Regulation of foods derived from genetically engineered crops
Donna H Mitten*, Rob MacDonald† and Dirk Klonus‡

Addresses
*AgriEvo USA, 414 Fourth Street, Suite A, Woodland, CA 95695, USA
†AgriEvo Canada Inc, 295 Henderson Drive, Regina, Saskatchewan, S4N 6C2, Canada
‡Hoechst Schering AgrEvo GmbH, 65926 Frankfurt am Main, Germany

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Abbreviations
EU European Union
FDA Food and Drug Administration
GMO genetically modified organism

Introduction
The application of biotechnology to agricultural production has resulted in a number of whole and processed foods in the world marketplace today. The primary safety evaluation and subsequent approval for the commercialization of these products occurs within the national framework of the producing country. As these products have entered international trade, additional safety assessments may or may not be required in accordance with the importing nations’ regulations. There is a growing gap created by the increasing numbers of products cleared for commercial production in North America and the longer period of review for pre-market approval in Europe. The multi-lateral agreements that guide international trade and the changing national regulations directed to food derived from genetically modified organism (GMO) crops are not in harmony. Increased agricultural production of GMO crops has placed certain commodities on the world market that some trading partners are not prepared to receive. It is the intent of this review to identify the regulatory bodies that must ultimately work together to ensure a safe food supply and respond to consumer concerns, and to provide an overview of the current rules and regulations that address foods derived from GMO crops.

A significant change since the last review on this topic [1] has been the issuance of uniform standards for the Member States of the European Union [2]. A long standing disagreement between two groups of Member States on labeling policy had delayed the approval of the regulatory proposal for eight years [3]. The details for implementation of the labeling policy have still to be determined; however, it is recognized that uniform interpretation and equitable enforcement of the Novel Food regulations on labeling are global issues that can impact trade.

Production of genetically engineered commodity crops
The United States of America and Canada have produced a majority of the commodities that have entered international trade as processed products derived from genetically engineered agricultural crops. Over the past two years, increased transgenic commodity crop production has been recorded in Argentina and China. Expansion in the area planted with four crops is responsible for most of the estimated 2.5-fold global increase in the cultivation of transgenic crops in 1998 [4]. Farmers in the USA planted 3.6 million hectares of herbicide-tolerant soybean, representing 36% of the area in soybean production. In Argentina, 4.4 million hectares were planted, equivalent to 55% of that nation’s soybean production. Insect-resistant corn in the US was planted on 6.5 million hectares, ~22% of the corn production. Herbicide-tolerant canola production in Canada was 2.7 million hectares, 51% of the acres seeded to oilseed rape. Insect-resistant cotton was planted on 2.5 million hectares in the USA. The area planted to insect-resistant cotton in China is considered to be substantial, but difficult to estimate. The total area planted to transgenic crops in China is thought to be about 0.1 million hectares, with the majority being planted to cotton [4]. The situation is similar in Australia with insect-tolerant cotton planted on approximately 80,000 hectares in 1998/99 and limited to 150,000 hectares in 1999/2000 [5].

The projected area to be planted in transgenic commodity crops (including herbicide- and insect-resistant crops and, in some cases, crops with both transgenic traits) for the 1999 season in the USA include 10 million hectares of corn, 18.4 million hectares of soybean and 2.3 million hectares of cotton. These predictions suggest that 65% of all the soybeans, 31% of the corn and 40% of the cotton grown in the USA will be transgenic by 1999 [6]. It is projected that for the 1999 season in Canada, the percentage of canola acres seeded to herbicide-tolerant cultivars will grow to greater than 70%.

International trade
Agricultural commodities are traded extensively around the globe. In 1996, more than a quarter of the world’s soybean production and one fifth of the canola yield were exported from the country of production and traded internationally. In the same year, a total of 35 million tons of soybeans were traded on the global market, of which 24 million tons were from the USA alone (Food and Agriculture Organization [FAO] URL: http://www.fao.org). For example, an estimated 86% of the soybeans used in Japan are imported from North America [7]. If the production projections hold true for 1999, the majority of the soy-based foods in Japan will be produced from transgenic crops.

The Organization for Economic and Commercial Development and the World Health Organization (WHO) have embraced the concept of ‘substantial equivalence’ as the cornerstone of GMO food safety assessment. The international food standards body Codex Alimentarius, an
agency of the United Nations WHO and the FAO, was created in 1961 as a food standards program. Its labeling committee is currently reviewing recommendations for the labeling of foods obtained through biotechnology; however, considerable disagreement still exists over the guiding principles for labeling. Many parties argue that labeling should be held to the same standard as current agricultural commodity segregation, that is, that a 2–4% level of ‘contamination’ is acceptable (e.g. a contamination of 3% soft wheat is allowed for hard wheat used for pasta). Unfortunately, the GMO food debate is based on ethical considerations, which may request more stringent standards. There is discussion instead for a de minimis quantitative threshold in the final food (which would allow minor deviations from a specified limit). If the level is below the set limit, no labeling would be required regardless of the origin. This would require testing of the final food product, as it is impossible to calculate single ingredient levels from a crop threshold. Consequently, a final recommendation is unlikely before 2001. Additionally, consideration is being given for the establishment of a committee to develop standards for foods derived from biotechnology, which would function under the auspices of the Codex Alimentarius.

Regulatory legislation
Underlying the growing gap in product review and commercial clearance is the basis for safety evaluation of genetically modified foods. In the USA, review of foods derived from genetically modified processes and/or crops falls within the current framework of food safety assessment in which government agencies and the food industry share responsibility. The source of any potential health risk is considered to be a characteristic of the product, not the use of genetic modification. In the European Union (EU), the use of genetic modification or new processes places the food product in a new legal class, novel foods and novel food ingredients, with a separate set of regulations that govern safety assessment and labeling.

Another way to underscore the impact of the delay in EU review and granting of authorization to genetically modified foods is to examine the record of pre-market approvals. The four commodity crops listed in Table 1 (corn, soybean, cotton, and canola) provide numerous food ingredients that are traded on a global basis. By the end of 1998, 35 product clearances were granted in North America, compared to eight granted in the EU. In the same timeframe, Japan had granted pre-market

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Genetically modified foods cleared via the pre-market approval process by the end of 1998.</th>
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<tbody>
<tr>
<td>USA and Canada (48)</td>
<td>EU (8)</td>
</tr>
<tr>
<td><strong>Commodity crops</strong></td>
<td></td>
</tr>
<tr>
<td>Soybean, herbicide tolerant (2)</td>
<td>Soybean, herbicide tolerant (1)</td>
</tr>
<tr>
<td>Soybean, modified oil (1)</td>
<td>Canola, herbicide tolerant and/or pollination control (11)</td>
</tr>
<tr>
<td>Canola, modified oil (2)</td>
<td>Oilseed rape, herbicide tolerant and/or pollination control (3)</td>
</tr>
<tr>
<td>Corn, insect resistant, herbicide tolerant, male sterile or stacked (14)</td>
<td>Corn, insect resistant (1)</td>
</tr>
<tr>
<td>Cotton, herbicide tolerant (3), insect resistant (1), herbicide/insect resistant (1)</td>
<td></td>
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<tr>
<td><strong>Other food crops</strong></td>
<td></td>
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<td>Potato, insect resistant (2), and combined insect disease resistant (2)</td>
<td>Potato, insect resistant (2)</td>
</tr>
<tr>
<td>Tomato, delayed ripening (3), and insect protected (1)</td>
<td>Tomato, delayed ripening (1)</td>
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<tr>
<td>Squash, disease resistance (2)</td>
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</tr>
<tr>
<td>Papaya, disease resistance (1)</td>
<td></td>
</tr>
<tr>
<td>Sugarbeet, herbicide tolerant (2)</td>
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</table>

Provided are the general class of product and, in parenthesis, the number of independent submissions cleared. In the USA and Canada, a submission may represent more than one line or transformation event, whereas in the EU and Japan, each event is often the subject of an independent submission. As the USA and Canada continue to harmonize their regulations, it is expected that expedited review and possibly mutual acceptance of assessments will lead to the same products being cleared in each country. Thus, for this table, we combined the product clearances of the two agencies (Health Canada and the FDA) and eliminated duplication. Clearances were compiled as of December 1998. Heath Canada, http://www.hc-sc.gc.ca; Canada Food Inspection Agency, http://www.cfia-acia.agr.ca; FDA, http://vm.cfsan.fda.gov/~lrd/bioncon.html. EU decisions were granted or notice to place on the market has been filed without objection for processed fractions that are substantially equivalent to non-GMO sources. Organization for Economic Cooperation and Development, http://oecd.org; Green Industry Biotechnology Platform, http://www.gibip.org. Combined website of Japanese ministries pertaining to biotechnology, http://ss.saffrc.go.jp/docs/sentan/eguide/commerc. List of food pre-market approvals are current as of December 1998.
approvals to allow the import of 19 products in the same group. A census of all the food products reviewed by the Food and Drug Administration (FDA) and Health Canada, recorded 48 unique product clearances granted by the end of 1998 (Table 1); the number for Japan is 22 and for the EU it is eight.

**European Union**
Perhaps the most significant change in the regulatory landscape in the past two years has been the adoption by the EU of regulation DOC 258/97/EC in May 1997 [2]. This resulted in harmonization of the national novel food laws in all the Member States and a uniform pre-market approval process. The procedure requires submission of an application for pre-market approval to a Member State and to the Commission. The data package is reviewed by the Member State and the Commission’s Scientific Committee on Plants. This technical body provides expert opinion for the review process. Once the submission has been accepted, the competent authority of the Member State has 90 days to complete a safety assessment and make a recommendation to the Commission. The recommendation and submission is distributed to the other Member States for a 60 day comment period. If the recommendation is favorable and no objections are raised by the Member States, the product is approved for the commercial market. If additional assessment is requested or objections are made, however, the European Standing Committee for Foodstuffs takes up the review with technical advice from the Scientific Committee on Plants [8,9].

Foods sold in at least one Member State before 15 May 1997 will not be covered by the new regulation. Thus, food ingredients derived from herbicide-tolerant soybean and insect-resistant corn that were reviewed and cleared under the deliberate release directive 90/220 and which were on the market in a variety of processed foods will not be reviewed again under the new directive. According to a separate EU decision (Council Labelling Regulation No. 1139/98), however, these products are subject to labeling requirements following the standards of the Novel Food Regulation that are currently on the market.

European nations with existing Novel Food regulations now need to conform to regulation 258/97 [2]. For example, some national rules are being changed to require the submission of technical information to be used for labeling of the new food products [3].

**Asia and the Pacific nations**
The legislative situation concerning genetically engineered food in Asia and the Pacific nations is very diverse. Crops which were developed with the help of recombinant methods are cultivated commercially only in China and in Australia.

China has no food legislation and is handling the food related aspects of genetically modified crop plants through their National Safety Committee for Agricultural Biological Genetic Engineering which was formed in January 1997. The committee operates under the principle of substantial equivalence. The government and the farmers of China are very positive towards GMO crops.

Japan is importing products or agricultural raw commodities that originate from genetically modified crops produced in North America, but so far is not cultivating transgenic crops on a commercial scale. Food safety of transgenic crops is assessed by the Ministry of Health and Welfare (MHW) in a well defined manner according to specific guidelines for such products. In a recent announcement [10], the MHW and the Ministry of Labor will merge to form the Ministry of Labor and Welfare with an organization and functions similar to the US FDA. The new agency will have responsibility for approval, testing and regulation of drugs, food products, medical devices and cosmetics.

Australia and New Zealand are in the process of finalizing regulatory legislation for food derived from transgenic plants. A guidance document has been released by the Australia and New Zealand Food Authority which describes the safety assessment for food produced using gene technology. The guidelines are proposed to become part of the Australia and New Zealand Food Standards Code and are due to be enacted on 13 May 1999.

To date, seven applications for food approval have been received by the Australian Authority, involving cotton, soybeans, corn and canola. Two applications (cottonseed and soybean) have been recommended as safe for use in Australian foods. Comments from the public will be considered before the final ruling is made.

**Africa**
In South Africa, existing laws that regulate the import of GMOs (Plant Pest Act) and novel foods and ingredients are regulated by the Department of National Health and Population Development. In 1998, the long-standing biosafety committee, SAGENE, was replaced by an advisory committee of scientists as the new GMO Act went into effect. Under the Ministry of Agriculture, all applications regarding GMOs (environmental and food safety assessments) will undergo technical review by the advisory committee and procedural review by the executive council, representing members of the various national government departments. Policy in South Africa for labeling genetically modified foods will probably adopt the Codex Alimentarius guidelines [11].

**South America**
South American nations have largely followed Canadian guidance for safety assessments. Argentina, Brazil and Chile have legislation and expert panels in place to evaluate and authorize the commercial development of GMO foods. The technical review panels are comprised of national experts and the level of review is rigorous.
The safety assessment process in the USA was most recently reviewed for food ingredients produced via biotechnology [12]. No change was noted in the consensus that the safety of food ingredients produced via biotechnology can be evaluated in the same manner as food ingredients produced by traditional processes.

**Labeling of novel foods**

The debate on the need to label foods derived from recombinant DNA technologies has two aspects: health and safety, and consumer choice. Experience now with the regulatory framework of case by case review has, in effect, removed the food safety and human health questions from the debate. There is consensus that if a novel food is not equivalent to an existing food, then an assessment of the health and safety is required and labeling may be warranted; however, key differences in approaches to labeling are becoming evident in the aspect of consumer choice. In the USA, the newly developed national standards for the certification of whole foods as ‘Organic’ will be administered by the United States Department of Agriculture and will prohibit the use of recombinant DNA crops in organic products at the request of the organic farming industry [13]. Thus, the US consumer will have a choice to purchase a special class of food that will be certified as organic, and thus by definition, not the product of genetic engineering. In Europe, consumer groups argue that choice should be based upon ethical considerations and have successfully demanded the labeling of both whole and processed foods that contain GMOs [14].

The EU Regulation (258/97) [2] requires that labeling of novel foods be considered on a case by case basis. The regulation guidance describes examples that it considers as health concerns, such as proteins from a known food allergen, as well as ethical concerns. Refined products, such as vegetable oil and sugar, derived from GMO crops will not require labeling, as the refined products do not contain recombinant DNA or the novel protein. All food and food ingredients containing or consisting of GMOs will require labeling. For commodity crops, the use of ‘may contain’ language in the label will meet the requirements of the regulation [9]; however, debate in the European Parliament has rejected this provision. Technical issues to verify the presence of GMO-derived components and to set tolerance limits represent the next challenge to the implementation of the new regulations.

In contrast, the principle guiding the draft labeling recommendations of the Codex Alimentarius labeling committee is linked to the concept of substantial equivalence and not to the process used to derive the product. The principle as outlined in the working document states that “When a food produced by biotechnology is not substantially equivalent to any existing food in the food supply and no conventional comparator exists, the labeling shall indicate clearly the nature of the product, its nutritional composition, its intended use and any other essential characteristic necessary to provide a clear description of the product” [15].

The policy of the US FDA has been one of no mandated labeling, unless warning of a potential human health risk is deemed necessary following the regulatory review. The agency requests a premarket consultation to review the attributes of the new food. A formal regulatory review is required if, by genetic engineering, a substance has been introduced which has not previously been a component of human food or animal feed, that is to say, without a history
of safe use. Review is also required if the recombinant DNA was derived from plants known to cause allergic reactions. To date, there have been no cases of mandated labeling of GMO food by the US FDA.

Currently, processed products of genetically modified crops are imported into Japan and may be sold without labeling. Distributors may choose to label or not; however, a special committee within the Ministry of Agriculture, Forestry and Fisheries is considering labeling requirements and will make a recommendation to the Japanese Government in 1999.

In Australia and New Zealand, an amendment to the Food Standards Code, requested by Health Ministers in December 1998, will require the labeling of all GMO food products, including sugars and oils. Clarification was also requested, however, on the definition of GMO food products. This amendment is currently under consideration.

Information on government regulations
A number of internet sites post the rules and regulations governing genetically engineered food, including safety assessment criteria, import requirements and agency decisions. Many sites are maintained by the respective agencies, but others provide a more global view. Three web sites with extensive links to government agencies and related sites are sponsored by the United Nations, the Organization of Economic and Commercial Development and the Information System for Biotechnology. For a short list of internet websites that provide broad-based information and links to specific government agencies, see Table 2. In this rapidly changing arena, internet posting is a key mode of communication.

Conclusions
The legal framework for the regulation of genetically engineered foods on a global level is now set for the leading nations. A general consensus on the key aspects of food safety assessment for human and animal health has been reached. The discussion is now shifting to questions of consumer choice and labeling. Implementation of labeling regulations will be key to the resolution of the product clearance gap between North America and the EU.

References