# Making 'safety first' a reality for biotechnology products

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A critical challenge facing the advocates of biotechnology is to fortify the biosafety of genetically engineered organisms. Readers of this journal have seen competing notions on how to achieve biosafety. For some, scientists carry the burden of designing better biosafety through 'backup safety precautions'[1] and 'molecular gene-containment strategies'[2]. Some have advocated that industry should take the lead in adopting more stringent safety criteria[3]. Others have argued that biosafety science requires significant public investment in order to assess the potential risks of biotechnological products[4]. All seem to agree that 'some form of control mechanism is needed' to minimize genetically modified (GM) product risks and maximize product and environmental safety[5]. Prospective and preventative approaches to strengthening biosafety science and policy, however, have been lacking.

Over the past three years, our colleagues and we have developed a new 'Safety First Initiative,' a public-private partnership for transparent development of proactive safety standards that anticipate and resolve safety issues as far upstream of commercialization as possible. The Initiative's purpose is to establish cross-industry (agriculture, biotechnology, food processing, food marketing and retail) and socially robust safety standards for designing, producing and monitoring the safety of agricultural biotechnology products from laboratory bench to the consumer's dinner plate, with safety a primary criterion from the outset. The Initiative's executive advisory board (John Block, former Secretary of Agriculture; Charles S. Johnson, former executive vice president, DuPont; Margaret G. Mellon, program director, Union of Concerned Scientists; Vin Weber, former US representative; John Woodhouse, former CEO, SYSCO Corp.) and steering committee (representatives of biotechnology businesses, farming, retail food business, consumer and environmental groups and diverse scientific experts) have decided to apply a consultative and transparent process to incorporate scientific, technical, social and governmental considerations in developing environmental and human health safety standards for genetically engineered products[6]. Our collaborations with a diverse range of stakeholders and responsible observers have demonstrated that public concerns about the risks of biotechnology can be addressed through such a participatory and open process to make safety a first priority in the development of biotechnological products. As a result, this Initiative is building a rare and extraordinary convergence among previously acrimonious parties in the agricultural biotechnology debate.

The genetic engineering industry, operating in different social and ecological contexts around the world, has yet to take the lead in establishing comprehensive and proactive cross-industry safety standards. Instead, biosafety governance has largely involved a reactive approach that places the burden on government or consumers to demonstrate safety or risk just before or after commercialization; that is, ten or more years after a firm has committed to developing a product. In the United States, for instance, the government's focus on assessing risks (where government regulation of commercial products exists) occurs long after completion of multiple steps of design and development of a GM organism. Waiting until this late stage to thoroughly address safety issues increases vulnerability to regulatory disapproval, consumer jitters and flawed decisions. Furthermore, scientific and governmental groups are only beginning to devise scientifically informed standards for acceptable risks, validation of scientific information related to risks and training for safe management of biotechnologies[7–12]. Meanwhile, products that are arriving from the 'next stage' of genetic engineering efforts, such as growth-enhanced

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fish and pharmaceutical-producing crops, are presenting daunting new challenges to food and environmental safety regulatory regimes for both industry and government[11,13].

## Elements of the 'Safety First' approach

There is a long history of efforts to improve safety within established industries, such as the steel, railroad and aircraft manufacturing industries, which have shaped the safety engineering profession[14,15]. Numerous industries eventually established industry-wide safety programs to strengthen their inadequate safety records and thus earn consumer confidence, reduce litigation and insurance costs, and assure business viability. For example, in the aircraft industry, actions taken by cross-representational groups over 30 years, and especially over the past 10 years, have resulted in safety improvements; the process was a transparent, respectful one of improving safety programs and incorporating the consensual standards into government regulations. In this case, an analytic-deliberative process of decision-making has evolved whereby potentially affected parties in the private and public sectors collectively identify key safety issues to be addressed[16], which in turn has produced knowledge and agreements about safety that met and moved beyond scientific 'reliability' to 'socially robust' and publicly credible arrangements[17].

The Safety First Initiative executive advisory board and steering committee are now forming cross-sectoral working groups that will conduct transparent negotiations to produce four categories of cross-industry safety standards. The Initiative will begin by focusing on the safety issues for two classes of products that are currently under development: nonfood uses of food crops (*e.g.*, genetically modified to produce pharmaceutical and industrial compounds) and food uses of genetically engineered fish and other aquatic species. Concerns about the environmental and human health safety, and related regulatory complexity, of these two classes of GM products have been an increasing focus of discussion for scientists, policy makers, developers and consumers. These products clearly promise benefits to a large number of consumers, while posing new and complex safety management issues—a situation that highlights the urgency for addressing the formulation of safety standards in these two cases.

On the basis of lessons learned in the formation of successful industry-wide safety programs, these working groups will negotiate and draft four elements of cross-industry safety standards necessary to establish credible safety planning and management for these two cases[6]:

**Safety criteria setting.** Designing safety criteria requires systematic analysis of possible harm, which involves the rigorous identification of hazards, the assessment of risk and planning to reduce and control risk. Establishing a complete and scientifically reliable set of safety design criteria for a product rests on two requirements: establishing rigorous criteria at the outset of development of a new product and independently validating these criteria before they are used. Both of these tasks become at once doable and highly credible when developers have an agreed-upon set of safety standards to start from. Safety criteria developed for a product from such safety standards might address such factors as the effects that release of the GM product would have on the abundance of wild relatives and nontarget organisms, and the allergenicity of foods derived from the GM product.

**Safety verification.** Rigorous tests need to be designed that will fully challenge the product and credibly demonstrate that the product meets the pre-set and government-approved safety criteria established in this process. Designing these tests requires the application of the best available scientific methodologies and information, from all relevant fields. Standards might address, for example, acceptable means of verification of the fitness of GM plants and fish compared with unmodified relatives.

**Follow-up.** The processes of setting criteria and conducting tests to verify that the product meets safety criteria cannot anticipate all problems. Open-minded and scrupulous monitoring of the product in all its uses is also required; the discovery of problems needs to be followed up with meaningful and timely corrective action. Standards might address risk-relevant monitoring and appropriate sampling of products in use.

**Safety leadership.** A well-designed set of safety criteria, verification processes and follow-up procedures will only be meaningful if they are implemented consistently and properly. This requires responsive and responsible safety leadership in three areas. The first area is the establishment of rigorously trained and independently certified safety engineers who would be valued employees of firms and government agencies. The second area is the encouragement of a company management style that fosters broad thinking, application of the best scientific methodologies and information, self-imposed responsibility to make safe products, responsiveness to evidence of real hazards and problems, and independent review of all aspects of the product safety program. The third area is the creation of a framework for managing the application of cross-industry safety standards, including an independent audit function.

The above four elements offer a means for galvanizing national and international participants from biotechnology firms, agriculture and aquaculture, food processing and retail firms, consumer and other public interest groups, academia, and government to organize and build on their existing knowledge and practices to establish scientifically reliable and publicly credible safety standards that would be applied throughout the research, development and commercialization processes for these two cases of GM products.

## Shared benefits, shared responsibilities

The Safety First Initiative can offer benefits to many groups simultaneously. Safety principles, applied early in the design process, can benefit multiple stakeholders concerned with environmental safety, food safety and the security of their investments. For an example of building safety into early stages of design and development, consider Davison's[18] proposals to enhance biosafety of recombinant microorganisms through the removal of unwanted genes, by increasing the stability of gene constructs, through inducing suicide in transgene hosts and in the use of "environmentally friendly genetic markers" in GM organisms. Consensual safety standards, developed by integrating ideas such as these, would work to improve biosafety management, and they would have other benefits, such as enhanced market competitiveness, higher investment ratings and an improvement in inter- and intra-industry relations.

Establishing these cross-industry safety standards would draw on existing national and transnational regulatory regimes but also would require industry leadership. Other industries, such as aircraft and steel, demonstrate that individual firms can be safety pioneers. Today, some life science companies that use genetic engineering have already established some components of a safety program and offer the foundation for building a cross-industry program. For instance, a consortium of safety experts from a variety of companies are informally organized around an effort to improve safety programs across the agricultural biotechnology industry, focused on pharmaceutical crops, in an effort supported by the Biotechnology Industry Organization (Washington, DC, USA). Some companies, such as Dow AgroSciences (Indianapolis, IN, USA) and DuPont (Wilmington, DE, USA) are applying safety

management programs developed in their pharmaceutical and chemical divisions to safety management of biotechnology products. Pioneering firms have not received appropriate recognition for their efforts because the efforts are undertaken in isolation rather than industry-wide, are implemented partially and are not vetted by independent, cross-representational groups. Smyth *et al.*[5] emphasized that the industries involved with GM products stand to gain from decreased risks of product failure and liability claims. To achieve these benefits, it is essential that the biotechnology industry develop private-sector safety governance regimes, from firm-level components, such as product safety verification, to cross-industry components, such as third-party certification of biotechnology safety engineers, as other industries have done.

The Safety First initiative also involves the kind of representative, independent and verifiable process that would be credible with consumers and other groups, a credibility that has eluded those biotechnology companies, despite the extensive efforts of some to ensure safety. Involvement of scientists and safety experts from multiple disciplines in the working groups that will draft the safety standards will ensure that industry safety programs are also scientifically reliable. Existing lessons suggest that the development of such effective, responsive and responsible safety standards can improve the trust of the public and affected industries (*e.g.*, food retail businesses) in genetic engineering and other biotechnologies.

In addition, the initiative also offers a process for national and international government units to make constructive progress toward addressing the gaps in the patchy nature of biosafety governance globally. New, government-certified, biotechnology-safety engineer training programs aimed at building a recognized safety professional career path would provide additional reassurance.

In proposing cross-industry safety standards for genetic engineering through the Safety First Initiative, we are well aware that safety failures in particular applications of GM organisms will still occur due to complex interactions among people's behavior, the technology, human social institutions and environmental factors. GM organisms are themselves complex, their potential interactions with and effects on the environment and human health are diverse and complex, and their present-day management—from the idea stage to final use—involves diffuse leadership and responsibility. Safety standards will necessarily be applied in a global economic context, and it will be a challenge to design their content and operation to be effective in different social and ecological settings without exacerbating existing disparities between nations in their capacities to govern genetic engineering. Acknowledging these complexities while focusing on making safety the first priority will require integrity, pragmatism and wide participation[6]. The first step is replacing the current retrospective risk-based paradigm for governing biotechnology with a proactive safety paradigm.

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