demand for poultry, swine, cultured tilapia, and other animals. In 2002, the average national yield using non-biotech corn was 2.65 tons per hectare per crop. Biotech corn yields are in the 4-9 ton-per-ha per-crop range. Having seen the increased yield, without any government support for the more expensive biotech corn seeds, farmers now plant about half the annual crop to biotech corn. With the increased yield, the Philippines is now on the cusp of exporting corn. Certainly, the availability of this locally produced biotech corn helps the Philippine compete in the international food market."

Dr. Peczon also believes that "as more people shed the shackles of ignorance, safe and responsible use of biotechnology will be widespread. People will demand better access to the fruits of this technology. Consumers will want a free choice in the products they consume, regardless of what pressure groups say or do. Moreover, in the primary health care arena, presently marketed biotechnology products and future applications are just too awesome to ignore. Let us hope and pray that onerous overregulation will not dry up the funding needed to reap the fruits of biotechnology."



Sutat Sriwatanapongse

- Former Director, Thailand Biodiversity Center
- Former Deputy Director, National Center for Genetic Engineering and Biotechnology (Thailand)
- Former Regional Maize Specialist for North Africa and Middle East Region, CIMMYT

"Modern technology, such as plant biotechnology and genetic engineering, is part of the arsenal to improve agricultural production not just to produce more food and feed, but also to develop value-added products in the areas of nutraceuticals and medicinal products."

Giving a Helping Hand to Biotech in Thailand

Supat Attathom and Mariechel Navarro

Dr. Sutat Sriwatanapongse, has long retired from public service but his commitment to see biotechnology thrive in Thailand keeps him busy and on the go. The former agronomy professor of Kasetsart University has already put in so much time and energy in getting government support for biotechnology. One senses a level of frustration and disappointment toward what he feels is lack of political will, but Dr. Sriwatanapongse does not lose hope that under the new coalition government, supporters in the Cabinet will provide an opportunity to encourage research and commercialization of biotech crops.

"Modern technology, such as plant biotechnology and genetic engineering, is part of the arsenal to improve agricultural production not just to produce more food and feed, but also to develop value-added products in the areas of nutraceuticals and medicinal products," Dr. Sriwatanapongse explains.

Early Foray into Biotech

Dr. Sriwatanapongse looks back at how he got involved in biotechnology. He had been invited to attend a meeting (where he was the only Asian) at Michigan State University in the mid-1980s. A distinguished professor from the University of Hawaii had stood up and encouraged participants to begin work on biotechnology, the new buzz word with its foundations in genetics, biology, and cytogenetics. "I was amazed at its potential use in agriculture, medicine, and industry." His segue to biotech was smooth, having earned MS and PhD degrees in plant breeding and genetics from Purdue University and Iowa State University, respectively. He eventually worked at the International Maize and Wheat Improvement Center (CIMMYT) as regional maize specialist for North Africa and the Middle East Region for 5 years.

"It is ironic that neighboring countries such as China, India, and the Philippines have been planting biotech crops such as Bt cotton and stacked-trait corn for over a decade, while Thailand continues to import many products and their derivatives from genetically modified (GM) cotton, soybean, and corn grown in countries that allow their planting," Dr. Sriwatanapongse says in disbelief. "China and India are exporting Bt cotton while the Philippines has attained self-sufficiency in corn production. Why can't we do the same?"

Dr. Sriwatanapongse reflects on the country's foray into the technology. "Thailand started on the right foot with its support of biotechnology in the early eighties. The Minister of Science and Technology (MoST) fully supported it and the government even sent an application to the United Nations when it was looking for a potential host country for the International Centre for Genetic Engineering and Biotechnology (ICGEB)." This center, eventually established in Delhi, India, is dedicated to advanced research and training in molecular biology and biotechnology with special regard to the needs of developing countries.

Establishment of BIOTEC

"Instead of getting discouraged from losing to India, the government decided to establish a local version of the center as a regular agency under the MoST. In 1992, the National Center for Genetic Engineering and Biotechnology (BIOTEC) became part of the National Science and Technology Development Agency (NSTDA). Dr. Sriwatanapongse was deputy director for 7 years before he became the first director of the Thailand

Biodiversity Center, also an organization under NSTDA.

His hands-on experience in the field enabled him to share in the glory of public sector-led research that put Thai researchers at par with the global science community. "We had good networking among five local universities then; we were able to send as many as 300 students for PhD degrees in UK, Germany, US, and Australia. All came back and worked in universities or research and development institutions. State-of-the-art laboratories and work facilities were built over time," Dr. Sriwatanapongse claims. Many GM crops were developed such as tomato, papaya, cotton, and chili pepper. Other imported transgenic plants were field-tested including GM papaya, tomato, and cotton. Results were significant and several products went into the pipeline for eventual commercialization. "We were advanced in tissue culture and genetic engineering. Thailand was the center for training on biotechnology in Southeast Asia."

> "Farmers continue to ask why they cannot plant GM papaya. We feel for them but we are helpless."

External Pressure

The clamor from opposition groups to stop work on transgenic crops won over the dedicated work of scientists. "Elected politicians were not ready to take the risk of the opposition's ire. The Ministry of Agriculture was about to do extensive field trials of Bt cotton in the late eighties, but external pressure convinced the government to ask scientists to restudy their research, which led to cessation of further work. "We missed a chance to try Bt cotton, and it happened again with GM papaya years later when the government, again due to mounting opposition from civil society groups, released an executive order prohibiting the planting of GM crops unless it is for research purposes only," Dr. Sriwatanapongse reminisces. "That was 10 years of rigorous research that was ripe for commercialization." It did not help that BIOTEC decided to take a neutral stance in all of these controversies.

> "China and India are exporting Bt cotton while the Philippines has attained self-sufficiency in corn production. Why can't we do the same?"

"Farmers continue to ask why they cannot plant GM papaya," Dr. Sriwatanapongse shares. "We feel for them but we are helpless." Green papaya salad, locally known as *som tam*, is a popular dish in Thai homes, which explains why 90% of total papaya production is consumed domestically. The rest is exported mostly as canned fruit cocktail, making Thailand the world's 12th largest producer. But the papaya ringspot virus (PRSV), which has affected production first in northeastern Thailand in 1975 and has since spread to other parts of the country, looms as a dreaded enemy.

Illegal Planting of GM Crops

Having seen how GM papaya is able to resist PRSV, which is a dreaded pest, farmers cannot understand why a better alternative to the conventional variety cannot be grown. Dr. Sriwatanapongse opines that "Thailand heavily uses chemical insecticides and is imported in great amounts. But even pesticides cannot completely solve the problem. Biotechnology is one way to cope with the predicament and at the same time conserve the environment. If there is a better way, let us use it." Dr. Sriwatanapongse shakes his head, noting that "illegal planting of GM papaya and Bt cotton (estimated at 80% of total production) has been observed in farmers' fields. There is a real need for better alternatives but, unfortunately, these have not been approved for cultivation."

Dr. Sriwatanapongse has the gait and energy of one much younger than his age. His optimism and dedication are contagious and inspiring. "We are relying on the power of the science community to get our message across to legislators. I believe that collective action and commitment can move mountains," he says. This time the science community in Thailand wants its voice heard.

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Emiliana N. Bernardo

- Professor of entomology, University of the Philippines Los Baños (UPLB) and Visayas State College of Agriculture (Philippines)
- Member, Department of Agriculture's Scientific and Technical Review Panel
- Member, Institutional Biosafety Committee of UPLB

> "Whenever I explain crop biotechnology to people, whether they are for or against it, I entertain all kinds of questions. Questions are important, in whatever form, because they demand that scientists be cautious and critical. We (scientists) have to make sure that everything has a scientific basis."

An Advocate of Environmental Stewardship

Ma. Monina Cecilia A. Villena

She is passionate about insects, and that is the world she has chosen to explore. Dr. Emiliana N. Bernardo is one of the most renowned entomologists in the Philippines. She belongs to the country's roster of multi-awarded scientists as attested by the numerous recognitions she has received for her notable research. Her expertise in entomology cover pest management, risk assessment, and host plant resistance to insect pests. She is currently a member of the Philippine Department of Agriculture's (DA) Scientific and Technical Review Panel, which assesses the safety of genetically modified (GM) crops. Dr. Bernardo is likewise a member of the Institutional Biosafety Committee of the University of the Philippines Los Baños (UPLB) for the multi-location field trial of Bt eggplant of the university.

For the commercialization of Bt corn in the Philippines, Dr. Bernardo leads the DA's Insect Resistant Management Advisory Team. This group of scientists looks out for signs of development of corn borer resistance to Bt corn and helps in the formulation and enforcement of insect resistance management strategies for GM insect-resistant crop varieties. The team also assists in environmental risk assessment for GM crops.

Dr. Bernardo's formal introduction to entomology started when she worked as a student assistant at the UPLB Department of Entomology tasked to *simply take care of insect cultures*. When she finished her BS in Agriculture degree, she taught at the Department of Entomology. During her long stint at the university, apart from teaching entomology, she later served as vice chancellor for instruction/academic affairs. Dr. Bernardo also taught at the Visayas State College of Agriculture (VISCA) in Baybay, Leyte (now Visayas State University). Some of her other appointments at VISCA included her being tapped as director of instruction and director of the Philippine Root Crop Research and Training Center.

In 1958, Dr. Bernardo received a scholarship grant from the International Cooperation Administration-National Economic Council for an MS degree in entomology. She was also given the Rockefeller Foundation Fellowship Grant in 1965 to pursue studies leading to a PhD degree major in host plant resistance to insect pests. She completed both her masters and doctorate degrees in entomology at Kansas State University in the United States.

> “Entomologists help take care of the environment. And one way of doing that is by minimizing the heavy use of pesticides. I'm not saying we should not use pesticides, no. There are cases when pesticides are absolutely necessary. But, when there are other safer alternatives, why not explore them?”

Involvement in Biotech

When asked how she got involved in crop biotechnology, she says, "It may be because of my field of specialization, which is host plant resistance to insect pests. I got involved in crop biotechnology because when Bt corn came into the picture, I was one of the senior entomologists in UPLB at that time. I was fortunate enough to have been trained under the guidance of the well-known researcher and professor in entomology in the United States, Dr. R.H. Painter of Kansas

State University." Dr. Painter is the author of the classic 1951 book *Insect Resistance to Crop Plants*, which is said to be the first textbook on host plant resistance to insect pests.

Dr. Bernardo cites her involvement in the assessment of Bt corn in the Philippines as her most notable contribution to crop biotechnology in the country. She states, "I'm so happy I became a member of the team that assessed the suitability of Bt corn in the Philippines because it was the first GM crop to be introduced here. During that time, it sparked a lot of interest among the various stakeholders." She reminisced that a lot of people then were wondering why the Philippines, a small country as compared with its neighbors in Asia, was the first to adopt GM technology. She prides herself in being one of the technical evaluators and advocates of the technology in the country, which, for the past many years, have benefited and improved financially the lives of numerous corn farmers.

> "The very basic question that we should ask ourselves is, which is safer, the present practice or the alternative: the Bt eggplant that is rigorously evaluated by experts or unharvested eggplant fruits bathed and dipped in chemicals, which would end up in our dinner tables?"

Fourteen years after her retirement, Dr. Bernardo remains a tireless advocate of GM crop acceptance. She was involved with Bt corn then; now she is hell-bent on pushing for the commercialization of Bt eggplant. Says Dr. Bernardo, "The current methods used by some eggplant growers in controlling the eggplant fruit and shoot borer (EFSB) are unacceptable. Many eggplant farmers spray chemical insecticides every other day or up to 80 times per growing season to control EFSB infestation in their farms. The practice is unacceptable and unhealthy to consumers, farmers, and the environment."

Insecticide Exposure

Dr. Bernardo adds, "Farmers, consumers, the environment — all these can be adversely affected by chemical insecticides if not properly selected, applied and managed. We have to be practical." She likewise cited studies conducted in major eggplant-producing provinces in the Philippines, which found that almost all farmers use chemical insecticides. Some even dip the unharvested eggplant fruits in a mixture of insecticides just to ensure that harvests are free from EFSB damage, thus marketable. "The insecticide exposure of our farmers and environment is too much," Dr. Bernardo points out.

"Entomologists help take care of the environment. And one way of doing that is by minimizing the heavy use of pesticides. I'm not saying we should not use pesticides, no. There are cases when pesticides are absolutely necessary. But, when there are other safer alternatives, why not explore them?," the lady scientist explains.

"The very basic question that we should ask ourselves is, which is safer, the present practice or the alternative: the Bt eggplant that is rigorously evaluated by experts or unharvested eggplant fruits bathed and dipped in chemicals, which would end up in our dinner tables?" she asks. Dr. Bernardo explains that Bt is very natural. "Cooking Bt eggplant or Bt corn can completely denature the Bt protein. It is not detectable in any cooked food and is therefore safe for human consumption," she said. "Moreover, we do not have the needed receptors for Bt toxin in our digestive system."

Safety Assurance

Despite the never-ending debate and opposition from other groups on the acceptance of GMOs, Dr. Bernardo believes that what is important is that farmers understand the science, and consumers are assured that government-approved GM crops are safe. "Whenever I explain crop biotechnology to people, whether they are for or against it, I entertain all kinds of questions. I never get tired of answering them. Questions are important, in whatever form, because they demand that scientists be cautious and critical. We (scientists) have to make sure that everything has scientific basis."

Agus Pakpahan

- Chairman of Biosafety Commission of Genetic Engineering Products (Indonesia)
- Founder of Max Havelaar Foundation

> "To achieve food security, better environmental quality, energy sufficiency, as well as improved farmers' welfare, we need some support, such as biotechnology."

Strengthen Policies for Biotechnology in Indonesia

Dewi Suryani Oktavia and Heryanto Lingga

Dr. Agus Pakpahan, chairman of Indonesia's Biosafety Commission of Genetic Engineering Products, remembers his first foray into biotechnology when he served as director general of Plantation in 1998. At that time, he saw biotechnology as a new tool that could provide an opportunity for Indonesia, particularly the use of genetically modified (GM) cotton. Cotton and rice have an ideological importance in the country. Both crop symbols are on the lower left quarter of the national emblem of Indonesia, representing the fifth *Pancasila* principle, "Social Justice for the Entire People of Indonesia." Rice and cotton represent sustenance and livelihood.

Focus on Cotton

Almost 99% of clothing requirement in Indonesia is satisfied by cotton. Domestic demand for the fiber cannot be met and importation becomes necessary, thus the need to focus on production. However, the experience to develop conventional cotton through IKR (*Intensifikasi Kapas Rakyat*) failed because cotton seeds were not resistant to *Heliothis* sp., the cotton bollworm.

At that time, the United States, China, and India were planting transgenic cotton seeds (called Bt cotton) which is resistant to the cotton bollworm. Indonesia wanted to follow suit, intending to gradually adopt transgenic cotton seeds after confined field trials in Bantaeng, Bulukuma and Jeneponto, South Sulawesi in 2002. The trials showed good results, but unfortunately, many issues regarding transgenic cotton plants arose.

"I now see the differences from the perspective of change and current development of the technology," says Dr. Pakpahan. Unfortunately, discussions on the pros and cons forced the government to suspend the use of transgenic cotton. "If, at that time, there was courage from all parties to accept the presence of transgenic cotton, Indonesia might have been able to follow India's success. In Mahatma Gandhi's country, transgenic cotton has been planted in 3.5 million ha in 2002; now it has reached 11 million ha. It means an additional 1 million ha of transgenic cotton field every year in India."

"Government policy should be clear and focused, and it should encourage through incentives, farmers and agricultural companies to use biotechnology efficiently and wisely."

Since the moratorium on growing transgenic cotton plants, the agricultural sector in Indonesia has not been involved with GM products. Biotech in Indonesia is still limited only for consumption and for research. Dr. Pakpahan says that the main constraint to adoption of biotech is the low priority given to it. He says, "The U.S. policy puts biotech as a priority after information technology. Likewise, the U.S. business world has entered a very dynamic and sophisticated environment in order to invest in biotech and agricultural support system as a whole. Thus, its agricultural productivity, within 40 years, has increased ten-fold. It means that a ton of corn, for instance, can now be obtained from one-tenth area of land compared with 40 years ago."

"Government policy should be clear and focused, and it should encourage through incentives, farmers and agricultural companies to use biotechnology efficiently and wisely," says Dr. Pakpahan who obtained his graduate degree from the Department of Agricultural Economics at Michigan State University.

Biotechnology will develop in Indonesia if the agricultural and agricultural processing industries also grow. "Hence, it is very important to develop these industries. Meanwhile, from an internal agricultural point of view, the most important thing is to increase the land area for farmers. Agrarian reform is pivotal if we want farmers to have the ability to implement new technologies, including biotechnology," adds the man from Sumedang, West Java.

Indonesia will increasingly be confronted by the need to find new ways of producing food, feed, fiber, energy, and medicine. Biotechnology provides an opportunity for solving many problems in the agricultural field. The wide use of transgenic cotton in many countries has reduced the use of pesticides. Likewise, the presence of drought-tolerant sugarcane strain NXI-4T produced by researchers from the University of Jember (East Java) and PTPN XI in East Java points to a great potential to confer drought stress tolerance in important crops.

Impact of Transgenic Seeds

Dr. Pakpahan notes the positive and negative impacts on the environment of transgenic seed utilization, which has been done on a wide scale in many countries for the last 20 years. In particular, he cites the findings of the Research Group of the Biotech Sector of the European Union. These results show that biotechnology products can (i) reduce the use of herbicides and improve land management, (ii) reduce the use of pesticides and mycotoxin level, and (iii) increase farmers' income and health because of good yield and lower cost of production inputs.

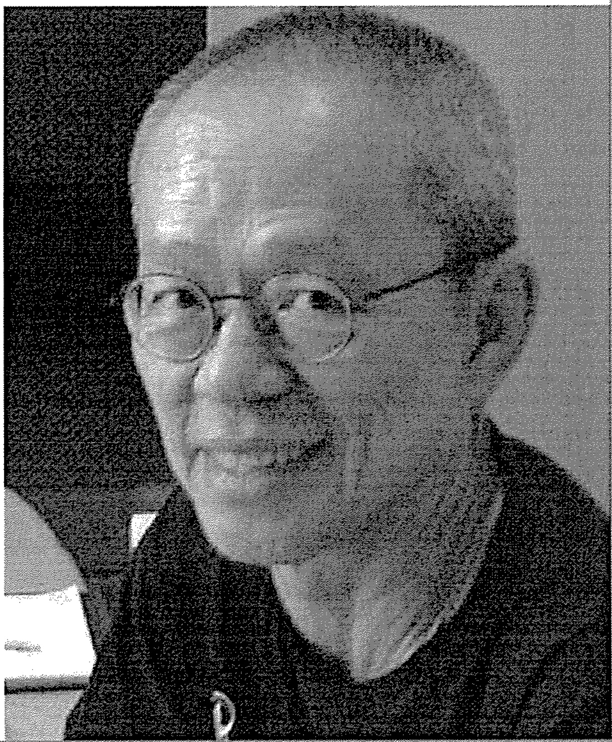
Lately, there is a reality that can not be denied — the implementation and utilization of transgenic seed have happened very fast. After the research and development phase was completed, the first transgenic seed was legally and safely commercialized in 1996. At that time, the area devoted to biotech crops was only 1.7 million ha. In 2014, the hectarage increased to 181.5 million ha in 28 countries. The countries with the most extensive planting of biotech crops among others were the U.S. (73.1million ha, Brazil by 42.2 million ha, Argentina by 24.3 million ha, India by 11.6 million ha), Canada (11.6 million ha, and China (3.9 million ha). This fact is enough to justify that the agricultural world has experienced a new revolution, replacing the so-called Green Revolution. "With such a reality, Indonesia's attitude toward biotechnology implementation has to adopt a precautionary approach, not one based on fear," says Dr. Pakpahan, also the founder of Max Havelaar Foundation that works for the empowerment of Indonesian farmers.

> "Biotechnology products must have satisfied food, feed, and environmental safety parameters as well as considered socioeconomic concerns, especially of farmers."

Addressing GM Issues

Indonesia should be able to be more realistic in addressing the issue of GMO, Dr. Pakpahan suggests. Indonesia already has a set of regulations that provides legal protection for their release. The legal framework related to GMO (Cartagena Protocol) which Indonesia helped ratify in 2004 has made the country a part of the world community. In 2005, a government regulation on biosafety of GM products initiated the establishment of the Biosafety Commission of GM Products (BC-GMP). The Commission is composed of a team that takes charge of biosafety, food and feed safety, environmental safety, and serves as a biosafety clearing house. "The presence of legal, institutional, and organizational dimensions that regulate GMO is a new reality in Indonesia. The Commission works using precautionary principle, valid scientific method, and parameters according to set guidelines," he adds.

Dr. Pakpahan concludes " We must build an institutional model that produces a win-win solution. It must be based on precautionary principle, must apply valid scientific principles, and must follow virtuous business ethics. To achieve food security, better environmental quality, energy sufficiency, as well as improved farmers' welfare, we need some support, such as biotechnology. Biotech products must have satisfied food, feed, and environmental safety parameters as well as considered socioeconomic concerns, especially of farmers."



Pornsil Patchrintanakul

- Executive at the Charoen Pokphand (CP) Company (Thailand)
- Vice Chairman of the Thai Chamber of Commerce
- President of the Thai Feed Mill Association
- Secretary of the Federation of Livestock and Aquaculture (Thailand)

> "The use of GM crops is not the only solution but if they open a door of opportunity, why not try it? Let us not wait for a crisis to happen for the government to understand why we need to explore other alternatives."

Mixing Business and Science for National Development

Supat Attathom and Mariechel Navarro

As a well-known business leader in Thailand, Pornsil Patchrintanakul knows that the key to success in the business world is to see that all actors in the food value chain are able to contribute to the greater good. "One weak link in the chain will affect the smooth running of the system. Farmers are often the weakest link, they need to use modern technology. With many players in the region and the world, we cannot compete in terms of prices. It is innovation through science and technology that can give the competitive edge. It is new ideas and technologies that will add value to our products. But we need political will to make this happen."

Mr. Patchrintanakul, who has an MA degree in political economy from Chulalongkorn University, notes with trepidation that with the regional economic integration by 2015, Thailand needs to overhaul its agricultural production structure so that it can compete with other countries. The ASEAN economic community (AEC) will involve (a) a single market and production base, (b) a highly competitive economic region, (c) a region of equitable economic development, and (d) a region fully integrated into the global economy.

Competition in Animal Feed Production

He cites the example of corn which is a major ingredient in the production of animal feed. Once AEC takes effect, tariffs for export and import of corn will be zero and they will be quota-free. "The government must find ways to help corn growers cut costs to compete with neighboring countries," the businessman says. "We need modern technology to help reduce production cost per unit, improve the use of natural resources, and address issues such as climate change and carbon emission." In addition, he notes that cheaper and better quality products will benefit a broad range of consumers across different income groups.

> "The irony is that the government is not approving the commercialization of genetically modified (GM) crops in the country but what we are importing in great amounts are the very products we oppose."

The other link that needs attention is the political system. Exports in Thailand account for around 65% of its gross domestic product. While manufactured goods account for 86% of total shipments, food items such as prawns and shrimps as well as poultry products are becoming big export commodities. The country has problems in producing sufficient animal feed, particularly protein products for its animal and aquaculture feed industry. It imports a substantial amount of soybean for crushing purposes that provide the Thai feed industry with soybean meal to meet both domestic and trade quotas.

"The irony is that the government is not approving the commercialization of genetically modified (GM) crops in the country but what we are importing in great amounts are the very products we oppose," says Mr. Patchrintanakul. Wearing several hats, he is vice chairman of the Thai Chamber of Commerce, president of the Thai Feed Mill Association, and secretary of the Federation of Livestock and Aquaculture. In addition, he has a day job as a high-ranking executive at the Charoen Pokphand (CP) Company, Thailand's largest agriculture-based conglomerate.

Having studied the literature on biotechnology, Mr. Patchrintanakul understands its benefits particularly for farmers and consumers. "The use of GM crops is not the only solution, but if they open a door of opportunity, why not try it? Let us not wait for a crisis to happen for the government to understand why we need to explore other alternatives," he warns. He has been known to be very vocal about urging the government to speed up plans to expand plantations by 500,000 to 1 million rai (about 80,000 to160,000 ha) or allow planting of GM corn to ease a possible grain shortage.

> Why do we deprive farmers and consumers with a viable choice that has been tested for safety and are less susceptible to pest infestation?

Illegal Planting

The senior business leader also shares the view that illegal planting of GM papaya is no longer a secret in the country. Farmers know that they should not be planting the crop without government approval, but the good yield and the pest-free produce tempt them to try a variety that is resistant to a problematic pest — the papaya ringspot virus (PRSV). Already, a German exporter of Thai tropical fruit cocktail has complained about detecting GM papaya in a batch. The issue of segregation, availability, and higher cost of non-GM fruits (if available) are issues that need to be addressed. Segregation of products as GM or not will entail a system where the Ministry of Agriculture will need to certify that papaya growers are planting only non-GM crops and that farmers will have to register to comply with this requirement. For a fruit industry that actually involves a very small market (5%), are the efforts and resources commensurate to doing so?

Mr. Patchrintanakul further asks, "Are consumers willing to pay higher premium for non-GM food? Why do we deprive farmers and consumers with a viable choice that has been tested for safety and are less susceptible to pest infestation? Who can guarantee that the seeds we import such as GM soybean will not spread to plantations and also be planted illegally?"

GM papaya resistant to PRSV has long been tested for possible commercialization in Thailand. "I know about the work of scientists in Kasetsart University and how they assure the product's safety following a regulatory process. We should give this product a chance to be planted by farmers who have long voiced out the need for a variety that can assure better yields and is resistant to PRSV," the business leader adds.

> I am convinced that we need innovation and business entities should share in the cost of research and development.

Business and Science

Committed to the interplay of business and science, Mr. Patchrintanakul sits on the executive boards of the National Center for Genetic Engineering and Biotechnology and the National Science, Technology and Innovation Policy Office, both under the Ministry of Science and Technology. As member of these boards, he shares his thoughts on science management policies, particularly the synergistic role of S & T and innovation for business. "I am convinced that we need innovation and business entities should share in the cost of research and development. Concomitantly, the government should encourage private sector participation by reducing tax incentives for innovation cost," Mr. Patchrintanakul elaborates. Sadly, however, much still has to be done to get the public and private sectors make this happen.

Time is of the essence. The clock is ticking and 2015 is now here. But Mr. Patchrintanakul thinks that so much can still be done. "We must put our acts together and think about how the country can benefit from all these endeavors. The easy way out is to be weak and to keep quiet. But we need to make strong and clear decisions about using modern technology...before time runs out, before a crisis looms."

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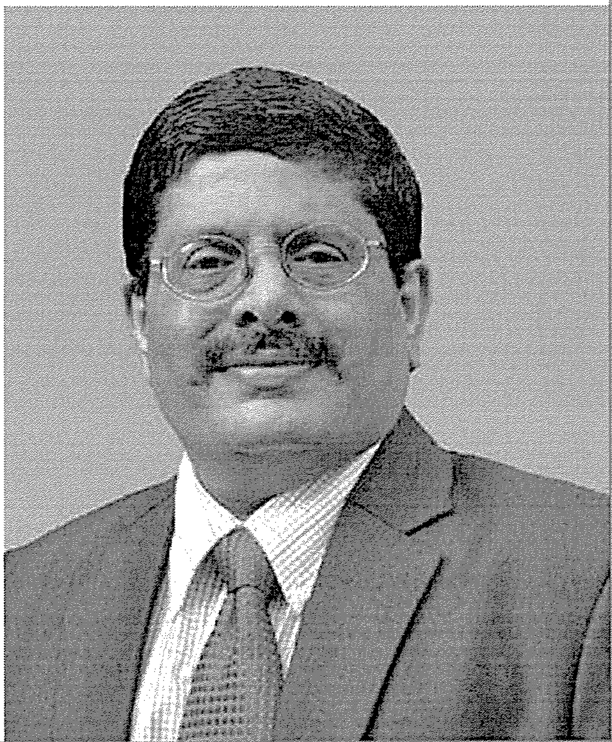
Communicating the Science



Channapatna Prakash

- Professor of plant genetics, biotechnology and genomics at Tuskegee University (USA)
- Morrison-Evans Outstanding Scientist awardee
- Top 30 social influencers on biotech and biopharma (NEMUS Bioscience)

“It is not an exaggeration to say that the 21st century is the century of biology, and biotechnology has already begun to impact so many aspects of our life — our food, our medicine, our environment, and even our law.”

Galvanizing Worldwide Support for Agri-biotech

Mariechel J. Navarro

In 2000, Dr. Channapatna Prakash spearheaded a 'Declaration in Support of Agricultural Biotechnology.' He posted the declaration online on his website www.agbioworld.org and asked members of the scientific community to sign it. The feedback was astonishing — it was signed by nearly 4,000 scientists. Twenty-five Nobel laureates, including Drs. Norman Borlaug, Paul Boyer, and James Watson, all signed the declaration.

"We, the undersigned members of the scientific community, believe that recombinant DNA techniques constitute powerful and safe means for the modification of organisms and can contribute substantially in enhancing quality of life by improving agriculture, health care, and the environment," the declaration said. It also urged policy makers to "use sound scientific principles in the regulation of products produced with recombinant DNA, and to base evaluations of those products upon the characteristics of those products, rather than on the processes used in their development."

Food Safety

The declaration likewise clarified that 'No food products, whether produced with recombinant DNA techniques or with more traditional methods, are totally without risk. The risks posed by foods are a function of the biological characteristics of those foods and the specific genes that have been used, not of the processes employed in their development." It stressed that, "Our goal as scientists is to ensure that any new foods produced from recombinant DNA are as safe or safer than foods already being consumed."

Aside from the declaration that gave agricultural biotechnology the limelight it deserved, Dr. Prakash ran an online newsletter *AgBioView*, a daily collection of news and comments on agricultural biotechnology. It generated wide interest among stakeholders as the newsletter was able to regularly gather all relevant viewpoints and developments that enabled transparent discussion and debate on the field.

The professor of plant genetics, biotechnology, and genomics at Tuskegee University, USA, continues his crusade, this time getting actively involved in enhancing awareness of food biotechnology concerns around the world. He tackles issues such as technical, societal, and ethical perspectives to a diverse audience that includes scientists, activists, and journalists.

> "We are going to see more of biotech in our future as it has the best potential to advance humanity by enhancing our quality of life."

Dr. Prakash has been instrumental in catalyzing the scientific community in many countries to engage in research and development on genetically modified (GM) crops. He also served on the USDA's agricultural biotechnology advisory committee and on the advisory committee for the Department of Biotechnology of the Government of India. Dr. Prakash has delivered lectures in more than 80 countries and at diverse locations such as the Vatican, the U.S. Congress, United Nations, Food and Agriculture Organization, Aspen Ideas Festival, and hundreds of universities across the world.

"It is not an exaggeration to say that the 21st century is the century of biology, and biotechnology has already begun to impact so many aspects of our life — our food, our medicine, our environment, and even our law. We are going to see more of biotech in our future as it has the best potential to advance humanity by enhancing our quality of life. Biotech has transformed the way we farm, the foods that we consume, and of course, the medicine that we take. Its impact is widely documented in enhancing our farm productivity, reducing the usage of insecticides, increasing farming efficiency, and reducing tillage through herbicide-tolerant crops," Prakash elaborates.

Research Interests

As a researcher, Dr. Prakash's interests include studies on transgenic plants, gene expression, tissue culture, and plant genomics. His group at Tuskeegee pioneered the development of transgenic sweet potato plants, identification of DNA polymorphism in peanut plants, and the development of a genetic map of cultivated peanut. They have recently enhanced the protein content of crops several-fold through genetic modification.

> “Biotechnology is a logical extension of many tools we have used over a few millenia to shape our crops and livestock, but with more precision, knowledge and power.”

"Wider adoption of molecular breeding tools, including GM and genomics, in agricultural research can foster greater food security and stability in the face of volatile climate changes, especially in the developing world. Agricultural biotechnology is already helping to develop novel crop varieties with improved attributes such as insect resistance and herbicide tolerance," says Dr. Prakash.

Future Benefits

In addition, the professor notes, "Potential future benefits include hardier crops tailored to tolerate climate changes including drought; smaller environmental footprint of farming (through reduced consumption of pesticides, fertilizers, and fuel); mitigating global warming through reduced emission of greenhouse gases; conserving biodiversity through reduced expansion of land for farming; nutritionally enhanced foods with added vitamins, antioxidants, protein quality and content; better foods with improved flavor, enhanced taste, and longer shelf life; developing hypoallergenic foods; making food more affordable; and developing greener energy alternatives."

Dr. Prakash recalls that he got into biotech almost by accident. "I was invited to attend a Student Pugwash conference on science and technology at Princeton University during June 1985 while I was completing my PhD at the Australian National University. I had to choose a section within this conference to participate in the discussion and prepare a paper. I chose the one on genetic engineering because it was already emerging as a hot area at that time and my background was in plant breeding and genetics. Later, when I came to the U.S. as a postdoctoral researcher at the University of Kentucky, I sat in many courses in molecular biology to learn more about biotech."

His interest in biotechnology paid off. As an awardee of the Morrison-Evans Outstanding Scientist Award by the Association of 1890 Research Directors, he was recognized for his lifetime contribution to agricultural research among the 1890 land grant universities in the U.S. He has also been honored by the Council for Biotechnology Information and the journal *Nature* as among the most influential biotechnologists. He was among a select group of scientists who was invited to speak at the Vatican in November 2013, and had an audience with Pope Francis. He, thus, walks the talk.

Social Networking

Dr. Prakash continues to engage and inform a global audience of more than 3,000 followers now on social networks. He can be found on Facebook at https://www.facebook.com/agbioworld and on Twitter at https://twitter.com/AgBioWorld. He was identified as one of the top 30 social influencers who have the largest digital and social presence and the most influence in the fields of biotechnology and biopharma. The agency Evolve was commissioned by the biopharmaceutical company NEMUS Bioscience to research top social influencers and out of 400 candidates, whittled down the number to 30.

"Biotechnology is a logical extension of many tools we have used over a few millenia to shape our crops and livestock, but with more precision, knowledge and power. I believe in biotech because I have been on the front row watching it develop in the past three decades and thus know it intimately to how it has evolved. I believe that it is the best bet to help ensure a better future for our children and their children," Dr. Prakash concludes.

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Chris Kakunta

- Development Journalist at the National Agricultural Information Services (Zambia)

> "As someone who has seen GMO crops in the lab and on the farms and who has witnessed the benefits accruing to farmers, I would say that the media, the industry to which I belong to, must work extra hard so that every farmer hears the facts and makes the right decision."

Media will Make or Break the Use of Biotechnology in Africa

Margaret Karembu, Faith Nguthi, and Brigitte Bitta

We invite them into our houses every day. We watch and listen to them, allowing them to influence our opinion on certain issues. In turn, they influence our attitude toward the said issue, and consequently, our behavior for or against the issue. In fact, Maxwell McCombs (internationally recognized for his research on how media influences public attention) writes that media appears to "not only tell us what to think, it also tells us how to think about it." [1] He also cites media's s ability to influence what we consider as important, as well as its key role in influencing decisions that we make [2].

That is the influence that the media yields over society. Mr. Chris Kakunta, a development journalist working for the National Agricultural Information Services (NAIS) in Zambia, thinks this influence produces an outcome that has a crippling effect on the adoption of agricultural biotechnology in Africa and in his country, in particular.

Take the case of the drought that affected Zambia in 2001-2002. In early 2002, Zambia was cited as facing an "extremely tight" food situation. There was no grain in storage, maize meal prices were at an all-time high, and there were hungry people everywhere. The government declared a state of emergency [3]. With nearly 30% of Zambia's 10.2 million people facing starvation, the government (then led by President Levy Mwanawasa) had to choose whether to take or reject relief food from the World Food Programme. As fate would have it, they rejected simply because the offer included genetically modified (GM) maize.[4]

According to Mr. Kakunta, this may well have been the time that the battle lines were drawn against agri-biotechnology in Zambia. He recalls that the government "bowed" to concerns about potential risks of GM foods and refused to accept the GM grain. President Mwanawasa repeatedly said that, until he had sufficient and credible information to the contrary, he would not risk feeding Zambians with a "poison that could have long-term effects." He was more so concerned with how the media covered the story.

Media Coverage

A survey of the media coverage relating to GM crops in five developing countries, including Zambia, showed that news stories covered during the GMO debate lacked a critical analysis of issues at stake, and these rarely represented the views of farmers. The average media had to follow what the government had said, with most papers uninterested in investigating and researching on whether what was said by politicians were true. Although he could not influence all media, Mr. Kakunta immediately vowed to personally take the issue head-on and find out the truth. To his dismay, a lot of what the media had covered was based on personal opinions and long-ago myths. He now produces more balanced stories, covering agri-biotechnology issues from all views.

He believes that the major concerns emerging in most cases is whether GM technology would work in Africa and whether the western world is sincere with its intention. He also thinks that most people lack the evidence showing that the technology can work and is working on African soil. This is why, in 2012, he quickly grabbed the opportunity to visit Burkina Faso, joining a study tour organized by the International Service for the Acquisition of Agri-biotechnology Applications (ISAAA). The tour, dubbed "Seeing is Believing", comprised a delegation from seven African countries representing eastern Africa (Ethiopia, Kenya, northern Sudan, and Uganda) and Southern

Africa (Malawi, Zambia, and Zimbabwe). The delegation, made up of farmers, researchers, legislators, ginners, journalists, and biosafety regulators, visited Bt cotton fields in the western part of Burkina Faso, in the regions of Houndé and Bobo-Dioulasso, which are major cotton production zones. Its objective was tied to ISAAA's key role in knowledge sharing, "making available science-based, authoritative information to the global community."[5]

> Burkina Faso remains an amazing country admirable in its desire to embrace science, without fear.

Burkina Faso is the second country in Africa, after South Africa, to have successfully tested, adopted and commercialized the growing of GM crops. In 2014, the country planted 547,124 ha of biotech cotton, approximately 68.6% of all cotton grown in the country. In 2013, the industry raked in US$37 million.[6] Burkina Faso's cotton industry stands as a beacon, visible to any African country willing to follow suit.

Study Tour

Of the study tour experience, Mr. Kakunta says, "We have written a lot of articles regarding GM crops but really, to touch a GM plant is something else, and to see the crop being grown on the ground is something that adds so much value." The study tour is indeed a game-changer because since then, he has become a firm believer in the benefits of GM technology.

"The farmers we talked to were articulate in explaining the benefits of Bt cotton. I equally observed that the development of the cotton industry also had some co-benefits on the entire cropping system. Burkina Faso's National Cotton Company, La Société Burkinabè des Fibres Textiles (SOFITEX), arranges credit facilities for farmers with local banks who charge reasonable interest rates on farm inputs such as work oxen and ox-cart; farmers were also given cash advances for harvesting. The banks find this arrangement appropriate with SOFITEX as back-up and they are able to recoup their monies without difficulty. Amidst strong anti-GMO sentiments, government provided support through research and extension. Burkina Faso remains an amazing country admirable in its desire to embrace science, without fear," adds Mr. Kakunta.

> We have written a lot of articles regarding GM crops but really, to touch a GM plant is something else, and to see the crop being grown on the ground is something that adds so much value.

At a Common Market for Eastern and Southern Africa (COMESA) meeting in Lusaka in 2014, Mr. Kakunta brought to the attention of the COMESA secretariat the demand of the Cotton Growers Association of Zambia for their government to facilitate the growing of Bt cotton, arguing that Zambian cotton was no longer competitive in the international market because of higher production cost. His greatest concern now is whether Zambia and other African countries will embrace biotechnology and GM crops in particular. He asks, "Will the opportunity bypass them just like the Green Revolution did?"

Media's Influence

"As someone who has seen GMO crops in the lab and on the farms and who has witnessed the benefits accruing to farmers, I would say that the media, the industry to which I belong, must work extra hard so that every farmer hears the facts and makes the right decision. There is no doubt that mass media today wields a more enormous influence over the daily lives of the people than before. As Donald Ferguson noted, while the media does not mold men's minds in the fashion once suspected, they do provide the information upon which persons in a democratic society can base their decisions, both in the polling place and the market place. It is essential that this information be as pure and untainted as human beings can make it. If the press errs, then the whole of society lives with the same mistake," Mr. Kakunta concludes.

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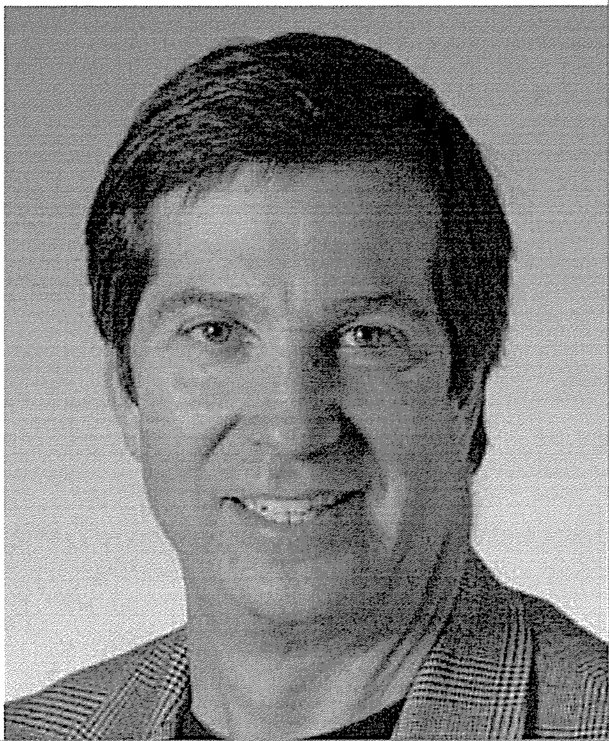

Jon Entine

- Founding Director of the Genetic Literacy Project
- Senior Fellow at the World Food Center's Institute for Food and Agricultural Literacy at the University of California-Davis (USA)
- Senior Fellow at the Center for Health and Risk Communication at George Mason University (USA)

> "We have no choice but to embrace innovation. Literally. The science is robust and checks and balances are in place. We are already seeing significant benefits."

Demystifying Genetics and Biotechnology

Mariechel J. Navarro

"The greatest challenge as this century progresses will be those posed by population growth and affluence, and the strains they will put on Earth's limited resources. In the next 50 years alone, we will add the equivalent in population of two Chinas. Yet, all of the most productive farmland is already being utilized. What can we, in the developed world, do to meet this challenge? Agricultural technology, and to a large degree, biotechnology, are our only hope. We could face a perilous future if we strangulate biotechnology advances because of misplaced fears."

Mr. Jon Entine, founding director of the Genetic Literacy Project (GLP), senior fellow at the World Food Center's Institute for Food and Agricultural Literacy at the University of California-Davis, and senior fellow at the Center for Health and Risk Communication at George Mason University, sees the potential for biotechnology. "There is no other word but revolutionary—at least the potential for being revolutionary. Facing ecological and demographic challenges, biotechnology offers the prospect of increasing farm yields while limiting environmental consequences. Some of that potential has been realized, dramatically decreasing toxins in the environment and improving yields." Yet, he cautions, "Only fear can prevent further advance."

As a "science journalist dedicated to analyzing the politization of biotechnology," how did he get into the field?

"I'm a long-time journalist, having spent the first 20 years of my career as a television writer and producer for NBC News and ABC News. In 1989, NBC's Tom Brokaw and I produced a documentary for NBC on the role of genetics on sports performance, focusing on the outsized success of African-descended athletes. It led to a best-selling book published in 2000, *Why Black Athletes Dominate Sports and Why We're Afraid to Talk About It*. That ultimately led to another book on population genetics, *Abraham's Children: Race, Identity and the DNA of the Chosen People*."

"The reaction to both books was fascinating but discouraging in some ways; many people are afraid of developing technologies, including those that unlock the mystery of evolution and disease. Although the parallels are not exact, the resistance to appreciating the revolutionary discoveries in human genetics was echoed in the agricultural field. I decided to devote my research going forward to helping the public demystify genetics and biotechnology. It eventually led to my founding of the Genetic Literacy Project (GLP) in 2011, which addresses the nexus of genetics and biotechnology with media and public policy," Mr. Entine explains.

> "The United States has been built on risk taking. Biotechnological research is cutting edge — it challenges paradigms."

Commitment to Science

Mr. Entine adds, "I have witnessed an explosion of misinformation and disinformation in the media and in policy debates about genetic innovation—human and agricultural. We now offer daily access to the best journalism, blogging and research on medical and human genetics, drug biotechnology, and agricultural biotech and food. There are no 'sacred cows' for the GLP; our only commitment is to the science. The GLP also offers an annual Biotech Bootcamp to train scientists how to more impactfully convey the science of biotechnology, hopefully containing the explosion of anti-science that is so prevalent in cyberspace and across so many media channels." GLP's tagline is "Where science trumps ideology."

Mr. Entine, who received his degree in philosophy from Trinity College and studied at the University of Michigan under a National Endowment for the Humanities Fellowship, further explains his views on biotechnology. "The United States has been built on risk taking. Biotechnological research is cutting edge—it challenges paradigms. There is no question that this country will continue to take a leadership position in biotechnology in the years ahead. That said, there is a discouraging technophobia that has arisen in the U.S., and sadly it's perceived as "progressive" when it is exactly the opposite. Those precautionary obsessions are even more prevalent in Europe and elsewhere. I'm cautiously optimistic that the exaggerated fears promoted by non-government organizations (NGOs) resistant to biotechnology will not prevail, but it is gumming up the regulatory structure, making it challenging to introduce innovations."

Politics and Trade Disputes

In his book *Let Them Eat Precaution: How Politics is Undermining the Genetic Revolution in Agriculture* published in 2006 that Mr. Entine edited and contributed to, experts from the U.S. and Great Britain explain why cultural politics and trade disputes, not science, pose the biggest hurdles in developing products. It notes that well-funded environmental groups, organic advocates, and religious groups among others exploit anxiety about science. The authors suggest that biotechnology proponents must address political, social, moral, and economic issues raised by critics instead of merely relying on scientific evidence.

"I'm cautiously optimistic that the exaggerated fears promoted by non-government organizations (NGOs) resistant to biotechnology will not prevail, but it is gumming up the regulatory structure, making it challenging to introduce innovations."

Also a visiting fellow at the American Enterprise Institute since 2003 where he focuses on science and public policy, Mr. Entine reiterates the critical role that biotechnology could and should play in the years ahead: "We have no choice but to embrace innovation. Literally. The science is robust and checks and balances are in place. We are already seeing significant benefits."

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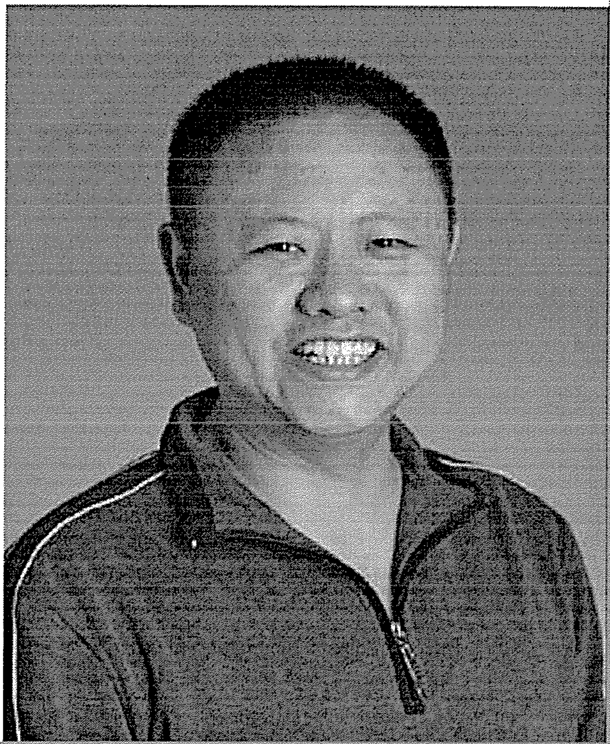

Jia Hepeng

- Science communicator (China)
- Former Editor-in-Chief of *Science News Magazine* affiliated with the Chinese Academy of Sciences
- Former Executive Director of the World Federation of Science Journalists

"I think the next-generation agri-biotechnology will play even a bigger role in the sustainable development of our society amidst various challenges, among them climate change and swelling global population, which are particularly important to China."

Good Journalists Never Stop Revealing the Truth

Tian Zhang

As one of the most prominent science journalists in China, Mr. Jia Hepeng had an early interest in agricultural biotechnology. "As an active journalist, I had an instinctive interest in and a deep concern about it. It was a hot topic and a controversial one and I wanted to protect public interest by exposing 'bad science' like agri-biotechnology," Mr. Jia says.

A former editor-in-chief of *Science News* magazine in China which is affiliated with the Chinese Academy of Sciences (CAS), Mr. Jia did extensive research and investigation on the topic. It was the evidence that changed his attitude toward the technology.

Interest in Biotech

"I remembered my interview with Professor Zhu Zhen, former deputy director of the Institute of Genetics and Developmental Biology, CAS, in early 2003. Zhu patiently explained every point raised by critics against agri-biotechnology and clarified nearly every concern I had. Another force to cause my shift was the chance for me to freelance for international science media, primarily the London-based *SciDev.Net* and *Nature Biotechnology*. During the freelancing process, I came to know of a few acceptable papers to prove the 'harm' of agri-biotechnology. My experience with the top international journals provided me the norm to base every claim of my reporting on solid evidence, but it was Prof. Zhu's candidness and clarity that made me trust scientists," he explains.

Mr. Jia's earlier work on agri-biotechnology mainly relied in his role as a science journalist and a science communication practitioner. He initiated and organized many communication-related events, including organizing one of China's earliest agri-biotechnology communication symposia, developing the first website on agri-biotechnology dialogue, and publishing a media handbook on agri-biotechnology in Chinese. He has been involved in drafting the communication section of a formal CAS scientific report on agri-biotechnology, which was submitted to top Chinese leaders. The central task surrounding these projects is to make people, particularly those in the communication process, to base their claims and judgment of agri-biotechnology on acceptable evidence. "As a science communicator, my role is to promote the sustainable development of science amidst various social and public concerns, at least to smoothen the increasing tension between fast-growing science and technology and the rising social uneasiness towards it," Mr. Jia says. In 2010, he won the honorary title "National Advanced Worker for Science Communication" awarded jointly by China's Ministry of Science and Technology, Propaganda Department of the Central Committee of the Communist Party of China, and China Association for Science and Technology.

Currently, Mr. Jia is pursuing his PhD in communication at Cornell University. As part of his academic work, he has been extensively studying and writing about public opinion on agri-biotechnology (as an example of scientific controversies). He is identifying and summarizing the key elements underneath people's resistance to agri-biotechnology.

"For my ongoing research on agri-biotechnology communication, I am focused on revealing the social, political, and psychological factors that predict people's attitude to agri-biotechnology. I have made a comprehensive literature review on previous research on the topic and the results of this research were published as several papers. But, most of the research is made in the developed countries, while China, as a transitional economy, may have quite different factors to explain the public attitude to the technology. I am trying to identify these factors," Mr. Jia adds.

A former executive director of the World Federation of Science Journalists and director of Science and Development Network in China, Mr. Jia is also a team member of the risk communication section of the National Key Research Program on Agri-biotechnology. He continues to freelance in China as a columnist, writing about genetic modification (GM) issues and concerns. While not as active as he was once as a journalist, Mr. Jia is disseminating mainstream scientific views on recent GMO developments. These include the widely refuted French study on GM maize's carcinogenicity and the referendum on GMO labeling in the US states of California and Washington, which he tackles in his columns and articles to encourage evidence-based rationality among Chinese readers.

> "We will have much more evidence to understand the mechanism underlying people's attitude to GMO and thus we will be able to promote its acceptance by strengthening those positive factors."

Future for Biotech

Now, Mr. Jia is a believer of biotechnology. His confidence comes not only from its power to create benefits for people but also from his conviction that, with progress in science communication, "biotechnologies in general and agri-biotechnology in particular will have a brilliant future in this world and in China." He notes, "It is one of the key forces to promote food security, social progress, and economic prosperity in the world. I think the next-generation agri-biotechnology will play an even bigger role in the sustainable development of our society amidst various challenges, among them climate change and swelling global population, which are particularly important to China as the world's most populous nation. We will have much more evidence to understand the mechanism underlying people's attitude to GMO and thus we will be able to promote its acceptance by strengthening those positive factors."

Making Benefits Available

"Traditionally, the influence or powerfulness of a new technology is embodied through the presentation of its benefits to the people," Mr. Jia adds. "But agri-biotechnology has to be different. Its primary benefits must accrue to farmers, who are either politically weak or demographically marginal. Substantial efforts should be made to embody its benefits to consumers, particularly poor people. Therefore, Golden Rice, with its potential benefit to improve nutritional deficiency, should be made available to the poor people as quickly as possible. It is the most persuasive way for people to accept GMO, at least morally."

"There has been a strong legacy of GMO resistance, so that many people have equated GMO resistance to environmental protection or to protesting against capitalism. Hype surrounding such a highly controversial product as GMO should always be avoided because any unmet promise could be disastrous. The world's leading charity groups, such as the Bill and Melinda Gates Foundation, should support research and development of biotech products like Golden Rice and the promotion of these products. It is crucial to have an early example of a crop that benefits people as a whole, rather than just big farmers who can afford expensive agri-biotechnological seeds and related herbicides," Mr. Jia explains.

> But agri-biotechnology has to be different. Its primary benefits must accrue to farmers, who are either politically weak or demographically marginal.

Evidence-based Reporting

Rational attitude and evidence-based reporting should always be the right attitude of journalists (whose composition has been expanded to citizen media workers who use blogs and other social media to report events) in dealing with any controversial topic, including GMO. To Mr. Jia's mind, a good journalist shall not avoid challenges and problems linked to technology.

A good journalist should never stop at revealing these problems. "He or she must ask 'why'? And all the 'whys' should be based on solid and authoritative evidence. In the same vein, a good journalist should also avoid hyping the sensational aspects of GMO. Many communication studies have indicated that the audiences are not reasonable enough. They would not take all knowledge seriously. This is human nature. So, do not think that you can make big sensational news and then balance the negative side by making thorough and clarified explanation. Never! Readers simply remember the 'bad' event and then go away. You, as a responsible journalist, will have no chance to clarify certain issues with your readers."

> "He or she must ask 'why'? And all the 'whys' should be based on solid and authoritative evidence."

Mr. Jia's career goal is to combine academic research on GMO communication and a practitioner's role in risk communication. The most ideal position for the task is a professorship of communication at a top Chinese university. "But that is not the goal, it is only a means. I do believe more and more studies on communication regarding agricultural biotechnology — including those done by me —will help us develop more effective communication strategies based on solid evidence and reasonable application."

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Bruce Chassy

- Professor of University of Illinois at Urbana Champaign (USA)
- Author, *History and Future of GMOs in Food and Agriculture, Crop Biotechnology and the Future of Food: A Scientific Assessment*, and *GMOs: A Plateful of Promises*
- Maintains GM food safety website at http://academicsreviews.org

"In the future, we can expect to see crops with improved nutrition and other desirable traits, crops that will cope with climate changes, will be intrinsically more productive, and which will make more efficient use of resources. The impact on agriculture has been phenomenally positive and beneficial."

Getting the Message Out and Clear

Mariechel J. Navarro

Scientists are expected to do more than disseminate information in their field of interest. They are also encouraged to participate in the debate and discourse on science and technology. But not many scientists are willing to venture beyond the laboratory and be actively part of the conversations and narratives that occur in the public sphere. Several reasons are forwarded: inadequate communication skills, difficulty in popularizing technical jargon, and lack of audience interest. Yet, studies show that university professors and public sector scientists are regarded by stakeholders as highly credible, trustworthy, and key information sources. They need to be part of the debate so that uncertainties, doubts, and fears about technology can be explained.

Dr. Bruce Chassy is one of those who have created a balance as a scientist and as a science communicator. As a professor and researcher at the University of Illinois at Urbana Champaign, he worked on the characterization and development of methods for the genetic manipulation of microorganisms used in food and dairy fermentation. His interest spans food safety and the safety evaluation of biotech foods.

Public Engagement

He has also found the time to explain the science of biotech and the controversy surrounding it to various stakeholders. He maintains a website (http://academicsreview.org) where he reviews claims about GM food safety. *Academics Review* stands against "falsehoods, half-baked assertions, and theories or claims not subjected to rigorous review." In addition, he speaks at national and international meetings and is often a guest on television and radio programs in addition to writing articles and blogs for several mainstream and online publications. In addition, he has authored papers on *The History and Future of GMOs in Food and Agriculture, Crop Biotechnology and the Future of Food: A Scientific Assessment,* and *GMOs: A Plateful of Promises.*

Early Interest in Molecular Biology

"As a student, I was fascinated by DNA, genetics, and the evolution of life on earth. I wrote several papers on the topic in high school and college. I considered several professions but probably always knew that I would be a scientist and a teacher," Dr. Chassy recalls.

"Three events stand out to me as shaping my career choice to focus on using the tools of molecular biology in my research. I can still remember the excitement that came one day in 1961 in my biochemistry class when the instructor came in and said that instead of the planned lecture we would review a new paper in the *Journal of Biological Chemistry* by Marshall Nirenberg (Nobel Prize, 1968) that reported the deciphering of the genetic code. A few years later, when I was a graduate student at Cornell, I remember Bob W. Holley (Nobel Prize, 1968) coming into the classroom for a class he taught in nucleic acids. Instead of talking, he walked to the blackboard and wrote a series of A's, U's, G's, and C's that represented the sequence of the yeast phenylalanine transfer RNA—the first nucleic acid ever sequenced. I earned a PhD in biochemistry and molecular biology from Cornell in 1966."

"In 1973, while working as a research chemist at the National Institutes of Health in Bethesda, Maryland, I read a paper by Herb Boyer and Stan Cohen in the *Proceedings of the National Academy of Sciences* (PNAS) that described the transformation of a bacterium (*E. coli*) by recombinant plasmid DNA. The transformed cells produced a new protein, ampicillinase. The ability to transfer genes from one organism to another and thereby introduce new traits opened the way for genetic engineering and formed the foundation of what came to be known as the "biotechnology industry." I decided, at that point, to apply this newly emerging technology first to medical and dental applications and later in food and agriculture," Dr. Chassy reminisces.

Biotech Applications

His early interest in biotechnology and its applications was eventually validated over the years. "Today, more than 100 pharmaceuticals are the products of biotechnology. New vaccines are being made using the techniques of biotechnology. Genetic engineering has been applied to the production of food ingredients and chemicals. Many useful enzymes are produced using biotechnology. Biotechnology has also been applied to the production of new and better seeds that have found widespread use in agriculture. There are many other applications of this science that range from creating art to remediating environmental contaminants. The possibilities are endless. Biotechnology is simply the science of putting life to work for useful purposes. Its products surround us in our everyday lives. I think the applications of biotechnology will be with us in the future. In my area of interest, food and agriculture, applications of biotechnology will continue to expand," Dr. Chassy explains.

"Today's biotech crops have offered a host of improvements in agriculture, which include improved yields, lowered input costs, less use of chemicals, better stewardship and less labor, disease resistance, and improved sustainability. In the future, we can expect to see crops with improved nutrition and other desirable traits, crops that will cope with climate changes, will be intrinsically more productive, and will make more efficient use of resources. The impact on agriculture has been phenomenally positive and beneficial. There are many studies and papers that document the benefits of biotechnology." Ironically, Dr. Chassy notes that he "continues to be astounded that there is opposition to and criticism of biotechnology after almost 20 years of successful use on billions of hectares of farmland." The University of Illinois professor notes, however, that it would be incorrect to say the prospects are endless. "Biotechnology is just a tool that is used to introduce new desirable traits in organisms or, in some cases, modulate or remove undesirable traits. No one technology can be a magic bullet that will solve all of the world's challenges. Many other technologies and management practices will be needed to improve foods and agriculture to meet future needs. The technology is, however, exceedingly useful for engineering changes into living organisms. It is often used in combination with other technologies that are used in breeding improvements into microbes, animals, and crops. It is also important to note that some kinds of genetic changes are easier to do with other breeding methods. All of these point to the conclusion that biotechnology is a powerful tool, but it is not the only tool we will need to manage future challenges. That said, I believe that we cannot meet the food and agricultural needs of the future without biotechnology."

> **"I am not pro-biotech. I see myself as a supporter of science and technology when it is used appropriately."**

Biotech Challenges

According to Dr. Chassy, biotechnology faces two important challenges. "The first is that a small but committed group of opponents have instilled fear in consumers, policy makers, and governments. Much of what these groups say is not factually correct; often, they deliberately spread misinformation. It is not unusual for humans to be cautious and concerned about new technologies about which we know little and which we have been told are untested — in fact, it makes good sense to be careful. As a result of widespread campaigning against biotechnology in agriculture and food, many people around the world are not certain that biotechnology is either necessary or safe. Society will need to move past this opposition in order to capture the benefits offered by biotechnology."

"Secondly, one consequence of the belief that biotechnology is somehow a new or different way to breed plants and animals is that governments around the world have applied strict regulations to the use of the science. It takes 5-10 years and can cost more than US$100 million to develop and gain approval for a new biotech crop. This means that few developments will come to the market and it also means that only the largest international corporations who have the needed resources will be able to introduce new products. Paradoxically, there is an overwhelming scientific consensus based on extensive scientific evidence that products produced using biotechnology are as safe as, or are safer than, products produced using other methods of breeding. From a purely scientific perspective, it makes better sense to regulate products produced by other methods of breeding or, at the very least, to regulate all new phenotypes regardless of the methods used to produce them. These unwarranted regulatory barriers need to be removed," Dr. Chassy opines.

> "Biotechnology is a powerful tool, but it is not the only tool we will need to manage future challenges."

Supporter of S&T

The scientist clarifies that biotech is just a scientific tool for introducing genetic changes. "It can be useful in research aimed at improving our knowledge of how living systems work, and it can help us produce better products. If products are produced that don't function correctly or which cause more harm than benefits, obviously we should not use them. I am not pro-biotech. I see myself as a supporter of science and technology when it is used appropriately. In the case of agricultural biotechnology, the benefits have been considerable and the harms have proven few and quite manageable to date. If products fail to meet that standard, I would not support their use."

To Dr. Chassy, it is a life mission to empower the public to make crucial decisions regarding acceptance and adoption of biotech but these must be based on what science has to say about it.

Nina Gloriani

- Medical researcher and doctor, University of the Philippines (UP) Manila
- President, Biotechnology Coalition of the Philippines
- Former Dean of the College of Public Health at UP Manila

> "Everything we do, everything we have, there are risks. We look at the risk, we assess the risk, and we manage the risk."

Taking Scientific Arguments to Public Engagement

Sophia Mercado

Shifting from the stereotyped scientist in the lab to a staunch educator and advocate came smoothly for medical researcher and doctor, Nina Gloriani.

Dr. Gloriani, who conducts a limited practice of her profession in clinical microbiology aside from being an esteemed professor and former dean of the College of Public Health at the University of the Philippines Manila (UP Manila), admits that she was normally just a quiet scientist immersed in research and the laboratory before she went into the biotech debate. But, after an encounter with a biotech critic from the academe, then director of the Institute of Biotechnology and Molecular Biology at the National Institutes of Health-University of the Philippines Manila (UP Manila), Dr. Gloriani felt driven to step up from being a scientist confined in a lab, clarify the truth, and present her professional take about the claims presented against biotech products, particularly genetically modified organisms (GMO). The experience somehow served as a catalyst for Dr. Gloriani's efforts on biotech education to start rolling. Since 1999, she has been a resource person more than five times a year in various local and international speaking engagements on GMOs, human health, and food safety.

Outstanding Scientist

Her expertise and caliber in her field cannot be denied with the numerous awards she received from national scientific and academic bodies and organizations, including UP Manila's Most Outstanding Researcher in 2001, the Philippine Society for Microbiology's Outstanding Microbiologist in 2006, UP Alumni Association's Outstanding Professional in Public Health in 2006, and other citations. With a PhD in microbial immunology and immunochemistry and having completed postgraduate training and fellowships in biotechnology, clinical microbiology, HIV/AIDS immunology and virology from universities such as the University of California, Los Angeles, Georgetown University in San Francisco, and Kobe University in Japan, Dr. Gloriani was involved and has led many research projects on molecular biology and biotech, particularly vaccines, human and animal seroepidemiology, and risk assessment of biotech-derived food, among others.

> "We are no longer the stereotypes with lab gowns, in the laboratory. More of us are out now. We explain what we are doing. We explain what the science is about, what the need is for."

In UP Manila, she became chairman of the Department of Medical Microbiology in the College of Public Health; director of the Institute of Biotechnology and Molecular Biology; and dean of the College of Public Health. She was also the director of SEAMEO-TROPMED Regional Center for Public Health, Hospital Administration, Environmental and Occupational Health from 2007 to 2013. Now, she is working on the development of *Leptospira* vaccines applicable in the Philippine setting and a project on risk factors in the outbreak of infectious diseases and psychosocial problems in the aftermath of disasters in the national capital region and neighboring provinces.

As an active voice in the biotech arena in the Philippines, Dr. Gloriani also shares that what fueled her desire to explain were the sudden and demanding questions from anti-GMO activists. She explains the need for information and data so as to accurately answer the questions. "We need to be very upbeat but careful in a sense that we do not become like them (anti-biotech groups). You cannot win battles that way, and it is not the truth. We just go by what is true. If there are possible side effects, then we also say those because of the risk." Still, Dr. Gloriani remains steadfast in countering anti-GMO efforts.

> **"With economic development, it is already certain that technologies will come in. There will be more products, and the public has to understand their applications and what good they will do for us."**

As the leader of the Biotechnology Coalition of the Philippines (BCP) since 2007, she acknowledges the need for continuous education for all stakeholders. BCP is a non-stock, non-profit membership association of multi-sectoral advocates from the academe, the scientific community, farmers' organizations, industries, the church, media, and other civil society organizations, "We are after those who will not use technology for good noble purposes." She also places emphasis on young students, believing that biotech education should start in the early years. "Maybe they're the best ones to teach because they don't have misconceptions and biases." Under her leadership, BCP has reached out and conducted biotech education activities all over the country, some in partnership with and involving ASEAN countries, while bringing together the various biotech stakeholders.

Dr. Gloriani also recognizes that more scientists like her are also out in the field. "We are no longer the stereotypes with lab gowns, in the laboratory. More of us are out now. We explain what we are doing. We explain what the science is about, what the need is for."

As an expert in the meticulous fields of medicine, public health, and microbial immunology and immunochemistry, Dr. Gloriani never concludes her talks and explanations on GMOs without emphasizing the nature of scientific research and risks.

Assessing and Managing Risks

"In any scientific experiment, we do not always have a hundred percent answer. That is why we keep on researching. But there is a point where we can say that this is already conclusive, based on the standards that we have set. Well, over the years, that will change, but, as I've said, there is no zero risk." She also highlights the importance of case-by-case assessment, which, she points out, is not just for biotech products, but for any new technology as well. "At some point, we already know the safety angle. We should arrive at certain conclusions, given what we do, depending on what we see... at some point, you can conclude based on very rigorous standards of your methodology which should be internationally accepted. That is why we have accreditations and certifications," she explains. "We cannot keep on saying these things that they (anti-GMOs) say," she adds, referring to safety issues posed by biotech detractors that have already been addressed globally.

During a consultative meeting of stakeholders for the Philippine position in the 7th Conference of Parties as Meeting of Parties to the Cartagena Protocol on Biosafety (COP-MOP), Dr. Gloriani puts into context the risk management in every technology. "Everything we do, everything we have, there are risks. We look at the risk, we assess the risk, and we manage the risk." She also puts forward the helpful intentions of Filipino scientists who choose to stay and serve the country, stating that they do their best in developing products that will benefit the Filipino people. "We will never put you in harm's way," she said.

Pushing for Biotech

She also distinguishes medicinal and agricultural biotechnology, understanding that it is harder to press the case for biotech in agriculture and food. Dr. Gloriani says the public is more accepting of biotechnology as applied to medicine and health because it is "curative" and "prevent a lot of infections." "But with crops, it's about something you eat everyday, so there are some questions."

By persistently echoing the principles in her medical fields through her own efforts and BCP's various outreach activities, Dr. Gloriani helps push forward biotechnology (be it in the medical or agricultural arena), recognizing the advantages it would bring to the Filipino people. "With economic development, it is already certain that technologies will come in. There will be more products, and the public has to understand their applications and what good they will do for us."

Mark Lynas

- Visiting Fellow at Cornell University's Office of International Programs at the College of Agriculture and Life Sciences (USA)
- Author, *The God Species: Saving the Planet in the Age of Humans* and *Six Degrees: Our Future on a Hotter Planet*
- Vice-Chair of the World Economic Forum's Global Agenda Council on Emerging Technologies

"It is not enough to sit back and hope that technological innovation will solve our problems. We have to be much more activist and strategic than that. We have to ensure that technological innovation moves much more rapidly, and in the right direction for those who most need it."

Uprooting the Weeds of Misinformation

Mariechel J. Navarro

It was a school holiday in August 2013 at the University of the Philippines Los Baños. Organizers were not too sure about a captive student audience where Mr. Mark Lynas, prize-winning author and former anti-genetically modified organism (GMO) activist, was the guest speaker at a convocation. Ten minutes before the afternoon talk, the auditorium was packed with students, scientists, and academics while others had to be turned away, many of them perhaps curious to listen to what this man had to say. After all, this was the man who was among those who joined the anti-GM movement and participated in the uprooting of GM crops in field trials in the United Kingdom in the mid-1990s. Today, he is singing another tune — that of the benefits of the technology — but not after going through a process of discernment in his quest for evidence-based answers.

Anti-GM Movement

Mr. Lynas' involvement with anti-biotech groups was a phase: "I helped to start the anti-GM movement where I assisted in demonizing an important technological option which can be used to benefit the environment." He attributes the initial ferment to the idealism of youth and the exciting times for environmental activism. The anti-science campaign in Europe, which he was initially part of, proved to be a most successful one, with fears about "scientific powers being used secretly for unnatural ends" spreading to Africa and Asia. So successful was the movement that, to this day, many countries ban the use of the technology.

Riding on his interest with the environment and its issues, the journalist-writer wrote a book *Six Degrees: Our Future on a Hotter Planet* in 2008, which won the prestigious Royal Society science book prize. The book was eventually made into a film by the *National Geographic*. He followed this up with *The God Species: Saving the Planet in the Age of Humans* in 2009. The book noted that humans are God species, being both creators and destroyers of life. It called for the use of technological mastery over nature by managing the planet successfully to continue life and civilization. In the course of doing research for a chapter in agriculture in the book, he discovered that his anti-GMO stance had no basis after reading articles in science journals.

Value of Science

"I'm not a doctor. I don't have any PhD [and] so I really have to start from the very beginning in terms of understanding scientific methodologies, appreciating the value of science as a form of knowledge as opposed to just campaigning, or assertion or argument or shouting. And on that basis, I wanted my books to be credible and to be authoritative," he explains. This awakening led him to call for the use of environment-friendly technologies such as genetic engineering and nuclear power.

Mr. Lynas, who was then a research associate at Oxford University's School of Geography and the Environment, kept this change of opinion to himself until the Oxford Farming Conference in January 2013 where he had been invited to give a talk. Without possibly realizing that he might have opened a Pandora's box of doubts and skepticism, he admitted retracting his decade-long negative position on GMO after carefully studying scientific data on which his assumptions were based.

To his audience, he posed the question: So I guess you'll be wondering— what happened between 1995 and now, that made me not only change my mind but come here and admit it? Well, the answer is fairly simple: I discovered science, and in the process I hope I became a better environmentalist." By reading the scientific literature, he discovered that one of his "cherished beliefs about GM turned out to be little more than green urban myths." His assumption that GM would increase the use of chemicals was unfounded. Rather, pest-resistant cotton and maize needed less insecticide. Still another assumption was debunked — that GM benefited only the big companies. Instead, billions of benefits were accruing to farmers needing fewer inputs.

"It is not enough to sit back and hope that technological innovation will solve our problems. We have to be much more activist and strategic than that. We have to ensure that technological innovation moves much more rapidly, and in the right direction for those who most need it," Lynas added.

In conclusion, Mr. Lynas emphatically stresses "I don't know about you, but I've had enough. So my conclusion here today is very clear: the GM debate is over. It is finished. We no longer need to discuss whether or not it is safe — over a decade and a half with 3 trillion GM meals eaten — there has never been a single substantiated case of harm.... So my message to the anti-GM lobby, from the ranks of the British aristocrats and celebrity chefs to the US foodies to the peasant groups of India is this: You are entitled to your views. But you must know by now that they are not supported by science. We are coming to a crunch point and, for the sake of both people and the planet, now is the time for you to get out of the way and let the rest of us get on with feeding the world sustainably."

The reaction to Mr. Lynas' confession was fast, winning the admiration of some for his bravery to speak up and losing close friends who had earlier shared his thoughts on the technology. The online feedback to his talk generated 532 comments before the system stopped posting more views. He has since become a sought-after speaker in different countries, not just on biotechnology but on climate change and nuclear power.

In October 2013, Mr. Lynas was appointed a visiting fellow at Cornell University's Office of International Programs at the College of Agriculture and Life Sciences. He is also a member of the advisory board of the science advocacy group Sense About Science and is vice-chair of the World Economic Forum's Global Agenda Council on Emerging Technologies. His appointment at Cornell now allows him to pursue his interest in assisting biotech work concerned with food security and environmental sustainability. He visits projects such as Golden Rice in the Philippines, advises the Bt brinjal (eggplant) project in Bangladesh, and goes to African countries for advocacy and research work on biotech.

"The GM debate is over. It is finished. We no longer need to discuss whether or not it is safe — over a decade and a half with 3 trillion GM meals eaten — there has never been a single substantiated case of harm."

Public Engagement

Mr. Lynas' website (http://www.marklynas.org/) features a wide range of topics on agriculture and the environment. On his homepage, he tackled media reports claiming that GM pest-resistant Bt brinjal has failed in the field and that farmers in Bangladesh are regretting that they have begun to grow it. "It is entirely false. I myself, along with various scientists and others from Cornell University and the Bangladesh Agricultural Research Institute, visited the same farm a day earlier and found the crop in good health and the farmer happy." He attached photos to prove otherwise.

But Mr. Lynas continues to be in the 'battlefield" of public debate. In July 2014, he spoke on climate change and biotechnology at an Argentinean university. Although used to the antics of the antis, he was surprised by a full-scale invasion of hecklers complete with shouting, banners, and dreadlocks. He tried to engage them to raise their points but the group became aggressive. Nevertheless, he stood his ground and eventually realized how irreconcilable his worldviews and those of the activists were.

But, to Mr. Lynas, evidence fuels science and it cannot be otherwise.

Further Reading

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Thinking Beyond Technology

Winarno Tohir

- Chairman of the National Outstanding Farmers and Fishermen Association (Indonesia)

“Farmers are ready to accept the latest technology, including biotech crops, as it can bring substantial benefits to farmers. I have had opportunities to be invited to several events that showcased the technology to enable me to come to this conclusion.”

Consider Ethics in Developing Transgenic Crops

Dewi Suryani Oktavia and Heryanto Lingga

Indonesia, an archipelago in Southeast Asia, is predominantly an agricultural country with 21 million farmers engaged in the industry. Perhaps, only 10% of these farmers are aware of biotech crops. This is expected, as currently, there is no biotech crop approved for commercialization. Local scientists, however, are developing genetically modified (GM) sugarcane and potato.

Nevertheless, Winarno Tohir, chairman of the National Outstanding Farmers and Fishermen Association (NOFA) in Indonesia, believes that "farmers are ready to accept the latest technology, including biotech crops, as it can bring substantial benefits to farmers. I have had opportunities to be invited to several events that showcased the technology to enable me to come to this conclusion."

Information on Biotech Crops

Winarno first heard about biotech crops in school. During a visit of the People's Representative Council in the region, students were informed of a tall and high-yielding biotech tomato. "As a son of a farmer in the village, I was amazed by that information and I have continued to seek information about this technology," says Winarno.

After graduating from high school, he heard about Golden Rice (GR), which contains beta-carotene or vitamin A precursor being studied by the International Rice Research Institute (IRRI) in the Philippines. At that time, the minister of agriculture, Mr. Syarifudin Baharsyah, introduced the concept of GR. "When is it going to be available, Mr. Minister?" asked Winarno. "It is still undergoing research at IRRI", said the Minister. Winarno admits that he did not fully understand about GM crops, particularly how it is possible to insert a specific gene into a high-yielding rice variety to improve the crop. But this information excited him. The farmer leader eventually graduated in 1990 from the Tanjung Sari Agricultural University, Sumedang, West Java.

International Exposure

In 2000, Winarno and a number of farmers from NOFA attended an international conference on agriculture in California, USA. In a round-table meeting, one of the resource speakers from the U.S. told them: "If Indonesia is ready to accept the presence of biotech crops, then we will be ready to help." In 2003, Winarno attended an agricultural meeting in Paris, France, which apparently also discussed the development of biotech crops. At that time, the U.S. representative talked about biotech crops. Later on, a reporter asked him about what Indonesian farmers felt about the technology. "As long as it can benefit us, why not?," Winarno answered.

> "As a product of the latest technology, biotech crops must also be applied within a stewardship context by assigning agricultural extension workers whom farmers could interact with and who could answer their questions about the technology."

A year later, Winarno got an opportunity to share experiences and knowledge with farmers in Gambia, Africa. During his three-month visit in Gambia, he saw wheat plants in experimental areas growing so well and lush in the middle of dry land.

He was surprised, saying "How could the crop grow in the middle of dry land with no other vegetation? A farmer told me that the wheat crops are products of biotechnology which are resistant to drought. That was the first time for me to actually see a biotech crop." The drought-resistant wheat plant was inserted with a gene obtained from a native plant called African Baobab tree, which can survive devastating droughts. Winarno wanted to bring home the seeds, but unfortunately he was not allowed to do so.

At the seeing-is-believing tour of the Philippines in 2011, Winarno got further interested about biotechnology. He witnessed various biotech applications in the country for livestock and crops.

Winarno's interaction with biotech crops continued. Between 2012 and 2013, he, along with some Indonesian farmers, biotech researchers, heads of agricultural bureaus, and the director general of the Ministry of Agriculture visited U.S. research laboratories. During the visit, he saw how gene crossing is done. Winarno was fascinated not only by the development of research in the field of genetic engineering but also by how developed countries practice precision farming. Farmers can bring soil samples to be assessed in the government laboratory facility, and they get recommendations as to the kind of crop to be planted and the type of fertilizer to use.

Problems with New Technology

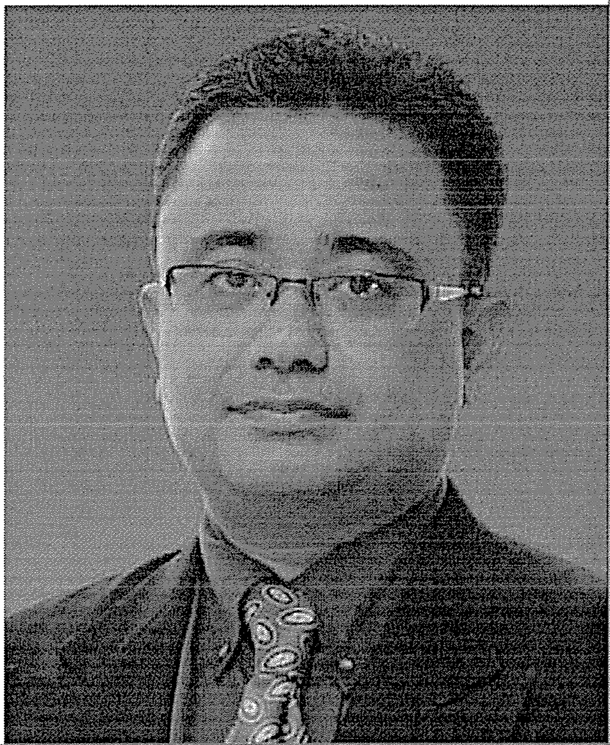
Since many Indonesian farmers have finished only elementary education and rely on their ancestral and family experiences with farming, Winarno is well-aware of fundamental problems when considering technological development in agriculture. He cites the case of hybrid rice seeds as a way to increase crop productivity. "Many farmers refused to use hybrid rice seeds because there's no one to guide them on how to cultivate them." Farmers rejected hybrid rice seeds because they made mistakes in following the cultivation procedures for hybrid seed. For instance, they soaked the seeds for two to three nights instead of only 2-3 hours. Because of this, they got unsatisfactory result. Farmers were disappointed and reluctant to use the superior seeds. "Since 2000, there has been no stewardship program to guide farmers in cultivating hybrid seeds properly and correctly," the farmer leader explains.

Stewardship of Biotech Crops

The farmer leader suggests that when new technologies such as biotech crops are introduced in the future, adequate briefing should be provided. "In addition, there should be a guide book on proper cultural recommendations, such as the one that accompanies electronic goods," says Winarno. "As a product of the latest technology, biotech crops must also be applied within a stewardship context by assigning agricultural extension workers whom farmers could interact with and who could answer their questions about the technology."

Based on his many experiences with biotech crops, he concludes that biotechnology development is a necessity. However, he emphasizes the need for an ethical foundation for biotech research and its products. "For example, we need to determine the origin of the gene that is inserted either into the plant or animal. Genes from pigs, for example, should not be used in biotechnology research projects because it is forbidden by the Muslim faith," Winarno elaborates.

As a farmer representative of NOFA, he is grateful that Indonesia has established the Biosafety Commission to monitor genetically engineered products. "They will make sure that products developed from biotechnology have thoroughly followed ethical considerations."



Shaikh Mohd Saifuddeen bin Shaikh Mohd Salleh

- Senior Fellow, Centre for Science and Environment Studies, Institute of Islamic Understanding Malaysia

"Biotechnology is a branch of knowledge that is important to mankind. It is therefore crucial that this field be developed."

The Voice of Islam for Biotechnology

Shaikh Mohd Saifuddeen bin Shaikh Mohd Salleh and Mahaletchumy Arujanan

The voice of Islam regarding knowledge, science, and technology has been clear from the time the religion was revealed to Prophet Muhammad almost 1,500 years ago. The first revelation as stated in verses 1 to 5 of Surah al-'Alaq says: "Read! In the name of thy Lord and Cherisher, Who created. Created man, out of a (mere) clot of congealed blood. Proclaim! And thy Lord is Most Bountiful. He Who taught (the use of) the pen. Taught man that which he knew not."

This verse emphasizes the need to pursue and have mastery of knowledge. A number of significant messages can be gleaned from this first revelation:

- Islam created and promoted one of the most vibrant civilizations in the world and it is believed that the Islamic civilization had created a second agricultural revolution as a number of new technologies and innovations in agriculture were introduced, resulting in an important transformation in this sector.

- This verse contains a scientific message in the form of a biological information with regard to the development of the embryo. This information was verified to be accurate by anatomists in the early 20th century. This further signifies the voice of Islam with respect to the importance of the biological sciences.

- The word *iqra'* in this verse is a directive for mankind to read. Reading is the key that can unlock many doors of knowledge. When reading becomes a culture, it would empower mankind with a vast amount of knowledge that has the ability to revolutionize the world.

- The word *qalam* in this verse is translated as "the pen." This gives the signal that, aside from reading, writing is equally important. One of the effective ways to disseminate knowledge is through writing, as ideas and thoughts are documented for others to dissect.

- Finally, the verse 5 of Surah al-'Alaq which gives the clear message to Muslims that all knowledge are made possible by the Will of God. For Muslims, all forms of knowledge belong to God. It is God who wills for mankind to know something through observation, trial and error, and research. In other words, knowledge, including biotechnology, are "taught" by God to mankind.

In essence, the first revelation of the Quran shows that Islam puts great emphasis on the pursuit and mastery of knowledge. There are many forms of knowledge, and it is the responsibility of Muslims to have someone within their midst to have mastery in the various branches of knowledge, including biotechnology.

Declaration on Biotech

Biotechnology is a branch of knowledge that is important in the modern world. Its applications can be found in many sectors — agricultural, biomedical, pharmaceutical, food production, and environmental sectors, to name a few. Such wide-ranging applications highlight the need for Muslims to view biotechnology as a critical branch of knowledge and to strive to pursue and master this knowledge.

Realizing this importance, the Islamic Academy of Sciences (IAS) drew up the "IAS Rabat Declaration on Biotechnology and Genetic Engineering for Development in the Muslim World", which was issued way back in October 2001.

The Declaration, among other things, noted the following:

- The applications of biotechnology could have far-reaching effects and favorable impact on the developing countries, many of which suffer from large and rapidly increasing populations, chronic food shortages and malnutrition, poor health, and profound environmental problems.

- Biotechnology and genetic engineering are areas where rapid and meaningful advancement can be readily made by the Organization of Islamic Countries (OIC), especially in attaining food security and promoting the pharmaceutical industry.

- Activities being carried out by many governments, academic institutions, and non-government organizations in the fields of biotechnology and genetic engineering, especially in agriculture, are appreciated by IAS.

- Advancement in biotechnology and genetic engineering underlines the importance of investment in basic sciences, which are the backbone of sustainable science and technology advancement, especially as there is very little biotechnological research and development in the developing countries.

- The significance of the sequencing of the human genome is acknowledged as an event compared to man's landing on the moon and described as a milestone in the history of science that will enhance research in human biology focused on diseases such as cancer, Alzheimer's, diabetes, and cardiovascular disorders.

- IAS takes into consideration the Universal Declaration on the Genome and Human Rights, adopted by the General Conference of UNESCO in 1997, which is the first worldwide instrument in the fields of biology, medicine, and genetics.

The IAS also highlighted some problems faced by Muslim countries vis-à-vis biotechnology in the 2001 Rabat Declaration. These problems include lack of a long-term biotechnology policy in many OIC countries, the small number of students enrolling in biotechnology-related disciplines, the lack of adequate infrastructure for biotechnology research in most OIC countries in order to sustain this fast-growing sector, the absence of coordination between agencies involved in biotechnology research and application, and the lack of up-to-date curricula for biotechnology as well as shortage of qualified teaching staff. The IAS proposed that an Islamic biotechnological fund be established in order to help "poorer OIC countries to transfer biotechnology know-how from other countries, and develop and utilize it to achieve national food security."

"It is important to ensure that biotechnological development would bring forth benefits to mankind and the environment and not the opposite."

Aside from the systemic problems identified by the IAS, it is also interesting to note that major breakthroughs in molecular biology and genetic engineering have raised many legal, ethical, and social questions. Such legal, ethical, and social dilemma are given serious attention by Islam and Muslim scholars. It is important to ensure that biotechnological development would bring forth benefits to mankind and the environment and not the opposite. On this matter, the IAS proposed that a multidisciplinary group made up of "scientists, technologists and Islamic scholars be set up to study the various facets of social and ethical issues."

It is also equally noteworthy that one point stressed in the Declaration was the recognition that genetic engineering has been defined as an unnatural insertion of a foreign sequence of genetic codes in the midst of the orderly sequence of genetic codes developed through millions of years, which is a profound intervention, with unpredictable consequences. Such sensibility would act as a reminder of the importance of not causing unwanted effects due to biotechnological developments.

It is not surprising then to see the IAS proposal for a moratorium on "the release of genetically engineered organisms and on the use of genetically engineered (GE) foods, until sufficient knowledge has been acquired to make it possible to judge how far it is safe for human health and the environment to exploit this technology. This is the "prevention is better than cure" approach suggested by the IAS.

Moving Forward

In essence, Islam stresses the need to preserve a harmonious three-dimensional relationship — i.e., relationship between mankind and God, relationship among mankind, and relationship between mankind and the environment. We can factor in biotechnology into this three-dimensional relationship to see how Islam views biotechnology.

Relationship between mankind and God: While "new" knowledge is welcomed by believers of Islam in line with the spirit of iqra', Islam also stresses the fact that all knowledge, including biotechnology, belongs to God, and only by God's Will is mankind able to obtain knowledge.

With regard to biotechnology, mankind has been given the tool to do many things that involve manipulation at the biomolecular level. From the perspective of Islam, what is important is for mankind not to have the inclination to "play God" or to "deny the existence of God." This is crucial in order to ensure that the relationship between mankind and God is protected. In other words, believing in what biotechnology can do for the betterment of mankind should strengthen one's belief in God.

Relationship among mankind: From Islam's point of view, biotechnology should not be the technology of the elite few. The benefits of biotechnology should not be accessible only to certain countries, certain companies, or certain individuals, as this would be tantamount to monopoly, which is not allowed in Islam. For Muslims, whatever is developed should be beneficial for the greater good of mankind.

Relationship between mankind and the environment: Biotechnological advancement has the potential to either improve or damage the environment. Believers of Islam are reminded of the need to ensure that the environment does not become a victim of mankind's greed.

Take Home Message

Biotechnology is a branch of knowledge that is important to mankind. It is therefore crucial that this field be developed. If its development falls within the ambit of the three-dimensional relationship mentioned above, Islam permits and supports it. What Islam stresses is the need to be cautious so as not to affect this all-important relationship.

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(https://biobricks.org/bpa/). It would be a small step to implement similar policies for synthetic biology standards, such as SBOL. Such an approach has recently been proposed by one of us for bioinformatics standards[9], and numerous readily available tools exist to assist with policy development[2]. Best outcomes for synthetic biology will result from simultaneous consideration of technical standards and IP issues.

Accordingly, although we commend the authors on their development of SBOL and other techniques for achieving interoperability of synthetic biology elements, we hope that they will also devote some attention to the IP issues noted above to avoid some of the pitfalls that have affected and increased costs associated with standardization in other industries.

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COMPETING FINANCIAL INTERESTS
The authors declare no competing financial interests.

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Michal Galdzicki, Linda J Kahl, Drew Endy & Herbert M Sauro reply:

We thank Contreras *et al.*[1] for drawing attention to the important couplings between technical standards and property rights in synthetic biology. In creating a first-ever standard for information exchange in synthetic biology[2], we are committed to ensuring that the synthetic biology open language (SBOL) remain free to use for all. Members of the SBOL development group, J. Christopher Anderson, Evan Appleton, Douglas Densmore, Drew Endy, Michael Fero, Michal Galdzicki, John H. Gennari, Raik Grünberg, Linh Huynh, Jeffrey David Johnson, Linda J. Kahl, Goksel Misirli, Chris Myers, Ernst Oberortner, Matthew Pocock, Jacqueline Quinn, Cesar A. Rodriguez, Nicholas Roehner, Herbert Sauro, Evren Sirin, Guy-Bart Stan, Neil Swainston, Mandy Wilson, individually and collectively, do not hold or plan to assert property rights claims against users of SBOL. Although we can never guarantee that third parties will not assert claims against SBOL users, our intention is to develop, release and, if needed, revise SBOL so that it remains free to use.

We therefore chose to work in an open and transparent manner using the BioBricks Foundation Request For Comments (BBF RFC) process (http://biobricks.org/programs/technical-standards-framework/), which allows us to document the development of the SBOL standard by means of a time-stamped world-readable digital archive. For example, BBF RFC #84 (ref. 3) and BBF RFC #87 (ref. 4) were issued on October 3, 2011, and October 11, 2012, respectively. We used these BBF RFCs to formally disclose the development of SBOL at specific points in time, name all process participants and establish various aspects of prior art.

We agree with Contreras *et al.*[1] that the time is right for the SBOL development group and others in the synthetic biology community to consider more formal policies requiring disclosure and licensing of property rights covering technical standards. Inevitably, there will be trade-offs in the time and resources needed for developing technical standards versus the time and resources needed to identify and evaluate property rights that may be essential for practicing those standards. As such, it will be important to establish policies for meaningful disclosure that are not overly burdensome and will not unduly hinder the standards development process.

We, together with the BioBricks Foundation and others in the synthetic biology community, would welcome additional work by legal professionals to analyze, establish and share opinions regarding the 'freedom to operate' for SBOL v1.1 and other standards from a property rights perspective. These opinions could, for example, be made available to the public by posting on the BioBricks Foundation's website. By engaging in a careful and active process of public documentation and disclosure of SBOL's development, and by working with legal experts that could assist in identifying potential third-party rights (thereby enabling workarounds if needed), we hope to realize our goal of keeping the SBOL standard free to use for all.

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Status and market potential of transgenic biofortified crops

To the Editor:

This month marks the 15th anniversary of the publication of pro-vitamin A–enriched 'Golden Rice'[1]. As the crop still awaits regulatory approval, its developers have little reason to celebrate. Golden Rice is not alone in facing a political and regulatory blockade. Several other biofortified transgenic crops also await authorization, in contrast to numerous staple crops with elevated micronutrient content developed through conventional breeding techniques that are available for consumption around the world.

Currently, genetically modified (GM) crops approved for cultivation are all products with improved agronomic traits—so-called first-generation traits that mainly benefit farmers in the developed and developing world[2,3], rather than consumers. Despite the global growth in transgenic acreage of first-generation crops, there is now a world-wide 'regulatory slowdown'[1,5] in approvals of GM crops, and agbiotech remains politically controversial in Europe[6] and elsewhere[7,8].

The case of Golden Rice illustrates how second-generation GM crops face commercialization barriers similar to those the preceding generation of crops faced[9], with their benefits often ineffectively

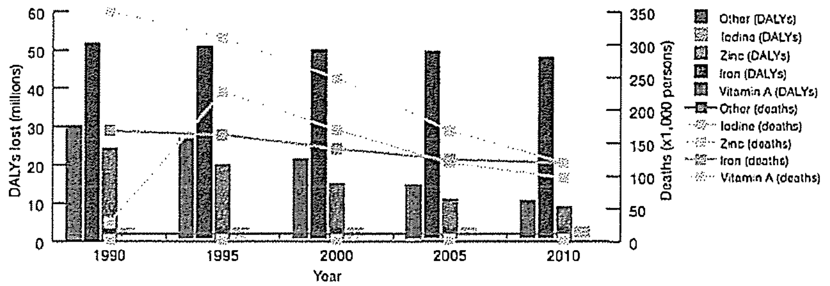

Figure 1 The global burden of micronutrient malnutrition. The number of DALYs and deaths attributable to deficiencies of key vitamins and minerals as risk factors. Source: Compilation based on IHME Global Burden of Disease database[31] (available at http://www.healthdata.org/search-gbd-data).

communicated to the public[10]. Nevertheless, in the past two decades, agbiotech research has steadily extended its focus toward food crops with enhanced quality traits that carry tangible benefits for consumers.

Golden Rice exemplifies the way in which transgenic technology can expand the range of micronutrient strategies available to malnourished populations, especially in poor rural regions, where industrial infrastructure and educational efforts are often lacking and/or can be difficult to implement. Indeed, despite numerous efforts to tackle vitamin and mineral deficiencies through supplementation, industrial fortification or dietary diversification, deficiencies remain widespread among two billion people (Fig. 1). This is especially the case in developing regions, where monotonous diets, mainly or solely consisting of staple crops, provide the daily caloric intake of the population[11]. Here, biofortified crops can play an important alternative, agriculture-based strategy to alleviate the burden of micronutrient malnutrition[12].

To build a case for these biofortification efforts, researchers have gradually started to anticipate the risk of market failure by joining forces with colleagues who—putting aside regulatory constraints—assess *ex-ante* the market potential of their new product developments. The following correspondence summarizes the current state of product development in the field of transgenic biofortification as well as applied consumer research at the microlevel (i.e., consumer studies on acceptance and willingness to pay) and macrolevel (i.e., health impact assessments, cost-effectiveness and/or cost-benefit analyses) (See **Supplementary Glossary**). Out of the 60 studies selected from the peer-reviewed literature, 35 reported key findings on the development of single- or multi-biofortified crops, with 19 and 6 studies conducting a micro- or macro-level analysis, respectively (**Fig. 2** and **Supplementary Dataset**).

Biofortification can be achieved by conventional breeding or by plant biotech. Conventional breeding is possible only between closely related (sexually compatible) individuals (and thus relies on natural variation of the target compound within parental lines) and is also time-consuming. Although marker-assisted breeding (MAB) and quantitative trait loci (QTL) mapping can accelerate conventional breeding, the minimum number of breeding generations for clonally propagated crops (e.g., potato, sweet potato, banana and cassava) is estimated to be 7 generations, for self-fertilizing crops (e.g., rice, wheat and sorghum), 9 generations and for cross-fertilizing crops (e.g., corn), 17 generations[13].

Pro-vitamin A–biofortified yellow corn is a prime example of a staple crop where breeding was successfully applied to increase micronutrient content to a desirable level[14]. In some cases, however, natural variation of the desired micronutrient is insufficient for conventional breeding. Moreover, in cereals, most of the vitamins and minerals are concentrated in the outer layers and the embryo of the kernel, which are usually removed upon milling to prolong storage, leaving only the endosperm. Thus, conventional breeding of cereals would have little or no effect on their vitamin and mineral content after milling. Enhancing micronutrient levels in staple crops by metabolic engineering greatly outpaces the results obtained by conventional breeding, MAB and QTL mapping (**Supplementary Fig. 1** and **Supplementary Table 1**). Moreover, engineering strategies can be redirected toward the accumulation of a target compound into the desired tissue, such as cereal endosperm, without compromising micronutrient content upon milling.

Great progress has been made in increasing vitamin content in staple crops by metabolic engineering. Although enhancing vitamin bioavailability could further improve their nutritional quality, vitamin engineering strategies to date have mostly relied on the accumulation of target compounds. Often, genes originating from nonrelated organisms, such as other plant species, mammals and/or bacteria, are overexpressed in the target crop (**Supplementary Table 2**). The best known example is Golden Rice[1,15], which was engineered with transgenes from daffodil and the bacterium *Pantoea* (formerly known as *Erwinia*)[1]. Golden Rice opened the door for the creation of other pro-vitamin A–enriched staple crops, such as corn, cassava, potato and wheat (**Supplementary Fig. 1**), whereas genes from other organisms appeared to further increase β-carotene content in target crops (for more details and references, see **Supplementary Table 2**).

Another well-known example is folate (vitamin B_9)-enhanced rice[16]. Here, transgenes from *Arabidopsis* were overexpressed in rice endosperm, which resulted in a 100-fold increase in folate content[16]. Again, conventional breeding was not an option because of the low folate content and low natural variation of this compound in rice kernels[17]. Attempts to increase ascorbate (vitamin C) content in staple crops were moderately successful (**Supplementary Table 2**), mainly because the metabolism of antioxidants is tightly regulated and therefore difficult to engineer. This clearly illustrates that to successfully engineer vitamin content in target crops not only a profound understanding of the biosynthesis pathways of vitamins is required, but also knowledge of the regulation of these biosynthesis routes, as well as the turnover and accumulation of the respective vitamins.

Over the past decade, interest in improving the mineral content in staple crops has grown as well, the focus being mostly on iron and zinc. Unlike vitamins, minerals cannot be synthesized by plants, which rely entirely on their availability in the soil. The Green Revolution, which coincided with large-scale irrigation and macronutrient fertilization, compromised mineral levels and availability in crop fields. Although soil fertilization would be an obvious way to increase mineral content in staple crops, foliar fertilization is often more successful[18]. Iron and zinc

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engineering strategies focus on enhancing both bioavailability and content. Cereals, for instance, contain antinutritional factors, such as phytic acid, which bind iron and zinc, limiting their absorption by the human intestine. Several attempts at lowering phytic acid levels both by conventional breeding and genetic engineering have been reported, mostly in cereals[18]. Engineering mineral content in staple crops is challenging because it involves many processes from mineral uptake by the roots, to transport throughout the plant, to accumulation in edible tissues. Metabolic engineers must correctly orchestrate these processes, which requires overexpression of multiple genes. Although numerous attempts to achieve mineral enhancement by engineering one or two processes have been reported, successful multiprocess engineering approaches are scarce.

A multi-biofortification approach is necessary to optimally tackle micronutrient deficiencies. Multivitamin white corn[19], with enhanced β-carotene, folate and ascorbate levels, sets a good example toward this goal, as well as mineral-enriched rice, where the overexpression of a single rice gene, resulted in enhanced iron, zinc and copper content[20]. However, there is a growing awareness of the importance of nutritional enhancement, in a broader range of essential and nonessential phytonutrients, in major crops consumed across the world.

Although an increasing number of studies report successful biofortification attempts, second-generation, staple GM crops remain unavailable to consumers, largely due to regulatory obstacles (for a discussion, see ref. 21 and **Supplementary Note** on GMO regulation. By building an evidenced-based case for the potential demand and impact of GM crops with health attributes, researchers hope to influence priority-setting and resource allocation, and thus facilitate decision-making by government authorities on whether or not to adopt them[22].

As biofortification efforts have proceeded furthest in rice[15,23], studies on consumer acceptance of, and willingness to pay for, transgenic biofortified crops have mainly focused on rice (14 studies); that is, rice fortified with pro-vitamin A, folate or vitamin C (9 studies, 4 studies and 1 study, respectively; **Fig. 2** and **Supplementary Table 3**). Six microlevel studies have been carried out on four products containing enhanced levels of vitamin E (in cookies and made from wheat flour, broccoli, tomato and potato), two on pro-vitamin A-enriched plants (cassava and apple) and one on a vitamin C–enhanced apple variety. Although targeting nonstaple crops is less relevant from a health policy point of view, their results are useful for evaluating consumer reactions toward transgenic biofortification. Asia (10 studies) is by far the most-often selected research location, followed by North America (5 studies), Europe (2 studies), Oceania or South America (1 study). Despite the lack of African studies, the geographical spread of consumer research is important, given the global need to tackle micronutrient malnutrition.

Whereas consumers often demand a discount when it comes to first-generation GM foods[24], the premiums they are prepared to pay for transgenic biofortified crops are relatively high, from 20% to 70%, regardless of the targeted crop, micronutrient and country (**Fig. 3a**). In regions with high prevalence of micronutrient deficiencies, such as China and Brazil, which are considered priority target markets, willingness-to-pay levels are as high as, and often exceed, those in developed regions. Together with the optimistic purchase intentions, preference rates and acceptance levels, these findings lend support for transgenic biofortification as an alternative micronutrient strategy, especially in developing regions (**Fig. 3b**).

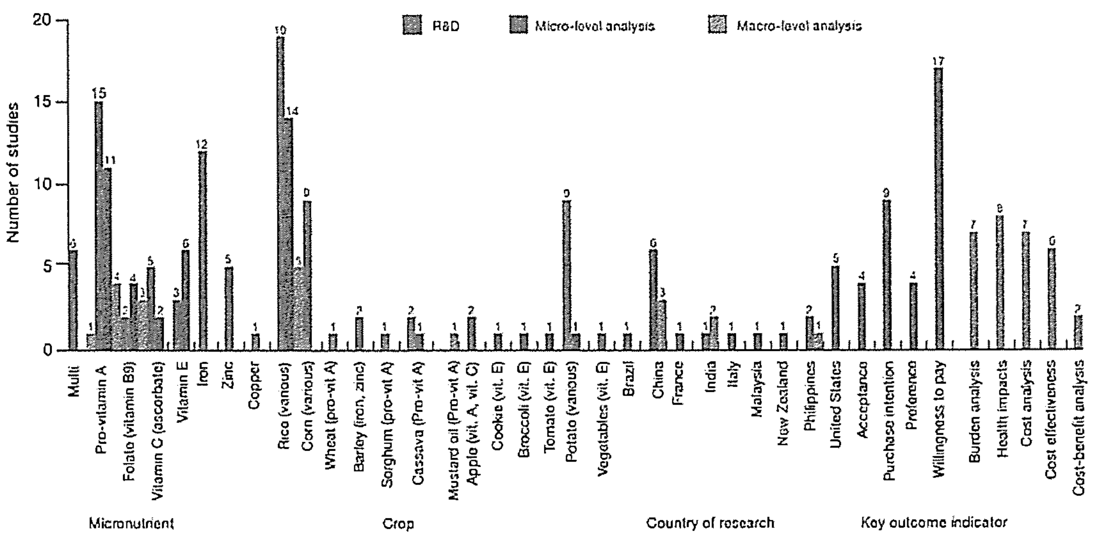

Figure 2 Number of studies on the development and market potential of transgenic biofortified products organized by micronutrient, crop and country categories, and key outcome indicator. Note: under the micronutrient category, multi-biofortification included several different types of crops, whether for research studies or for macrolevel analysis (no microlevel analysis was identified in our literature survey). R&D studies included one study on pro-vitamin A- + folate- + vitamin C–enriched corn, three studies on iron- + zinc-enriched rice, one study on iron- + zinc-enriched barley, one on iron + zinc + copper rice. The one macrolevel analysis of multi-biofortification was for a pro-vitamin A + folate + conventional traits zinc + iron rice. Under the crop category, 'various' refers to rice (fortified with multiple micronutrients folate +pro-vitamin A+zinc+iron; excl. 3 R&D studies on multi-biofortification or one of pro-vitamin A, folate, vitamin C, vitamin E, iron, zinc or copper), corn (fortified with pro-vitamin A, folate, vitamin C, vitamin E or iron) and potato (fortified with pro-vitamin A, vitamin C or vitamin E). The targeted multi-biofortified crop contains transgenic (pro-vitamin A or folate) and conventional traits (zinc or iron). The 'cookie' is made from transgenic wheat (vitamin E). Several studies examine different micronutrients, crops and/or outcome indicators. For detailed information, see **Supplementary Tables 2, 3 and 5.**

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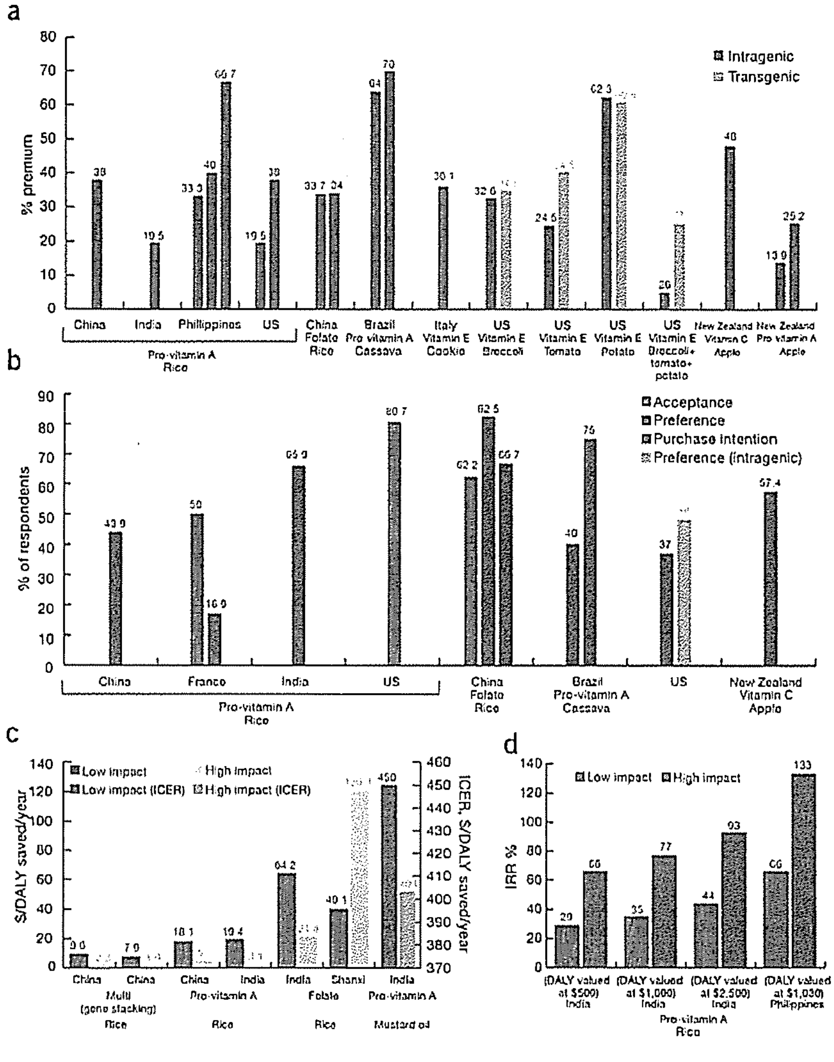

Figure 3 Market potential of biofortified crops. (**a**) Willingness to pay (percentage premium). (**b**) Percentage of respondents with acceptance of, purchase intention for and preference for, transgenic and intragenic biofortified crops, per target crop, micronutrient and country. Premium and preference levels are compared with a conventional, non-GM crop. Multiple blue or purple bars for one country refer to premium differences within (Brazil) or among studies (China and Philippines), except for willingness-to-pay premiums for pro-vitamin A apples in New Zealand, which were compared with apples treated with vacuum-infiltration of apples with vitamin A and irradiation (UV-treatment boosts the production of vitamin A in the latest stage of apple development), respectively. Preference levels exclude the group of indifferent respondents. Purchase intentions refer to the share of respondents that is prepared to pay a premium. All values are based on a sample of . adults, except for the studies in the Philippines (students) and one study in China (34.0% and 62.2% women of childbearing age). Values based on partial data sets are not presented. (**c**) Cost effectiveness and (**d**) cost-benefits of transgenic biofortified crops. Impact scenarios differ in terms of efficacy (e.g., improved micronutrient content, post-harvest losses and, in the case of pro-vitamin A, bioavailability) and estimated market coverage (i.e., consumption levels), by which low-impact scenarios are rather pessimistic compared with the more optimistic high-impact scenarios. Shanxi Province is a high-risk region of folate deficiency in China. $/DALY refers to the monetary cost to save one DALY. The internal rate of return (IRR) is a common measure to evaluate the economic feasibility of an intervention by calculating the annual percentage yield for each dollar invested. The IRRs on biofortification attach a monetary value to one DALY saved (i.e., $500, $1,000 or $2,500 in India or the national per capita income in the Philippines, $1,030). Only interventions with an IRR that exceeds the cost of capital (i.e., the minimum required return of the investments or 10–12% for health-related projects[32]) are worth implementing. Incremental cost-effectiveness ratio (ICER) figures (right *y* axis) represent the additional cost to save a DALY when choosing biofortification over supplementation. Data from **Supplementary Dataset**.

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With respect to biofortified rice in India and China, for example, all market-share figures obtain a level above 60%, except for a study in urban China, where 43.9% of respondents still intend to purchase Golden Rice. When also taking the share of indifferent consumers into account (**Supplementary Table 4**), transgenic biofortified crops appear to be commercially viable.

To date, all macrolevel analyses have studied rice, enriched with pro-vitamin A (two studies), folate (two studies) or a combination of micronutrients (i.e., pro-vitamin A, folate, zinc and iron), with the exception of one on pro-vitamin A–biofortified mustard oil (Fig. 3c). Studies on folate- and multibiofortified rice were conducted for China and, in the case of the former in Shanxi, Shanxi Province, where there is high risk for folate deficiency, whereas India and the Philippines were selected for evaluating the potential introduction of Golden Rice and/or mustard oil, respectively.

All studies build upon the disability-adjusted life year (DALY) framework to measure the burden of micronutrient deficiencies (in DALYs lost per year) on the one hand, and to determine the potential health benefits of transgenic biofortified crops (in DALYs gained per year) on the other. DALY is a health measure that describes both mortality and morbidity associated with a health condition (e.g., vitamin deficiency) as a single index: years of life lost plus years lived with disability. To evaluate whether the resources that accrue from the implementation justify the health impacts, six cost-effectiveness and two cost-benefit analyses were undertaken (**Supplementary Table 5**).

When comparing the potential health benefits of introducing transgenic biofortified crops, substantial differences exist between the targeted products, micronutrients and countries (for disease burden and health impact figures, see **Supplementary Table 6**). Golden Rice, for example, has the potential to lower the burden of vitamin A deficiency in China, India and the Philippines by 17–60%, 9–59% and 6–32%, respectively. In China, both folate deficiency and micronutrient malnutrition can be reduced by, respectively, 20–82% and 11–46% when folate-biofortified or multi-biofortified (pro-vitamin A, folate, iron and zinc-enriched) rice is placed on the market. And when it comes to saving lives, Golden Rice and mustard oil both would have a substantial impact, which is largely attributable to the strong association between vitamin A deficiency and child mortality.

The cost effectiveness of enhancing several micronutrients simultaneously is by far the most promising option because it generates aggregated health benefits at a relatively low additional cost ($1.9–9.6 per DALY saved); followed by Golden Rice and folate-biofortified rice (**Fig. 3c**). Even so, all transgenic, biofortified rice varieties fall well below the standard benchmark for evaluating micronutrient interventions (i.e., the upper boundary for highly cost-effective interventions of $267.4 per DALY saved in 2013, as set by the World Bank[25]). This demonstrates that from a public health perspective, these interventions are a worthwhile undertaking. Moreover, the generally low (recurrent) costs are often put forward as a major advantage. Even if biofortification is expected to be more costly than supplementation, which is the case for Golden mustard oil, its potential health impact is (among) the highest. Cost-benefit analyses, though conducted only for Golden Rice in India and the Philippines (**Fig. 3d**), further support the sizable health benefits of transgenic biofortified crops and justify the $15.7-million and $21.4- to 27.9-million investments to put Golden Rice on the Indian and Philippine market, respectively (for cost figures, see **Supplementary Dataset**). Although caution is needed when interpreting these findings, owing to crop-, micronutrient- and country-dependent data assumptions and methodological choices, they all confirm the market potential of transgenic biofortification research.

Given the market potential of transgenic biofortified crops, their cost effectiveness and the positive consumer reactions, one might argue that their authorization could break the legacy of first-generation GM crops and become a catalyst for the adoption of transgenic crops in the future. According to a recent review on GM rice, for example, the global value of the second-generation varieties that are currently in the R&D pipeline amounts to about $56 billion per year[26]. Golden Rice, in particular, of which delayed adoption in Asia alone results in an annual economic loss of about $16 billion, would generate large welfare gains that outweigh those of first-generation GM rice varieties[27]. Nevertheless, to successfully market such crops, an (economic) incentive should be provided to farmers. Therefore, the targeted micronutrient trait should be crossed into high-yielding varieties, as intended for Golden Rice in the Philippines[28]. Improving both micronutrient and yield traits will increase the likelihood of farmer adoption, as such crops deliver benefits for consumers and, both directly and indirectly, for farmers. A humanitarian license, similar to 'future' Golden Rice[29], or a governmental subsidized credit for seed purchases should also be considered.

At a time of repeated delays in Golden Rice commercialization, despite the extensive campaigning to reverse this trend (e.g., see the recent launch of the Allow Golden Rice Society), research continues to produce important new transgenic biofortification traits and economists demonstrate their market potential. Notwithstanding the positive outcomes in both fields, the anti-GM organisms lobby continues to block the introduction of these products. Meanwhile, the hidden hunger of micronutrient deficiencies remains a major public health problem, calling for alternative strategies that aim to help those who need it the most. Though using staple crops for transgenic biofortification is an appropriate strategy to reach poor, malnourished populations, these crops remain a meager source of various other untargeted micronutrients.

Certainly, transgenic biofortification is not a panacea for eliminating malnutrition[30], but it does offer a complementary, cost-effective intervention. In this context, we hope the data presented in this study can be used constructively not only by those developing biofortified crops, but also by those seeking a combined approach to reduce the burden of micronutrient malnutrition.

Note: Any Supplementary Information and Source Data files are available in the online version of the paper.

COMPETING FINANCIAL INTERESTS
The authors declare no competing financial interests.

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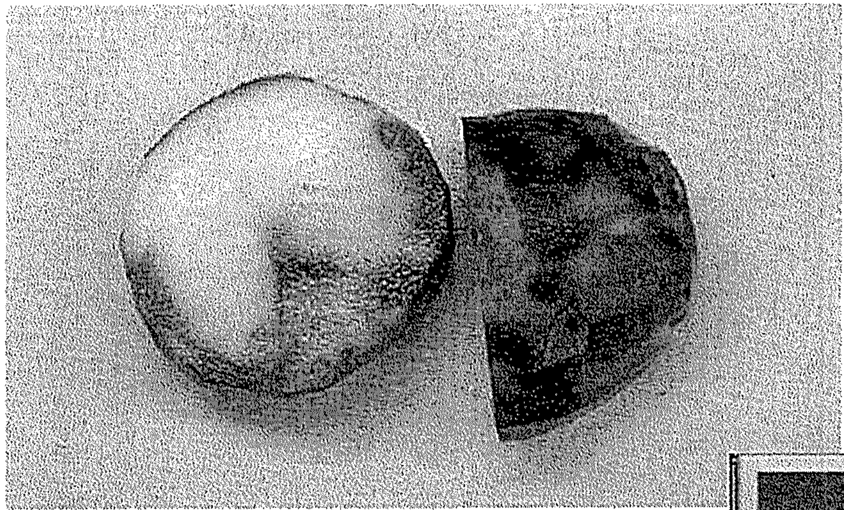
Exemplars of the pipeline of new plant GMOs and their traits

Irish potato blight – famine and emigration



Potato infested with
phytophthora infestans

Saving trees

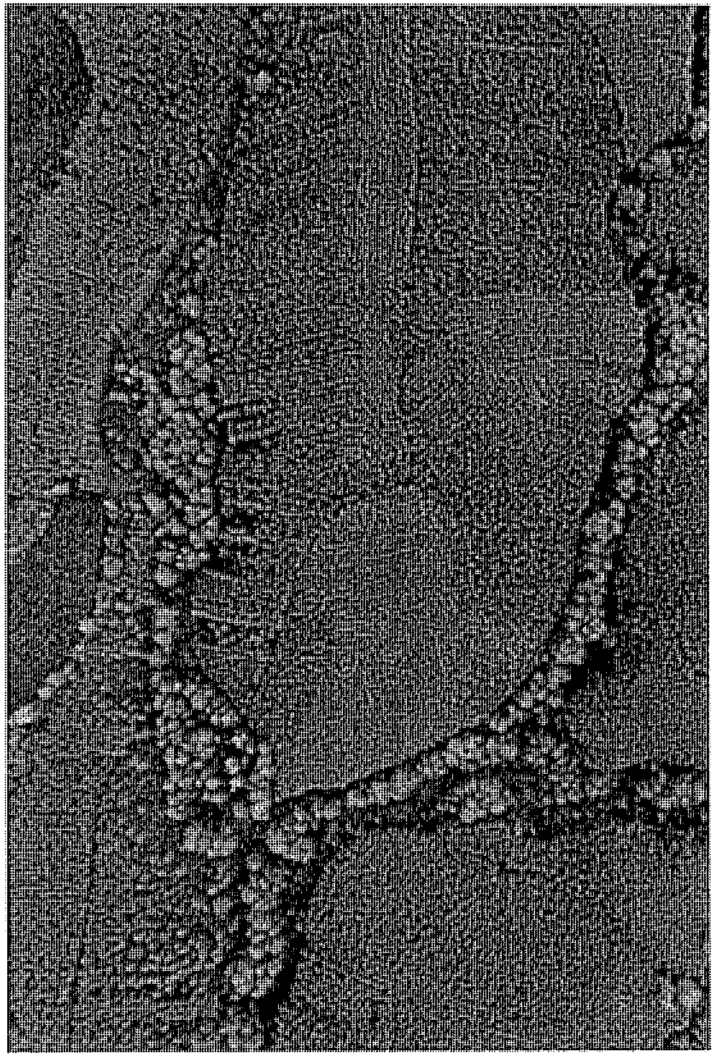
American chestnut was an iconic, keystone forest tree in the USA

It became extinct as a forest tree by Chestnut Blight

GM technology is being used to reinstate chestnut in forests

Commercial release of biotech trees

- Brazil: ~4m hectares Eucalyptus;
  - Suzano, Brazil (500,000ha Euc, sells to Europe, partners in China, Thailand, Sth Africa), 2015-6 release of biotech Euc=increase wood mass 20%, harvest 5 years;11 years field trials 100ha plots, 3 countries. Less land, more wood.
- US: plantation pine and Eucalyptus
  - ArborGen, US, application to release freeze tolerant Euc. Many field trial sites; US, Brazil. Targets altered lignin, sterility, drought tolerance, bioenergy. Recent partners for water and N use efficiency
- China: 1m BT poplar planted (490ha)



scion forests · products · innovation

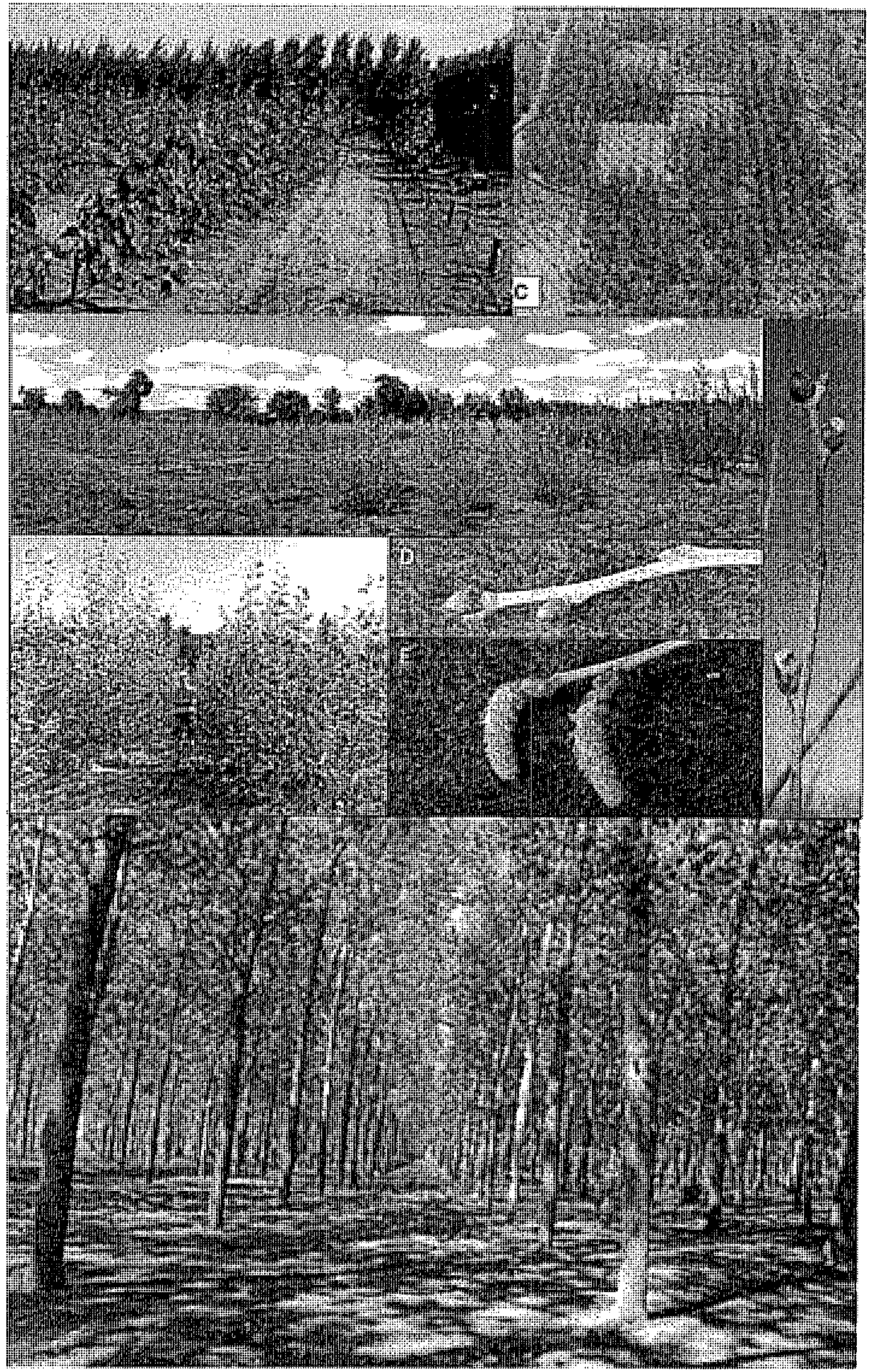
Biotech trees

>700 field trials of GM trees globally, eg

- herbicide tolerance
- sterility
- wood-pulp properties (better products)
- more biochemicals
- pest resistance
- disease resistance
- wood density
- growth rates
- cold tolerance
- yield improvements
- drought resistance

Swetree (Sweden, Brazil, China): screened >1000 genes; 35 in field trials Eucalyptus, poplar

EU: Belgium, Poland, Sweden, Finland



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Production of first and second generation biofuels: A comprehensive review

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ABSTRACT

Sustainable economic and industrial growth requires safe, sustainable resources of energy. For the future re-arrangement of a sustainable economy to biological raw materials, completely new approaches in research and development, production, and economy are necessary. The 'first-generation' biofuels appear unsustainable because of the potential stress that their production places on food commodities. For organic chemicals and materials these needs to follow a biorefinery model under environmentally sustainable conditions. Where these operate at present, their product range is largely limited to simple materials (i.e. cellulose, ethanol, and biofuels). Second generation biorefineries need to build on the need for sustainable chemical products through modern and proven green chemical technologies such as bioprocessing including pyrolysis, Fisher Tropsch, and other catalytic processes in order to make more complex molecules and materials on which a future sustainable society will be based. This review focus on cost effective technologies and the processes to convert biomass into useful liquid biofuels and bioproducts, with particular focus on some biorefinery concepts based on different feedstocks aiming at the integral utilization of these feedstocks for the production of value added chemicals.

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Contents

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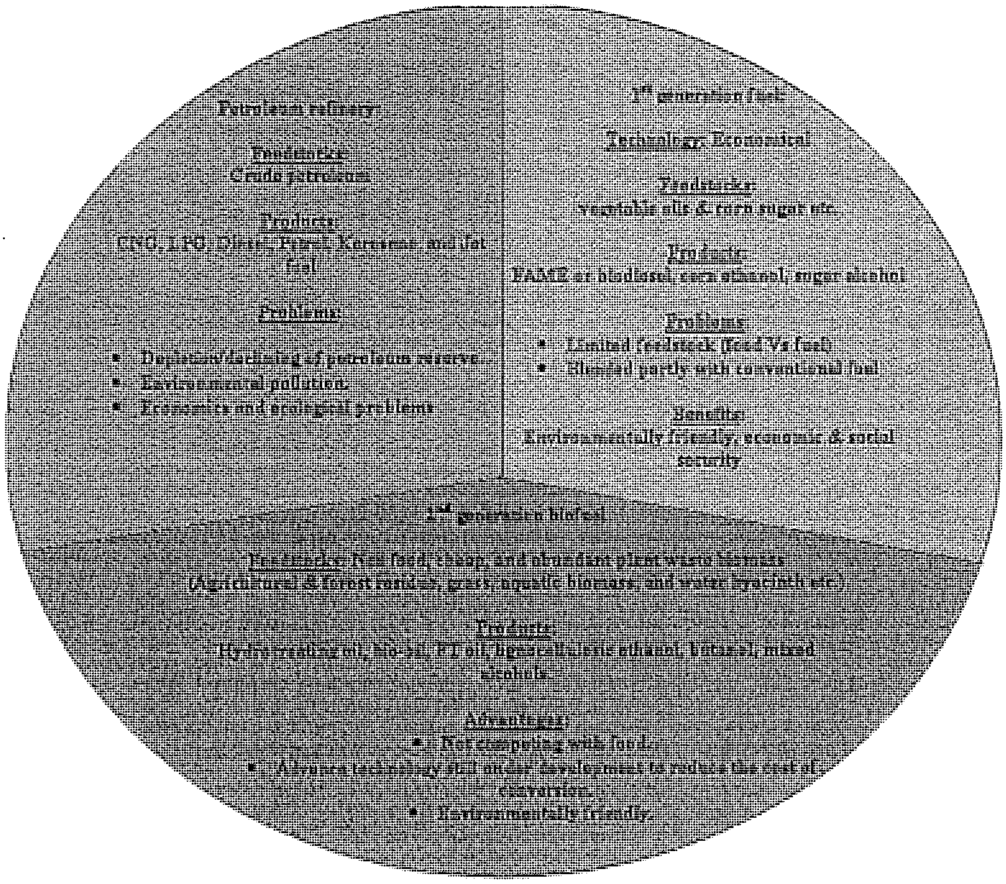


Fig. 1. Comparison of first, second generation biofuel and petroleum fuel.

to review the literature on first and second generation biofuels and anticipated biochemicals from the non-food crop biomass. In this respect, the present paper is a part of research program aiming at the integrated utilization of Jatropha in India and cereal crop residues in Canada, attempting to contribute to the first generation biofuels production (i.e. biodiesel) and parallel use of the residues for energy and 2nd generation biofuels production. In addition some biorefinery concepts based on different biomass feedstocks for 2nd generation biofuels and their bioproducts with example have been discussed.

2. Biomass as multiple feedstocks for biorefinery

Biomass derived from trees, agro-forest residues, grasses, plants, aquatic plants and crops are versatile and important renewable feed stock for chemical industry as shown in Fig. 2. Through photosynthesis process, plants convert carbon dioxide and water in to primary and secondary metabolite biochemicals. Both of these are industrially important chemicals. Primary metabolites are carbohydrate (simple sugar, cellulose, hemicellulose, starch, etc.) and lignin called lignocellulose present in high volume in biomass. The lignocellulosic biomass can be converted into biofuels. The secondary metabolite are high value biochemicals such as gums, resins, rubber, waxes terpenes, tepenoids, steroids, triglyceride, tannin, plant acids, alkaloids, etc. are present in low volume in the plants [15]. The secondary metabolites can be utilized for production of high value chemicals such as food flavors, feeds, pharmaceuticals, cosmoceuticals, and nutraceutical, etc. using integrated processing technique.

Enhancement of biomass utilization requires tremendous effort to develop new biomass systems in which production, conversion and utilization of biobased products are carried out efficiently in near harmony with nature [6]. However, success depends on how far it is possible to change today's production of goods and services gradually from fossil to biological raw materials. Therefore many researchers around the World are working on the development of possible biomass integrated conversion technologies. For example, Huang et al. [14] reviewed on separation methods and technologies related to lignocellulosic biorefineries for production of ethanol and other products. The paper critically has reviewed the current and future technologies used for corn to ethanol biorefinery, lignocellulosic biomass to ethanol biorefinery, integrated lignocellulose/forest biorefinery (ILCB), pre extraction of hemicellulose and other value added chemicals (corn germ, fiber, zein or gluten from corn–ethanol plant), detoxification of fermentation hydrolyzates, and ethanol product separation and dehydration. For future biorefineries separation processes like extractive distillation with ionic liquids and hyperbranched polymers, adsorption with molecular sieve and biobased adsorbents, nanofiltration, extractive-fermentation, membrane pervaporation in bioreactors, and vaccum membrane distillation (VMD) hold significant potential and great promise for further investigation, development and application. Clark et al. [16] reported the use of green chemical technologies to transform low value waste biomass to green chemicals like, waxes and ethanol, etc. However, Chew et al. [17] have reported on different types of catalysts and their role in the catalytic processes for production of biofuels in a typical palm oil and oil palm based refinery in Malaysia. Rowlands et al. [18] reported the biorefinery challenges,

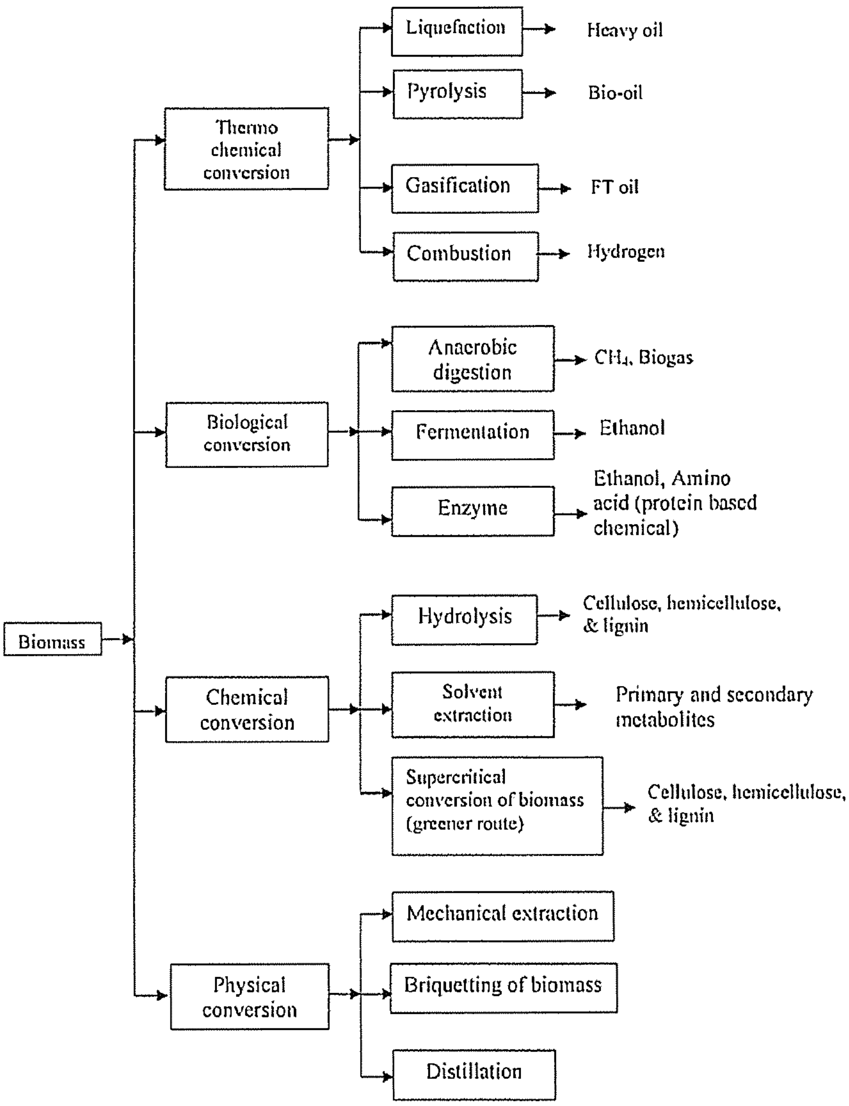


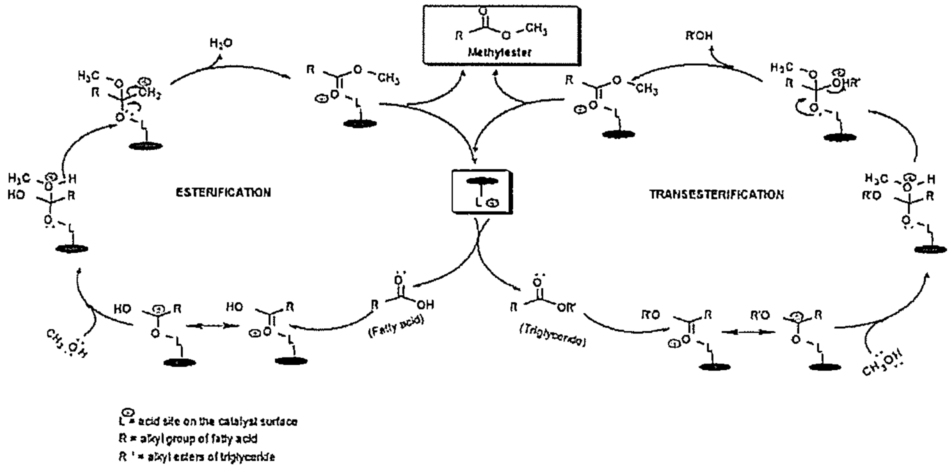
Fig. 3. Biomass conversion processes.

(bio-esters), ethanol, and biogas of which world wide large quantities have been produced so far and for which the production process is considered 'established technology'. Biodiesel is a substitute of diesel and is produced through transesterification of vegetable oils, and residual oils and fats, with minor engine modifications; it can serve as a full substitute as well. Bioethanol is a substitute of gasoline and it is a full substitute for gasoline in so-called flexi-fuel vehicles. It is derived from sugar or starch through fermentation. Bioethanol can also serve as feedstock for ethyl tertiary butyl ether (ETBE) which blends more easily with gasoline. Biogas, or biomethane, is a fuel that can be used in gasoline vehicles with slight adaptations. It can be produced through anaerobic digestion of liquid manure and other digestible feedstock. At present, biodiesel, bioethanol and biogas are produced from commodities that are also used for food. The demands of edibles oils are increasing trend, so it difficult to use the agricultural food crop for biofuel production [22]. There are some potential crops for biodiesel production, which can be taken up as Industrial crop on unproductive lands. Such multipurpose uses oilseeds crops can be introduced, so that the biomass produced by them can be utilized for production of various bioproducts. In that respect, example of whole crop biorefinery as shown in Fig. 4, has been discussed aiming at the integrated utilization of Jatropha in India, attempting to contribute to sustainable biodiesel production and parallel use of its solid residues for production of other valuable chemicals and utilization of its lignocellulosic biomass for 2nd generation biofuels production.

3.1. Conversion processes for first generation biofuels

3.1.1. Transesterification

The vegetable oil based fatty acid methyl esters (FAME), popularly known as biodiesel, is gaining importance as an environment-friendly diesel fuel substitute or extender. Biodiesel is an alternative diesel, made from renewable biological sources such as vegetable oils and animal fats by chemically reacting oil or fat with an alcohol, in the presence of a homogeneous and heterogeneous catalyst. The product of the reaction is a mixture of methyl esters, which are known as biodiesel, and glycerol, which is a high value co-product [23,24].



Scheme 1. Solid acid catalyzed simultaneous esterification and transesterification [23].

nucleophilic attack of alcohol to the carbocation produces a tetrahedral intermediate (Scheme 1). During esterification the tetrahedral intermediate eliminates water molecule to form one mole of ester ($RCOOCH_3$). The transesterification mechanism can be extended to tri- and di-glyceride. It is well known that transesterification is a stepwise reaction. In the reaction sequence the triglyceride is converted stepwise to di- and monoglyceride and finally glycerol. The tetrahedral intermediate formed during reaction eliminates di-, monoglyceride and glycerol when tri-, di- and monoglyceride come in contact with the acidic sites, respectively, to give one mole of ester ($RCOOCH_3$) in each step. In cases, esterification and transesterification produce methyl ester, the same final product. Also, as shown in Scheme 1, the catalyst is regenerated after the simultaneous esterification and transesterification reactions. Use of excess alcohol favors forward reaction and thus maximizes the ester yield [23].

3.1.1.3. Ethanol conversion processes. A wide variety of carbohydrates containing raw materials have been used for production of ethanol by fermentation process. These raw materials are classified under three major categories:

(a) Sugar containing crops: Sugar cane, wheat, beet root, fruits, palm juice, etc.
(b) Starch containing crops: Grain such as wheat, barely, rice, sweet sorgum, corn, etc. and root plants like potato, cassava.
(c) Cellulosic biomass: Wood and wood waste, cedar, pine, wood, etc. agricultural residues, fibers.

The alcohol produced from food crops like corn, wheat, barley, sweet sorgum is called grain alcohol, where as ethanol produced from lingo-cellulosic biomass such as agro residue (i.e. rice straw, wheat straw) grasses (switch grass) is known as biomass ethanol or bioethanol. Both these alcohols are produced through biochemical process [25].

Chemical structure of starch consists of long chain polymer of glucose. The macromolecular starch cannot be directly fermented to ethanol by conventional fermentation technology. The macromolecular structure first broke down in to simpler and smaller glucose. In this process, starch feedstocks are grounded and mixed with water to produce a mash typically contained 15–20%starch. The mash is then cooked at or above its boiling point and treated subsequently with two enzyme preparation. The first enzyme hydrolyzes starch molecules to short chains to glucose. The first enzyme is amylase, amylase liberates "maltodextrin" oligosaccharides by liquefaction process. The dextrin and oligosaccharides are further hydrolyzed by enzyme such as pullulanase and glucoamylase in a process known as saccharification. Saccharification converts all dextrans to glucose, maltose and isomatose. The mash is then cooled to 30 ßC and yeast is added for fermentation [26].

Ethanol production is usually obtained via enzymatic hydrolysis of starch containing crops like corn wheat. Corn ethanol production facilities can be classified into two groups i.e. wet &dry mill processes [25]. Dry mills are usually smaller in size (capacity) and are built primarily to manufacture ethanol only. According to Shapouri et al. [27] modern wet milling plants are able to produce 1 gal ethanol consuming 35150 Btu of thermal energy and 2134 KWh of electricity. If molecular sieves are used the thermal energy input drops to 32150 Btu/gal. The starch grain is prepared for ethanol fermentation by either wet milling or dry grinding as shown in Fig. 5a and b. Wet mill ethanol process produced variety of valuable coproducts such as nutraceuticals, pharmaceuticals, organic acids and solvent. Dry grinding mill process is specially designed for production of ethanol and animal feed.

3.1.1.4. Fermentation process. The term fermentation can generally be defined as the metabolic process in which an organic substrate

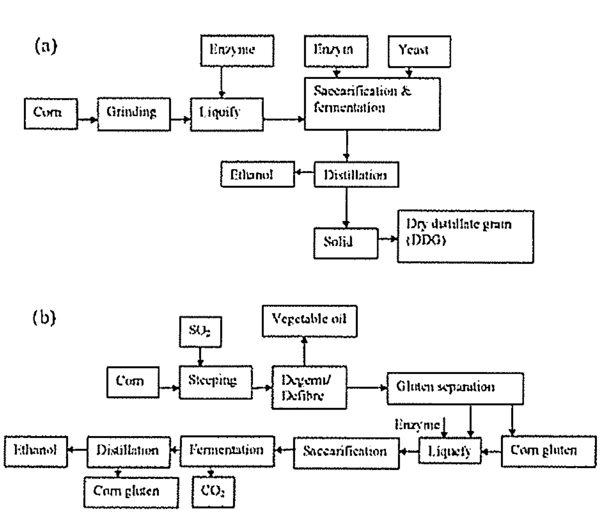


Fig. 5. (a) Dry mill process and (b) Wet mill process.

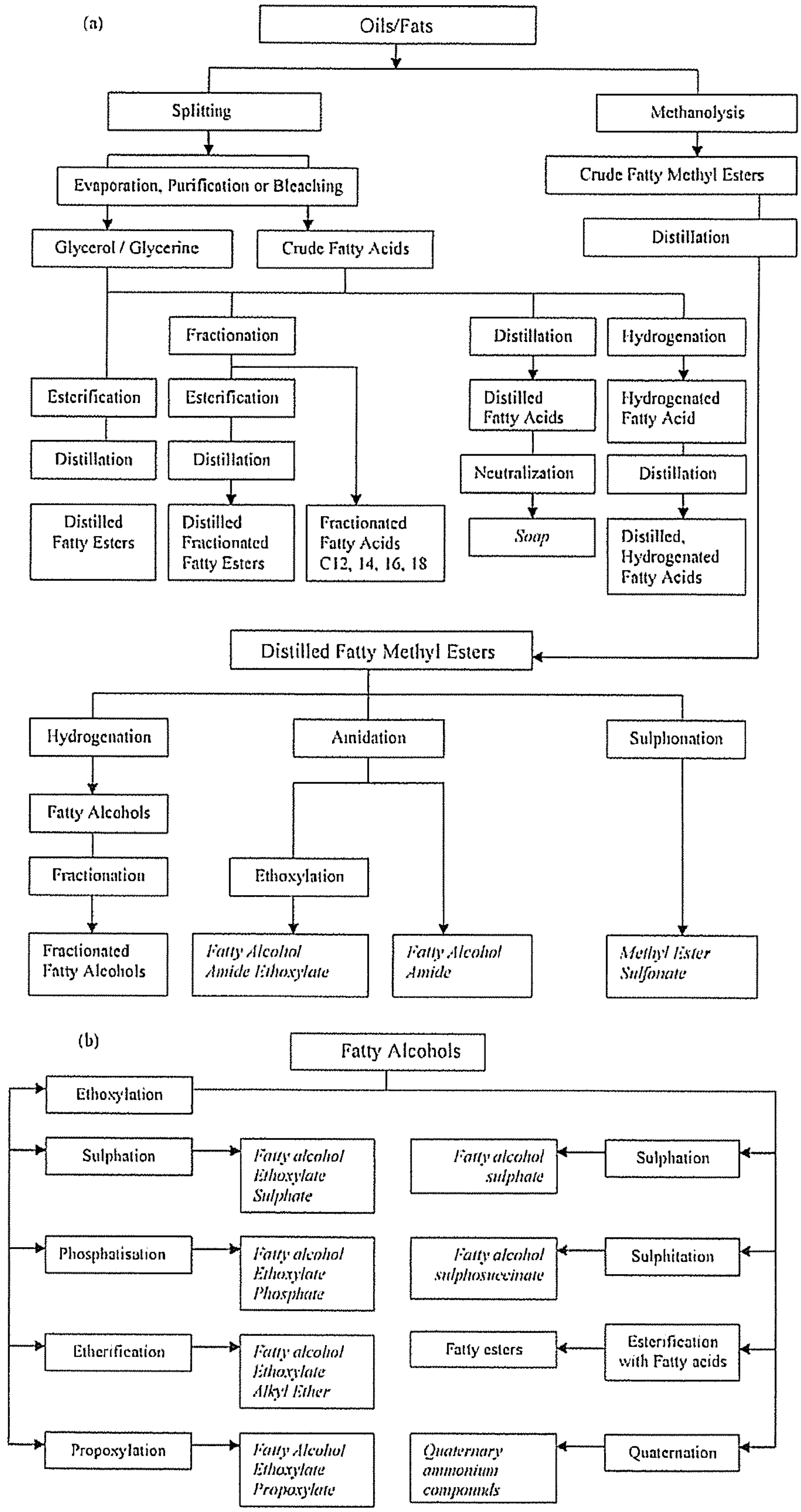


Fig. 7. (a) Basic oleochemicals and downstream oleochemicals and derivatives and (b) basic oleochemicals and downstream oleochemicals and derivatives production flow.Soon [29].

hydrolysis, sugars are extracted from lignocellulosic feedstock, after which the sugars are fermented into ethanol. Fischer–Tropsch diesel (FT-diesel) or BTL (Biomass-to-Liquids) is a full substitute of diesel. Lignocellulosic biomass is gasified to produce syngas which is in turn transformed into liquid hydrocarbons, mostly diesel and kerosene. Bio-SNG (Synthetic Natural Gas) is a fuel that can be used in gasoline vehicles with slight adaptations. Lignocellulosic biomass is gasified to produce syngas which is in turn transformed into methane. Bio-DME (Dimethyl Ether) is a fuel that can be used in diesel vehicles with slight adaptations. Lignocellulosic biomass is gasified to produce syngas which is in turn transformed into DME [33].

4.1. Conversion processes for second generation biofuels

There are two main routes available for producing liquid biofuels from biomass; one involves thermochemical processing and the other biochemical processing. Thermochemical processing defines the conversion of biomass into a range of products, by thermal decay and chemical reformation, and essentially involves heating biomass in the presence of different concentrations of oxygen. The clear advantage of thermochemical processing is that it can essentially convert all the organic components of the biomass compared with biochemical processing which focuses mostly on the polysaccharides [11]. This section onwards paper mainly focuses on the conversion processes for lignocellulosic biomass and utilization of combination of technologies for production of other value added chemicals (Fig. 9) and example of some biorefineries based on different feedstocks have been discussed aiming at the integrated utilization of biomass.

4.1.1. Physical conversion

4.1.1.1. Mechanical extraction. Crude vegetable oils are recovered from the oil seeds by applying a mechanical pressure using screw press (expeller). Screw press can be applied in two ways: pre-pressing and full pressing. In pre-pressing, only part of the oil is recovered and the partially de-oiled meal (cake with 18–20%oil) is further treated by solvent extraction. Combined pre-pressing and solvent extraction is commonly applied for oilseeds with high oil content (30–40%). Full pressing requires 95,000 kPa to squeeze out as much oil as possible, preferably up to 3–5% residual fat for animal materials. Full-pressing can also be carried out in a pre-press and a final press [7].

4.1.1.2. Briquetting of biomass. Agricultural, forestry residues and other waste biomass materials are often difficult to use as biofuels because of there uneven bulky and troublesome characteristics. This draw back can be overcome by means of densification of the residual into compact regular shapes. During densification biomass enclosed in compression chambers presses. There are two major methods of densification, i.e. pressing and maceration. Some time these two processes are combined, in pressing there is a close correlation of an increase in density with an increase in applied pressure in the early stage of compression, but the rate of increase in density fall rapidly as the density of pressed material approaches the density of water. There is no such close correlation of density change and degree of maceration, which may be chopping, grinding, and pulverizing. A coarse chopping of some materials may be as effective as ultrafine grinding. For example tree branches undergo extensive volume reduction when chipped, but fine grinding would provide little, if any, additional reduction in volume [6,7].

4.1.1.3. Distillation. Distillation is the most important method for extracting essential oil and relies on the evaporation of the more volatile constituents of a blend to separate them from the non-volatile parts. Plants are crushed to encourage them to release their oils. The plants are steam distilled, and the essential oils vaporize and rise up with the steam. The vapours are captured, and are allowed to condense back into liquids. A more high tech chemical process is molecular distillation. It is used to produce fragrances that cannot be distilled by conventional methods [7].

4.1.2. Thermo-chemical conversion

Biomass can be converted to energy by mainly two processes. They are either thermo-chemical or biological. The thermo-chemical conversion process includes direct combustion, gasification, liquefaction, and pyrolysis as shown in Fig. 10. When biomass is heated under oxygen deficient conditions, it generates synthesis

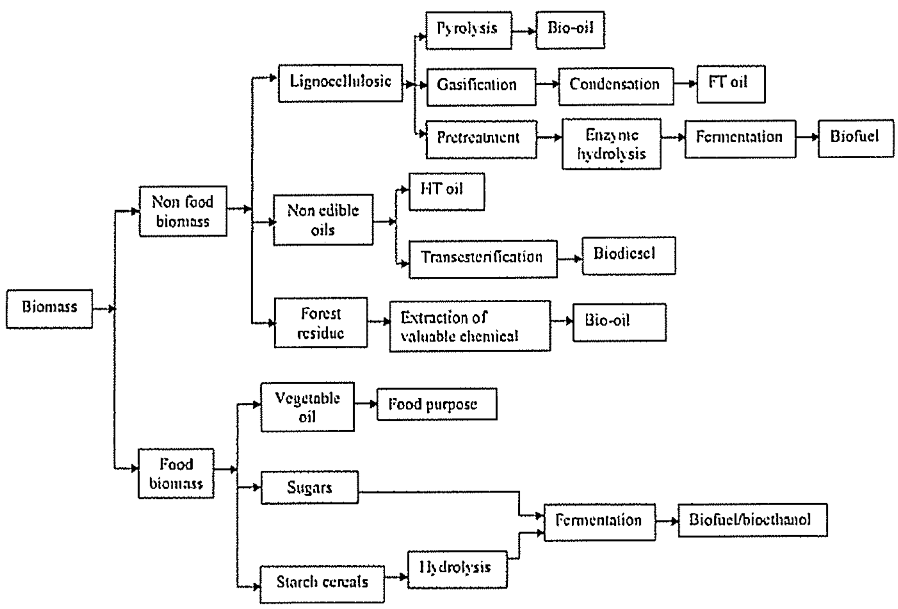


Fig. 9. Second generation biofuel production from biomass.

power [35]. Depending on the operating conditions, the pyrolysis process can be divided into three subclasses: (a) Conventional pyrolysis, (b) Fast pyrolysis, and (c) Flash pyrolysis.

4.1.2.4.1. Conventional pyrolysis. Conventional pyrolysis occurs under a slow heating rate (0.1–1 K/s) and residence time is 45–550 s and massive pieces of wood. In the first stage of biomass decomposition which occurs in between 550 and 950 K is called pre-pyrolysis. During this stage, some internal rearrangement such as water elimination, bond breakage, appearance of free radicals, formation of carbonyl, carboxyl and hydroperoxide group take place [37]. The second stage of solid decomposition corresponds to the main pyrolysis process. It proceeds with a high rate and leads to the formation of pyrolysis products. During the third stage, the char decomposes at a very slow rate and it forms carbon rich solid residues.

4.1.2.4.2. Fast pyrolysis. It occurs in the high temperature range of 850–1250 K with fast heating rate (10–200 K/s), short solid residence time (0.5–10 s) and fine particle (<1 mm). The fast pyrolysis is recommended for production of liquid and/or gaseous products. In fast pyrolysis process biomass decomposes to generate vapours, aerosol, and some charcoal like char. After cooling and condensation of vapours and aerosol a dark brown mobile liquid is formed that has heating value that is half that of conventional fuel oil. Fast pyrolysis produced 60–75% of bio-oil, 15–25% solid char and 10–20% non condensed gases depending upon feedstocks [37].

4.1.2.4.3. Flash pyrolysis. It differs strongly from that of conventional pyrolysis, which is performed slowly with massive pieces of wood. It occurs in the temperature range of 1050–1300 K, fast heating rate (>1000 K/s), short residence time (<0.5 s) and very fine particle (<0.2 mm). Bio-oil production from biomass pyrolysis is typically carried out via flash pyrolysis [35] the produced oil can be mixed with the char to produce bioslurry. Bioslurry can be more easily fed to the gasifier (gasifier condition: 26 bars; 927–1227 K) for efficient conversion to syngas. The conversion of biomass to crude oil can have an efficiency of up to 70% for flash pyrolysis process. The so called bio-crude can be used in engines and turbines. Its use as feedstocks for refineries is also being considered [35,38].

4.1.3. Hydrotreating of vegetable oils/green diesel

Vegetable oils are renewable feedstock currently being used for production of biofuels from sustainable biomass resources. The existing technology for producing diesel fuel from plant oils such as rapeseed, soybean, canola and palm oil are largely centered on transesterification of oils with methanol to produce fatty acid methyl esters (FAME) or biodiesel. The future widespread use of biofuels depends on developing new process technologies to produce high quality transportation fuels from biologically derived feedstocks. These new biofuels need to be compatible with the existing fuel and transportation infrastructure to be economically feasible.

Researchers around the world are in pursuit of different processing routes to convert vegetable oils into a high quality diesel fuel or diesel blend stock that would fully compatible with petroleum derived diesel fuel. The isoparaffin-rich diesel known as 'green diesel' is produced from renewable feedstock containing triglycerides and fatty acids by process of catalytic saturation, hydrodeoxygenation, decarboxylation and hydroisomerization. This technology can be widely used for any type of oil feedstock to produce an isoparaffin-rich diesel substitute. This product, referred to as green diesel, is an aromatic and sulfur free diesel fuel having a very high cetane blending value. The cold flow properties of the fuel can be adjusted in the process to meet climate-specific cloud point specifications in either the neat or blended fuel [39]. Table 2 compares the Green diesel fuel properties with petroleum diesel, and biodiesel. Green diesel has a higher cetane value and good cold flow properties. It is also has excellent storage stability and is completely compatible for blending with the standard mix of petroleum derived diesel fuels. In contrast to fatty acid methyl esters, green diesel properties do not depend on feed origin and process configuration and the fully deoxygenated biofuel is readily blended with diesel fuel.

Table 2
Green diesel fuel properties.

	Petroleum ULSD	Biodiesel (FAME)	Green diesel
%oxygen	0	11	0
Specific gravity	0.84	0.88	0.78
Sulphur (ppm)	<10	<1	<1
Heating value (MJ/kg)	43	38	44
Cloud point (8C)	−5	−5 to +15	−10 to 20
Distillation (8C)	200–350	340–355	265–320
Cetane	40	50–65	70–90
Stability	Good	Marginal	Good

Kalnes et al. [39].
ULSD: is ultra low sulphur diesel.

4.1.4. Bio-oil

Bio-oil/pyrolysis oil is produced by fast pyrolysis process. In this process, organic class of compounds, such as cellulose, hemicellulose, and lignin, etc. are thermally decomposed at moderate temperature (400–600 8C) in absence of oxygen to produce liquid product viz. bio-oil (60–70%), char (13–25%), and gas such as CO, H_2, light hydrocarbons (13–25%). The yield and chemical composition of bio-oil depends upon feed stocks and process condition: particle size of biomass (2–5 mm), residence time (0.1–2 s), and reactor type. In general, reactor types which are presently used are; fluidized bed reactor, circulating fluid bed, fast fluidized bed, etc. (Fig. 11). The bio-oil is a dark brown viscous, corrosive and acidic with distinctive smoky odor used as fuel for boiler, gas turbine, diesel engines, furnaces and stationary engines. Bio-oil has a complex chemical composition contained chemical products of lignocelluloses biomass like aliphatic alcohols/aldehydes, furanoids, pyranoids, benzenoids, fatty acids and high molecular mass hydrocarbons, etc. these constituents are mixed with water (25–45%), which is formed in pyrolysis process to form an emulsion with organic constituents. Therefore a wide range of "Green

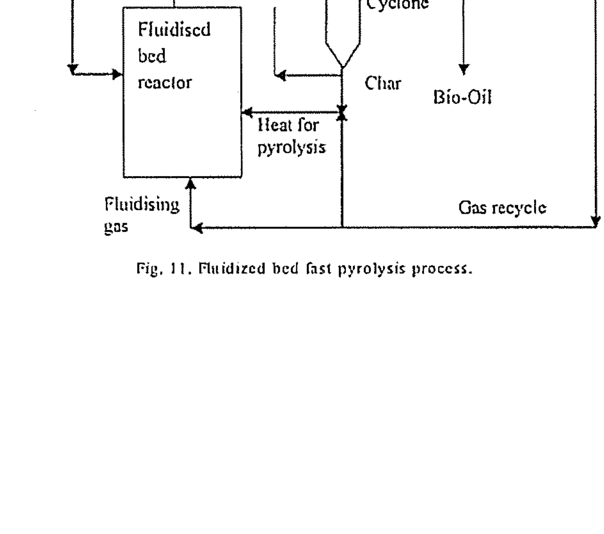


Fig. 11. Fluidized bed fast pyrolysis process.

vessel (i.e. digester) and vaporized using saturated steam for a short time (20 s to 20 min) at a temperature 473–543 K and high pressure 14–16 bar. The pressure in digester is then dropped quickly by opening the steam and the material is exposed to normal atmospheric pressure to cause explosion which disintegrate lignocellulosic biomass. Different types of devices are available for steam explosion. Steam explosion causes the hemicellulose and lignin from the wood to be decomposed and converted into low molecular weight fractions which can be easily extracted. Therefore most of the water soluble fraction of hemicellulose can be removed by water extraction. At the same time, a part of the low molecular weight fraction of lignin is also extracted. The xylose can be fermented to ethanol and the lignin can be further processed to produce other fuels. The crystalline cellulose remains solid after the pretreatment and later break down to glucose by enzymatic hydrolysis process. The glucose is further fermented to alcohol and the hemicellulose fraction is converted to xylose. The conversion of xylose to ethanol is a difficult process, therefore, pretreatment is necessary to reduce the crystallinity of cellulose to lessen the average polymerization of the cellulose and hemicellulose–lignin sheath that surround the cellulose and to increase available surface area for the enzyme to attack [25].

Ethanol can be blended with gasoline to produce an oxygenated fuel with lower hydrocarbon and green house gas emissions, certain aldehydes are increased, which could cause health issues. Automobiles can be operated on ethanol/gasoline blends from 5% to 25% without any alterations in engine equipments or setting [25]. The fuel properties of alcohol blended gasoline and pure gasoline are given in Table 4. The major engine operation issue with alcohol blended fuels is fuel quality, volatility, octane number, cold start, hot operation, and fuel consumption.

4.1.7. Chemical conversion

4.1.7.1. Chemical hydrolysis. The important specific factors in chemical hydrolysis are surface to volume ratio, acid concentration, temperature, and time. The surface to volume ratio is especially important, in that it also determines the magnitude of the yield of glucose. Hence smaller the particle size the better the hydrolysis in terms of the extent and rate of reaction. With respect to the liquid to solid ratio, the higher the ratio the faster the reaction [48].

4.1.7.2. Solvent extraction. Solvent extraction involves different unit operations: extraction of the oil from the oil seeds using hexane as a solvent; evaporation of the solvent; distillation of the oil–hexane mixture (called miscella); and toasting of the de-oiled meal. In special cases, other solvents can be used: halogenated solvents (mostly dichloromethane), acetone, ethanol or isopropanol. Supercritical extraction can also be performed using CO_2 [7].

Extraction refers to a process in which the desired substance is selectively removed from the raw materials by allowing the desired substance to dissolve into the solvent, and subsequently recovering the substance from the solvent. To remove the particular substance from biomass, extraction and separation are both essential. Typically biomass (wood, wheat straw, aromatic grasses, etc.) contains high volume of macromolecular compounds (polysaccharide, cellulose, hemicellulose, and lignin) called primary metabolite. The other low volume and high value biochemical molecules like terpenoids, waxes, resins, sterols, and alkaloids are known as secondary metabolites or extractive biomass. In the biorefinery process these chemicals are initially extracted from biomass by using solvent extraction or supercritical fluid extraction. Recently Dewarte et al. [49], Clark et al. [16] reported integrated straw based biorefinery and isolated high value chemicals like waxes, polycosanol, and sterol by using supercritical carbon dioxide. Supercritical fluid extraction can be used for extraction of aromatic woods (cedar wood, sadal wood, pine wood) to isolate extractives. The extracted lignocellulosic biomass is further used for hydrolysis and fermentation for production of biofuels. The other solvent like, ethanol, acetone, methanol, water can be used to isolate desired extractive from biomass [7].

Table 4
Fuel properties of ethanol, gasoline, blended gasoline.

Property	Ethanol	Gasoline	E_{10}	E_{20}
Specific gravity	0.79	0.72–0.75	0.73–0.76	0.74–0.77
Heating value	76000	117000	112900	109000
Vapor pressure	17	59.5	64	63.4
Oxygen content	35	0	3.5	7

Shelley [25].

4.1.7.3. Supercritical water conversion of biomass. A supercritical fluid is defined as a substance that is at temperature and pressure conditions which are above its vapour liquid critical point (for water it is 644 K and 22 MPa; for CO_2 it is 304 K and 7.4 MPa). At supercritical conditions a fluid is neither liquid nor gas as it can not be made to boil by decreasing the pressure at constant temperature, and it would not condense by cooling at constant pressure [50].

Supercritical fluid processing of biomass to chemicals represents an alternative path to acid hydrolysis, enzymatic hydrolysis of cellulose to sugars. With acid hydrolysis acid recovery is a costly and polluting issue. Enzymatic saccarification needs pretreatment of lignocellulosic biomass. Supercritical water can quickly convert cellulose to sugar and convert biomass into a mixture of oils, organic acids, alcohol and methane. In supercritical (i.e. 300–644 K; pressure 200–250 bar) and near critical state (523–573 K) acid (H^+) and base components (OH^-) of water are separate and dissolve in the biomass. The dissolved supercritical water breaks the bonds of cellulose and hemicellulose rapidly to produce small sugar molecules, glucose, xylose and oligosaccharide [51,52]. These properties make supercritical water a very promising reaction medium without using any catalyst for the conversion of biomass to value added products. The scheme of supercritical water conversion of biomass and integral utilization side streams of the process is shown in Fig. 14. Supercritical water gasification technology has been demonstrated for conversion of cellulose into glucose in the range of 10–20 s and above 45 s pyrolysis start. As temperature increases to 873 K supercritical water becomes strong oxidant and results in complete disintegration of the substrate structure by transfer of oxygen from water to the carbon atoms of the substrate. The hydrogen atom of water is set free and form hydrogen. Supercritical water also breaks the cellulosic bonds and also formed gaseous products. The typical overall reaction for biomass is as follows [53].

$$2C_6H_{12}O_6 + 7H_2O \rightarrow CO_2 + 2CH_4 + CO + 15H_2$$

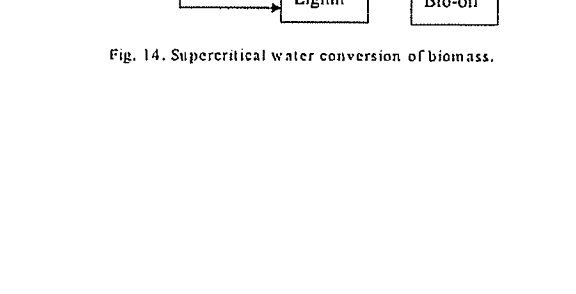


Fig. 14. Supercritical water conversion of biomass.

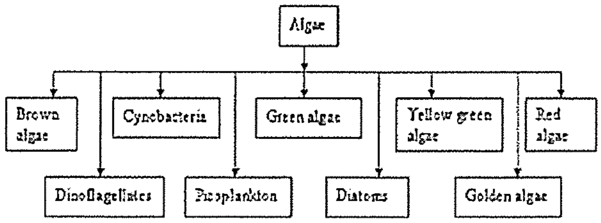


Fig. 17. Classification of algae species.

mainly uses hard fibrous plant materials generated by lumber or municipal waste. In the initial step plant material is cleaned and broken down into three fractions (hemicellulose, cellulose, and lignin) using chemical digestion or enzymatic hydrolysis. Hemicellulose and cellulose can be produced by alkaline (caustic soda) and sulfite (acidic, bisulfite, alkaline, etc.). The sugar polymers (cellulose and hemicellulose) are converted to their component sugars through hydrolysis. In case of hemicellulose, it consists of short, highly branched chains of sugars. It contains five carbon sugars usually D-xylose and arabinose, six carbon sugars and uronic acid. The hydrolysis of cellulose to glucose can be carried out either by enzymatic processing or chemical processing which produces useful products such as ethanol, acetic acid, acetone, butanol, and other fermentation products. Although the hemicellulose and cellulose fractions have numerous uses it is not yet the case for lignin. However, there are still some unsatisfactory parts within the LCB, such as utilization of lignin as fuel, adhesive or binder. It is unsatisfactory because the lignin scaffold contains considerable amounts of mono-aromatic hydrocarbons which, if isolated in an economical way, could add a significant value to the primary processes. Because the primary technologies would generate primary chemicals from which industry could make a wide range of fuels, chemicals, materials, and power. Therefore five stages have been suggested: sugar stage, thermochemical or syngas stage, biogas stage, carbon rich chains, and plant products. The concept of LCB based on these stages is described in Fig. 16.

5.3. Aquatic or algae-based biorefinery

Algae are photosynthetic microorganisms that convert sunlight, water and carbon dioxide to lipids or triacylglycerol. The lipids may include neutral lipids, polar lipids, wax esters, sterols and hydrocarbons as well phenyl derivatives such as tocopherols, cartenoids, terpenes, quinones, and phenylated pyrole derivatives such as chlorophylls. Algae have high growth rates and tolerance to varying environmental conditions. They can survive and reproduce in low quality high saline water [6]. This feature has allowed algae to be used in wastewater treatment plants for sludge treatment (Gray). In addition, since they have high CO_2 tapping and fixation ability, so the algae can be utilized to reduce carbon dioxide emission from power plants and other industries with high carbon dioxide emission [55]. Algae or cynobacteria can be used in bioreactors to reduce CO_2 emission from power plants and use the algae biomass for oil extraction and biodiesel production. There are over 40,000 species of algae have been identified and many more yet to be identified, algae are classified in multiple major groupings and its classification is shown in Fig. 17.

Algae synthesize fatty acids principally for esterification of glycerol based membrane lipids which constitutes about 5–20% of their dry cell weight (DCW). Fatty acids include medium chain (C_{10}–C_{14}), long chain (C_{16}–C_{18}) and very long chain (≥C_{20}) species of fatty acid derivatives. Hydrocarbons and other types of neutral lipid are found in algae at a quantity less than 5% Bortyococcus braunii has been shown to produce large quantities of (upto 80% DCW) of very long chain (C_{23}–C_{30}) hydrocarbons, similar to those found in petroleum and thus explored as feedstocks for biofuel and biomaterials. Oil content of some algae species exceeds 80% of the dry weight of algae [56]. Agricultural oil crops such as soybean, rapeseed and oil palm are widely used to produce biodiesel. For

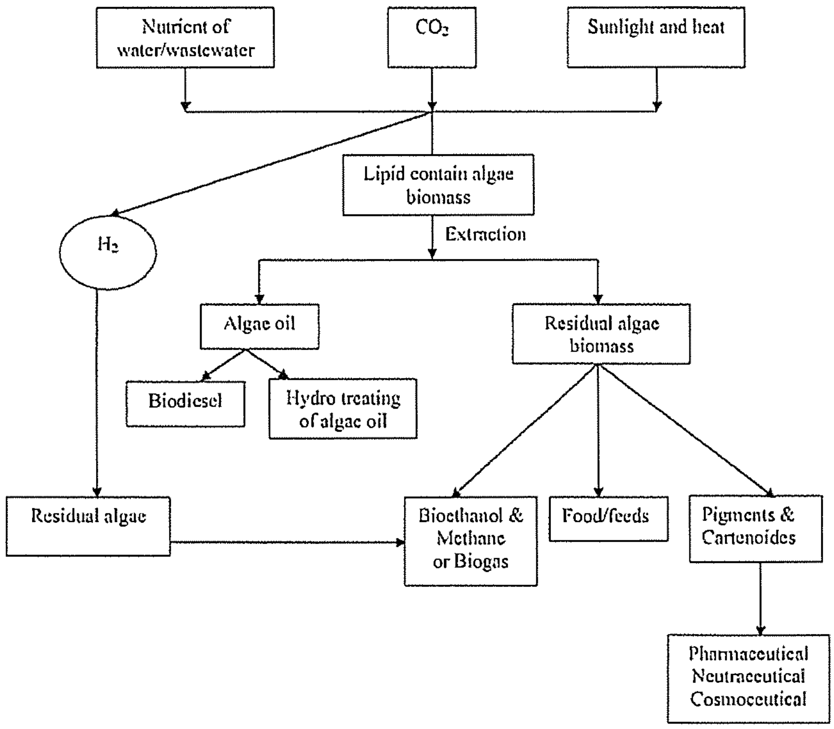


Fig. 18. Algae bio-refinery.

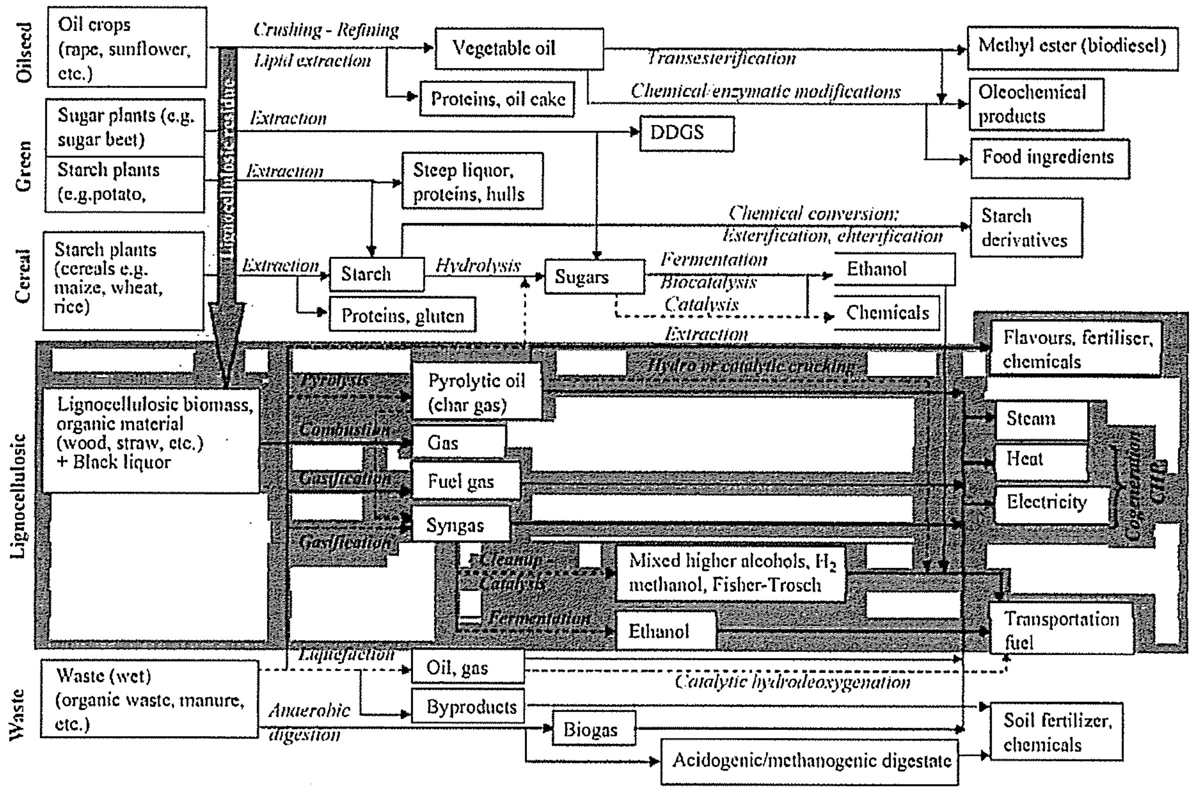


Fig. 20. Integrated biorefinery. www.biorefinery.euroview.eu [52].

Three different platforms, namely: thermochemical, sugar, and nonplatform or existing technologies are integrated. An integrated biorefinery produces various products, which include electricity produced from thermochemical and bioproducts from the combination of sugar and other existing conversion technology platforms.

An emerging concept in the biorefinery arena is conversion of bio-oil, the product from biomass pyrolysis, which could be routed via a conventional petrochemical refinery to generate various chemicals, the typical schematic of the process in shown in Fig. 20. The advantage of this route is that all necessary infrastructures for the separation and purification of products generated are already in place. This concept makes perfect sense since most petroleum refineries are well equipped to handle variable feedstock with the assumption that no two batches of crude oil are the same. Table 5 gives the composition of bio-oil compounds. Bio-oil chemical properties vary with the feedstock but woody biomass typically produces a mixture of 30% water, 30% phenolics, 20% aldehydes and ketones, 15% alcohols, and 10% miscellaneous compounds [58]. A process known as hydrodeoxygenation (HDO) could be applied to replace oxygen by hydrogenation of the raw bio-oils. After several HDO treatment steps the bio-oil could be transformed into a liquid hydrocarbon with properties similar to those of petroleum crude oil. The deoxygenated bio-oils can potentially be refined in existing petroleum refineries, with only minor adjustments to the current petroleum industry refinery infrastructure that is set up for hydrodesulfurization (HDS) process [59].

6. Conclusions

The paper has discussed first and second generation biofuel, concept of biorefineries, different types of biorefineries, and associated technical challenges. However, growing concerns over first generation biofuels in terms of their impact on food prices and the environment have led to an increasingly bad press in the last year. The unfortunate effect is that biofuel is starting to generate resistance particularly in poor countries with environmental agendas. As the replacement of fossil fuels takes place irrespective of these concerns, the way to avoid the negative effects of producing biofuels from food supplies is to make lignocellulosic-derived fuels available within the shortest possible time (i.e. second generation biofuels). However the immediate use of first generation biofuels involves putting in place logistic changes to use biofuels. This commitment to biofuels in the present will make the transition to the second generation biofuels more economically convenient. But at present the technology to produce these replacement fuels is still being developed. Biorefineries based on lignocellulosics will be able to access a much wider variety of feedstock, including forest biomass. Therefore, there is a need to integrate process operation, reactor and catalyst design to improve the effectiveness of different processes used for bioproducts and biofuels production in a typical biorefinery system. The main objective of the biorefinery is to produce multiple products using combination of technologies. Moreover the commitment of the chemistry, particularly the organic chemistry, needed for the concept of bio-based products and biorefinery systems and to force the combination of the biotechnological and chemical conversion of substances.

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REVIEW

Planted forest health: The need for a global strategy

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Several key tree genera are used in planted forests worldwide, and these represent valuable global resources. Planted forests are increasingly threatened by insects and microbial pathogens, which are introduced accidentally and/or have adapted to new host trees. Globalization has hastened tree pest emergence, despite a growing awareness of the problem, improved understanding of the costs, and an increased focus on the importance of quarantine. To protect the value and potential of planted forests, innovative solutions and a better-coordinated global approach are needed. Mitigation strategies that are effective only in wealthy countries fail to contain invasions elsewhere in the world, ultimately leading to global impacts. Solutions to forest pest problems in the future should mainly focus on integrating management approaches globally, rather than single-country strategies. A global strategy to manage pest issues is vitally important and urgently needed.

Forests and woodland ecosystems are a hugely important natural resource, easily overlooked and often undervalued (1–3). Globally, one in six people is estimated to rely on forests for food (3), and many more depend on forests for other critical ecosystem services, such as climate regulation, carbon storage, human health, and the genetic resources that underpin important wood and wood products–based industries. However, the health of forests, both natural and managed, is more heavily threatened at present than ever before (4–6). The most rapidly changing of these threats arise from direct and indirect anthropogenic influences on fungal pathogens and insect pests (hereafter referred to as pests), especially their distribution and patterns of interactions.

Here we focus on the importance of pests of planted forests, which are particularly vulnerable to invasive organisms yet are of growing importance as an economic resource and for various ecosystem services. Planted forests are typically of a single species. In plantations in the tropics and Southern Hemisphere, they are usually of nonnative species, such as species of *Pinus*, *Eucalyptus*, and *Acacia*. Northern Hemisphere plantations often comprise species of *Pinus*, *Picea*, *Populus*, *Eucalyptus*, and other genera, often in native areas or with closely related native species. These intensively managed tree farms cover huge areas [currently 7% and potentially 20% of global forests by the end of the century (1)], and they sustain major industries producing wood and pulp products. These tree genera have become natural resources of global importance, much like major agricultural crops, and are unlikely to be easily replaced.

Planted forests face various serious health threats from pests (Fig. 1). Non-native trees in plantations are in part successful because they have been separated from their natural enemies. However, when plantation trees are reunited with their coevolved pests, which may be introduced accidentally, or when they encounter novel pests to which they have no resistance, substantial damage or loss can ensue (7). The longer these non-native trees are planted in an area, the more threatened they become by native pests. Where the trees are of native species, they can be vulnerable to introduced pests. But the relative species uniformity of monoculture stands in intensively managed native plantation forests can make them especially susceptible to the many native pests occurring in the surrounding natural forests (8–10).

There are many opportunities to mitigate potential losses caused by pests in planted forests through exclusion (e.g., pre-export treatments and quarantine), eradication of newly established pests, and avoidance of disease through pest containment and management. Yet the lack of investment and capacity, especially in poorer countries, as well as the limited coordination of efforts at a global level, means that the impact of these tools to stem the global problem is limited. Unless this is addressed, pest problems will continue to grow and will threaten the long-term sustainability of forests and forestry worldwide. It should be recognized that the sustainable use of these tree "crops" will require the same global focus and investment to manage pest threat as that of agricultural crops.

Prevention is important but remains porous

Biological invasions of alien pests have been shown to be growing at constant or even increasing rates—and not only for those affecting trees (4–6, 11). Few pests are ever eradicated or completely suppressed, leading to an an ever-changing and increasing number of management programs to juggle. Phytosanitary measures are the major line of defense available to limit the global movement of pests, and various international policies seek to promote them [such as the International Standards For Phytosanitary Measures No. 15 (ISPM 15)

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found in a wide range of environments, of which more than 10 and their hybrids are commonly planted commercially around the world today. This diversity of genetic background has provided opportunities to capture traits for fast growth in many different environments, favorable wood properties, and resistance to many different fungal and insect pests.

Vegetative propagation has underpinned the rapid growth of the Eucalyptus forestry industry—and similarly for poplars, pines, and acacias. Mastering vegetative propagation has made it possible to produce and intensively propagate hybrids between tree species, leading to a paradigm shift for the global forest plantation industry. It has also provided one of the most important opportunities to avoid pest problems. A classic example is the case of the stem disease known as Cryphonectria canker, now recognized to be caused by a suite of cryptic species in the fungal genus Chrysoporthe (20). In the early 1980s, Cryphonectria canker was a major threat to the sustainability of Eucalyptus propagation in Brazil and later South Africa. Yet the selection of clones and particularly clonal hybrids with resistance made it possible to avoid the disease to the point where it is hardly considered important today (10).

An approach that is increasingly contemplated is to promote resistance to pest threats by increasing diversity through mixed plantings of species rather than monocultures (9, 21). From a managed forest perspective, this approach can be useful, but it is typically at odds with the needs of commercial forestry when done at a stand level. Nevertheless, introducing this form of resistance could be considered at a landscape level—for example, using clones in uniform but smaller blocks and including a diversity of genes rather than a diversity of species or even genotypes. Exploring the use of tree species and genera other than those currently used could offer further opportunities for mitigating the impact of pests and contribute to the resilience of the industry.

For introduced insect pests, biological control has provided superb solutions. Early examples of biological control in forestry date back to the early 1900s, using two introduced predators against the scale insect Eriococcus coriaceus on Eucalyptus in New Zealand and an egg parasitoid against the Eucalyptus snout beetle, known then as Gonipterus scutellatus (22). There have been many subsequent examples in planted forests, such as, for example, the widely applied Sirex woodwasp biological control using the parasitic nematode Deladenus siricidicola (23). Dealing with native insect pests is somewhat more complex, and in the absence of resistant planting stock, the application of biocides such as formulations of the insect pathogenic bacterium Bacillus thuringiensis and insect pathogens (e.g., Beauvaria bassiana) and behavior-altering semiochemical-based strategies provide opportunities (24, 25). But there also remains a strong dependence on synthetic chemical insecticides that may be harmful to the environment and inconsistent with environmental certification (see http://pesticides.fsc.org).

Invest in research and innovation

Our capacity to deal with tree pest problems far outstrips the level of investment in exploring and applying these opportunities. At the outset of dealing with pest problems, we are challenged by our ability to accurately identify the pest in question. There are many examples where new pests appear that are misidentified or unknown elsewhere in the world. This is largely the result of poor or unequal levels of investment in global surveys and in our knowledge of global biodiversity. Hundreds of known pests and pathogens remain undetected, especially in poorer countries, and this problem is significantly more severe in forestry (26).

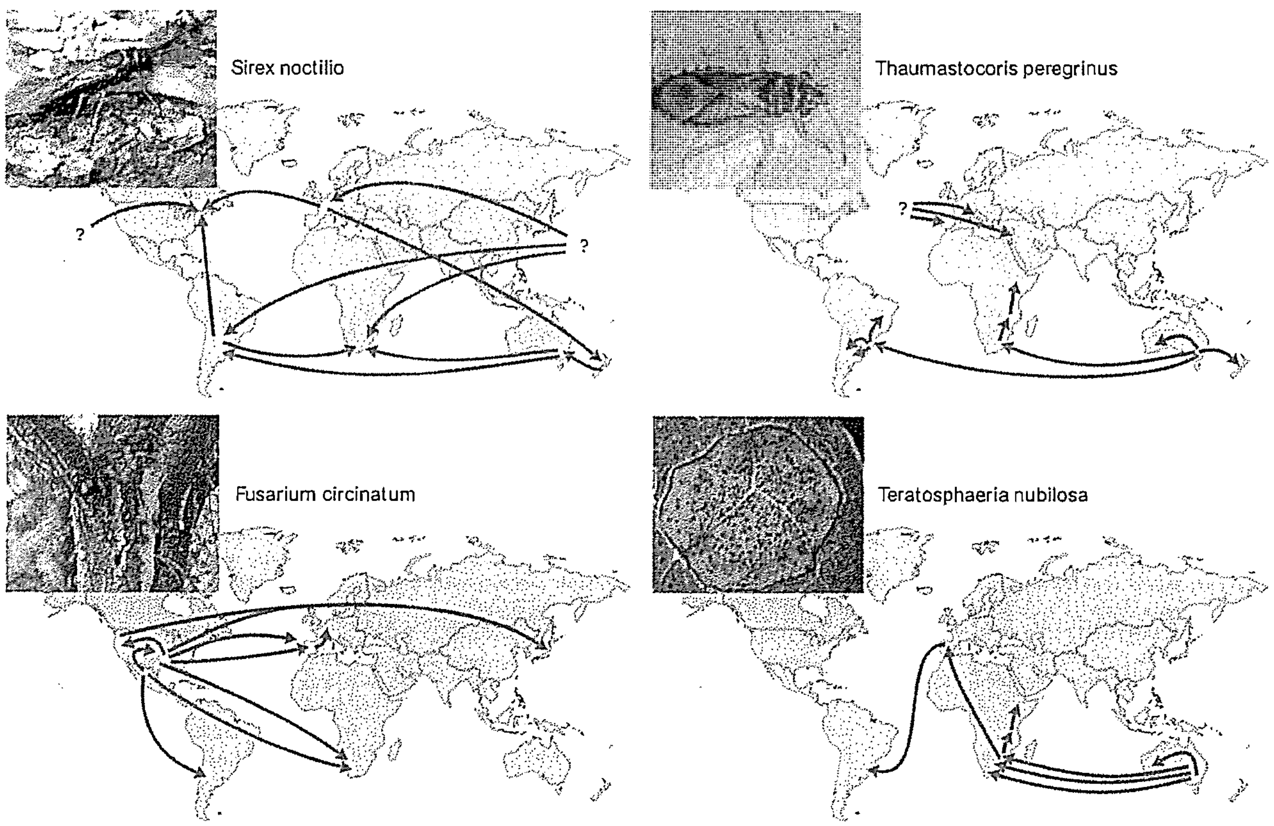

Fig. 2. Examples of invasion routes of pests of planted forests that illustrate an apparently common pattern of complex pathways of spread to new environments, including repeated introductions and with either native or invasive populations serving as source populations (18). Invasion routes of the pine pitch canker pathogen Fusarium circinatum (origin in Central America) (39), eucalypt leaf pathogen Teratosphaeria nubilosa (origin in southeast Australia) (40), the pine woodwasp Sirex noctilio (origin in Eurasia) (23), and the eucalypt bug Thaumastocoris peregrinus (origin in southeast Australia) (41) were determined through historical and genetic data. [Photo credits: (top left) Brett Hurley; (top right) Samantha Bush; (bottom left) Jolanda Roux; (bottom right) Guillermo Perez]

capacity to deal with tree pest problems (not exclusive to managed and planted forests), answering the "who pays" question is much more challenging (36). Various models are in operation, but the answer most likely lies in collaborations between governments and the commercial sector. They would need to jointly take responsibility for preparedness and for the consequences of incursions, such as in the Government Industry Agreement for Biosecurity Readiness and Response in New Zealand (www.gia.org.nz/) or the Tree Protection Cooperative Program that has been jointly funded by the South African commercial sector, government, and university system for over 25 years. At present, however, it is clear that tree pest problems are made worse by the lack of clear global objectives, priorities, funding, and collaboration. This needs to be addressed, and externally supported where necessary, in developed and less-developed countries, because the overall goal will depend on a more uniform participation.

Outlook

The future of planted forests will be influenced by our ability to respond to damaging pests and the threat of biological invasions. The trends are clear, with at best a constant suite of emerging pests and sometimes a dramatically increasing rate of pest impacts. Increasing numbers of damaging hybrid genotypes and abiotic influences linked to global changes in the environment are further increasing the impact of these pests (4). It would be naïve to believe that local solutions such as quarantine at national borders can present a complete barrier to the global impact of pests on forests. For this reason, much greater focus will need to be placed on global strategies aimed at reducing pest movement and improving pest surveillance and incursion response, as well as optimizing the use of the most powerful tools to mitigate damage.

Genetics offers many outstanding opportunities to mitigate damage from pests, either alien invasive or native and that have undergone some form of adaptation. For managed forests and especially plantation forestry, traditional selection and breeding of species, provenances, clones, and clonal hybrids will increase in importance even further. Beyond this point, genetic engineering with genes conferring resistance to pests will be a valuable additional tool. Such genetic modification is already well advanced for Eucalyptus and poplar. They will also need to be managed with care, as has been true in agriculture, so as to avoid the development of resistance. The rapid decrease in the cost of generating relevant -omics data for nonmodel species, as well as inexpensive tools for gene editing such as CRISPR, will make these technologies available for more plant species sooner than previously anticipated (37). There are, however, valid concerns beyond the management of resistance that will require efficient platforms where the research community and various other societal interest groups can discuss the use of these technologies and collectively inform their regulation.

Pest problems in forests are well recognized and of considerable concern in many parts of the world, but this is not balanced with the investment that would be required to make a significant difference. This is a situation that should change, but funding and coordinated efforts from across a variety of disciplines and institutions would be needed to make this possible. For example, all the tools and much of the knowledge exist to develop an international database on the diversity of insects and fungi associated with trees used in plantations [there are various unlinked databases on pests and diseases, and with various levels of accessibility, that could be linked via a central database such as, for example, QBOL: Quarantine organisms Barcode Of Life (www.qbol.org)]. Such a database could be powerfully linked to metadata related to host use, natural enemies, climate, surveillance tools and information, and more.

It is not possible to predict which tree pest problems are likely to be most important and damaging in the future. The so-called unknown unknowns and black swan diseases will remain a challenge (35). The appearance of new pests can still surprise local industries and governments, and responses are often erratic and inadequate. Through a more coordinated global investment in relevant research, it should be possible to respond more rapidly and mitigate problems more effectively in the future. There are also increasing opportunities to capture the imagination and support of the public, to create awareness, and to expand the capacity for surveillance beyond the limited number of specialists, through the implementation of citizen science and crowdsourcing mechanisms.

Bill Gates recently called for new thinking about global systems to deal with human infectious disease problems in order to avoid a global health disaster (38). Although the situations for tree pests and human disease are not fully comparable, there are many similarities. Tree health specialists as well as funding agencies concerned with global tree health should learn from these. In particular, it should be recognized that although the impact of tree health disasters is experienced locally, the drivers of their emergence are global. This makes uncoordinated local efforts to slow the overall emergence all but futile. Our capacity to deal with serious tree pest problems will remain minimal unless we can find the support and vision to launch a more global and holistic approach to study these problems and to implement mitigation strategies.

A global strategy for dealing with pests in planted forests is urgently needed and should include:

• A clearly identified body with the mandate to coordinate and raise funds for global responses to key pests and to monitor compliance with regulations.

• A central database on pests and diseases of key forest plantation species.

• Shared information on tools for and information from the surveillance of pests and pathogens in planted forests.

• Identification of measures with potentially high global impact for pest mitigation, and support for the development and sharing of capacity.

• More-structured systems for facilitating biological control, including global sharing of knowledge, best practices, and the selection of agents (organisms).

• Protection of the genetic resources of the key forest plantation genera.

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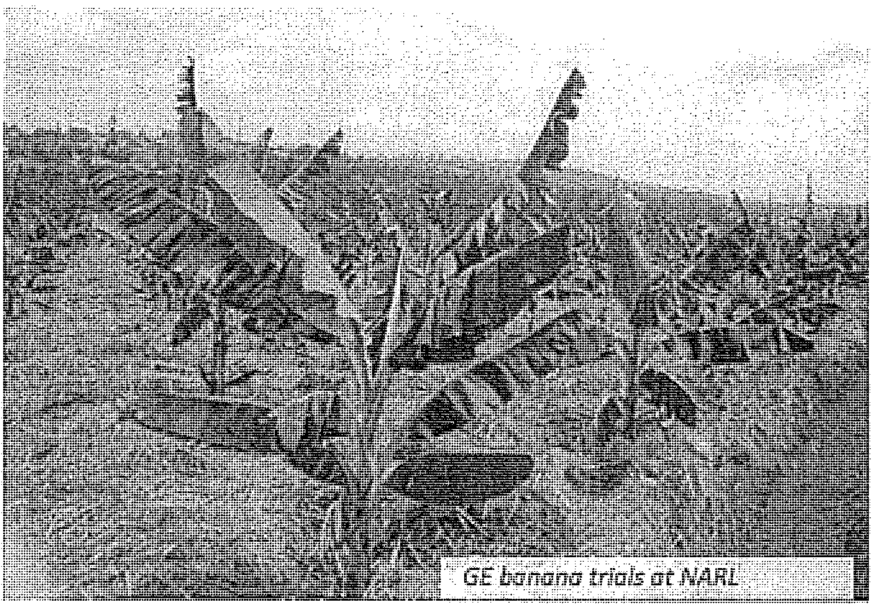
Vitamin A and Iron rich banana under trial in Uganda


GE banana trials at NARL

Peter Wamboga, Scifode

A biotechnology-based research for bananas enriched with Vitamin A, Iron and for varieties resistant to the devastating banana bacterial wilt (BXW), should be prioritized in passing a National Biotechnology and Biosafety law, stakeholders in agricultural modernization have demanded. Based on the information they received during a workshop at Kawempe near Kampala and from a tour of Vit. A and Iron-enriched bananas currently in a confined field trial (CFT), at NARL, Kawanda—the diversity of stakeholders asked the Government to prioritize expeditious processing of the biosafety law, as research was already showing exciting opportunities.

Dr. Andrew Kiggundu, head of the National Agro-Biotechnology Centre (NABC) at the Kawanda-based National Agricultural Research Laboratories (NARL), a key constituent institute of NARO, said that ongoing biotechnology-based research—of which he was part—had prioritized saving staple crops from virulent pests such as: weevils,nematodes and diseases like: banana bacterial wilt (BBW, and fungal black sigatoka also in bananas, cassava mosaic and cassava brown streak disease (CBSD) in cassava; and the sweet potatoes virus disease.

"This research is by Ugandan scientists and is at confined field trial (CFT) stages at NABC, Kawanda (bananas) and at the National Crops Resources Research Institute (NaCRRI), Namulonge—for cassava and sweet potatoes. We're determined to provide resistant lines against these serious constraints using biotechnology. But unless the draft bill is passed into law, technology from this useful research cannot get to would-be beneficiaries," Kiggundu said, while responding to questions from the diversity of stakeholders who included local leaders; representatives from National Association of Professional Environmentalists (NAPE); Uganda National Farmers' Federation (UNFFE); faith-based organisations; the ministries of Tourism, Trade and Industry, Agriculture, Water and Environment, local seed breeders, rural farmers and the media.

These stakeholders' sentiments for enacting of a biotech law, were also voiced after they toured the NABC laboratory, the Biosafety Level II greenhouses and the confined field trials (CFT) site for genetically-modified bananas: sukali ndizi (apple banana) which is a dessert and nakyinyika (a cooking banana)—both bearing Vitamin A and Iron micronutrients, which are already expressing signs of integration of the two micronutrients.

The workshop held at Tick Hotel, Kawempe—north of Kampala city, was sponsored by the Strengthening Agricultural Biotechnology Management in Sub-Saharan Africa (SABIMA) project of the Forum on Agricultural Research in Africa (FARA) being implemented by the National Agricultural Organisation (NARO) in Uganda.

Cont. pg 4

Inside This Issue:

Editorial

GMO debate: Biosafety is key

Theresa Sengooba

The deployment of modern biotech tools such as genetic engineering (GE) to agricultural production has created significant discourse among various interest groups. Following the introduction of transgenic plant varieties for use by farmers 15 years ago, groups opposed to the technology have criticised it as fulfilling less than it promises while developers and proponents have already demonstrated evidence of the technology increasing productivity of agricultural crops, even to smallholder farmers.

No farmer will adopt a technology that is not useful or profitable. Whereas the benefits of the GE technology have been demonstrated in adopting areas, the key focus of debate has been the safety of the technology to the environment, human health, and animal health. Socio-economic issues largely focussed on Intellectual Property Rights over the technology have also been viewed as a major concern with the technology. A lot of media attention has in the past six months been devoted to discussion of the concerns with GE technology.

An honest and credible debate is useful as long as facts or plausible theory based on sound science are presented. The potential risks associated with modern biotechnology use especially in agriculture is a subject of global interest and the Cartagena Protocol on Biosafety was established to assist countries develop laws and regulatory systems that can provide for assessment of GE products and allow only those that are safe to the environment and to human health. These laws and regulations collectively known as biosafety, form the key to mitigating any potential negative effects of using the technology. Biosafety regulatory frameworks are designed to address potential risks right from product development stages to post release monitoring of approved technologies. In Uganda for instance, the national competent authority (Uganda National Council for Science and Technology) has established guidelines and procedures for conducting any research with modern biotech in the country. This is to assure the citizenry of safety of such advances. The UNCST in this regard currently conducts thorough review of applications for GE plant field experiments and ensures that those that are approved are adequately inspected to observe compliance to agreed standards of specific experiments.

Other countries in the region, notably Kenya and Tanzania, have fully established legal frameworks for managing aspects of modern biotech related to agriculture. Uganda is also in process to fine-tune its biosafety regulatory framework by developing the hitherto missing sections such as a biotechnology safety law and regulations to govern advanced and general uses of products of modern biotechnology, It is important to recognize that in all research efforts, the key emphasis has been, and will be, the safety of any technologies developed for the Ugandan farmers and consumers. The agricultural research organization in Uganda has a system of vetting and monitoring all research activities in the country and only products that can make a positive contribution to livelihood and the country's development are released. In the case of GE technology, additional responsibility for proper assessment is undertaken by the Competent Authority and the overall biosafety framework.

Scientists and other stakeholders are encouraged to contribute to this process through appropriate discourse so that concerns are addressed where they occur but otherwise helping the country to competitively benefit from technology. ■

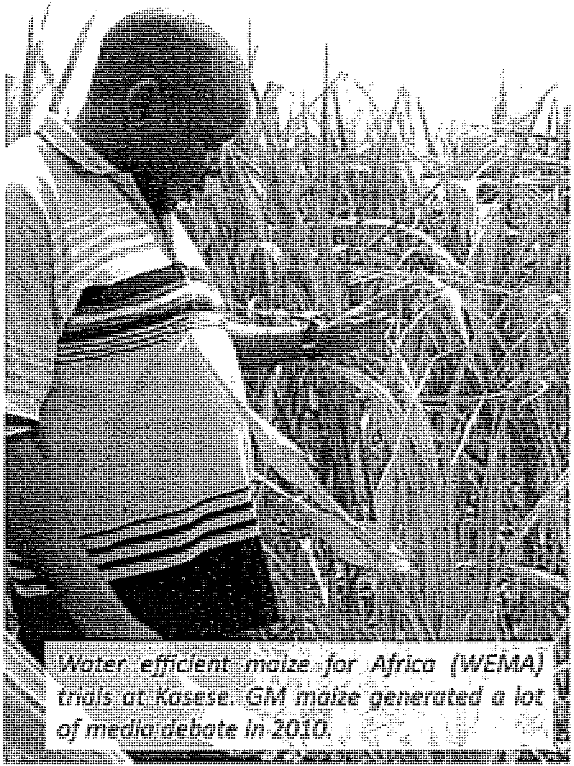
News Briefs

Biotech Crops Surge Over 1 Billion Hectares

International: In just 15 years after commercialization, accumulated biotech crops exceeded 1 billion hectares in 2010, a milestone that signifies biotech crops are here to stay, according to Clive James author of the annual report released in March 2011 by ISAAA (International Service for the Acquisition of Agri-biotech Applications). The 1 billionth hectare was planted in 2010 by one of the 15.4 million farmers in 29 countries who now benefit from the technology. With an unprecedented 87-fold increase between 1996 and 2010, biotech crops are the fastest-adopted crop technology in the history of modern agriculture. "Growth remains strong, with biotech hectarage increasing 14 million hectares - or 10 percent – between 2009 and 2010," said James. "That's the second highest annual hectare growth ever – bringing 2010 global plantings to 148 million hectares." ■

Kenyan government to publish biosafety guidelines

Nairobi, Kenya: The Kenyan government has said it will publish guidelines on biosafety in about two months, setting the country on course to join developing countries in commercialising genetically modified (GM) crops. The country enacted a law on Biosafety in 2008/2009 but has yet to publish regulations and guidelines for commercial releases of GM crops. The current guidelines allows only field trials with biotech crops but the National Biosafety Authority in Kenya says they are in the process of developing requisite regulations for the country to responsibly take advantage of biotech developments in the country and beyond. ■



Water efficient maize for Africa (WEMA) trials at Kasese. GM maize generated a lot of media debate in 2010.

Science journalists recognised at the first-ever Uganda biotech media awards

Makara Arthur, Scifode

The Science journalists in Uganda have been awarded for excellence in scientific reporting by a tripartite consortium of organisations—the Science Foundation for Livelihoods and Development (Scifode), the National Agricultural Research Organisation (NARO) and the Africa Harvest Biotech Foundation International (AHBFI). These awards, the first of its kind in Sub-Saharan Africa were aimed at recognizing the efforts of Ugandan scientists in reporting issues of Biotechnology and genetic engineering. The function which took place on 21st December 2010 at the Kampala Serena Hotel was presided over by the Uganda's First Deputy Prime Minister and Minister for East African Community Affairs Rt. Hon. Eriya Kategaya. Speaking at the function, the Deputy Prime Minister congratulated the organizers of the awards Ceremony upon organizing a colorful ceremony to recognize the efforts of journalists that are normally never given credit of informing and educating the public. He strongly supported the cause for using modern approaches in scientific research including genetic engineering and pledged Government support to these novel approaches especially to increasing food security and addressing effects of climate change.

The function saw five science journalists scooping awards for their great contribution to public understanding and awareness of biotechnology in Uganda and the Easten African region as a whole. The overall winner of the first-ever Uganda Biotech Media Awards was Ms. Lominda Afedraru from the Daily Monitor newspaper, a Uganda independent daily, the first runner-up was Mr. Joseph Miti from the same paper and these were followed by Mr. John Kasozi from the government owned The New Vision, also a daily. The electronic Media was represented by Ms. Sarah Mawerere from the government-run Uganda Broadcasting Corporation (UBC) radio whereas the regional media were represented by Ms. Halima Abdallah from The East African, a weekly. Key personalities present at this debut Ceremony included the Director General of the National Agricultural Reasearch Organisation, Dr. Denis Kyetere who presented a keynote paper on "Biotechnology Research, Development and Public Engagement: Key Challenges and Opportunities". In his keynote paper, Dr. Kyetere called for the bridging of the big gap that exists between scientists and journalists and pledged scientists support to journalists work by availing them information whenever they are called upon to do so.

Others present were the Executive Director of Science Foundation for Livelihoods and Development (Scifode), Mr. Arthur Makara (author); the regional coordinator of the Program for Biosafety Systems (PBS) who was also the Chairperson of the Vetting Committee, Dr. Theresa Sengooba; Ms. Julia Kagunda who represented the CEO of Africa Harvest Biotech Foundation, Dr. Florence Wambugu, among other notables that included scientists, media executives and journalists. The partners pledged for the continuation of this noble effort in the years to come and encouraged the Journalists to mentor others and to continue reporting and educating the public on issues of Biotechnology and Biosafety especially in the face of a wide range of challenges including drought, crop and animal diseases, food insecurity and climate change. ■

Journalists and other stakeholders on a recent trip to NARL, Kawanda

Biofortified Banana

from pg 1

The ongoing experiment is the first of the kind in a developing country. "What we see this year is clearly that the gene we inserted promoting vitamin A has got fully integrated and it is a positive development. It is exciting to us because it's the first indicator that the genes are working. This is what we wanted and it is called gene-expression. After that, the next thing we expect is expression of the same pro-vitamin A in the pulp (banana fingers). We shall only confirm this when bunches [now forming] finally mature and we open them up for examination." Solvents used in the testing of plants for vitamin and iron micronutrients' presence, have been ordered by NARL to arrive in the country, in time for the GM bananas' maturing stage.

Dr. Arinaitwe—who in 2004 transformed a *gros michel (bogoya)* banana with rice *chitinase* genes for resistance to fungal black sigatoka disease—reveals that the pro-iron promoters in nakinyika bananas were extracted from soya beans (the protein and iron rich leguminous crop).

The first research of the kind in the world involving transfer of pro-vitamin A and iron genes into bananas, was conducted in Australia in 2007-8 by scientists at Queensland University of Technology (QUT). The research was led by Prof. James Dale as Principal Investigator who tested cavendish—bananas closely-related to bogoya. NARL's GM *sukali ndizi* and GM *nakinyika*—both containing genes for enhanced Vit. A and iron, are first being grown in a CFT as a requirement under the Cartagena Protocol on biosafety—an international law regulating GMOs for safety to humans and the environment to which Uganda is signatory.

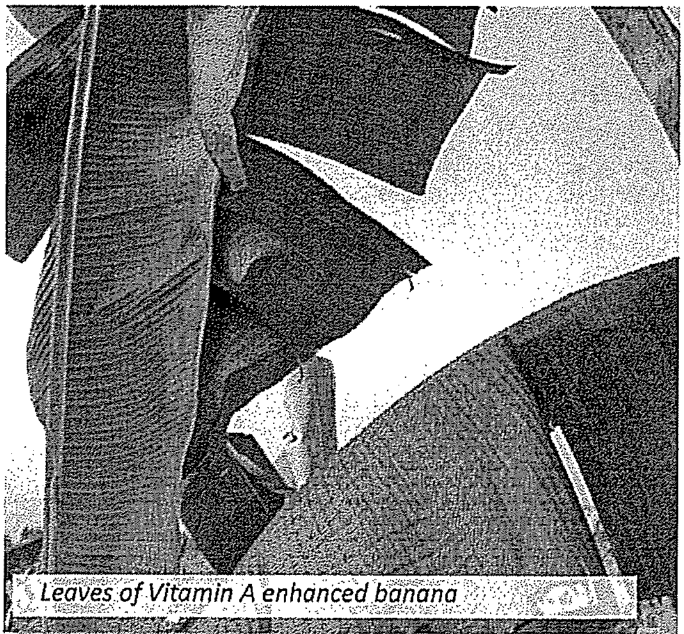
Dr. Arinaitwe says the National Biosafety Committee (NBC) at the Uganda National Council for Science and Technology (UNCST) gave NARO/NARL permission to undertake this cutting-edge research mid-2010, led by Prof. Wilberforce Tushemereirwe (Principal Investigator) and Head Banana Research Team in NARO. "It's the same pro-vitamin A genes used in bio-fortification of golden rice in Asia that we have used in biofortifying our bananas," Dr. Arinaitwe explains, adding that they are vital in the fight against blindness in children, due to Vit. A Deficiency (VAD). Meanwhile Iron deficiency in humans leads to anaemia—a state of poor blood levels in the body, with dire consequences particularly to pregnant women. Both cases lead to hundreds of deaths of blind children and anaemic pregnant women in Uganda.

According to another NARL molecular scientist specializing in bananas, Dr Andrew Kiggundu, severe vitamin A deficiency was identified in 31 out of 36 Ugandan districts surveyed in 1994. ..."and in 1999, it was concluded that more than 50% of children consumed inadequate vit-A...... Like Vit-A deficiency, iron-deficiency is a major public health problem and is common in both women and children. For example in early 1990s in eastern Uganda, 40% of children less than 5 years old had Iron Deficiency Anaemia (IDA). In 1998, IDA was

severe vitamin A deficiency was identified in 31 out of 36 Ugandan districts surveyed in 1994. ..."and in 1999, it was concluded that more than 50% of children consumed inadequate vit-A

cont. pg 5

Nutrient enhanced banana on trial at NARL



Leaves of Vitamin A enhanced banana

Dr. Kiggundu (L) describes the field trials

from pg 4

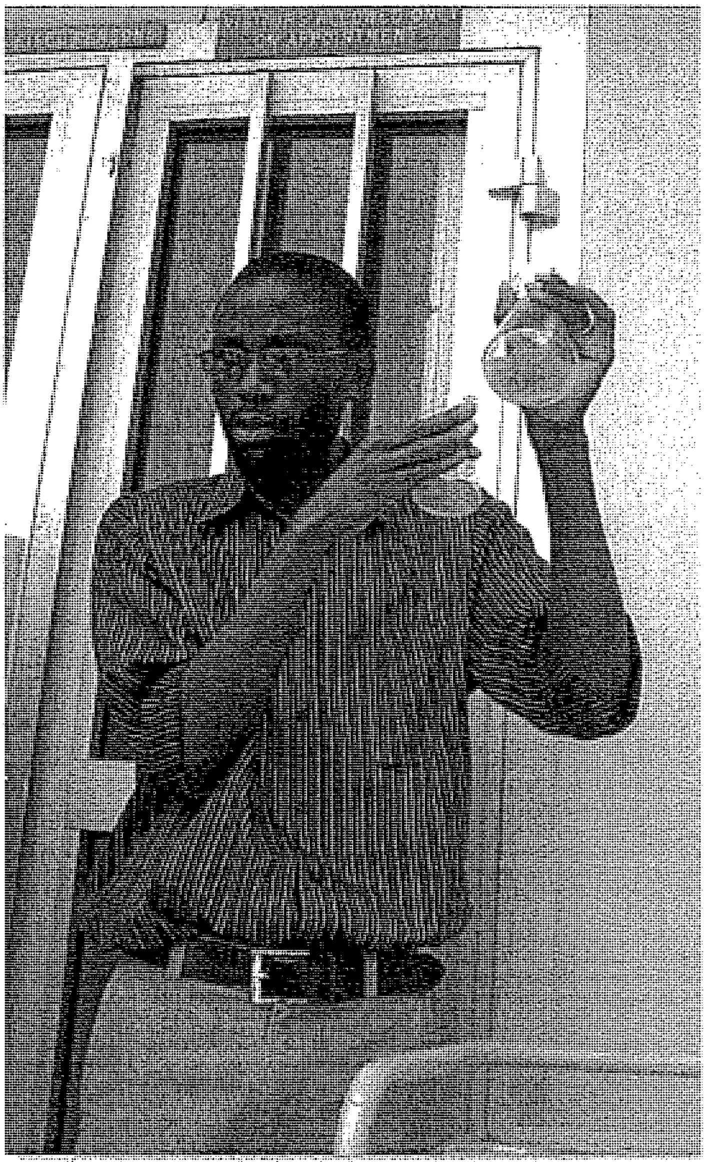
recognized in approximately 50% of pregnant women and about 30% of maternal deaths were attributable to IDA......," adds Dr. Kiggundu.

The highly-anticipated Vit. A and Iron-biofortified banana (enriching) project is funded by American philanthropist—Bill and Melinda Gates Foundation under its Grand Challenges program. It aims at providing a dietary fortification of staple foods, as an option to Vit-A and Iron-rich capsules distributed through the national health system.

Principal Investigator, Prof. Tushemereirwe says their research is well-intended to provide Ugandans with a more beneficial staple banana crop for both farmers/ traders and consumers. "We're the key stakeholders in this project as we scientists also consume bananas like the rest of the people. Therefore, what we shall come up with is a safe product both to humans and the environment," Tushemereirwe told a contingency of visitors to NARL from civil society, the media and NGO activists. "In fact, he added, we've asked government for permission to eat the first GM bananas from here, before anybody else eats them. We want to demonstrate to the world, the high level of confidence we have in the food from crops we have genetically-modified here, that it is as safe as any other banana". He added.

Arinaitwe says the biotech-based research is a continuous process as there are various stages yet to cover-including the conduct of the second-phase of biofortified sukali ndizi and nakinyika banana suckers that have stacked (combined) genes for pro-vitamin and iron promoters, in one sucker. This young trial was planted besides the old one (single-gene) on Nov. 23, 2010.

NARL has been gazetted as a centre of excellence in agro-research by global and African bodies, such as NEPAD's Bio-Sciences for Eastern and Central Africa Network (BecA-Net) that has sponsored Rwandan, Burundi, Congolese and



Mr Tindamanyire Jimmy, a scientist at NARL explains GE techniques to participants

Ugandan graduate students to study biotechnology at the National Agro-Biotech Centre (NABC), at NARL, Kawanda.

Beta-carotene (pro-Vitamin A), is the pre-curser of vitamin A in animals, including humans. It is a naturally occurring chemical and dietary intake is the primary source and most important source of vitamin A for humans. Vitamin A plays very many crucial roles in humans including supporting vision, boosting immunity, reproduction, as an anti-oxidant, and in development of various body tissues and organs. A deficiency in Vitamin A causes blindness, stunting and in severe cases, death in children as well as maternal mortality among expectant mothers. Deficiency in iron (Fe) causes the most common form of anaemia in the world as the nutrient is a major component of red blood cells and these cells cannot be formed without sufficient quantities of the nutrient in the body. In Uganda and in other developing countries, vitamin A and Fe deficiencies are commonly compounded, further worsening the situation. Fighting these two problems will go a long way in achieving the Millennium Development Goals of reducing Maternal Mortality and reducing Child Mortality.

Malaysia to release GM mosquitoes into the wild

Pond and bush, typical breeding grounds for mosquitoes

KUALA LUMPUR: Malaysia will soon take the controversial step of releasing genetically modified (GM) mosquitoes into the wild as part of an experiment to test their survival in natural conditions. The move was approved by the country's National Biosafety Board last year and will make the nation the first major country in the world to release GM *Aedes aegypti* mosquitoes for field testing — second only after the Cayman Islands in 2009. The mosquitoes, known as OX513A, have been developed by Malaysia's Institute for Medical Research (IMR) and the UK-based biotech company Oxitec to control the dengue virus, which is transmitted by *A. aegypti*.

A total of 4,000–6,000 male GM mosquitoes are expected to be released within the next couple of months, along with a similar number of unmodified male mosquitoes. The male GM mosquitoes mate with normal females to produce larvae that are unusual because of an extra enzyme they produce. This enzyme accumulates in the larvae to a level where it becomes toxic and kills them. The larvae's only hope for survival is if the antibiotic tetracycline is present — because it mops up the enzyme.

The developers hope male GM mosquitoes will compete with normal males for females so that repeated releases cut numbers of *A. aegypti* in dengue-prone areas. The mosquitoes will be released in the inland districts of Bentong in the state of Pahang, and Alor Gajah and Melaka in the state of Malacca, according to the National Biosafety Board. Each location will have two release phases: the first at a site 0.5–1 kilometres from the nearest human settlement, and the second at an inhabited site. They will be recaptured using mosquito traps, which will be monitored for at least one month, while the inhabited release sites will also be fogged with insecticide when the experiment is over. The board made its decision after its Genetic Modifications Advisory Committee (GMAC) analysed the risk factors for the experiment. The issue was opened for public consultation.

Ahmad Parveez Ghulam Kadir, head of the GMAC, told reporters in October 2010 that the committee had been concerned that lab tests had shown that three per cent of the offspring of male GM mosquitoes and normal females actually survive into adulthood rather than dying as larvae as intended. Ricarda Steinbrecher, a geneticist and co-director of EcoNexus, a UK-based non-profit research organisation, said that it is not clear how the offspring of the male GM mosquitoes survive into adulthood and do not die as 'programmed', but it raises the possibility that they could breed and pass on this — as yet unknown — mechanism for overcoming the lethality. "I would suggest that it is far too early for any open field releases. More data are needed from laboratory experiments. Furthermore, trials in field cages [large outdoor enclosures made from netting, i.e. confined field trials] are needed," she said.

The advisory committee had also been worried that female GM mosquitoes might accidentally be released. The technicians separate the male from the female GM mosquitoes based on the size of the pupae — the stage after the larval stage — and is therefore not completely accurate. Because of this, Parveez said, the board has insisted that scientists sort through the pupae twice — first mechanically and then manually. The 'self-limiting' strategy theoretically poses little threat of genes being released uncontrolled into the environment because of the death of the offspring. But future strategies, in which the aim is to overwhelm mosquito populations with those that are resistant to disease, are more controversial because the mosquitoes survive and breed.

A Malaysian geneticist, who declined to be named, said he hopes the experiments will be carried out under rigorous safety protocols. "We have the best laws on biosafety in the world, but the problem is the enforcement," he said. Liow Tiong Lai, health minister of Malaysia, told a press conference last year that the Malaysian government views the GM mosquitoes "as one of the most efficient and fast ways of getting rid of the Aedes mosquito from our local environment".

Source: SciDev.net

The Nagoya–Kuala Lumpur Supplementary Protocol on Liability and Redress to the Cartagena Protocol on Biosafety

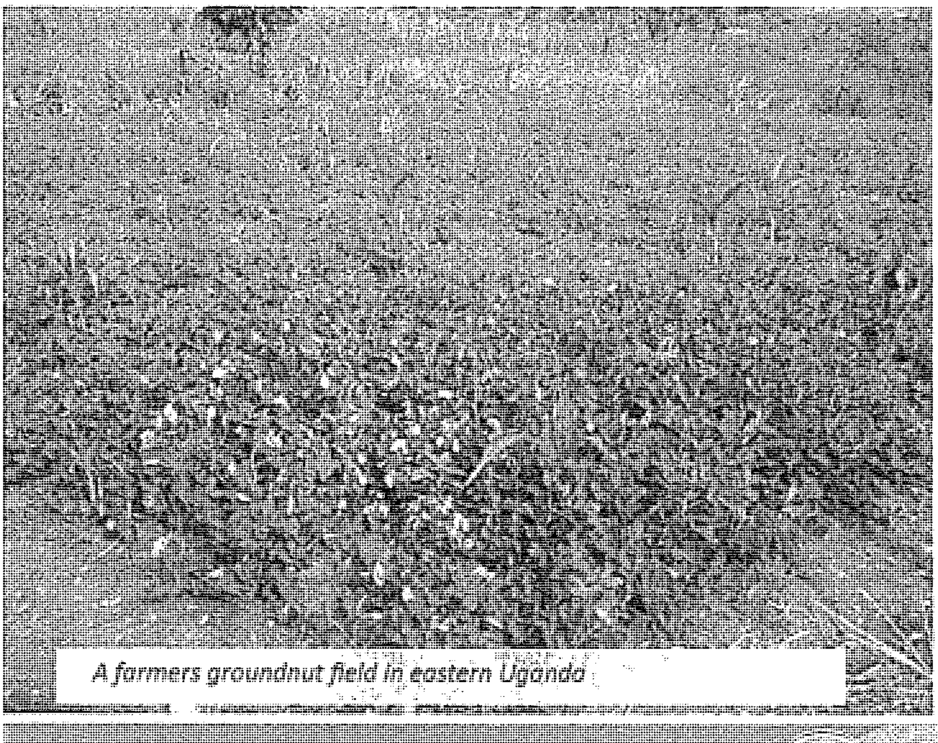
World community adopts a new UN treaty on living modified organisms

Nagoya, 16 October 2010. At 6.15 p.m. Friday in Japan, a new international treaty, the Nagoya – Kuala Lumpur Supplementary Protocol on Liability and Redress to the Cartagena Protocol on Biosafety, was adopted at one of the largest intergovernmental meetings ever held on the safe use of modern biotechnology.

The adoption of the new treaty came at the end of the five-day meeting of the governing body of the Cartagena Protocol on Biosafety (known as the Conference of the Parties serving as the meeting of the Parties to the Protocol or COP-MOP 5) and concluded six years of negotiations.

The new supplementary Protocol provides international rules and procedure on liability and redress for damage to biodiversity resulting from living modified organisms (LMO). Setting the stage for its adoption, small group of government negotiators had resolved contentious issues and agreed on the text of the supplementary Protocol just six hours before the opening of the COP-MOP 5 meeting on Monday.

Mr. René Lefeber of the Netherlands, one of the Co-Chairs of the Group of the Friends who facilitated the negotiations of the text of the new treaty said: "It has been many years since the last global environmental agreement was agreed. The adoption of new supplementary Protocol during the International Year of Biodiversity will give new impetus to multilateral environmental negotiations. This agreement will also make important contribution to the on-going work under the Convention on Biological Diversity to protect life on earth."



A farmers groundnut field in eastern Uganda

The new treaty shall be open for signature at the United Nations Headquarters in New York from 7 March 2011 to 6 March 2012 and will enter into force 90 days after being ratified by at least 40 Parties to the Cartagena Protocol on Biosafety.

The historic meeting of the Parties to the Protocol, held in the city of Nagoya, in Aichi prefecture, Japan, took seventeen other decisions. These included the adoption of a ten-year Strategic Plan for the implementation of the Protocol, a programme of work on public awareness, education and participation concerning LMOs, and further guidance on risk assessment and risk management.

At the closing ceremony of COP-MOP 5, Ms. Masayo Tanabu, Parliamentary Secretary of Ministry of Agriculture, Forestry and Fisheries, speaking on behalf of the Government of Japan, stated:

"The new supplementary Protocol is a turning point for the Cartagena Protocol on Biosafety. There have been many challenges successfully overcome. Let us rekindle the spirit of cooperation to confront the biodiversity challenges as well."

Mr. Ahmed Djoghlaf, Executive Secretary of the Convention on Biological Diversity praised Japan as an outstanding host and paid tribute to delegates for the outcomes of the meeting. He said: "I congratulate all of you on this remarkable achievement. We have dreamt of this event for more than six years. This is indeed a historic event not only for the biodiversity family but also for the world community at large."

CBD Secretariat

Biosafety in Biotechnology

1. What is biosafety?

Biosafety is the safe development, application and utilization of biotechnology and its products.

2. Why biosafety?

Biosafety systems are established worldwide to minimize or control potential risks of biotechnology on human health, the environment, as well as socio-economic impacts of such risks.

3. What is a biosafety legal framework?

A biosafety legal and regulatory framework is a coordinating platform for implementation of biosafety laws and regulations. The framework consists of laws, regulations, and guidelines, together with specific institutional arrangements such as a Competent Authority; a National Focal Point; and related institutional mandates of the various government agencies in the regulation of biotechnology.

4. Why is GMO use regulated in the world?

Being a new technology, GMO use in the world is regulated to: guarantee and assure safety to humans, animals and the environment; to keep abreast with advances in the field of scientific knowledge and appropriately tap any potential; and to address public consciousness about environmental and food safety issues.

5. Do we need a law on biosafety?

Yes. A law to regulate biotechnology use is necessary so that a framework of operation is available to safely harness the benefits of biotechnology tools without creating undue negative effects on society and the environment. A biosafety law will thus encourage development of useful products from biotechnology and prevent or minimise any potential risks.

6. Where is Uganda and EA region?

Uganda has established a National Policy on Biotechnology and Biosafety that among others, seeks to promote the safe use for biotechnology tools in contributing to the country's sustainable development goals. The country also has a national Biosafety Framework in place that has been used in coordinating and regulating research and development activities involving biotechnology tools. An explicit law on Biosafety is under preparation in the responsible government departments. Kenya and Tanzania have already enacted their respective laws on biosafety.

7. Do we have capacity to manage biosafety in Uganda?

Over the past 15 years, the country has been steadily building both human and institutional capacity to administer the various aspects of biosafety. There is a functional National Biosafety Committee (NBC) consisting of a team of biosafety experts to oversee research involving modern biotechnology tools. In addition, human capacity has been developed to conduct monitoring and evaluation of biotech related activities in the environmental, agricultural, and health sectors.

8. Can biosafety framework assure safety?

A fully functional biosafety framework will without doubt, assure safety to humans and the environment. This is through a robust risk assessment process conducted for each biotech initiative with potential risk. An effective system will ensure that only safe biotech products are released to the environment.

9. And the Cartagena Protocol on Biosafety (CPB)?

This is an internationally binding legal instrument (already ratified by EA countries) that mandates countries to establish mechanisms for safe handling, use, and transfer of living products of modern biotechnology such as living modified organisms (LMOs). Under this protocol, Uganda is charged with a responsibility of establishing mechanisms to regulate, manage or control potential risks associated with modern biotechnology.

10. How do other countries regulate biotech use?

Different countries in the world have established laws, regulations, and guidelines to address various potential biosafety and ethical concerns as regards application of biotechnology tools in increasing agricultural production, improving human health and protecting the environment. Whereas some countries enacted explicit laws on biosafety, others regulate biotech through existing environmental and food/health safety laws. In all cases, new guidelines/ regulations are issued, or existing ones modified to cope with advances in science and new evidence from risk assessment studies. The release of biotech products, especially those arising from modern biotech tools such genetic engineering, is conducted on a case by case basis taking into account the possible interaction of the said product with the environment in which it is to be released. ■

Compiled by PBS

More FAQs to come in the next edition

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A Meta-Analysis of the Impacts of Genetically Modified Crops

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Abstract

Background: Despite the rapid adoption of genetically modified (GM) crops by farmers in many countries, controversies about this technology continue. Uncertainty about GM crop impacts is one reason for widespread public suspicion.

Objective: We carry out a meta-analysis of the agronomic and economic impacts of GM crops to consolidate the evidence.

Data Sources: Original studies for inclusion were identified through keyword searches in ISI Web of Knowledge, Google Scholar, EconLit, and AgEcon Search.

Study Eligibility Criteria: Studies were included when they build on primary data from farm surveys or field trials anywhere in the world, and when they report impacts of GM soybean, maize, or cotton on crop yields, pesticide use, and/or farmer profits. In total, 147 original studies were included.

Synthesis Methods: Analysis of mean impacts and meta-regressions to examine factors that influence outcomes.

Results: On average, GM technology adoption has reduced chemical pesticide use by 37%, increased crop yields by 22%, and increased farmer profits by 68%. Yield gains and pesticide reductions are larger for insect-resistant crops than for herbicide-tolerant crops. Yield and profit gains are higher in developing countries than in developed countries.

Limitations: Several of the original studies did not report sample sizes and measures of variance.

Conclusion: The meta-analysis reveals robust evidence of GM crop benefits for farmers in developed and developing countries. Such evidence may help to gradually increase public trust in this technology.

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Data Availability: The authors confirm that all data underlying the findings are fully available without restriction. All relevant data are within the paper and its Supporting Information files.

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Introduction

Despite the rapid adoption of genetically modified (GM) crops by farmers in many countries, public controversies about the risks and benefits continue [1–4]. Numerous independent science academies and regulatory bodies have reviewed the evidence about risks, concluding that commercialized GM crops are safe for human consumption and the environment [5–7]. There are also plenty of studies showing that GM crops cause benefits in terms of higher yields and cost savings in agricultural production [8–12], and welfare gains among adopting farm households [13–15]. However, some argue that the evidence about impacts is mixed and that studies showing large benefits may have problems with the data and methods used [16–18]. Uncertainty about GM crop impacts is one reason for the widespread public suspicion towards this technology. We have carried out a meta-analysis that may help to consolidate the evidence.

While earlier reviews of GM crop impacts exist [19–22], our approach adds to the knowledge in two important ways. First, we include more recent studies into the meta-analysis. In the emerging literature on GM crop impacts, new studies are published continuously, broadening the geographical area covered, the methods used, and the type of outcome variables considered. For instance, in addition to other impacts we analyze effects of GM crop adoption on pesticide quantity, which previous meta-analyses could not because of the limited number of observations for this particular outcome variable. Second, we go beyond average impacts and use meta-regressions to explain impact heterogeneity and test for possible biases.

Our meta-analysis concentrates on the most important GM crops, including herbicide-tolerant (HT) soybean, maize, and cotton, as well as insect-resistant (IR) maize and cotton. For these crops, a sufficiently large number of original impact studies have been published to estimate meaningful average effect sizes. We estimate mean impacts of GM crop adoption on crop yield, pesticide quantity, pesticide cost, total production cost, and farmer profit. Furthermore, we analyze several factors that may influence outcomes, such as geographic location, modified crop trait, and type of data and methods used in the original studies.

Materials and Methods

Literature search

Original studies for inclusion in this meta-analysis were identified through keyword searches in relevant literature databanks. Studies were searched in the ISI Web of Knowledge, Google Scholar, EconLit, and AgEcon Search. We searched for studies in the English language that were published after 1995. We did not extend the review to earlier years, because the commercial adoption of GM crops started only in the mid-1990s [23]. The search was performed for combinations of keywords related to GM technology and related to the outcome of interest. Concrete keywords used related to GM technology were (an asterisk is a replacement for any ending of the respective term; quotation marks indicate that the term was used as a whole, not each word alone): GM*, "genetically engineered", "genetically modified", transgenic, "agricultural biotechnology", HT, "herbicide tolerant", Roundup, Bt, "insect resistant". Concrete keywords used related to outcome variables were: impact*, effect*, benefit*, yield*, economic*, income*, cost*, soci*, pesticide*, herbicide*, insecticide*, productivity*, margin*, profit*. The search was completed in March 2014.

Most of the publications in the ISI Web of Knowledge are articles in academic journals, while Google Scholar, EconLit, and AgEcon Search also comprise book chapters and grey literature such as conference papers, working papers, and reports in institutional series. Articles published in academic journals have usually passed a rigorous peer-review process. Most papers presented at academic conferences have also passed a peer-review process, which is often less strict than that of good journals though. Some of the other publications are peer reviewed, while many are not. Some of the working papers and reports are published by research institutes or government organizations, while others are NGO publications. Unlike previous reviews of GM crop impacts, we did not limit the sample to peer-reviewed studies but included all publications for two reasons. First, a clear-cut distinction between studies with and without peer review is not always possible, especially when dealing with papers that were not published in a journal or presented at an academic conference [24]. Second, studies without peer review also influence the public and policy debate on GM crops; ignoring them completely would be short-sighted.

Of the studies identified through the keyword searches, not all reported original impact results. We classified studies by screening titles, abstracts, and full texts. Studies had to fulfill the following criteria to be included:

- The study is an empirical investigation of the agronomic and/or economic impacts of GM soybean, GM maize, or GM cotton using micro-level data from individual plots and/or farms. Other GM crops such as GM rapeseed, GM sugarbeet, and GM papaya were commercialized in selected countries [23], but the number of impact studies available for these other crops is very small.
- The study reports GM crop impacts in terms of one or more of the following outcome variables: yield, pesticide quantity (especially insecticides and herbicides), pesticide costs, total variable costs, gross margins, farmer profits. If only the number of pesticide sprays was reported, this was used as a proxy for pesticide quantity.
- The study analyzes the performance of GM crops by either reporting mean outcomes for GM and non-GM, absolute or percentage differences, or estimated coefficients of regression models that can be used to calculate percentage differences between GM and non-GM crops.
- The study contains original results and is not only a review of previous studies.

In some cases, the same results were reported in different publications; in these cases, only one of the publications was included to avoid double counting. On the other hand, several publications involve more than one impact observation, even for a single outcome variable, for instance when reporting results for different geographical regions or derived with different methods (e.g., comparison of mean outcomes of GM and non-GM crops plus regression model estimates). In those cases, all observations were included. Moreover, the same primary dataset was sometimes used for different publications without reporting identical results (e.g., analysis of different outcome variables, different waves of panel data, use of different methods). Hence, the number of impact observations in our sample is larger than the number of publications and primary datasets (Data S1). The number of studies selected at various stages is shown in the flow diagram in Figure 1. The number of publications finally included in the meta-analysis is 147 (Table S1).

Effect sizes and influencing factors

Effect sizes are measures of outcome variables. We chose the percentage difference between GM and non-GM crops for five different outcome variables, namely yield, pesticide quantity, pesticide cost, total production cost, and farmer profits per unit area. Most studies that analyze production costs focus on variable costs, which are the costs primarily affected through GM technology adoption. Accordingly, profits are calculated as revenues minus variable production costs (profits calculated in this way are also referred to as gross margins). These production costs also take into account the higher prices charged by private companies for GM seeds. Hence, the percentage differences in profits considered here are net economic benefits for farmers using GM technology. Percentage differences, when not reported in the original studies, were calculated from mean value comparisons between GM and non-GM or from estimated regression coefficients.

Since we look at different types of GM technologies (different modified traits) that are used in different countries and regions, we do not expect that effect sizes are homogenous across studies. Hence, our approach of combining effect sizes corresponds to a random-effects model in meta-analysis [25]. To explain impact heterogeneity and test for possible biases, we also compiled data on a number of study descriptors that may influence the reported effect sizes. These influencing factors include information on the type of GM technology (modified trait), the region studied, the type of data and method used, the source of funding, and the type of publication. All influencing factors are defined as dummy variables. The exact definition of these dummy variables is given in Table 1. Variable distributions of the study descriptors are shown in Table S2.

Statistical analysis

In a first step, we estimate average effect sizes for each outcome variable. To test whether these mean impacts are significantly

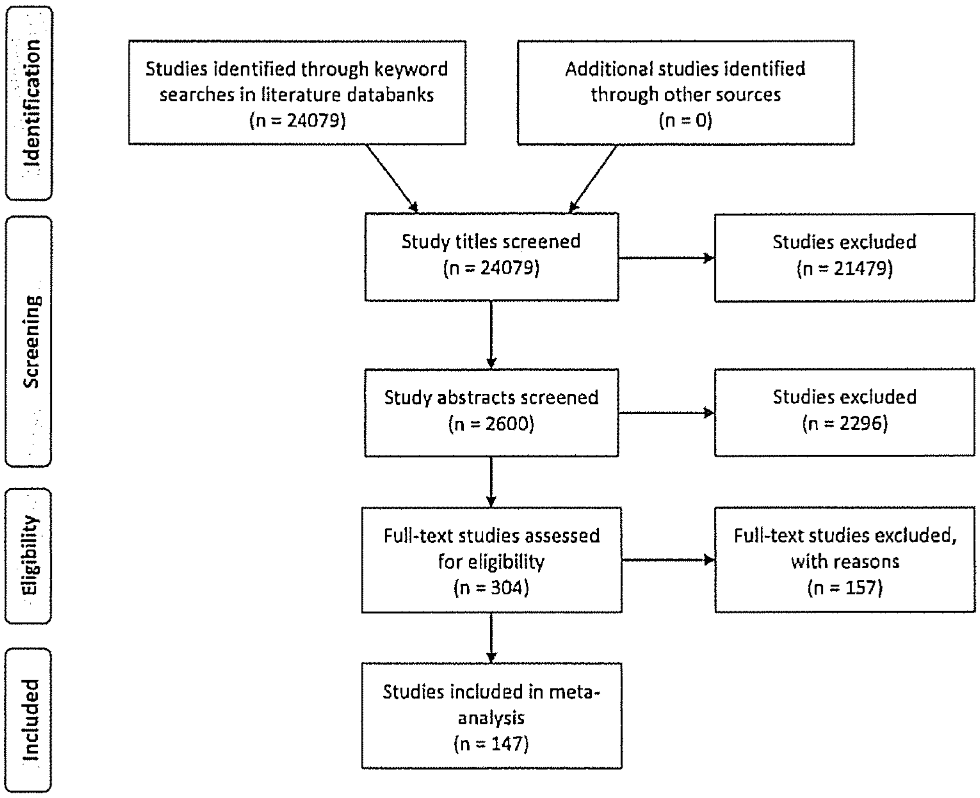

Figure 1. Selection of studies for inclusion in the meta-analysis.
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different from zero, we regress each outcome variable on a constant with cluster correction of standard errors by primary dataset. Thus, the test for significance is valid also when observations from the same dataset are correlated. We estimate average effect sizes for all GM crops combined. However, we expect that the results may differ by modified trait, so that we also analyze mean effects for HT crops and IR crops separately.

Meta-analyses often weight impact estimates by their variances; estimates with low variance are considered more reliable and receive a higher weight [26]. In our case, several of the original studies do not report measures of variance, so that weighting by variance is not possible. Alternatively, weighting by sample size is common, but sample sizes are also not reported in all studies considered, especially not in some of the grey literature publications. To test the robustness of the results, we employ a

Table 1. Variables used to analyze influencing factors of GM crop impacts.

Variable name	Variable definition
Insect resistance (IR)	Dummy that takes a value of one for all observations referring to insect-resistant GM crops with genes from *Bacillus thuringiensis* (Bt), and zero for all herbicide-tolerant (HT) GM crops.
Developing country	Dummy that takes a value of one for all GM crop applications in a developing country according to the World Bank classification of countries, and zero for all applications in a developed country.
Field-trial data	Dummy that takes a value of one for all observations building on field-trial data (on-station and on-farm experiments), and zero for all observations building on farm survey data.
Industry-funded study	Dummy that takes a value of one for all studies that mention industry (private sector companies) as source of funding, and zero otherwise.
Regression model result	Dummy that takes a value of one for all impact observations that are derived from regression model estimates, and zero for observations derived from mean value comparisons between GM and non-GM.
Journal publication	Dummy that takes a value of one for all studies published in a peer-reviewed journal, and zero otherwise.
Journal/academic conference	Dummy that takes a value of one for all studies published in a peer-reviewed journal or presented at an academic conference, and zero otherwise.

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different weighting procedure, using the inverse of the number of impact observations per dataset as weights. This procedure avoids that individual datasets that were used in several publications dominate the calculation of average effect sizes.

In a second step, we use meta-regressions to explain impact heterogeneity and test for possible biases. Linear regression models are estimated separately for all of the five outcome variables:

$$\%\Delta Y_{hij} = \alpha_h + \mathbf{X}_{hij}\beta_h + \varepsilon_{hij}$$

$\%\Delta Y_{hij}$ is the effect size (percentage difference between GM and non-GM) of each outcome variable h for observation i in publication j, and $\mathbf{X}_{hij}$ is a vector of influencing factors. α_h is a coefficient and β_h a vector of coefficients to be estimated; ε_{hij} is a random error term. Influencing factors used in the regressions are defined in Table 1.

Results and Discussion

Average effect sizes

Distributions of all five outcome variables are shown in Figure S1. Table 2 presents unweighted mean impacts. As a robustness check, we weighted by the inverse of the number of impact observations per dataset. Comparing unweighted results (Table 2) with weighted results (Table S3) we find only very small differences. This comparison suggests that the unweighted results are robust.

On average, GM technology has increased crop yields by 21% (Figure 2). These yield increases are not due to higher genetic yield potential, but to more effective pest control and thus lower crop damage [27]. At the same time, GM crops have reduced pesticide quantity by 37% and pesticide cost by 39%. The effect on the cost of production is not significant. GM seeds are more expensive than non-GM seeds, but the additional seed costs are compensated through savings in chemical and mechanical pest control. Average profit gains for GM-adopting farmers are 69%.

Results of Cochran's test [25], which are reported in Figure S1, confirm that there is significant heterogeneity across study observations for all five outcome variables. Hence it is useful to further disaggregate the results. Table 2 shows a breakdown by modified crop trait. While significant reductions in pesticide costs are observed for both HT and IR crops, only IR crops cause a consistent reduction in pesticide quantity. Such disparities are expected, because the two technologies are quite different. IR crops protect themselves against certain insect pests, so that spraying can be reduced. HT crops, on the other hand, are not protected against pests but against a broad-spectrum chemical herbicide (mostly glyphosate), use of which facilitates weed control. While HT crops have reduced herbicide quantity in some situations, they have contributed to increases in the use of broad-spectrum herbicides elsewhere [2,11,19]. The savings in pesticide costs for HT crops in spite of higher quantities can be explained by the fact that broad-spectrum herbicides are often much cheaper than the selective herbicides that were used before. The average farmer profit effect for HT crops is large and positive, but not statistically significant because of considerable variation and a relatively small number of observations for this outcome variable.

Impact heterogeneity and possible biases

Table 3 shows the estimation results from the meta-regressions that explain how different factors influence impact heterogeneity. Controlling for other factors, yield gains of IR crops are almost 7 percentage points higher than those of HT crops (column 1). Furthermore, yield gains of GM crops are 14 percentage points higher in developing countries than in developed countries. Especially smallholder farmers in the tropics and subtropics suffer from considerable pest damage that can be reduced through GM crop adoption [27].

Most original studies in this meta-analysis build on farm surveys, although some are based on field-trial data. Field-trial results are often criticized to overestimate impacts, because farmers may not be able to replicate experimental conditions. However, results in Table 3 (column 1) show that field-trial data do not overestimate the yield effects of GM crops. Reported yield gains from field trials are even lower than those from farm surveys. This is plausible, because pest damage in non-GM crops is often more severe in farmers' fields than on well-managed experimental plots.

Table 2. Impacts of GM crop adoption by modified trait.

Outcome variable	All GM crops	Insect resistance	Herbicide tolerance
Yield	21.57*** (15.65; 27.48)	24.85*** (18.49; 31.22)	9.29** (1.78; 16.80)
n/m	451/100	353/83	94/25
Pesticide quantity	−36.93*** (−48.01; −25.86)	−41.67*** (−51.99; −31.36)	2.43 (−20.26; 25.12)
n/m	121/37	108/31	13/7
Pesticide cost	−39.15*** (−46.96; −31.33)	−43.43*** (−51.64; −35.22)	−25.29*** (−33.84; −16.74)
n/m	193/57	145/45	48/15
Total production cost	3.25 (−1.76; 8.25)	5.24** (0.25; 10.73)	−6.83 (−16.43; 2.77)
n/m	115/46	96/38	19/10
Farmer profit	68.21*** (46.31; 90.12)	68.78*** (46.45; 91.11)	64.29 (−24.73; 153.31)
n/m	136/42	119/36	17/9

Average percentage differences between GM and non-GM crops are shown with 95% confidence intervals in parentheses. *, **, *** indicate statistical significance at the 10%, 5%, and 1% level, respectively. *n* is the number of observations, *m* the number of different primary datasets from which these observations are derived.
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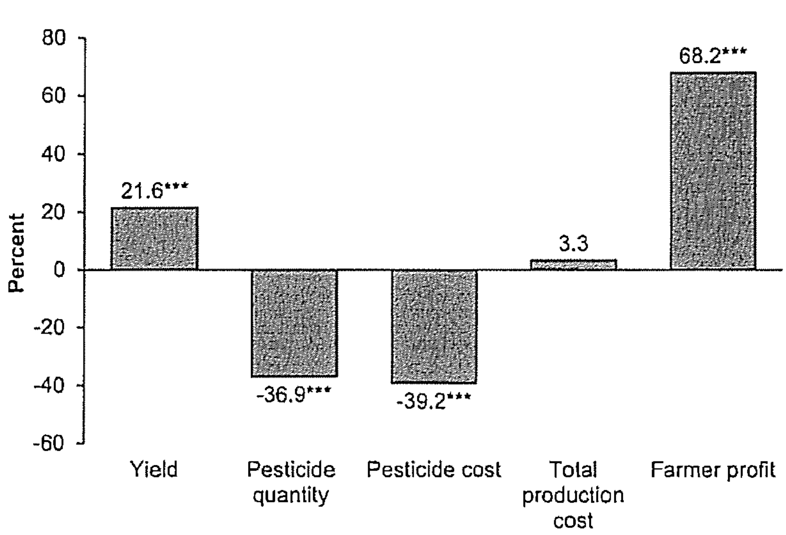

Figure 2. Impacts of GM crop adoption. Average percentage differences between GM and non-GM crops are shown. Results refer to all GM crops, including herbicide-tolerant and insect-resistant traits. The number of observations varies by outcome variable; yield: 451; pesticide quantity: 121; pesticide cost: 193; total production cost: 115; farmer profit: 136. *** indicates statistical significance at the 1% level.
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Another concern often voiced in the public debate is that studies funded by industry money might report inflated benefits. Our results show that the source of funding does not significantly influence the impact estimates. We also analyzed whether the statistical method plays a role. Many of the earlier studies just compared yields of GM and non-GM crops without considering possible differences in other inputs and conditions that may also affect the outcome. Net impacts of GM technology can be estimated with regression-based production function models that control for other factors. Interestingly, results derived from regression analysis report higher average yield effects.

Finally, we examined whether the type of publication matters. Controlling for other factors, the regression coefficient for journal publications in column (1) of Table 3 implies that studies published in peer-reviewed journals show 12 percentage points higher yield gains than studies published elsewhere. Indeed, when only including observations from studies that were published in journals, the mean effect size is larger than if all observations are included (Figure S2). On first sight, one might suspect publication bias, meaning that only studies that report substantial effects are accepted for publication in a journal. A common way to assess possible publication bias in meta-analysis is through funnel plots [25], which we show in Figure S3. However, in our case these funnel plots should not be over-interpreted. First, only studies that report variance measures can be included in the funnel plots, which holds true only for a subset of the original studies used here. Second, even if there were publication bias, our mean results would be estimated correctly, because we do include studies that were not published in peer-reviewed journals.

Further analysis suggests that the journal review process does not systematically filter out studies with small effect sizes. The journal articles in the sample report a wide range of yield effects, even including negative estimates in some cases. Moreover, when combining journal articles with papers presented at academic conferences, average yield gains are even higher (Table 3, column 2). Studies that were neither published in a journal nor presented at an academic conference encompass a diverse set of papers, including reports by NGOs and outspoken biotechnology critics. These reports show lower GM yield effects on average, but not all meet common scientific standards. Hence, rather than indicating publication bias, the positive and significant journal coefficient may be the result of a negative NGO bias in some of the grey literature.

Concerning other outcome variables, IR crops have much stronger reducing effects on pesticide quantity than HT crops (Table 3, column 3), as already discussed above. In terms of pesticide costs, the difference between IR and HT is less pronounced and not statistically significant (column 4). The profit gains of GM crops are 60 percentage points higher in developing countries than in developed countries (column 6). This large difference is due to higher GM yield gains and stronger pesticide cost savings in developing countries. Moreover, most GM crops are not patented in developing countries, so that GM seed prices are lower [19]. Like for yields, studies published in peer-reviewed journals report higher profit gains than studies published elsewhere, but again we do not find evidence of publication bias (column 7).

Conclusion

This meta-analysis confirms that in spite of impact heterogeneity the average agronomic and economic benefits of GM crops are large and significant. Impacts vary especially by modified crop trait and geographic region. Yield gains and pesticide reductions are larger for IR crops than for HT crops. Yield and farmer profit gains are higher in developing countries than in developed countries. Recent impact studies used better data and methods than earlier studies, but these improvements in study design did not reduce the estimates of GM crop advantages. Rather, NGO reports and other publications without scientific peer review seem to bias the impact estimates downward. But even with such biased estimates included, mean effects remain sizeable.

One limitation is that not all of the original studies included in this meta-analysis reported sample sizes and measures of variance. This is not untypical for analyses in the social sciences, especially when studies from the grey literature are also included. Future

Table 3. Factors influencing results on GM crop impacts (%).

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Variables	Yield	Yield	Pesticide quantity	Pesticide cost	Total cost	Farmer profit	Farmer profit
Insect resistance (IR)	6.58** (2.85)	5.25* (2.82)	−37.38*** (11.81)	−7.28 (5.44)	5.63 (5.60)	−22.33 (21.62)	−33.41 (21.94)
Developing country	14.17*** (2.72)	13.32*** (2.65)	−10.23 (8.99)	−19.16*** (5.35)	3.43 (4.78)	59.52*** (18.02)	60.58*** (17.67)
Field-trial data	−7.14** (3.19)	−7.81** (3.08)	–#	−17.56 (11.45)	−10.69* (5.79)	–#	–#
Industry-funded study	1.68 (5.30)	1.05 (5.21)	37.04 (23.08)	−7.77 (10.22)	–#	–#	–#
Regression model result	7.38* (3.90)	7.29* (3.83)	9.67 (10.40)	–#	–#	−11.44 (24.33)	−9.85 (24.03)
Journal publication	12.00*** (2.52)	–	9.95 (6.79)	−3.71 (4.09)	−3.08 (3.30)	48.27*** (15.48)	–
Journal/academic conference	–	16.48*** (2.64)	–	–	–	–	65.29*** (17.75)
Constant	−0.22 (2.84)	−2.64 (2.86)	−4.44 (10.33)	−16.13 (4.88)	−1.02 (4.86)	8.57 (24.33)	−1.19 (24.53)
Observations	451	451	121	193	115	136	136
R^2	0.23	0.25	0.20	0.14	0.12	0.12	0.14

Coefficient estimates from linear regression models are shown with standard errors in parentheses. Dependent variables are GM crop impacts measured as percentage differences between GM and non-GM. All explanatory variables are 0/1 dummies (for variable definitions see Table 1). The yield models in columns (1) and (2) and the farmer profit models in columns (6) and (7) have the same dependent variables, but they differ in terms of the explanatory variables, as shown. *, **, *** indicate statistical significance at the 10%, 5%, and 1% level, respectively. # indicates that the variable was dropped because the number of observations with a value of one was smaller than 5.

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impact studies with primary data should follow more standardized reporting procedures. Nevertheless, our findings reveal that there is robust evidence of GM crop benefits. Such evidence may help to gradually increase public trust in this promising technology.

Supporting Information

Figure S1 Histograms of effect sizes for the five outcome variables.
(PDF)

Figure S2 Impacts of GM crop adoption including only studies published in journals.
(PDF)

Figure S3 Funnel plots for the five outcome variables.
(PDF)

Table S1 List of publications included in the meta-analysis.
(PDF)

Table S2 Distribution of study descriptor dummy variables for different outcomes.
(PDF)

Table S3 Weighted mean impacts of GM crop adoption.
(PDF)

Data S1 Data used for the meta-analysis.
(PDF)

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Author Contributions

Conceived and designed the research: WK MQ. Analyzed the data: WK MQ. Contributed to the writing of the manuscript: WK MQ. Compiled the data: WK.

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Prevalence and impacts of genetically engineered feedstuffs on livestock populations

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Prevalence and impacts of genetically engineered feedstuffs on livestock populations[1]

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ABSTRACT: Globally, food-producing animals consume 70 to 90% of genetically engineered (GE) crop biomass. This review briefly summarizes the scientific literature on performance and health of animals consuming feed containing GE ingredients and composition of products derived from them. It also discusses the field experience of feeding GE feed sources to commercial livestock populations and summarizes the suppliers of GE and non-GE animal feed in global trade. Numerous experimental studies have consistently revealed that the performance and health of GE-fed animals are comparable with those fed isogenic non-GE crop lines. United States animal agriculture produces over 9 billion food-producing animals annually, and more than 95% of these animals consume feed containing GE ingredients. Data on livestock productivity and health were collated from publicly available sources from 1983, before the introduction of GE crops in 1996, and subsequently through 2011, a period with high levels of predominately GE animal feed. These field data sets, representing over 100 billion animals following the introduction of GE crops, did not reveal unfavorable or perturbed trends in livestock health and productivity. No study has revealed any differences in the nutritional profile of animal products derived from GE-fed animals. Because DNA and protein are normal components of the diet that are digested, there are no detectable or reliably quantifiable traces of GE components in milk, meat, and eggs following consumption of GE feed. Globally, countries that are cultivating GE corn and soy are the major livestock feed exporters. Asynchronous regulatory approvals (i.e., cultivation approvals of GE varieties in exporting countries occurring before food and feed approvals in importing countries) have resulted in trade disruptions. This is likely to be increasingly problematic in the future as there are a large number of "second generation" GE crops with altered output traits for improved livestock feed in the developmental and regulatory pipelines. Additionally, advanced techniques to affect targeted genome modifications are emerging, and it is not clear whether these will be encompassed by the current GE process-based trigger for regulatory oversight. There is a pressing need for international harmonization of both regulatory frameworks for GE crops and governance of advanced breeding techniques to prevent widespread disruptions in international trade of livestock feedstuffs in the future.

Key words: genetic engineering, genetically modified organisms, livestock feed, safety

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INTRODUCTION

The first genetically engineered (GE) feed crops were introduced in 1996. Their subsequent adoption has been swift. In 2013, GE varieties were planted on more than 95% of sugar beet, 93% of soy, and 90% of all cotton and corn acres in the United States (USDA National Agricultural Statistics Service, 2013). Global livestock populations constitute the largest consumers of GE feed crops. Independent studies have shown the compositional equivalence of the current generation of GE crops (Cheng et al., 2008; Garcia-Villalba et al., 2008; Herman and Price, 2013; Hollingworth et al., 2003), and no significant differences in feed digestibility, performance, or health have been observed in livestock that consume GE feed (Flachowsky et al., 2012). Similarly, it is not possible to detect differences in nutritional profiles of animal products after consumption of GE feed (Guertler et al., 2010; Tufarelli and Laudadio, 2013).

Despite these findings, some states have considered legislation that would require mandatory GE labeling

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of meat, milk, and eggs derived from animals that have eaten GE feed (CAST, 2014). Furthermore, some food companies are actively targeted by campaigns to promote products from animals that are fed non-GE diets. Given the widespread adoption of GE crops, the segment of animal agriculture that is currently feeding non-GE diets is relatively small. Approximately 0.8% of U.S. cropland and 0.5% of U.S. pasture were certified organic in 2011 (USDA National Agricultural Statistics Service, 2012), and only a portion of organic crops are used for animal feed.

Our objective was to briefly review the literature on livestock GE feeding studies and the composition of animal products derived from animals fed a GE diet. We gave special attention to health studies of animals, including an analysis of publicly available data on the health of commercial livestock populations since the introduction of GE crops in 1996. Also, we summarized the global usage and trade of GE feedstuffs along with the estimated size of GE-sensitive markets. Finally, we discussed issues regarding pipeline and regulation of GE crops with modified output traits, asynchronous regulatory approvals, and novel breeding technologies.

Livestock Feeding Studies with Genetically Engineered Feed

A total of 165 GE crop events in 19 plant species, including those used extensively in animal feed (alfalfa, canola, corn, cotton, soybean, and sugar beet), have been approved in the United States (James, 2013). Before approval, each new GE crop goes through a comprehensive risk assessment. The risk analysis of GE organisms is governed by internationally accepted guidelines developed by the Codex Alimentarius Commission (www.codexalimentarius.org). One leading principle is the concept of substantial equivalence, which stipulates that any new GE variety should be assessed for its safety by comparing it with an equivalent, conventionally bred variety that has an established history of safe use. Over the past 20 yr, the U.S. Food and Drug Administration found all of the 148 GE transformation events that they evaluated to be substantially equivalent to their conventional counterparts, as have Japanese regulators for 189 submissions (Herman and Price, 2013). By contrast, plant varieties developed through other processes of achieving genetic changes (e.g., radiation mutagenesis) go through no formal risk assessment before being placed on the market. There have been instances where plants bred using classical techniques have been unsuitable for human consumption. For example, the poison α-solanine, a glycoalkaloid, was unintentionally increased to unacceptable levels in certain varieties of potato through plant breeding resulting in certain cultivars being withdrawn from the U.S. and Swedish markets due to frequently exceeding the upper safe limit for total glycoalkaloid content (Petersson et al., 2013).

The difficulties associated with the safety and nutritional testing of whole foods/feed derived from GE crops, which contain thousands of bioactive substances, are well known (reviewed in Bartholomaeus et al., 2013). These include the fact that the quantity of the GE food that can be included in the diet of test animals is limited by the potential to generate nutritional imbalances and might not be high enough to detect adverse effects. Substantial differences in composition could be present without producing a recognizably meaningful difference between treatment groups fed whole foods. Many toxicologists concur that animal feeding trials of whole GE food have a low power to detect adverse effects and contribute little, if anything, to the safety assessment of whole foods (Kuiper et al., 2013). Far more sensitive analytical, bioinformatical, and specific toxicological methods exist to identify unintended effects resulting from plant breeding and provide more precise and quantifiable data for the safety evaluation of whole foods.

In 2013, the European Union (EU) Standing Committee on the Food Chain and Animal Health (Brussels, Belgium) adopted a regulation mandating a 90-d subchronic rodent feeding study (OECD, 1998) for every single GE transformation event. This is despite the fact that the European Food Safety Authority (2008; Parma, Italy) states that such testing is only warranted when driven by a specific hypothesis indicated by molecular, compositional, phenotypic, agronomic, or other analysis (e.g., metabolic pathway considerations) of the particular GE event. This mandate is seen by some as interference in the risk assessment of GE foods based on pseudoscience or political considerations (Kuiper et al., 2013). The United States and Australia/New Zealand explicitly do not require a 90-d subchronic rodent feeding study or actively discourage their conduct due to their negligible scientific value.

Studies in which GE crops are fed to target (food-producing) animals have focused less on GE risk assessment and more on evaluating the nutritional properties of the GE crop as well as resulting animal performance and health as compared to the results when fed an isogenic counterpart. Clear guidelines on experimental design for these types of studies have been developed (International Life Sciences Institute, 2003, 2007).

Multiple generations of food animals have been consuming 70 to 90% of harvested GE biomass (Flachowsky et al., 2012) for more than 15 yr. Several recent comprehensive reviews from various authors summarize the results of food-producing animal feeding studies with the current generation of GE crops (Deb et al., 2013; Flachowsky, 2013; Flachowsky et al., 2012; Tufarelli and Laudadio, 2013; Van Eenennaam, 2013). Studies have

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been conducted with a variety of food-producing animals including sheep, goats, pigs, chickens, quail, cattle, water buffalo, rabbits, and fish fed different GE crop varieties. The results have consistently revealed that the performance and health of GE-fed animals were comparable with those fed near-isogenic non-GE lines and commercial varieties. Many authors came to the same conclusion a decade ago (Aumaitre et al., 2002; Faust, 2002), suggesting that little contradictory data has emerged over the past 10 yr, despite the increased global prevalence of GE feed.

A number of long-term (of more than 90 d and up to 2 yr in duration) feeding trials and multigenerational studies conducted by public research laboratories using various animal models including pigs, cows, quail, and fish have also been reviewed (Ricroch, 2013; Ricroch et al., 2013; Snell et al., 2012). Significant among these studies are 2 thorough multigenerational studies that examined the long-term effects of feeding a GE corn variety (MON810, expressing the insecticidal Cry1Ab protein from *Bacillus thuringiensis* [**Bt**], one of the few GE corn varieties approved for cultivation in the EU) to food-producing animals, specifically, a German study in dairy cattle and an Irish study in pigs (Guertler et al., 2010, 2012; Steinke et al., 2010; Walsh et al., 2011, 2012 a, b, 2013; Buzoianu et al., 2012 a, b, c, d, 2013 a, b). The results from the multiple papers resulting from these 2 studies are summarized in Table 1. These studies were notable in that they included appropriate controls consuming isogenic non-GE lines of corn, and both comprehensively examined a range of phenotypes and indicators of growth and health and also used sophisticated techniques to look for the presence of recombinant DNA (**rDNA**) and Bt protein in the tissues and products derived from these GE-fed animals.

Results from these comprehensive studies revealed the compositional and nutritional noninferiority of GE corn to its isogenic control and an absence of long-term adverse effects from GE corn consumption. Organ pathology and function were similar between animals fed GE and non-GE corn, and there were no adverse effects of feeding GE corn on small intestinal morphology or the gut microbiota. Antibodies specific to the GE corn protein (Cry1Ab) were not detected in the blood, indicating the absence of an allergic-type immune response to the protein. Neither the *cry1Ab* gene nor the Cry1Ab protein was found in the blood, organs, or products of animals fed GE corn, indicating that neither the intact rDNA nor the intact recombinant protein migrated from the digestive system of the animal into other body tissues or edible animal products.

Even though these 2 comprehensive studies overwhelmingly revealed that a diet of Bt corn was not associated with long-term deleterious effects on the immune systems or animal performance, there were statistically significant differences in some of the parameters measured. Although the authors concluded that these differences were not of biological relevance, significant findings in any parameter in animal feeding studies have been interpreted by some as evidence of harm (Dona and Arvanitoyannis, 2009). Others have pointedly responded that statistical differences per se are not "adverse effects" and need to be considered in terms of their biological importance (Rickard, 2009). The European Food Safety Authority clarified the difference between statistical significance and biological relevance (European Food Safety Authority, 2011). In the absence of some predefined understanding of what changes might be of biological relevance, studies risk becoming "hypothesis-less fishing trips." Post hoc analysis of a large number of variables in a data set with a small sample size can lead to spurious conclusions because such studies "are fraught with differences that are not biologically significant between groups from simple variation and probability" (DeFrancesco, 2013).

The Federation of Animal Science Societies maintains an extensive bibliography of food-producing animal GE feeding studies (FASS 2014). Given the large number of 90-d subchronic rodent and food-producing animal GE feeding studies that currently exist in the literature, it is worth questioning the value of more animal feeding studies as part of a GE risk assessment for crops that are substantially equivalent to conventional comparators (Flachowsky, 2013). The rationale for conducting long-term feeding trials and multigenerational studies need to be explicitly stated, especially given that GE proteins are digested in the gut and no intact GE protein has been found in the bloodstream. Once compositional equivalence has been established for a GE crop, animal feeding studies add little to the safety assessment (Bartholomaeus et al., 2013).

There are less than 100 long-term (>90 d) and multigenerational target animal GE feeding studies in the peer-reviewed literature, which has prompted some to call for more of these types of feeding studies (DeFrancesco, 2013). Although such studies may seem intuitively appealing, they must result in novel useful data to justify the additional time, expense, and animal experimentation. Objective analyses of available data indicate that, for a wide range of substances, reproductive and developmental effects observed in long-term studies are not potentially more sensitive endpoints than those examined in 90-d rodent subchronic toxicity tests (European Food Safety Authority, 2008). There is no evidence that long-term and multigenerational feeding studies of the first generation of GE crops that have been conducted to date have uncovered adverse effects that were undetected by short-term rodent feeding studies (Snell et al., 2012). In the context of GE feed risk assessment, they argue that the decision to conduct long-term and

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Table 1. Summary results of 2 comprehensive evaluations of target animal effects of long-term feeding of genetically engineered feed (Bt-MON810 corn) to dairy cattle and pigs[1]. Table adapted from Ricroch et al. (2013)

Study Design	Methods	Results	Conclusions	Reference
A. Dairy cattle study				
36 Simmental dairy cows (9 primiparous and 9 multiparous per treatment group) were assigned to 2 feeding groups and fed with diets based on whole-crop silage, kernels, and whole-crop cobs from GE corn (Bt-MON810) or its isogenic non-GE counterpart as main components. The 765-d study included 2 consecutive lactations.	Feed intake, milk production and composition, and body condition over 25 mo	There were no consistent effects of feeding GE corn or its isogenic control on milk composition or body condition. All changes fell within normal ranges.	Compositional and nutritional equivalence of GE corn to its isogenic control. No long-term effects	Steinke et al. (2010)
	Gene expression pattern of markers for apoptosis, inflammation, and cell cycle from gastrointestinal tract and samples from liver	Statistical analysis of the examined gene expression pattern revealed no significant difference in the gene expression profile of cows fed transgenic or near-isogenic feed ration	Genetically engineered maize MON810 does not have any effect on major genes involved in apoptosis, inflammation, and cell cycle in the gastrointestinal tract and in the liver of dairy cows.	Guertler et al. (2012)
	Fate of *cry1Ab* DNA and recombinant protein	All blood, milk, and urine samples were free of recombinant DNA and protein. The *cry1Ab* gene was not detected in any fecal samples; however, fragments of the Cry1Ab protein were detected in feces from all cows fed transgenic feed.	Milk of dairy cows fed GE corn for 25 mo should be classified not different from milk of cows fed non-GE corn.	Guertler et al. (2010)
B. Pig study				
Large white × landrace cross-bred male 40-d-old pigs (n = 40) were fed 1 of the following treatments: 1) isogenic corn-based diet for 110 d (isogenic), 2) Bt corn-based diet (MON810) for 110 d (Bt), 3) isogenic corn-based diet for 30 d followed by Bt corn-based diet for 80 d (isogenic/Bt), and 4) Bt corn-based diet (MON810) for 30 d followed by isogenic corn-based diet for 80 d (Bt/isogenic).	Feed intake, growth, characteristics, and body composition. Heart, kidneys, spleen and liver weight and histological analysis. Blood and urine analysis.	No difference in overall growth, body composition, organ weight, histology and serum and urine biochemistry. A significant treatment × time interaction was observed for serum urea, creatinine, and aspartate aminotransferase.	Serum biochemical parameters did not indicate organ dysfunction; changes were not accompanied by histological lesions. Long-term feeding of GE maize did not adversely affect growth or the selected health indicators investigated.	Buzoianu et al. (2012a)
	Effect on intestinal microbiota	Counts of the culturable bacteria enumerated in the feces, ileum, or cecum were not affected by GE feed. Neither did it influence the composition of the cecal microbiota, with the exception of a minor increase in the genus *Holdemania*.	Feeding Bt corn to pigs in the context of its influence on the porcine intestinal microbiota is safe.	Buzoianu et al. (2012d)
	Hematological analysis, measurement of cytokine and Cry1Ab-specific antibody production, immune cell phenotyping, and *cry1Ab* gene and truncated Bt toxin detection	On d 100, lymphocyte counts were higher (P < 0.05) in pigs fed Bt/isogenic than pigs fed Bt or isogenic. Erythrocyte counts on d 100 were lower in pigs fed Bt or isogenic/Bt than pigs fed Bt/isogenic (P < 0.05). Neither the truncated Bt toxin nor the *cry1Ab* gene was detected in the organs or blood of pigs fed Bt corn.	Perturbations in peripheral immune response were thought not to be age specific and were not indicative of Th 2 type allergenic or Th 1 type inflammatory responses. No evidence of *cry1Ab* gene or Bt toxin translocation to organs or blood following long-term feeding.	Walsh et al. (2012b)
Large White × Landrace cross-bred male pigs (9 per treatment group) fed diet containing 38.9% GE or non-GE isogenic parent line corn for 31 d.	Growth performance, intestinal histology, and organ weight and function.	Short-term feeding of Bt MON810 corn to weaned pigs resulted in increased feed consumption, less efficient conversion of feed to gain, and a decrease in goblet cells/mum of duodenal villus. There was a tendency for an increase in kidney weight, but this was not associated with changes in histopathology or blood biochemistry.	The biological significance of these findings is currently being clarified in long-term exposure studies in pigs.	Walsh et al. (2012a)
	Effects on the porcine intestinal microbiota were assessed through culture-dependent and -independent approaches.	Fecal, cecal, and ileal counts of total anaerobes, Enterobacteriaceae, and Lactobacillus were not significantly different between pigs fed the isogenic or Bt corn-based diets. Furthermore, high-throughput 16S rRNA gene sequencing revealed few differences in the compositions of the cecal microbiotas.	*Bacillus thuringiensis* corn is well tolerated by the porcine intestinal microbiota.	Buzoianu et al. (2012c)
	Immune responses and growth in weanling pigs. Determined the fate of the transgenic DNA and protein in vivo.	Interleukin-12 and interferon gamma production from mitogenic stimulated peripheral blood mononuclear cells decreased in GE-fed pigs. Cry1Ab-specific IgG and IgA were not detected in the plasma of GE corn-fed pigs. The detection of the *cry1Ab* gene and protein was limited to the gastrointestinal digesta and was not found in the kidneys, liver, spleen, muscle, heart, or blood.	No evidence of *cry1Ab* gene or protein translocation to the organs and blood of weaning pigs. The growth of pigs was not affected by feeding GE corn. Alterations in immune responses were detected; however, their biologic relevance is questionable.	Walsh et al. (2011)

continued

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Table 1. (cont.)

Large White × Landrace cross-bred female pigs (12) – Fed for approximately 143 d throughout gestation and lactation F_0 + 1 generation (offspring at birth). Large White × Landrace cross-bred pigs (10) – Corn dietary inclusion rate identical between treatments (isogenic parent line corn from service to weaning and GE corn from service to weaning [Bt]) and ranged from 86.6% during gestation to 74.4% during lactation). Offspring (72) fed in 4 dietary treatments as follows: 1) non-GE corn-fed sow/non-GE corn-fed offspring (non-GE/non-GE), 2) non-GE corn-fed sow/GE corn-fed offspring (non-GE/GE), 3) GE corn-fed sow/non-GE corn-fed offspring (GE/non-GE), and 4) GE corn-fed sow/GE corn-fed offspring (GE/GE) for 115 d.	Hematological and immune functions to detect possible inflammatory and allergenic responses at various times. Attempts to detect Cry1Ab protein in blood and feces at various times.	Cytokine production similar between treatments. Some differences in monocyte, granulocyte, or lymphocyte subpopulations counts at some times, but no significant patterns of changes.	No indication for inflammation or allergy due to GE corn feeding. Transgenic material or Cry1Ab-specific antibodies were not detected in sows or offspring.	Buzoianu et al. (2012b)
	Pig growth performance, BW, and feed disappearance recorded at the time of each dietary change (at weaning [d 0] and on d 30, 70, and 100) and at harvest (d 115). At harvest, organ weight, histological observations, and cold carcass weight. Serum biochemistry.	No pathology observed in the organs. Offspring of sows fed Bt corn had improved growth throughout their productive life compared to offspring of sows fed non-GE corn, regardless of the corn line fed between weaning and harvest. Some minor differences in average daily gain, carcass and spleen weights, dressing percentage, and duodenal crypt depths for offspring from GE fed or in average daily feed intake for offspring from sows fed GE and for GE-fed pigs or in liver weight for pigs in the GE/GE.	Feeding GE Bt corn from 12 d after weaning to slaughter had no adverse effect on pig growth performance, body composition, organ weights, carcass characteristics, or intestinal morphology. Transgenerational consumption of GE corn diets not detrimental to pig growth and health.	Buzoianu et al. (2013a)
	Sequence based analysis of the intestinal microbiota of sows and their offspring fed GE corn	At d 115 postweaning, GE/non-GE offspring had lower ileal Enterobacteriaceae counts than non-GE/non-GE or GE/GE offspring and lower ileal total anaerobes than pigs on the other treatments. Genetically engineered corn-fed offspring also had higher ileal total anaerobe counts than non-GE corn-fed offspring, and cecal total anaerobes were lower in non-GE/GE and GE/non-GE offspring than in those from the non-GE/non-GE treatment. The only differences observed for major bacterial phyla using 16S rRNA gene sequencing were that fecal Proteobacteria were less abundant in GE corn-fed sows before farrowing and in offspring at weaning, with fecal Firmicutes more abundant in offspring.	While other differences occurred, they were not observed consistently in offspring, were mostly encountered for low-abundance, low-frequency bacterial taxa, and were not associated with pathology. Therefore, their biological relevance is questionable. This confirms the lack of adverse effects of GE corn on the intestinal microbiota of pigs, even following transgenerational consumption.	Buzoianu et al. (2013b)
	The effects of feeding GE corn during first gestation and lactation on maternal and offspring health serum total protein, creatinine and gamma-glutamyltransferase activity, serum urea, platelet count, and mean cell Hb concentration	Genetically engineered corn-fed sows were heavier on d 56 of gestation. Offspring from sows fed GE corn tended to be lighter at weaning. Sows fed GE corn tended to have decreased serum total protein and increased serum creatinine and gamma-glutamyltransferase activity on d 28 of lactation. Serum urea tended to be decreased on d 110 of gestation in GE corn-fed sows and in offspring at birth. Both platelet count and mean cell Hb concentration (MCHC) were decreased on d 110 of gestation in GE corn-fed sows; however, MCHC tended to be increased in offspring at birth.	There was a minimal effect of feeding GE corn to sows during gestation and lactation on maternal and offspring serum biochemistry and hematology at birth or BW at weaning.	Walsh et al. (2013)

[1]GE = genetically engineered; Bt = *Bacillus thuringiensis*; Hb = hemoglobin.

multigenerational studies should be reserved for cases where some reasonable doubt remains following a 90-d feeding trial triggered by a potential hazard identified in the compositional analysis of the GE crop or other available nutritional or toxicological data.

Field Datasets of Livestock Populations Fed with Genetically Engineered Feed

Although a small number of controlled long-term and multigenerational feeding trials of commercialized GE crops in food-producing species are available in the peer-reviewed literature, large numbers of livestock in many countries have been consuming GE feed for over 15 yr. Hence, a very large and powerful set of GE-fed target animal data has been quietly amassing in public databases. United States agriculture feeds billions of food-producing animals each year, with annual broiler numbers alone exceeding the current size of the global human population (Table 2). During 2011, less than 5% of U.S. animals within each of the major livestock sectors were raised for certified National Organic Program (NOP) markets that specifically prohibit the feeding of GE feed (Table 2). Given the increase in GE adoption rates between 2000 and 2013, it can be predicted that the vast majority of conventionally raised livestock in

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Table 2. Organic livestock production statistics in the United States (2011)

Industry	Number of organic farms in the United States[1]	Number of animals on organic farms[1]	Total number of livestock animals in the United States[2]	Organic livestock numbers as percent of the U.S. total[3]
Broilers	153	28,644,354	8,607,600,000	0.33%
Layers	413	6,663,278	338,428,000	1.97%
Turkeys	70	504,315	248,500,000	0.20%
Beef cows	488	106,181	30,850,000	0.34%
Dairy cows	1,848	254,711	9,150,000	2.78%
Hogs	97	12,373	110,860,000	0.01%

[1]USDA National Agricultural Statistics Service, 2012.
[2]USDA Economics, Statistics, and Market Information System, 2013.
[3]USDA Economic Research Service, 2013.

the United States consumed feed derived from GE crops over the past decade. Cumulatively, this amounts to over 100 billion animals consuming some level of GE feed between 2000 and 2011 (Table 3).

The duration and level of exposure to GE feed would be expected to vary depending on the animal industry. For example, in a typical U.S. broiler operation, chickens are fed for 42–49 d on diets that are composed of approximately 35% soybean meal and 65% corn grain, whereas in others species, longer-term exposure would be the norm (e.g., dairy cows over recurrent lactations). The average U.S. dairy cow has a productive life of 5 yr with 3 conceptions, 3 gestations, and 3 lactations. A typical U.S. dairy diet contains 50% corn silage, 20% corn grain, and 10% dehulled soybean meal. Also, many cows receive large portions of their rations as ground corn grain, fuzzy cottonseed (no processing except for removal of the lint), or roasted full-fat soybeans. Other GE sources of animal feed include alfalfa hay, sugar beet pulp, corn distillers grains or other coproducts from corn processing, cottonseed meal, canola meal, and soy hulls. A beef cow on the range might consume only some GE alfalfa hay, but her progeny entering the feedlot might be expected to consume a ration containing high quantities of GE feed during their 120 d in the feedlot before harvest. Depending on the feeding stage and relative feed prices, feedlot rations will consist of about 80 to 85% grain (usually corn); distillers' grains and/or other sources of starch/energy; and 10 to 15% hay, silage, or other forage. The remaining share of the ration will include some protein source such as soybean or cottonseed meal (Mathews and Johnson, 2013), also likely to be of GE origin.

Table 3. Estimated cumulative number of livestock raised in the United States during the period from 2000 to 2011

Industry[1]	United States
Broilers	94,683,600,000
Layer Hens	3,722,708,000
Turkeys	2,733,500,000
Beef cattle	339,350,000
Dairy Cows	33,550,000
Hogs	1,219,460,000
Total	102,732,168,000

[1]Numbers for broilers, hogs (barrows and gilts), and beef cattle (steers) are for slaughtered animals during calendar year. Dairy animals are number of dairy cows in a calendar year divided by 3 to account for 3 lactations per animal.

It would be reasonable to hypothesize that if animal feed derived from GE crops had deleterious effects on animals consuming GE feed, then animal performance and health attributes in these large commercial livestock populations would have been negatively impacted. To examine this hypothesis further, in October 2013, data on livestock health were collated from publicly available sources in the United States from before the introduction of GE crops in 1996 through 2000 through 2011, a decade when high levels of GE ingredients would be expected to be present in livestock feed based on the known extent of GE crop cultivation. Data were collected for the broiler, dairy, hog, and beef industries. In general, USDA data sets were from the Economics, Statistics, and Market Information System (2013). Additional data for broilers were available from the National Chicken Council (2011) and were 1) days to market, 2) feed efficiency (feed to meat gain ratio), and 3) percent mortality.

Yearly data on cattle condemnation rates were available for 1999 through 2002 from the USDA Food Safety and Inspection Service (**FSIS**) website (USDA Food Safety and Inspection Service, 2003) and from 2003 through 2007 based on a Freedom of Information Act request as reported (White and Moore, 2009). Data from 1994 was collected from the National Non-Fed Beef Quality Audit as reported (Boleman et al., 1998). Non-fed beef is from culled cows and bulls (i.e., animals that do not spend a significant amount of time being "fed" in a feedlot). Data were analyzed to compare trends before and after the introduction of GE feed into livestock diets. Regression analyses were performed for the period 1983 through 1994 as representative of a period with no GE feed and for the period from 2000 through 2011 as a period with high levels of GE feed based on high rates of GE crop adoption. Where data were available for both time periods, the slope of the regression lines between periods was compared using an unpaired *t* test.

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Table 4. Livestock production statistics in the United States before and after the introduction of genetically engineered feed in 1996

Year	Milk yield, kg	Somatic cell count, cells/mL, 1,000s	Carcass wt, kg, broiler	Carcass wt, kg, hog	Carcass wt, kg, cattle	Broiler				Cattle postmortem condemned, %			
						Condemned, %	Market age, d	Mortality rate, %	Feed to gain	Fed cattle		Non-fed cattle	
										Steers	Heifers	Cows	Bulls
1983	5,708		1.82	75.3	318.8	1.54							
1984	5,667		1.85	75.7	317.5	1.60							
1985	5,910		1.87	76.6	329.3	1.74	49	5	2				
1986	6,029		1.89	77.1	327.4	1.90							
1987	6,252		1.91	77.6	325.2	1.91							
1988	6,446		1.92	78.5	330.2	1.95							
1989	6,460		1.93	78.0	336.1	1.95							
1990	6,640		1.95	79.4	336.1	1.83	48	5	2				
1991	6,742		1.97	79.8	343.3	1.87							
1992	6,995		2.01	79.8	344.7	1.72							
1993	7,054		2.03	81.2	338.8	1.58							
1994	7,315		2.06	81.6	351.9	1.68						2.6	
1995	7,461	304	2.08	82.1	348.8	1.79	47	5	1.95				
1996	7,485	308	2.12	82.1	347.4	1.80							
1997	7,671	314	2.14	83.9	346.5	1.82							
1998	7,797	318	2.16	83.9	357.8	1.86				0.09	0.10	2.22	0.26
1999	8,059	311	2.22	84.8	359.6	1.74				0.11	0.20	2.11	0.31
2000	8,256	316	2.22	86.6	361.9	1.56	47	5	1.95	0.13	0.17	2.71	0.32
2001	8,226	322	2.24	87.5	361.9	1.31				0.09	0.10	2.67	0.31
2002	8,422	320	2.28	87.5	373.2	1.07				0.08	0.09	2.77	0.24
2003	8,503	319	2.31	88.0	359.2	1.00				0.09	0.08	2.92	0.75
2004	8,597	295	2.34	88.0	361.0	1.13				0.08	0.08	2.44	0.35
2005	8,878	296	2.39	89.3	370.5	1.04	48	4	1.95	0.07	0.07	2.59	0.30
2006	9,048	288	2.44	89.8	377.8	1.22	48	5	1.96	0.06	0.07	2.34	0.30
2007	9,191	276	2.45	89.8	376.4	1.16	48	4.5	1.95	0.05	0.06	2.21	0.28
2008	9,250	262	2.48	89.8	380.0	1.10	48	4.5	1.93				
2009	9,332	233	2.48	90.7	384.1	0.91	47	4.1	1.92				
2010	9,591	228	2.53	91.2	378.7	0.88	47	4.0	1.92				
2011	9,680	217	2.58	92.1	381.4	0.87	47	3.8	1.91				

Livestock production statistics for the United States before and after the introduction of GE feed crops in 1986 are summarized in Table 4. In all industries, there were no obvious perturbations in production parameters over time. The available health parameters, somatic cell count (an indicator of mastitis and inflammation in the udder) in the dairy data set (Fig. 1), postmortem condemnation rates in cattle (Fig. 1), and postmortem condemnation rates and mortality in the poultry industry (Fig. 2) all decreased (i.e., improved) over time.

All animals arriving at USDA-inspected slaughter facilities undergo both antemortem and postmortem inspections to identify abnormalities. Carcasses are condemned postmortem if there are visible lesions or tumors present on organs and carcasses. Of the more than 163 million cattle arriving at USDA-inspected slaughter facilities for the years 2003 through 2007, a total of 769,339 (0.47%) were condemned (White and Moore, 2009). Cattle fed or finished in feedyards, typically for 120 d before slaughter on high concentrate diets containing corn and soy as major ingredients, made up the majority (82%) of the cattle at harvest but represented a minority (12%) of the cattle condemned. Condemnation rates for non-fed cattle, particularly cows, were higher than for fed cattle, but the rate in 2007 (2.49%), the last year for which data are available, was similar to that reported in cattle in 1994 (2.6%; Boleman et al., 1998), before the introduction of GE crops.

The broiler data are particularly important due to the large number of animals involved (approximately 9 billion broilers are processed annually in the United States) and the fact that there are several variables that are indicative of health (Fig. 2). The rate of broiler carcass condemnation decreased significantly over time and was at its lowest in 2011. Moreover, mortality was essentially unchanged throughout the years presented and was also at its lowest in 2011. Although broilers are exposed to large amounts of corn and soybean meal during their 42- to 49-d lifespan, they increase their body size 60-fold during this period, making them very sensitive to

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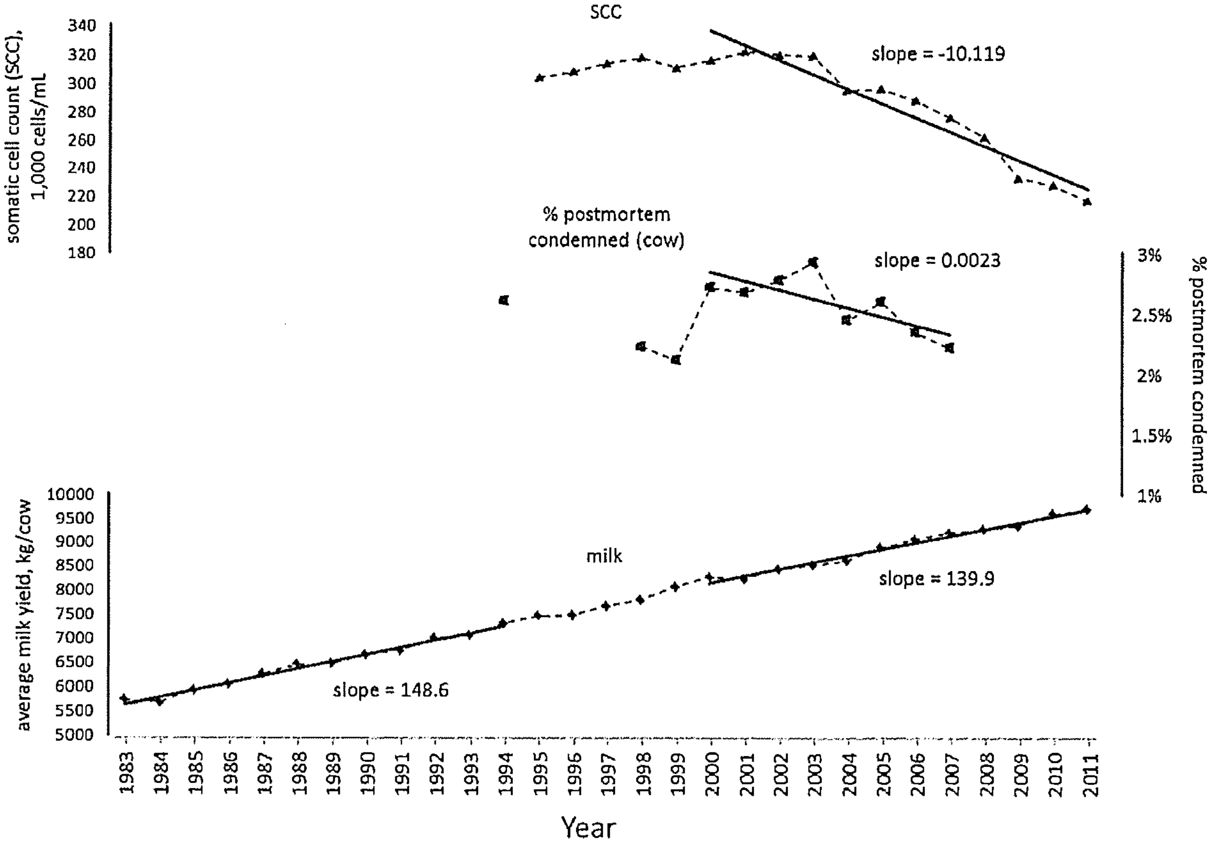

Figure 1. Milk production, percent postmortem condemned, and somatic cell counts for the United States before and after the introduction of genetically engineered crops in 1996. Sources: USDA National Agricultural Statistics Service, 2013; USDA Food Safety and Inspection Service, 2003; White and Moore, 2009; Boleman et al. (1998). Slope does not differ significantly between time periods 1983 through 1994 and 2000 through 2011.

dietary perturbations (European Food Safety Authority, 2008; International Life Sciences Institute, 2003). The conversion of feed to gain continuously decreased from 5 in 1985 to 3.8 in 2011, attributable most likely to improved genetics (Havenstein et al., 2003) and management, but this ratio is something that would be expected to worsen (i.e., increase) if the health of these animals was deteriorating following exposure to GE feed. An estimated 24 consecutive generations of broilers would have been consuming GE feed during the time period 2000 to 2011.

These field data sets representing billions of observations did not reveal unfavorable or unexpected trends in livestock health and productivity. The available health indicators from U.S. livestock suggest that these rates actually improved over time despite widespread adoption of GE crops in U.S. agriculture and increasing levels of GE content in livestock diets. There was no indication of worsening animal health after the introduction of GE feed, and productivity improvements continued in the same direction and at similar rates as those that were observed before the introduction of GE crop varieties in 1996.

A small number of experimental animal feeding studies have generated highly controversial results suggesting deleterious health effects of GE feed. Some of these reports were published and then retracted (Séralini et al., 2012), although recently and controversially republished without further peer review (Séralini et al., 2014), and others were never subjected to peer review (Ermakova, 2005; Velmirov et al., 2008). Adverse effects, including high rates of tumorogenesis, sterility, premature mortality, and histopathological abnormalities have been reported. These studies have been criticized for nonadherence to Organisation for Economic Co-operation and Development (Paris, France) consensus documents and standard protocols. Methodological flaws variously include the use of control feed that was not derived from near-isogenic lines, insufficient animal numbers to enable appropriate statistical power, lack of dose response or insufficient or no information on natural variations in test parameters, overinterpretation of differences that lie within the normal range of variation (i.e., the biological significance of differences is more important than their mere presence), and poor toxicological and/or statistical

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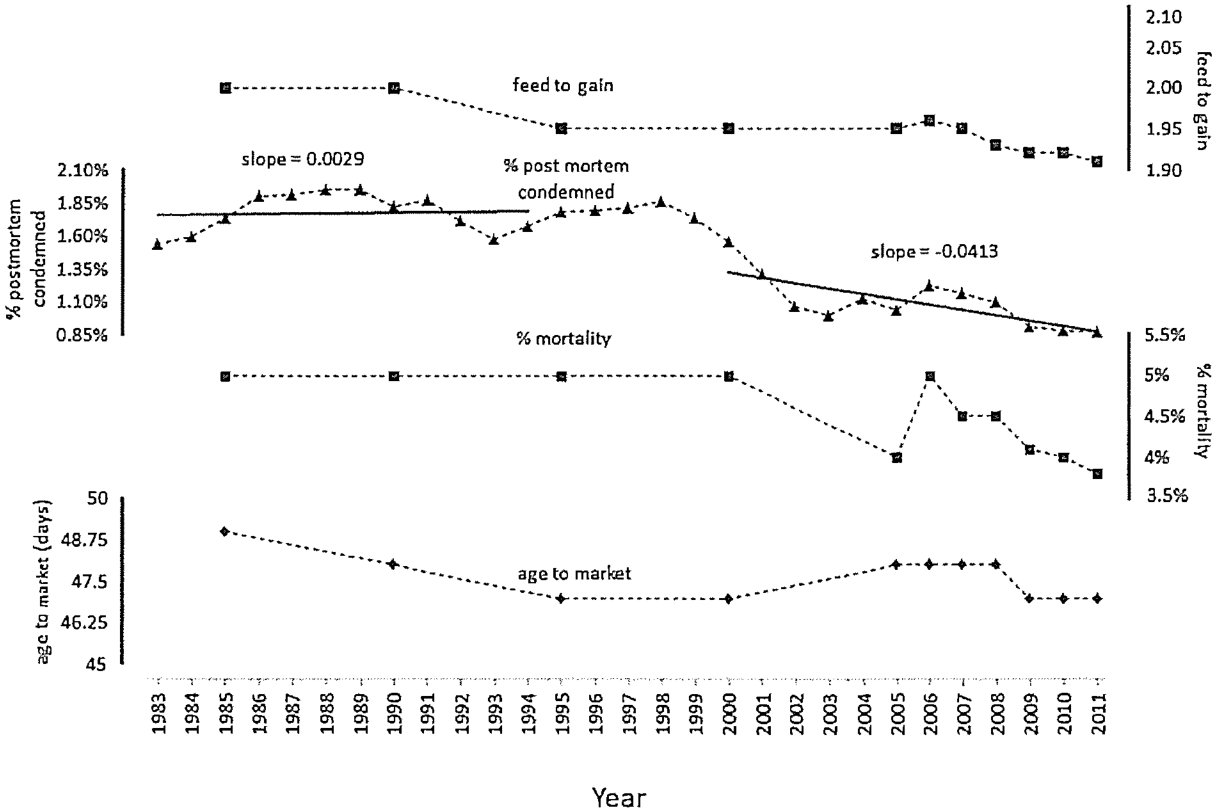

Figure 2. United States broiler statistics before and after the introduction of genetically engineered crops in 1996. Sources: USDA National Agricultural Statistics Service, 2013; National Chicken Council, 2011. Slope differs between time periods 1983 through 1994 and 2000 through 2011 (*$P < 0.05$).

interpretation of the data (Bartholomaeus et al., 2013; European Food Safety Authority, 2012; Marshall, 2007; Schorsch, 2013; The Australian and New Zealand Food Standards Agency, 2013, 2012). A particularly succinct summary of the methodological design flaws is presented in Table 5 (Bartholomaeus et al., 2013).

Despite a wealth of studies and literature to the contrary, these isolated and poorly designed studies have resulted in the promulgation of new regulations, including a mandatory 90-d rodent subchronic toxicity feeding study for all new GE approvals in the EU (Kuiper et al., 2013), and have generated a great deal of media attention (Arjó et al., 2013). They are also contrary to the field experience as documented by the health and production data collected on the billions of commercial food-producing animals that have primarily been consuming GE feed for over a decade. The media attention devoted to these sensational studies is exacerbating the continued controversy associated with the safety of GE food and feed and is bolstering arguments calling for the mandatory labeling of milk, meat, and eggs from GE-fed animals.

Summary of Data on Recombinant DNA/protein in Milk, Meat, and Eggs from Animals Fed Genetically Engineered Feed

Studies have concluded that animals do not digest transgenic and native plant DNA differently and that rDNA from GE crops has not been detected in animal products (Einspanier, 2013). Fragments of highly abundant plant DNA (e.g., chloroplast genomes) have been found in the digestive tracts and tissues of some species (Einspanier et al., 2001); however, neither recombinant DNA nor protein has ever been found in milk, meat, or eggs from animals that have eaten GE feed with the exception of a single study that reported the presence of fragments of transgenic DNA in both "organic" and "conventional" milk in Italy (Agodi et al., 2006). The organic milk was derived from animals not fed GE crops, so the authors postulated that the rDNA was due to feed and fecal contamination during milking of cows offered GE diets. This result has not been repeated despite recent studies using more sophisticated techniques that have looked for the presence of transgenic material in animal products (Buzoianu et al., 2012b; Deb et al., 2013; Guertler et al., 2010; Tufarelli and Laudadio, 2013). It is important to

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Table 5. Examples of limitations in experimental design, analyses, and interpretation in some whole food toxicity studies with genetically engineered (GE) crops (Bartholomaeus et al., 2013). Table reproduced with permission

Best practices	Deficiencies observed	References
Experimental design		
Identity of test and control substances	The identity of the GE test substance was not confirmed through an appropriate analytical method. Confirmation of correct control and test crop presence in diet was not conducted.	Brake and Evenson (2004), Ermakova (2005), Ewen and Pusztai (1999), Kilic and Akay (2008), and Malatesta et al. (2002a,b, 2003, 2005, 2008)
Use of appropriate control crops	The control crop was not of similar genetic background to the GE test crop. In some studies the control was simply identified as a "wild" variety.	Ermakova (2005), Ewen and Pusztai (1999), Malatesta et al. (2002a,b, 2003, 2005, 2008), and Rhee et al. (2005)
	The test and control substances were not produced under similar environmental conditions and/or no information was provided on the production of test and control substances.	Ermakova (2005), Ewen and Pusztai (1999), and Malatesta et al. (2002a,b, 2003, 2005, 2008)
Acceptable levels of contaminants (e.g., pesticides, mycotoxins, other microbial toxins) in control and test crops	Study results were not interpreted in light of differences in antinutrient or mycotoxin levels in test and control diets.	Carman et al. (2013) and Velmirov et al. (2008)
Nutritionally balanced diet formulations for control and test diets	Compositional analyses were not performed on the test and control substances to confirm that test and control diets had similar nutrient content and were nutritionally balanced.	Ewen and Pusztai (1999)
Description of study design, methods, and other details sufficient to facilitate comprehension and interpretation	Inadequate information was provided on the source of animals used, age, sex, animal husbandry practices followed, collection, and evaluation of biological samples to confirm that the procedures followed met accepted practices.	Ermakova (2005), Ewen and Pusztai (1999), and Séralini et al. (2012, 2014)
Statistical analyses and study interpretation		
Use of appropriate statistical methods for the design of the study	Statistical methods were sometimes not provided in sufficient detail to confirm if they were conducted appropriately for the data that were collected; statistical methods were documented but were not appropriate. Estimates of statistical power were based on inappropriate analyses and magnitudes of differences.	de Vendomois et al. (2009), Ewen and Pusztai (1999), Malatesta et al. (2003, 2005), and Séralini et al. (2007, 2012, 2014)
Appropriate interpretation of statistical analyses	Statistical differences were not considered in the context of the normal range for the test species, including data from historical and/or concurrent reference controls; the toxicological relevance of the difference was not considered (i.e., the reported finding is not known to be associated with adverse changes). Observed differences were not evaluated in the context of the entire data collected to determine if changes in a given parameter could be correlated with changes in related parameters.	Carman et al. (2013), de Vendomois et al. (2009), Ewen and Pusztai (1999), Kilic and Akay (2008), Malatesta et al. (2002a,b, 2003, 2005), and Séralini et al. (2007, 2012, 2014)
Adequate numbers of animals or test samples collected to be able to make meaningful comparisons between test and control groups	Too few animals/group were used to make meaningful comparisons; tissue sampling did not follow acceptable guidelines and was too limited to provide an accurate assessment of what was occurring in the organ being examined.	Ermakova (2005), Malatesta et al. (2002a,b, 2003, 2008), and Séralini et al. (2012, 2014)
Study publication and availability		
Publication of studies in peer-reviewed journals	Circumvention of the peer-review process removes a level of review that may contribute to ensuring that WF studies are appropriately designed and interpreted.	Ermakova (2005) and Velmirov et al. (2008)

note that animals and humans regularly ingest DNA and RNA as part of traditional diets without consequence. The DNA from GE crops is chemically equivalent to DNA from other sources and both are thoroughly broken down in the gastrointestinal tract during digestion (Beever and Kemp, 2000; Jonas et al., 2001; CAST, 2006).

Intact recombinant proteins have never been detected in tissues or products of animals fed GE crops (Alexander et al., 2007). This is particularly important when considering the prospect of labeling secondary products such as milk, meat, and eggs. In some countries, mandatory food labeling regulations target the presence of GE components in the finished product (e.g., Australia, New Zealand, and Japan), whereas in other countries, regulations target foods that use GE technology as a part of the production process (e.g., the EU, Brazil, and China). It should be noted, however, that only Brazil currently requires mandatory labeling of products from animals that consume GE feed. Technically, the Brazilian law requires the label to state "(name of animal) fed with rations containing a transgenic ingredient" or "(name of ingredient) produced from an animal fed with a ration containing a transgenic ingredient.", but has yet to fully implement these laws. Given that there are no detectable and reliably

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quantifiable traces of GE materials in milk, meat, and eggs, any proposed labeling of animal products derived from GE-fed livestock would have to be based on documenting the absence of GE crops in the production chain, thereby necessitating the need for identity preservation and segregation requirements for producers and importers (Bertheau et al., 2009). This difference is important for verification: a product-based system can be enforced with testing equipment to analyze for the presence of GE materials and can filter a cheater, whereas a tracking system segregating indistinguishable products cannot guarantee the absence of products from animals that might have eaten GE feed (Gruère and Rao, 2007).

In 2012 the USDA's FSIS approved a voluntary process-based label for meat and liquid egg products that allows companies to label that they meet the Non-GMO Project's standard (<0.9% tolerance for GE presence) for the avoidance of GE feed in the diet of the animal producing the product. The FSIS allows companies to demonstrate on their labels that they meet a third-party certifying organization's standards, provided that the claims are truthful, accurate, and not misleading. A similar approach of certifying the absence of prohibited methods in the production chain, rather than testing for some quantifiable attribute in the end product, is used for other voluntary process-based labels such as certified organic and the USDA's Agricultural Marketing Service (AMS) Process Verified Never Ever 3 (NE3) Program which requires that animals are never treated with antibiotics or growth promotants or fed animal byproducts. Again, because the products raised using these methods are indistinguishable from conventional animal products, the USDA Process Verified Program ensures that the NE3 requirements are supported by a documented quality management system.

2013 Data on Global Production and Trade in Genetically Engineered Feedstuffs and Sources of Non-Genetically Engineered Feedstuffs

Global grain production is currently 2.5 billion t, of which approximately 12% (300 million t) is traded. Soy and corn make up two-thirds of global grain trade and these are the main players in commercial animal feed. Figure 3 illustrates the major global producers of these 2 crops and the proportion of global production that is from GE crop varieties. It is estimated that approximately 85% of soybean and 57% of corn grain production (USDA Foreign Agricultural Service, 2014b) are used in global livestock diets annually. The demand for livestock products has been increasing in response to population growth and income, particularly in developing countries. In Asia alone, consumption of meat and dairy products has been increasing annually by approximately 3 and 5%, respectively (Food and Agriculture Organization of the United Nations, 2012). Increase in demand for animal products, especially meat, will drive demand for grain and protein feeds (USDA Economic Research Service, 2008). The Food and Agriculture Organization of the United Nations (Rome, Italy) predicts that by 2050 global grain trade will double to 600 million t (Bruinsma 2009).

Of the protein sources available, soybean meal has one of the best essential AA profiles for meeting the essential AA needs of livestock and poultry. It is a good source of both lysine and methionine, which are the first limiting AA for swine and poultry, respectively. It is estimated that 79% (85 million ha) of global soybean hectarage is planted to GE varieties (Fig. 3). In 2013, 36.5% of global soybean production (97.2 million t) was exported and 97% came from 3 countries that grow GE soybeans—the United States, Brazil, and Argentina (Fig. 4).

Soybean meal is also an important component of animal feed globally (Fig. 5). In the 2011 to 2012 marketing year, domestic animal agriculture used 27.6 million t of U.S. soybean meal. Poultry continue to be the single largest domestic user of soybean meal, consuming about half of all meal, followed by swine. Soybean meal is a very important protein source for animal feeds in the EU, supplying 46% of the lysine supply overall. The EU imports 65% of its protein-rich feedstuffs, for which there are no alternative sources grown in the EU (Popp et al., 2013), and is the largest importer of soybean meal and the second largest importer of soybeans after China (Fig. 4 and 5). About 70% of soybean meal consumed in the EU is imported and 80% of this meal is produced from GE soybeans.

Corn is an important subsistence crop in many parts of the world and hence the majority of production is consumed within the country of production. Although only 32% (57 million ha) of global corn hectarage is planted with GE varieties (Fig. 3), 71% of global trade came from those countries that grow GE corn varieties (Fig. 6). Approximately 11.6% (100 million t) of global corn production was internationally traded in 2013. Three of the top 5 corn exporting countries—the United States, Brazil, and Argentina—currently grow GE corn. The remaining 2 countries—Ukraine and India—do not have officially registered and approved GE corn varieties.

Of the top 5 corn importing countries—Japan, Mexico, the EU, South Korea, and Egypt—only 5 countries within the EU (Spain, Portugal, Romania, Czechoslovakia, and Slovakia) grew a small amount (148,013 ha) of Bt-MON810 corn (USDA Foreign Agricultural Service, 2014a). Corn is the second largest category of GE products imported into the EU after soy. Unlike soybean, EU corn production is sufficient to meet most of its own corn consumption, with imports accounting for only 10% of total supply. Annual EU imports of corn products include US$1.8 billion of corn, $151 million of corn seed for

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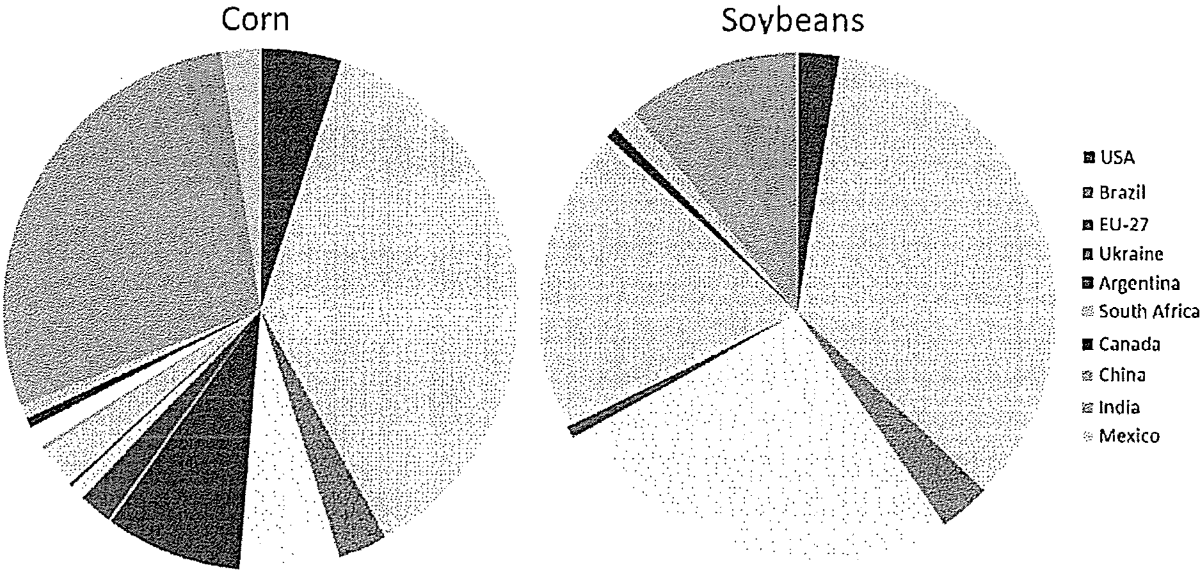

Figure 3. Genetically engineered (GE) and conventional corn and soy produced (million t) by selected countries 2012. Pattern represents production from GE varieties and solid slices represent conventional varieties. Sources: United States Department of Agriculture Foreign Agricultural Service; individual country Global Agricultural Information Network reports 2013; Food and Agriculture Organization of the United Nations (FAOSTAT). EU-27 = the 27 member states of the European Union (EU); production and trade database searches (faostat3.org/faostat-gateway/go/to/download/Q/*/E).

planting, and $87 million of dried distillers grains (USDA Foreign Agricultural Service, 2013a).

Prevalence of Markets Sourcing Non-Genetically Engineered Feed Globally for Livestock Populations as Compared to Conventional

World markets for grains can be separated into 4 segments: the conventional market (non-GE grain that is not certified as such), the mixed market (GE and conventional undifferentiated), the identity-preserved (certified non-GE) market, and the organic market. It is diffi-

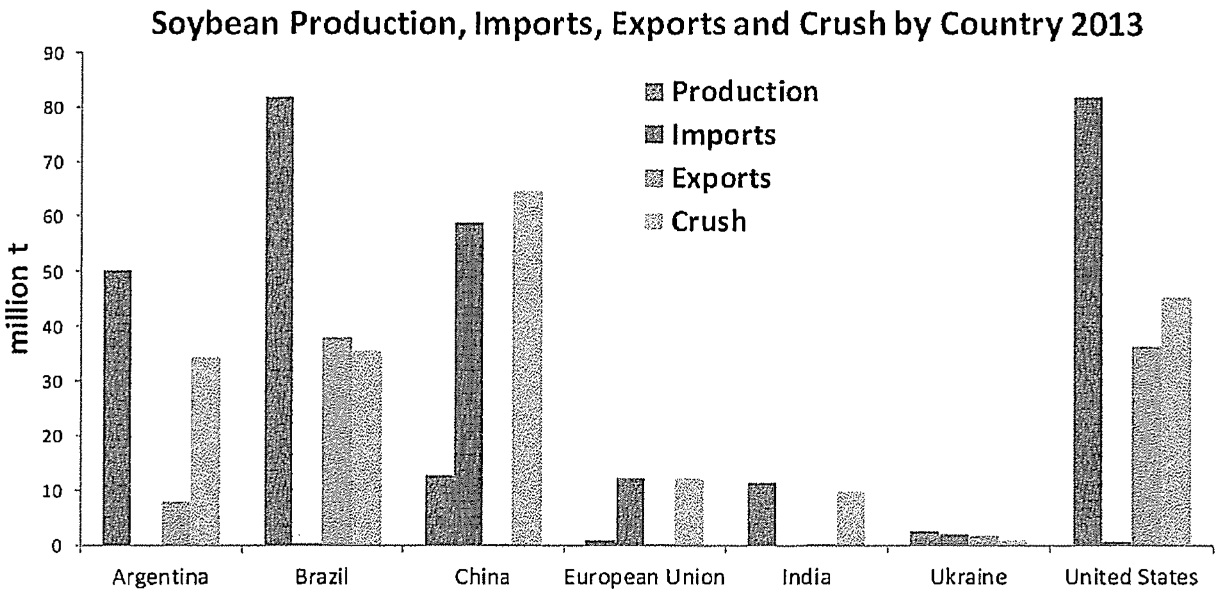

Figure 4. Soybean production, imports, exports, and crush (million t) by major import and export countries, 2013. Source: United States Department of Agriculture Foreign Agricultural Service; Production and trade database searches (http://faostat3.fao.org/faostat-gateway/go/to/download/G1/*/E).

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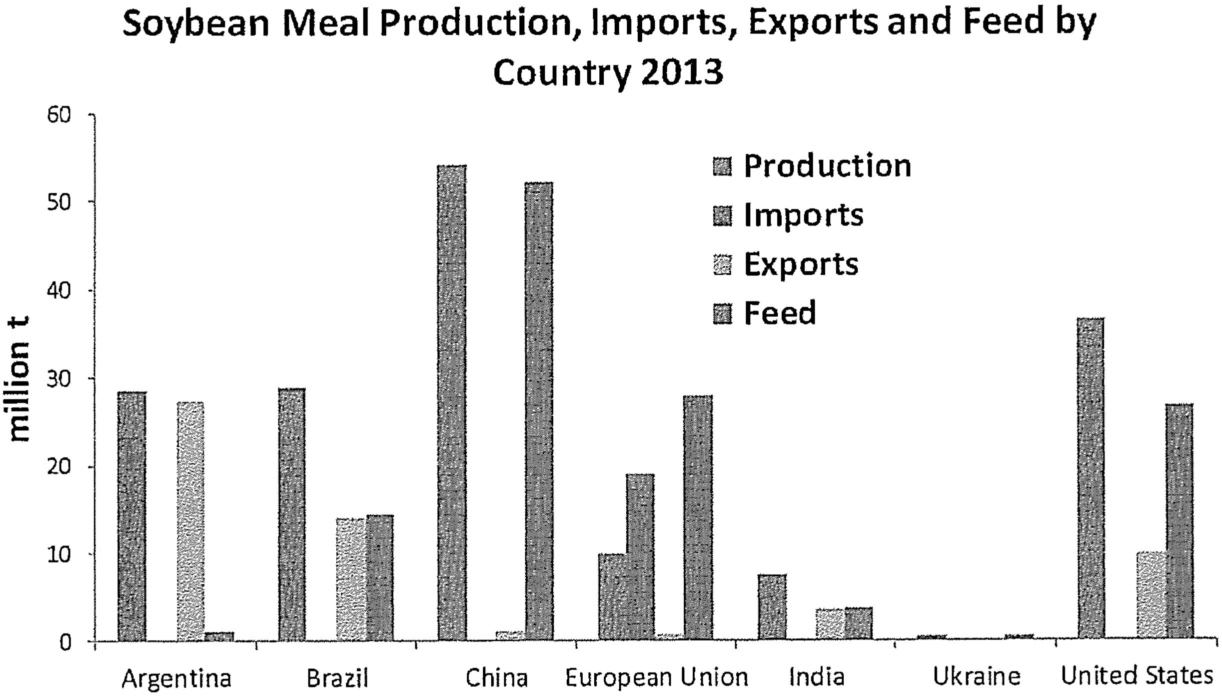

Figure 5. Soybean meal production, imports, exports, and feed (million t) by major import and export countries, 2013. Source: United States Department of Agriculture Foreign Agricultural Service; production and trade database searches (http://faostat3.fao.org/faostat-gateway/go/to/download/G1/*/E).

cult to determine exact size estimates for these different markets, although it can be stated that the conventional and mixed markets are much larger than the remaining 2.

Of the top 5 soybean meal exporting countries in 2013—Argentina, Brazil, the United States, India, and Paraguay—only India does not allow the cultivation of GE soybeans. Of the top 5 soybean meal importing countries in 2013—the EU, Indonesia, Thailand, Vietnam, and Iran—none grow GE soybeans (USDA Foreign Agricultural Service, 2014a). It is estimated that between 4.0 and 4.5% of global trade in soybeans is required to be identity-preserved certified non-GE, and if it is assumed that this volume of traded soybeans is segregated from supplies that may contain GE soybeans, then the GE share of global trade is in the range of 93 to 96% (Table 6). A similar pattern occurs in soybean meal, where 88% of globally traded meal likely contains GE material (Table 7).

The estimated size of the export market requiring certified non-GE corn is 7.3 million t or 7% (Table 6). This excludes countries with markets for certified non-GE corn for which all requirements are satisfied by domestic production (e.g., corn in the EU). Farm animal feed in the 27 member states of the European Union (EU-27) is composed of 50% roughages and 10% grains produced on farm, 10% purchased feed materials, and 30% industrial compound feed. It has been estimated that in the EU, less than 15% of the animal feed market is identity-preserved certified non-GE, although there are great variations between countries. The main driver for non-GE feed is the poultry sector (17%) followed by the cattle (9%) and pig sectors (2%; European Feed Manufacturers' Federation, 2013).

The United States used to be a major supplier of corn to the EU in the 1990s but GE corn plantings in the United States caused a drastic decline in corn exports to the EU because of trade disruptions due to asynchronous approvals (i.e., cultivation approvals of specific GE varieties in the United States occurring before food and feed import approvals in the EU). The result is that the United States is no longer a major supplier of corn to the EU. Similarly, in 2007 there was a problem with asynchronous approval of a GE corn variety approved for cultivation in Argentina but unapproved for food and feed use in the EU. This concentrated demand on corn grown in Brazil, which increased prices an estimated €50/million t for compound feed producers in the EU (Popp et al., 2013).

China, which imported an estimated 5 million t of corn in 2013, making it the sixth largest corn importer, began rejecting shipments of U.S. corn in November 2013 after tests found a GE variety of corn that had been approved for cultivation in the United States, Argentina, and Brazil since 2011 but was not approved for food and feed import into China, despite a 2010 regulatory submission requesting such approval. China has a zero-tolerance policy for unapproved events. Since these trade disruptions began, a total of 3.3 million t of U.S. corn have been subject to re-

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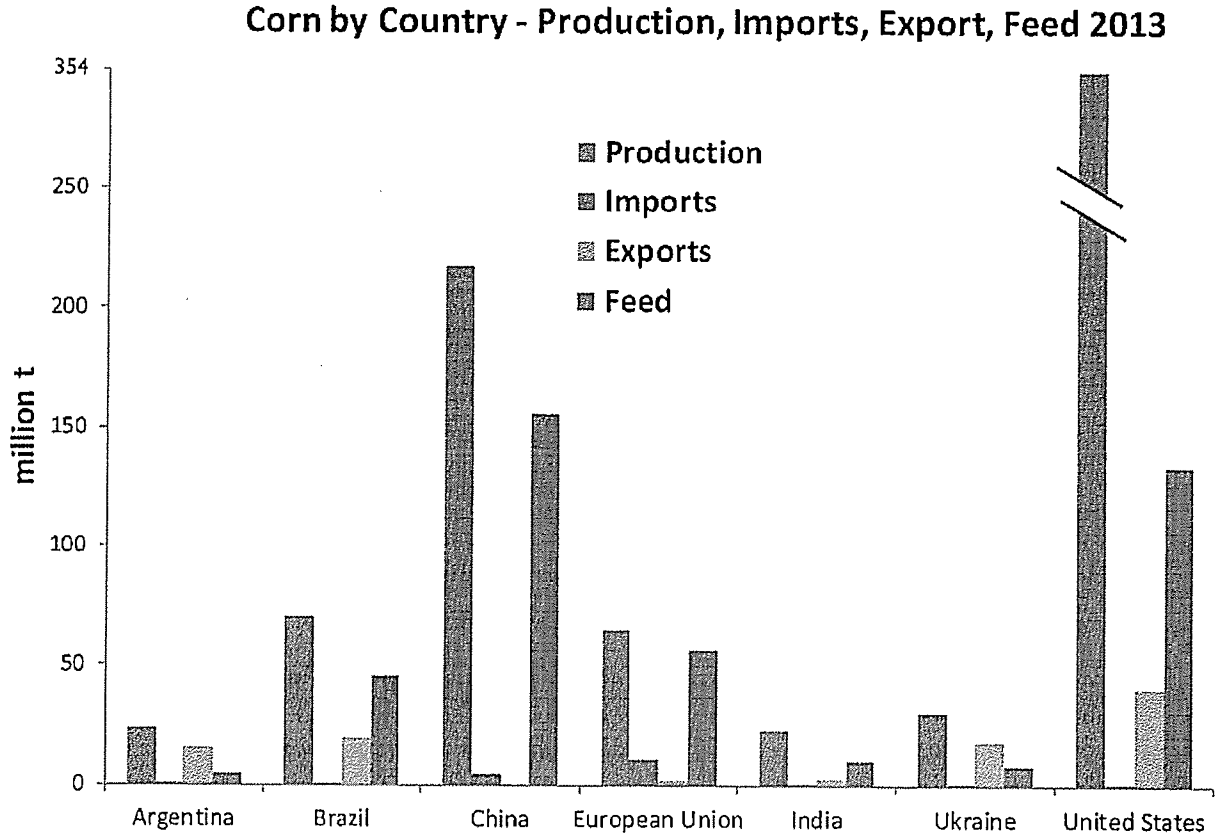

Figure 6. Corn production, imports, exports, and feed (production and trade database searches (http://faostat3.fao.org/faostat-gateway/go/to/download/G1/*/E)) by major import and export countries, 2013. Source: United States Department of Agriculture Foreign Agricultural Service; production and trade database searches(http://faostat3.fao.org/faostat-gateway/go/to/download/G1/*/E).

jection and diverted shipments (1.4 million t) or canceled or deferred sales. It has been estimated that up to $2.9 billion in economic losses were sustained by the U.S. corn, distillers' grains, and soy sectors in the aftermath of the zero-tolerance enforcement policy on U.S. export shipments to China (National Grain and Feed Association, 2014).

Interestingly, Ukraine signed a 3-yr agreement with China in 2013 for the delivery of 4 to 5 million t of corn per year. Ukraine does not export or import GE products as none are officially registered and approved for commercial use or sale in the country. However, private sources estimate approximately 60% of the Ukraine soybean crop and 30% of the corn crop consist of GE varieties (USDA Foreign Agricultural Service, 2013b). China only accepts GE-positive cargo if the shipment is marked accordingly and contains only those GE events that are approved for import in China as well as cultivation in the country of origin. Given asynchronous regulatory approvals and the realities of agricultural production systems where harvesting machinery and storage facilities are shared among different production systems, trade disruption appears almost unavoidable if importing countries enforce a "zero-tolerance" policy for unapproved events that have been approved for cultivation in exporting countries.

Reliance on imported animal feed is becoming increasingly complicated for countries that wish to source non-GE products due to the significant GE adoption rate worldwide. In 2013, 4 major United Kingdom food supermarket groups—Tesco, Cooperative, Marks and Spencer, and Sainsbury's—ceased requiring that poultry and egg suppliers use only non-GE feed (Popp et al., 2013). Likewise, in 2014, the German poultry industry, which feeds 0.8 million t of soybean meal annually, abandoned its commitment to use only non-GE soybeans in poultry feed (USDA Foreign Agricultural Service, 2014c). This was largely due to the fact that Brazil is growing more GE soybeans and therefore has less identity-preserved certified non-GE soybeans available for export. As the global production of GE feed crops continues to rise, the EU's stringent GE tolerance levels (0.9% GE material limit plus 0.05% measuring uncertainty tolerance) and zero tolerance for unapproved events are complicating the maintenance of non-GE supply chains (Popp et al., 2013).

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Table 6. Share of global crop trade accounted for by genetically engineered (GE) crop production 2012/2013 (million t; Brookes and Barfoot, 2014c). Table reproduced with permission

Variable	Soybeans	Corn	Cotton	Canola
Global production	266	862.9	26.8	62.6
Global trade (exports)	97.2	100.1	10.0	12.0
Share of global trade from GE producers	94.6 (97.3%)	71.3 (71.2%)	6.9 (69%)	10.2 (85%)
Estimated size of market requiring identity-preserved (certified non-GE) market (in countries that have import requirements)[1]	4.0–4.5	7.3	Negligible	0.1
Estimated share of global trade that may contain GE (i.e., not required to be segregated)	90.1–93.2	64–92.8	6.9	10.1
Percentage of global trade that may be GE	92.75–95.9%	64–92.7%	69%	84.2–85%

[1]Estimated size of market requiring certified conventional in countries with import requirements excludes countries with markets for certified conventional for which all requirements are satisfied by domestic production (e.g., corn in the European Union [EU]). Estimated size of certified conventional market for soybeans (based primarily on demand for derivatives used mostly in the food industry): main markets: EU, 2.5 to 3.0 million t bean equivalents, and Japan and South Korea, 1 million t.

Current U.S. Options for Products from Non-Genetically Engineered Fed Livestock

Consumers wishing to purchase products from animals fed non-GE diets in the United States currently have that choice available through certified NOP products, the FSIS-approved Non-GMO Project verified label claim for meat and liquid eggs, and other non-genetically modified organism certification programs. Additionally, some private retailers are pursuing voluntary labeling. For example, in March 2013, the retail chain Whole Foods Market set a deadline that by 2018, animal products sold in its U.S. and Canadian stores must be labeled to indicate whether or not they came from animals that had consumed GE feed (Whole Foods Market, 2013). These voluntary process-based labels, in effect, verify that GE crops were not used in the production process, rather than testing for the presence of GE content in the animal products themselves as such products contain no detectable and quantifiable traces of GE materials.

Given the high rates of GE adoption in major feed crops, U.S. producers wishing to purchase non-GE feed for their livestock likely contract with growers or source identity-preserved (certified non-GE) or organic feed. In 2011, the United States had 1.26 million ha of certified organic cropland and 0.93 million ha of certified organic pasture and range (USDA National Agricultural Statistics Service, 2012). This translates into roughly 0.8 and 0.5% of total U.S. cropland and pasture/rangeland, respectively (Fig. 7). The availability and cost of certified organic feeds is a major challenge for U.S. organic livestock producers. The costs of certified organic feedstuffs are 2 to 3 times greater than non-organically-grown feeds (Hafla et al., 2013).

United States feed grain distributors and soy product manufacturers report sourcing organic soybeans from other countries. Organic farmers and handlers anywhere in the world are permitted to export organic products to the United States if they meet NOP standards and are certified by a USDA-accredited organic certification body. In 2007, USDA-accredited groups certified 27,000 producers and handlers worldwide to the U.S. organic standard, with approximately 16,000 in the United States and 11,000 in over 100 foreign countries (Grow and Greene, 2009). In 2007, approximately half of the accredited foreign organic farmers and handlers certified to NOP standards were in Canada, Italy, Turkey, China, and Mexico. Organic farming is often labor intensive, and developing countries with lower farm labor costs may have a competitive advantage in the production of some organic products.

In 2009, Canada was the main market for U.S. organic exports, while countries in Latin America, including Mexico, Brazil, Argentina, and Uruguay, along

Table 7. Share of global crop derivative (meal) trade accounted by genetically engineered (GE) product 2012/2013 (million t; Brookes and Barfoot, 2014c). Table reproduced with permission

Variable	Soymeal	Cottonseed meal	Canola/rape meal
Global production	179.3	20.5	34.9
Global trade (exports)	57.2	0.6	5.6
Share of global trade from GE producers	50.4 (88%)	0.29 (46%)	3.6 (64%)
Estimated size of market requiring identity-preserved (certified non-GE) market (in countries that have import requirements)[1]	2.1	Negligible	Negligible
Estimated share of global trade that may contain GE (i.e., not required to be segregated)	48.3	0.63	3.6
Percentage of global trade that may be GE	84.4%	45%	64%

[1]Estimated size of certified conventional market for soymeal: European Union, 2 million t, and Japan and South Korea, 0.1 million t (derived largely from certified conventional beans referred to in Table 6).

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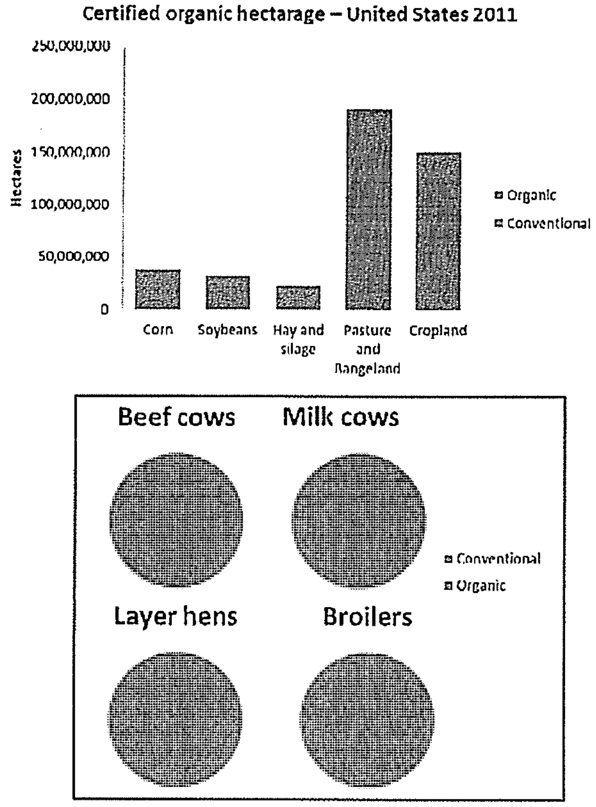

Figure 7. Certified National Organic Program hectarage and livestock numbers as a percentage of conventional U.S. numbers, 2011. Source: USDA National Agricultural Statistics Service, 2012. www.ers.usda.gov/datafiles/Organic_Production/National_Tables_/CertifiedandtotalUSacreageselectedcropslivestock.xls. See online version for figure in color.

with China and other countries in Asia are major sources of organic imports (Grow and Greene, 2009). The countries with the fastest growth in organic production are those that produce organic products for export including China, Bolivia, Chile, Uruguay, and Ukraine. The amount of organic farmland increased well over 1,000% in these countries between 2002 and 2006, while organic farmland in Europe and North America showed slower (27–80%) expansion rates (Grow and Greene, 2009). In 2013, the United States imported over $100 million of organic soybeans primarily from China and India (Fig. 8; Global Agricultural Trade System online [GATS] organic products www.fas.usda.gov/commodities/organic-products). The proportion of organic imports used for livestock feed versus human food purposes is unavailable as import product codes do not distinguish between these uses. Improved data collection is necessary to better describe international trade patterns in organic and identity-preserved (certified non-GE) feed.

Dairy

Organically raised livestock accounted for $1.31 billion in sales in 2011, the last year with a complete set of data on production and sales. Organic milk led livestock commodities, accounting for $765 million, or 58%, of organic animal product sales; however, less than 2% of U.S. dairy production is currently organic (Hafla et al., 2013). During 2011, approximately 254,700 dairy cows (2.78% of the total U.S. dairy herd; Table 2) on 1,848 dairy operations were certified organic. Production costs for organic dairies are greater than for conventional dairies due to the increased cost of organic feed and the increased use of labor and capital, which is not scale neutral as the total costs per unit of production drops sharply as herd size increases. Using pasture as a source of dairy forage is more common on organic dairies, which can help to reduce feed costs per cow but also contributes to lower production per cow. The U.S. organic dairy systems depend on the willingness of consumers to pay a premium (Hafla et al., 2013). The retail price for organic milk between 2004 and 2007 averaged 3 times the cost of conventional milk (USDA Economic Research Service, 2012b), and in 2013, organic milk made up 4.38% of total U.S. fluid milk market sales.

Beef

Natural, organic (grain-fed or otherwise), and grass/forage-fed (including cattle finished on grasses/forages to a specific quality standard) account for about 3% of the U.S. beef market (Mathews and Johnson, 2013). The term "natural" is not associated with an official production process standard so natural beef may come from animals that have consumed GE feed. Likewise, the USDA NE3 Process Verified Program does not mandate or specify the use of non-GE feed.

Beef from grass-fed ruminants can be labeled with a "grass (forage) fed" marketing claim through the AMS Process Verified Program if fed according to USDA standards. Under this verification standard, grass or forage must be the exclusive feed source throughout the lifetime of the ruminant animal except for milk consumed before weaning. The animal cannot be fed grain or any grain byproduct before marketing and must have continuous access to pasture during the growing season. However, silage is an accepted feed that can consist of relatively large portions of grain. For example, corn silage, which averages 10 to 20% grain and can consist of up to a third or more grain, blurs the distinction between grain fed and forage fed (Mathews and Johnson, 2013).

In a survey of certified organic beef producers in the United States, 83% reported that cattle were raised exclusively or predominantly on grass and hay until

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slaughter, while the remaining 17% reported using a grain finishing system (Hafla et al., 2013). Organic beef cattle may be finished in feedlots for no more than 120 d and must have access to pasture during this time. In 2011, 106,181 beef cows (0.34% of the total U.S. beef cows; Table 2) and 113,114 unclassified cows and young stock were raised in certified organic production systems. The price of natural/organic beef averaged $12.08/kg in the first quarter of 2011, which represented a premium of $3.75/kg.

Poultry

The largest volume of organic meat sales is for poultry. In 2011, the number of certified organic broilers totaled more than 28 million (0.33% of the total U.S. broilers; Table 2), layer hens totaled more than 6.6 million (1.97% of the total U.S. layers), and turkeys totaled 504,000 (0.20% of the total U.S. turkeys). In 2011, sales of U.S. organic broilers and eggs totaled $115 million and $276 million, representing 0.5 and 3.7% of total sales, respectively. The retail price for organic poultry and eggs between 2004 and 2006 was approximately twice that of conventional products (USDA Economic Research Service, 2012a).

Currently, the size of the market for products derived from animals raised in production systems that use either identity-preserved certified non-GE or organic feed is less than 5% (Fig. 7). Voluntary labeling programs and market premiums exist for products derived from animals that have not consumed GE feed. Mandating the labeling of products derived from animals that have eaten GE-feed at the current time would result in labeling essentially all products derived from conventionally raised livestock (i.e., >95% of all animal products) in the United States.

If suppliers and marketers respond to mandatory labeling of products from animals fed GE feed by increasing the offering of products from animals fed non-GE feed, an increase in the non-GE feed supply would be required. This could come from non-GE feed sources (e.g., wheat and barley), from contracting with U.S. growers to plant non-GE crop varieties, or from imported feed sources. Reversion from GE to conventional crop varieties would require the adoption of altered agronomic practices to manage those crops and relinquishment of the documented environmental and economic benefits associated with the adoption of GE crops (Areal et al., 2013; Fernandez-Cornejo et al., 2014; Green, 2012; NRC, 2010). The prices received by U.S. non-GE corn and soybean producers in recent years have averaged 15% more than the prices received by conventional commodity producers (CAST, 2014), and globally traded non-GE soybean meal is roughly at a 13% premium to conventional soybean meal prices. Given the importance of feed costs in overall

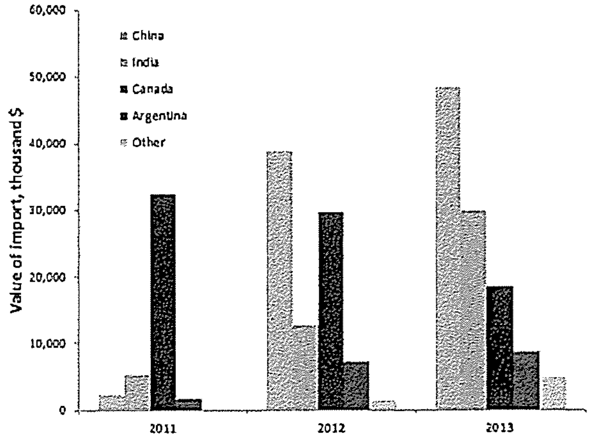

Figure 8. Value of certified National Organic Program soybeans imported into the United States, 2011 through 2013. Source: United States Department of Agriculture Foreign Agricultural Service (2014a). See online version for figure in color.

animal production costs, the cost of animal products from animals fed non-GE feed would be more expensive.

Impact of Genetically Engineered Feedstuffs on the Sustainability of Livestock Production

Feedstuffs are a major contributor to life cycle assessments in the production of meat, milk, and eggs on a national and global scale. By 2020, developing countries will consume 107 million t more meat and 177 million t more milk than the annual average of the years 1996 through 1998. The projected increase in livestock production will require annual feed consumption of cereals to rise by nearly 300 million t by 2020 (Delgado, 2003). Despite the fact that the first generation of GE crops with so-called "input" traits (those that potentially alter inputs needed in production) were not designed to increase crops yields per se, GE technology has added an estimated 122 and 230 million t to the global production of soybeans and corn, respectively, since the introduction of GE varieties in the mid 1990s (Brookes and Barfoot, 2014a).

In 2013, approximately 175.2 million ha of GE crops were cultivated worldwide (James, 2013) by 18 million farmers. Over 90% (>16.5 million) were small-scale, resource-poor farmers in developing countries. This planting was greater than a 100-fold increase from the 1.7 million ha that were planted in 1996, making GE the fastest-adopted crop technology in recent history. India cultivated 11.0 million ha of Bt cotton with an adoption rate of 95%. In China, 7.5 million farmers cultivating an average of approximately 0.5 ha collectively grew 4.2 million ha of Bt cotton, an adoption rate of 90%. Farmers have planted these GE varieties to enable the adoption of improved agronomic practices (e.g., reduced insecticide applications) providing environmental, economic,

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and food security benefits in various countries (Ali and Abdulai, 2010; Burachik, 2010; Fernandez-Cornejo et al., 2014; Huang et al., 2010; Kathage and Qaim, 2012; Qaim and Kouser, 2013).

During the period 1996 through 2012, it has been estimated that the cumulative economic benefits from cost savings and added income derived from planting GE crops was $58.15 billion in developing countries and $58.45 billion in industrial countries (Brookes and Barfoot, 2014a). The adoption of the technology also reduced pesticide spraying by 499 million kg (–8.7%), and has decreased the environmental impact of these crops by 18.1% (as measured by the indicator the Environmental Impact Quotient [a method that measures the environmental impact of pesticides]; Kovach et al., 1992) as a result of the use of less-toxic herbicides and reduced insecticide use (Brookes and Barfoot, 2014b). As a result of fuel savings associated with making fewer spray runs, the adoption of production systems with reduced tillage, and additional soil carbon sequestration, GE crops have also resulted in a significant reduction in the release of greenhouse gas emissions, which, in 2012 alone, was equivalent to removing 11.88 million cars from the roads (Brookes and Barfoot, 2014b).

Although some weed resistance has developed as a result of poor pest management practices and overreliance on a single herbicide (i.e., glyphosate), which may impact future benefits, the adoption of GE technology by the major livestock feed producing countries over the past 16 yr has had a positive sustainability outcome both in terms of increased global yield as a result of improved pest control and reduced overall environmental impacts per kilogram of animal feed produced.

The Future

There are numerous GE crops enhanced for animal nutrition in the research and development pipeline, with almost 100 events under research in many countries of the world (Tillie et al., 2013). This reflects both the importance of feed markets for GE crops and the potential nutritional improvements that can be brought to the quality of feedstuffs using this technology. There are 2 ways in which plant breeding might increase the efficiency of livestock production; the first is by raising the crop yield per hectare (e.g., improved drought tolerance or N use efficiency) and the second is by improving the rate of conversion of vegetable calories into animal calories (e.g., altered output traits or crop composition). Genetic engineering offers new possibilities for approaching both of these objectives, including improving the nutritional value of feed (e.g., AA content; Huang et al., 2006), lowering N and P pollution through altered crop composition (e.g., low phytate; Chen et al., 2008), and reducing manure excretion through a higher NE value (e.g., reduced lignin; Jung et al., 2012). Several of these crops are far advanced in the regulatory pipeline (Table 8; Tillie et al., 2013)

These so-called "second generation" crops modified for output traits will pose some regulatory and commercialization challenges. The first is that they will not, by definition, be substantially equivalent to isogenic non-GE varieties. Protocols have been developed to address the safety testing of these crops (International Life Sciences Institute, 2007). However, given the different regulatory approaches that are in place for crops that are compositionally equivalent, it is unclear how regulatory requirements may vary between countries in terms of the number and length of target animal feeding studies for these crops with altered output traits. Additionally, if the benefits derived from growing these crops accrue to the livestock producer or feeder and not directly to the farmer growing the crop, there will need to be some form of supply chain segregation in place to ensure a price premium is obtained for the value-added output trait.

An additional concern is the increasing problem of asynchronous regulatory approval, or regulatory asynchronicity. Currently, 33 countries have regulatory systems that handle approval for the cultivation or importation of new GE crops (International Service for the Acquisition of Agri-Biotech Applications, 2014). There are considerable discrepancies in the amount of time required to review and approve new GE crops in different countries. This leads to a situation where GE crops may be cultivated and marketed in some countries and remain unapproved in others. As discussed previously, this has resulted in trade disruptions, especially when countries use a "zero-tolerance" policy for unapproved events, meaning that even minute traces of unapproved GE crops are illegal and must be withdrawn from the market. Under a zero-tolerance policy, trade of relevant commodities between asynchronous countries will likely cease as importing and exporting firms will act to avoid the risk associated with a positive test (Kalaitzandonakes et al., 2014). Countries with zero-tolerance policies will be perceived as risky export markets, and importers will pay higher prices and insurance premiums to offset risks taken by the supplier.

Currently, the most accepted techniques for the detection of rDNA and protein products are PCR and ELISA, respectively. Various analytical methods have been developed and are routinely used for the monitoring of GE origin in raw materials and processed foods and have been reviewed elsewhere (Alexander et al., 2007; Marmiroli et al., 2008). Although efforts have been taken to harmonize analytical methodology for the detection of GE products at national, regional, and international levels, no international standards have yet been established (Holst-Jensen et al., 2006). Sampling, testing, and cer-

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Table 8. Summary of genetically engineered crops modified for output traits in the latest stages of the pipeline. Modified from Tillie et al. (2013).

Crop	Identifier	Stage[1]	Commercial name	Trait	Developer[2]	Regulatory approval status					
						United States	Argentina	Brazil	China	European Union	Japan
Soybean	DP-305423-1	1	Treus-Plenish	High oleic acid	Pioneer	All uses – 2009	None	None	Food and feed – 2011 (expires 2014)	Food and feed application; additional data request – 2012	All uses – 2010
Safflower		1	Sonova 400	Omega-6	Arcadia BioSciences	Grown under permit; dietary supplement	None	None	None	None	None
Corn	BVLA430101	2		Phytase expression	CAAS/Originally in Agritech	None	None	None	None	None	Cultivation – 2009
Corn	REN-00038-3	2	Mavera	High lysine	Monsanto	All uses – 2006	None	None	None	Application withdrawn – 2009	All uses – 2007
Corn	REN-00038-3 × MON00810-6	2	Mavera YieldGard	High lysine + herbicide tolerance	Monsanto	All uses – 2006	None	None	None	Application withdrawn – 2009	All uses – 2007
Soybean	DP-305423-1 × MON04032-6	2		High oleic acid + herbicide tolerance	Pioneer	All uses – 2009	None	None	None	Food and feed application; additional data request – 2012	All uses – 2012
Soybean	MON-87705-6	2	Vistive Gold	High oleic acid	Monsanto	All uses – 2011	None	None	None	Imports and domestic use – 2012	Food and feed – 2013
Soybean[3]	DD-026005-3	2		High oleic acid	Pioneer	All uses – 1997	None	None	None	None	All uses – 2007
Alfalfa	MON-00179-5	3	None	Low lignin	Forage Genetics/ Monsanto	Food and feed – 2013	None	None	None	None	None
Rapeseed	MPS961-5	3	PhytaSeed	Phytase expression	BASF	Food and feed – 1999	None	None	None	None	None
Soybean	MON87769	3	None	Omega-3	Monsanto	All uses– 2011/2012	None	None	None	Food and feed application; additional data request – 2012	None

[1]Development stage: 1 = commercialized; 2 = commercial pipeline; 3 = regulatory pipeline.

[2]Pioneer, Johnston, IA; Arcadia Biosciences, Davis, CA; CAAS, Beijing, China; Monsanto, St. Louis, MO; Forage Genetics, Nampa, ID; BASF, Ludwigshafen, Germany.

[3]Events whose development is currently discontinued. The information regarding the regulatory status of the events reported in this table was updated in May 2014.

tification depend on statistical processes, however, and hence all are subject to some error, which increases at very low tolerances (Lamb and Booker, 2011).

Kalaitzandonakes et al. (2014) succinctly summarizes some emerging trends in terms of likely increased regulatory asynchronicity in the future. These include 1) the expanding pipeline of novel GE crop events, including second generation crops modified for output traits; 2) the expanding range of GE crop species being grown and traded; 3) the expanding global hectarage of GE crops and the growing number of countries that raise them; and 4) the nascent and inexperienced regulatory expertise in many countries that will be called on to manage a large number of regulatory submissions for new GE crops in the future. Given the scope of trade of livestock feedstuffs and the increasing importance of GE crops in this supply, trade disruptions appear imminent, especially in countries that have slow approval processes for GE imports and yet are heavily dependent on commodity imports from exporting countries that are cultivating and developing a large number of GE crop varieties.

The emergence of precise gene-editing technologies (e.g., zinc finger nucleases [ZFN], meganucleases, transcription activator-like effector nucleases [TALEN], oligonucleotide-directed mutagenesis, and clustered regulatory interspaced short palindromic repeat [CRISPR]/Cas-based RNA-guided DNA endonucleases) that enable targeted editing of specific nucleotides in the endogenous genome (Kim and Kim, 2014) will further complicate this situation. Gene editing could be considered a form of directed mutagenesis and it is unclear whether gene-editing technologies for crops and animals will be encompassed by the GE regulatory system. This is especially uncertain where gene editing results in the substitution of 1 naturally occurring allelic form of a gene for another of the same gene or induces a mutation in an existing gene through a single base pair change analogous to the spontaneous mutation process (Wells, 2013). Whether these types of modifications should be subject to regulation is a topic of dis-

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cussion among the global regulatory community (Bruce et al., 2013; Hartung and Schiemann, 2014; Lusser and Davies, 2013). Given that the regulatory process takes years and costs millions of dollars (Prado et al., 2014), the governance of emerging gene-editing technologies will have a great influence on the future development of crops carrying these genetic modifications and will significantly impact the ability of the public sector and small companies to bring gene-edited products to market.

Of particular practical importance is that there will be no way to differentiate a gene-edited DNA alteration from a naturally occurring mutation and hence no way to trace and track "genetically modified" gene-edited crops or differentiate them from genetic modifications resulting from spontaneous mutations. Many of the existing PCR-based tests for GE crops are designed using primers that amplify unique DNA sequences that are common to a variety of transgenic crops (e.g., exogenous promoter sequence or gene coding sequence). As new GE crops with multiple novel regulatory and coding region sequences are developed, it will be increasingly difficult to use PCR-based assays to detect all possible events. Furthermore, PCR-based screening methodology may be unable to detect the genetic modifications that are under development through precise breeding techniques (Lusser et al., 2012). Likewise, some gene-editing techniques generate genetic changes that cannot be distinguished from conventionally bred crops or from crops produced by natural genetic variation or unregulated radiation mutagenesis (Broeders et al., 2012). Process-based regulatory frameworks that rely on PCR-based detection of specific transgenic constructs will be unable keep pace with technological developments when the products of these advanced breeding techniques are indistinguishable from those produced using conventional breeding techniques.

These developments may lead to a revaluation of the current rDNA process-based regulatory trigger for GE organisms to a more scientifically defensible product-based approach centered on the novelty and any unique risks associated with the phenotype of the product rather than the process used to accomplish the genetic modification (Bradford et al., 2005; McHughen, 2007). The need for international coordination and synchronization of regulatory frameworks for GE products is becoming increasingly urgent as both research and development of GE crops and animals are proceeding at an accelerated rate in an ever increasing number of countries in the world. In the absence of international harmonization, costly trade disruptions are likely to become increasingly widespread in the future to the detriment of global food security.

Conclusions

Commercial livestock populations are the largest consumers of GE crops, and globally, billions of animals have been eating GE feed for almost 2 decades. An extensive search of peer-reviewed literature and field observations of animals fed diets containing GE crop products have revealed no unexpected perturbations or disturbing trends in animal performance or health indicators. Likewise, it is not possible to distinguish any differences in the nutritional profile of animal products following consumption of GE feed. Animal agriculture is currently highly dependent on GE feed sources, and global trade of livestock feed is largely supplied by countries that have approved the cultivation of GE crops. Supplying non-GE-fed animal products is likely to become increasingly expensive given the expanding global planting of GE crops and the growing number of countries that raise them. The market for animals that have not consumed GE feed is currently a niche market in the United States, although such products are available to interested consumers via voluntary process-based marketing programs. The cost of these products is higher than conventionally produced products due to both the higher cost of non-GE feed and the costs associated with certifying the absence of GE crops in the production process and product segregation. There is currently a pipeline of so-called "second generation" GE crops with improved output traits for livestock production. Their approval will further complicate the sourcing of non-GE feedstuffs. Additionally, recent developments in techniques to induce precise genetic changes in targeted genes offer both tremendous opportunities and a challenge for global regulatory oversight. Given these developments, there is an urgent need for international harmonization of both regulatory frameworks for GE crops and governance of advanced breeding techniques to prevent widespread disruptions in international trade of livestock feedstuffs in the future.

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Erratum

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An error was found in the article "Prevalence and impacts of genetically engineered feedstuffs on livestock populations" (J. Anim. Sci. 2014 92:4255–4278). In the section ***Field Datasets of Livestock Populations Fed with Genetically Engineered Feed***, page 4262, feed conversion values were inadvertantly switched in the text (the values read correctly in both Fig. 2 and Table 4). Bolding below shows the correct wording. The authors apologize for the error:

The conversion of feed to gain continuously decreased from **2** in 1985 to **1.91** in 2011, attributable most likely to improved genetics (Havenstein et al., 2003) and management, but this ratio is something that would be expected to worsen (i.e., increase) if the health of these animals was deteriorating following exposure to GE feed.