Conventional crops are the test of GM prejudice

Sir — Millstone *et al.*, in their Commentary in last week's issue[1], claim that 'substantial equivalence', a rule governing toxicity testing of genetically modified (GM) crops, is a pseudo-scientific concept.

One of their arguments is that it is insufficient to test glyphosate-tolerant soybeans (GTSBs) for toxicity and health problems; beans must be tested specifically after glyphosate treatment when isoflavone levels are modified. Millstone *et al.* suppose that toxicity could result from unspecified interactions with the single gene incorporated in the GTSB. The GTSB (Roundup) technology actually requires glyphosate spraying only early in the season when soybean plants are small and weeds a strong competitor for soil and light resources. The beans themselves form months later when the effects of the biodegradable glyphosate sprays have disappeared.

As in all discussion about GM plants, it is important to ascertain the applicability of these arguments to conventionally bred crops, either to avoid, or to expose, simple prejudice against the technology itself. We are unable to think of any environmental stress condition in the quality or supply of light, in the supply of water, minerals or a host of pests and diseases which does not modify isoflavone levels and indeed the content of a host of potential carcinogens that are found in most plants[2].

Using the logic of Millstone *et al.*, every new crop seed variety would have to be separately tested for toxicity when it has been treated with every herbicide, every pesticide, fertilizer variations, attack by every individual predator, infection with every individual disease and grown in an astronomically large number of different environmental combinations. We would be drowning in toxicity tests. And all these tests would be simply to eliminate the remote possibility that a particular balance of carcinogenic chemicals inside the plant induced by a unique set of conditions might interact in some unexpected way with the many new genes that are combined by conventional plant breeding in the new seed variety.

If this phenomenon ever happens it is more likely to occur in conventional new-variety crops, because many new genes are present rather than the single well characterized *trans* gene and its protein product in a GM plant. Only two examples, to our knowledge, of the environmental induction of a toxic compound that was not detected during routine testing have ever emerged out of the many millions of conventional crop lines produced. Psoralen was found to accumulate in one line of insect-resistant non-GM celery in response to light, and to cause skin burns[3]. Cool weather-induced toxic accumulations of solanine caused the withdrawal of the non-GM Magnum Bonum potato line in Sweden[4].

The UK Health and Safety Executive concluded, after 25 years of intensive scrutiny, that GM food technology is one of the safest yet developed[5]. GM soya has been eaten for 3–4 years by hundreds of millions of people in the United States and Europe with no untoward effects. The type of ill-informed logic expressed by Millstone *et al.* obstructs the acceptance of a new and far safer technology, simply because the authors don't like it. Their arguments are a distraction from the task of developing a sustainable and environmentally friendly agriculture, which combines the best of conventional plant breeding approaches with the new technologies.

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Substantial equivalence is a useful tool

Sir — We would like to respond to last week's Commentary[1] in which Millstone *et al.* incorrectly assert that: "Substantial equivalence is a pseudo-scientific concept because it is a commercial and political judgement masquerading as if it were scientific. It is, moreover, inherently anti-scientific because it was created primarily to provide an excuse for not requiring biochemical or toxicological tests."

The concept of substantial equivalence was developed proactively before any new genetically modified (GM) foods came to the market. It was first described in an OECD (Organization for Economic Co-operation and Development) publication in 1993[2,3] produced by about 60 experts from 19 OECD countries, who spent more than two years discussing how to assess the safety of GM foods. Most of these experts, all nominated by governments, were regulatory scientists from government agencies and ministries responsible for consumer safety.

In 1996, participants at an expert World Health Organization/Food and Agriculture Organization consultation[4] recommended that "safety assessment based upon the concept of substantial equivalence be applied in establishing the safety of foods and food components derived from genetically modified organisms". This represented an endorsement by experts based on three years' experience in the safety assessment of various GM foods.

Substantial equivalence is not a substitute for a safety assessment. It is a guiding principle which is a useful tool for regulatory scientists engaged in safety assessments. It stresses that an assessment should show that a GM variety is as safe as its traditional counterparts. In this approach, differences may be identified for further scrutiny, which can involve nutritional, toxicological and immunological testing. The approach allows regulators to focus on the differences in a new variety and therefore on safety concerns of critical importance. Biochemical and toxicological tests are certainly not precluded.

Since the concept of substantial equivalence was first described, several new foods have been assessed and knowledge has accumulated on how to use the concept. In parallel, the OECD, its governments and others have continued to review its adequacy in food safety assessment and to develop supporting tools[5]. The OECD's task force on the safety of novel foods and feeds (chaired by P. M.), in particular, continues to focus on the application of the concept. This includes work on assessment methodologies when substantial equivalence cannot be applied, as well as efforts to identify the critical nutrients and toxicants found in major crop plants, as a focus for the demonstration of substantial equivalence.

More than a decade of work by the OECD and its member governments was recognized by the heads of state and government of the G8 countries when they met in June in Cologne and invited the OECD task force to undertake a study of the implications of biotechnology and other aspects of food safety. This additional challenge is certain to lead to further reflections on the concept of substantial equivalence.

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No GM conspiracy

Sir — Last week's Commentary by Millstone *et al.*[1] is misleading and inaccurate. The authors do not seem to be

aware of a meeting organized by the Organization for Economic Co-operation and Development, held in Aussois, France, in March 1997, which is about to be published. Hence they present an outdated view of the use of substantial equivalence, while their characterization of this tool as the outcome of an international conspiracy to foist genetically modified (GM) foods on a gullible public is beyond belief. Do Millstone *et al.* really believe in a worldwide conspiracy? They have no evidence for this assertion.

Second, by such accusations, Millstone *et al.* denigrate the whole regulatory process and all the hard-working academics who make up the British regulatory committees. Throughout their article, they reveal their ignorance of the way the regulatory process works. Substantial equivalence is a tool only: the 'first cut' at the decision-making rather than a quick solution, as the authors infer. I was chairman of the Advisory Committee on Novel Foods and Processes (ACNFP) from 1989 to 1997, and we never received any political or commercial pressure when making decisions. I totally reject the slur on our integrity.

Finally, Millstone *et al.* are wrong in what they say about GM soya. They imply that a herbicide that has no effect on the target enzyme, and that does not persist in the plant, has far-reaching effects on intermediary metabolism. If the herbicide does not affect its target, how can it affect the plant? Not only is this idea bizarre, it is wrong: GM beans have been analysed after treatment with herbicide and their composition is unaffected[2–4]. Millstone *et al.* are also wrong to say that treatment with herbicide alters the isoflavone content; they do quote one paper reporting some variation but ignore others showing that this difference is well within the normal range of isoflavone content[4]. More than 1,400 compositional analyses of Roundup Ready soya beans have been conducted, showing that there are no significant differences in the key soya bean nutrients and anti-nutrients; these data have been reviewed by the ACNFP. The authors use the literature selectively to make their point, which is not good enough for any scientific journal.

I contend that these data establish that GM soya beans are as safe as conventional soya beans. This conclusion was reached by the ACNFP after a thorough safety assessment, using substantial equivalence as a key safety assessment approach. This conclusion has been confirmed by regulatory agencies in the 13 countries that have approved these GM soya beans. This food has been used commercially for four years, and 300 million Americans are currently eating it with no sign of a problem.

How did such a mish-mash of old hat sociology and poor science get published? I would like an assurance from the editor that all such contributions — especially from activists — are rigorously refereed. *Nature*, in my view, damages its reputation by publishing such propaganda.

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4. Taylor *et al. J. Agric. Food Chem.* (in the press).

● **The publication policy of Commentaries is long established. The Commentary section, like the Book Reviews and Correspondence sections, is intended to convey original and stimulating opinions, both solicited and unsolicited, from outside contributors. Publication does not imply endorsement by *Nature* of the authors' views. In contrast to Articles, Letters and Brief Communications, not all Commentaries are refereed, but it is *Nature*'s policy to seek advice especially where we believe there is a risk of readers being misled. On the few occasions when, despite that policy, falsehoods or significant misrepresentations have been published, rebuttals or corrections have been published as soon as possible.** — Editor, *Nature*

Putting transparency into ethical balance

Sir — Science nowadays often responds to a particular ethical challenge in isolation from others, so that any overall philosophical perspective might not be apparent to the public. This can contribute to an impression that scientists muddle through on the defensive when it would be fairer and more persuasive if they displayed the relationships and consistencies between ethical positions on different matters. How might it be possible to achieve this?

People make ethical decisions by weighing opposing arguments, pressures and concerns, drawing on their feelings about the issues as well as on their thinking. Is earning a profit from drug or seed sales less ethical than providing these commodities cheaply or free to the needy? Is whistleblowing in public better than a quiet warning? Should the integrity of experimental animals take priority over prospects for medical advances?

Most people would probably agree that the answer to each of these questions is sometimes yes and sometimes no. Judgements are personal and specific to the circumstances. When people disagree it is usually because they assign different weights to particular factors, rather than differing on what the considerations should be.

I believe that most people could agree on generic principles which cover most or all issues in current contention, deep though their differences might be over interpretation and application. I suggest that these three would suffice:

(1) Fair shares of burdens and fruits. Goods and services for one population should not bring undue disadvantage to another, for example in the form of chemical, radioactive or noise pollution. Areas of risk include genetically modified crops; information technology and its use (on whom and for whom); databases and copyright law and intellectual property law for private versus public benefit, among others. Some inequities arise through omission, especially of the application of science to agriculture, health and education in the poorer countries (a theme of UNESCO's recent World Conference on Science).

(2) Obedience to truth. Honesty over details must be reconciled with perspectives on what is important in academic and corporate science and their applications. This should apply to the use, abuse and fabrication of data; commitment to establishing and acknowledging the whole truth; and the ethical tensions that arise from private research funding in public institutions.

(3) Respect for life. The uniqueness and integrity of all life forms and the environments that support them must be protected, whether as elements of the planet's gene pool or as individuals with conscious lives. This will expose conflicts between the needs of one organism and another, but although conflicts have existed throughout biological evolution, it is inevitable that we now accept the responsibility of resolving them by human decision.

Each of these principles is formulated as a balance to reveal why people think and feel differently about given problems, and even why they change between related issues. Ethical positions will and should always shift at the levels both of individuals and of society as a whole, and consensus will not and should never be complete or stable. We need challenge to recognize danger and test responsibility, and we also need to understand the patterns in different judgements to develop the democratic mandate for science to go forward to meet the needs and aspirations of society. Engagement with critics of science needs to shift from tactics to strategy; namely from whether in the short term new technologies are to be developed, to how in the long term they are to be certified and introduced.

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