ISP response to the GM Science Review Panel First Report

Note: The Independent Science Panel (ISP) response to the GM Science Review Panel First Report collates individual ISP members' responses. ISP members are responsible for those areas where they have specific competence, while giving overall endorsement to the response as a whole. Each ISP member also recognizes the expertise and authority of other ISP members in those areas where they themselves do not have specific competence.

Dr. Mae-Wan Ho, Prof. Joe Cummins & Prof. Peter Saunders

GM Science Review Deeply Flawed

Commercialisation by Stealth

The most serious shortcoming of the GM Science Review is that it entirely ignores the substantial body of evidence on the *proven* successes and benefits of organic farming, agroecology and other forms of sustainable agriculture. Not even to consider these, while dealing at length with the *projected* potential benefits of GM is to restrict the scope of the debate from the very outset.

At first glance, the Report looks reasonable enough. Chapters 5, 6 and 7, each 50 pages long, claim to address all the objections that critics have raised on health and environmental impacts and gene flow from GM to non-GM crops and wild weedy relatives. They contain sections with such promising titles as, "Possible nutritional toxicological differences in GM food", "Food allergies for GM crops", "The fate of transgenic DNA", "The effect of GM-derived feed in the food chain", "Invasiveness/persistence of GM plants", "Toxicity to wildlife", "Can DNA from GM crops transfer to soil microbes?" and "Can genetic material in GM plant transfer to viruses?"

But the promise of the headings is not fulfilled by the contents. No one can be surprised that the review panel, widely perceived as dominated by pro-GM scientists, found no evidence that GM crops pose a threat to health or the environment, as reported in the media. The precise wording (p. 10), however, is full of qualification and equivocation, and this runs through the entire report: "To date there have been no verifiable untoward toxic or nutritionally deleterious effects resulting from the cultivation and consumption of products from GM crops. However, absence of readily observable adverse effects does not mean that these can be completely ruled out and there has been no epidemiological monitoring of those consuming GM foods."

The Review does not give blanket approval for growing GM crops in Britain. Instead, it recommends that each application for approval should be considered and assessed for risks on its own merits. This may sound reassuring, but in fact it is not. For the "case by case" approach that is being advocated is based on the unsupported assumption that there is nothing wrong with GM technology in general. The most that is being investigated is whether any particular crop presents specific hazards.

At no point are the important and fundamental issues addressed. Worse, each application that is approved serves as a precedent for approving later ones, and in the end, it will be claimed that the entire technology has been properly investigated and approved when in fact it was never investigated at all.

And sure enough, the Review states openly (p. 24) that the "appropriate agriculture for the UK" would be, among other things, one that would "allow coexistence of farming systems." In other words, the Review clearly accepts from the outset and the principle that GM crops based on current technology should be grown in Britain – which is precisely the point that they were supposed to be deciding. The only question is whether some individual crops might be excluded.

The "case by case" approach is thus a slowly-but-surely tactic for commercial approval of GM crops.

We are given plenty of false reassurances – repeated with monotonous regularity at the end of every subsection. It goes like this.

"Is there general scientific agreement?" Yes, generally, after paragraphs riddled with equivocation, misrepresentation, omission, half-truths and worse, that the risk from eating GM food,

horizontal transfer of transgenic DNA, or of allergy, toxicity, cross-pollination, whatever, is *very* low, as the perceived hazard is *very* rare, if it happens at all.

"Is the issue unique to GM?" No, not at all, or not in many cases, or not usually.

"Are there gaps in our knowledge or scientific uncertainties and are they important?" Yes and no. We should proceed with caution on a "case by case" basis.

"Likely future developments"? Looks good if not great; they will overcome the uncertainties and bring many potential benefits. At one point (pp. 74-77), the Report even promises "safer, nutritionally enhanced" GM foods, including "golden mustard" as follow-on from "golden rice", supposedly to cure vitamin A deficiency in the Third World, and failing to mention that "golden rice" has already been widely exposed to be worthless. Many kilograms of the rice would have to be consumed each day to get the minimum daily requirement of vitamin A, while leafy greens that can be grown in every backyard would provide a much richer source of the vitamin plus other essential vitamins, minerals and micronutrients.

"Where there is important scientific uncertainty, what is the way forward?" Research and more research, and regulation, with "cautious commercial approval" and "post-release monitoring" and yes again, a "case by case" approach.

The "case by case" approach is not just a tactic for commercialising GM crops. *It is also a subterfuge for sidestepping fundamental criticisms of the GM technology itself, which the Report has singularly failed to acknowledge. In other words, it has given blanket approval for GM technology, which can only be justified by ignoring critical scientific evidence.*

Some of the most powerful critics – the two dozen prominent scientists who have constituted themselves as an Independent Science Panel (ISP) on GM, who oppose the official GM Science Review - are saying that the GM technology is *inherently* unsafe, that the hazards are *unique* to GM, and that *the evidence, incomplete though it is, already supports that view,* but is being obfuscated, suppressed, or otherwise not addressed by the pro-GM establishment.

To have a useful, informed debate, the key areas of scientific disagreement must be clearly laid out before the public, as is done in the ISP Report, *The Case for a GM-Free Sustainable World*, released on June 15, 2003 (www.indsp.org), which includes extensive review of the evidence on the successes and benefits of non-GM sustainable agriculture as well as the many problems and hazards of GM crops. The ISP Report, widely adopted by civil society organisations in Britain and around the world, was submitted to the GM Science Review, but it has not been posted on the official website. Our closely argued case as a whole also remains to be answered.

It will be instructive to give some glaring examples of how the Report sidesteps the major scientific criticisms in its attempt to ultimately mislead and cajole the public into accepting the commercialisation of GM crops.

Evidence that GM is inherently unsafe remains unanswered

1. GM is distinct from conventional breeding methods, including mutations induced by X-rays or chemicals. It is unreliable, uncontrollable, unpredictable and unstable; and introduces new risks (see below).

It is not just the rate of success that is at issue. To say that the rate of success in conventional breeding is no better than for GM (pp. 9, 49, 52) is not an answer to the genetic instability unique to GM lines that

comes from the GM technology itself. Making a GM plant or animal involves breaking and joining the DNA of the host genome at many unspecifiable locations, a process referred to as "illegitimate recombination", which distinguishes GM from all conventional methods. This process leads to substantial scrambling of both foreign and host DNA at the sites of integration.

Moreover, even the 'successes' in GM are unstable, and prone to further changes. These changes include silencing of the foreign genes, further rearrangement of the DNA and loss of the genetic material, *all of which are unique to the process*. The instability of GM lines is hardly addressed in this Report. We are told (p. 54) that in studies carried out largely by biotech companies there were no significant deviations from Mendelian ratios; but to infer stability from this is to make an elementary error in both statistics and genetics.

2. GM greatly increases the scope of horizontal gene transfer and recombination, which pose the most insidious dangers.

The genetic material of any and every species on earth can be recombined and transferred in the laboratory, even DNA from species that have been extinct for 400 000 years. There is no evolutionary precedent for this situation. New genes and new combinations can be introduced into our environment and food chain that have never existed. This important issue too, is not addressed in the GM Science Report.

3. GM DNA is definitely not the same as non-GM or natural DNA.

The claim is made repeatedly in the Report (pp.11, 90 and elsewhere) that GM DNA is no different from natural or non-GM DNA. This is simply not true. Many GM DNAs are combinations of genes and genetic material that have never existed, and would never have come into being but for genetic engineering in the laboratory. For example, promoters (genetic signals for boosting gene expression) from plant viruses are frequently joined to genes from bacteria and other species, and synthetic DNA sequences are often incorporated into GM DNAs.

More importantly, GM DNA is often designed to cross species barriers and to invade genomes, i.e., to enhance horizontal gene transfer and recombination, *the very process that creates new disease agents and spreads antibiotic and drug resistance, and could trigger cancer in the event of integrating into the genome of mammalian cells.*

The risk of creating disease agents and spreading antibiotic resistance is further increased by the fact that GM DNAs are predominantly from bacteria and viruses that cause diseases, and antibiotic resistance marker genes are a routine tool of the GM trade, and frequently remain in GM crops released into the environment.

That antibiotic resistance is already common (p.12) is no justification for using antibiotic resistance marker genes. Millions of hectares of GM crops with antibiotic resistance genes are bound to exacerbate existing problems of antibiotic resistance in deadly pathogens. The proposed methods of removing them with 'site-specific' recombination tools (p.97) have to be evaluated most carefully, as some, like the *Cre-Lox* and similar systems from bacteria, are already known to scramble genomes.

GM DNA has been known to be structurally unstable from the beginning of genetic engineering, i.e., it has a tendency to fragment, and can disintegrate from the genome, which is one reason why GM lines are unstable. (The other reason is that the host cell can silence the transgene by chemical

modification of its promoter.) This instability leads to genetic rearrangement in the host genome, changing the GM line in unpredictable ways, and increases the likelihood that the GM DNA can transfer horizontally and recombine in part or in whole.

Monsanto's Roundup Ready soya was the first transgenic line to be characterised by independent scientists several years after commercial release. The insert had altered substantially from what was claimed by the company in its application for commercial release. Not only was the gene order scrambled, the plant genome at the site of insertion was also scrambled, and a 534 bp fragment of unknown origin had got in as well.[1]

4. Many GM DNAs possess 'recombination hotspots' making them extra-unstable, and hence extra-prone to horizontal gene transfer and recombination, with all the attendant risks.

Recombination hotspots in GM DNA include sequences such as the left and right borders of integrating viruses and plasmids, artificial polylinkers containing multiple restriction sites, and genetic signals such as the origin of replication, and, in the case of transferable plasmids, the origin of transfers.

One prominent example is the isolated cauliflower mosaic virus (CaMV) 35S promoter, widely incorporated into GM crops before its unsafe properties became known. It not only possesses a recombination hotspot, but is also promiscuously active in making genes over-express in species across the living world, including human cells. The GM Science Review Report continues to suppress this and other damning evidence, as before, by giving the totally unjustified impression that the CaMV 35S promoter is just the same as the virus itself or its genome, which we are said to have eaten for millennia without harm (p. 70). The Report also fails to cite two further key scientific publications from ISIS, which we have drawn attention to more than once. By way of refuting our concerns that the CaMV 35S promoter is unsafe, the Report even cites a submission from Roger Morton, noted for his *ad hominem* attacks, and apparently behind a recent attempt to discredit MWH on the eve of the launch of the Independent Science Panel on GM.

5. Direct evidence of hazards inherent to the technology is swept aside and misrepresented.

Topping the list of the direct evidence of hazard inherent to the technology is the study of Pusztai and co-workers, who found dramatic 'growth-factor like' effects in the stomach and intestinal lining of young rats fed GM potato for just 10 days, which were not present either in rats fed non-GM potatoes or in rats fed non-GM potatoes spiked with the transgene product. The experiment suggested that the effects were due to the GM process or the GM construct, which happens to contain the CaMV 35S promoter. This raises a host of key questions, including the role of CaMV 35S promoter in producing the 'growth factor'-like effects.

To refute this work, the GM Science Review Report cites the Scottish Executive's bald statement that the work was "fundamentally flawed", and claimed, "subsequent work has failed to substantiate the findings" referenced to Derek Burke's submission (p.66). Derek Burke has never carried out experiments to substantiate or refute the findings, *nor has anyone else*. If the findings have not been confirmed by subsequent work that is because no such work has ever been attempted.

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[1]Windels P, Taverniers I, Depicker A, Van Bockstaele E and De Loose M (2001). Characterisation of the Roundup Ready soybean insert. *Eur Food Res Technol* DOI 10.1007/ s002170100336, © Springer-Verlag; see also "Scrambled genome of Roundup Ready soya" by Mae-Wan Ho, *ISIS Reprints on Transgenic Instability, 1999-2001*, ISIS Publications, London.

Thereafter, Monsanto's feeding studies are liberally cited as evidence of "no harm" (p.68). Those studies carry as much weight as the repeatedly cited 'evidence' that (p.105 and elsewhere), "many hundreds of millions of people" have been eating GM foods or GM-fed animals "for up to seven years with no substantiated adverse effects reported." That latter 'experiment', carried out on hundreds of millions of people who never gave their informed consent, could not have revealed any but the most immediately obvious harmful effects, as there was no control group, and no systematic health monitoring. The Report omitted to mention, however, that scientists at the Centers for Disease Control in the United States found that between 1994, when GM food was first introduced, and 1999, foodborne illnesses in the United States have increased two- to ten-fold.[2] The precise causes of the diseases are still largely unknown, and the possibility that they may be linked to genetically modified food cannot be dismissed *a priori*. That, at least, is a peer-reviewed scientific publication, as opposed to pure speculation that there have been no adverse effects from eating GM foods.

6. Positive evidence of horizontal gene transfer denied and dismissed as "very rare".

It is remarkable that there has been only *one single* field monitoring experiment after millions of hectares of GM crops have been planted, and just *one* human feeding trial involving 19 individuals fed *a single meal* containing GM soya flour. Despite that, positive evidence of horizontal transfer of GM DNA to bacteria in the soil and in the human gut has been found. More remarkable still, our Government's science advisors persist in denying and dismissing this evidence. And in the case of the human feeding trial, there is no plan to carry out longer-term studies. Page 90 of the Report contains a statement that directly conflicts with existing evidence: "Trans-kingdom transfer of transgenic DNA from GM plant material to bacteria is unlikely to occur due to a series of well-established barriers and this is supported by experimental evidence."

One main excuse for denial is that the bacteria that have taken up the DNA cannot be isolated as cultures (p.96), even though molecular probes and selection by marker trait both indicated that horizontal gene transfer had occurred. This is either a remarkable example of ignorance or a deliberate attempt to mislead. It is generally accepted that less than 1% of the bacteria in the environment can be isolated by current culture methods. The failure to isolate the bacterial culture, therefore, can in no way be construed as evidence that horizontal gene transfer did not happen.

Not only that, several of the papers cited in the Report itself (pp 90-92) actually provided further evidence of horizontal gene transfer, which the Report fails to make fully explicit. For example, Duggens and coworkers (2003) found that the entire coding sequence of the *Cry1A(b)* transgene could still be detected in sheep rumen fluid 5 hours after feeding GM maize grains, and fragments more than 200bp long were detected 24 hours later. Plasmid containing the transgene and kanamycin resistance marker gene could still transfer the entire transgene as well as kanamycin resistance to *E. coli* after being kept for 5 minutes in the sheep's mouth. The authors remarked, "DNA released from feed material within the mouth has potential to transform naturally competent oral bacteria." Similarly, Mercer and coworkers (2001) showed that both plasmid and chromosomal DNA fragments were incompletely degraded after incubation in the human mouth, and can still transform *Streptococcus gordonii*, which normally lives in the mouth.

[2] Mead PS, Slutsker L, Dietz V, McCaig LF, Bresee JS, Shapiro C. Griffin PM and Tauxe RV. Food-related illness and death in the United States. *Emerging Infectious Diseases* 1999, 5, 607-25.

In fact, horizontal gene transfer could occur during food processing, long before the food is consumed, for most food processing fails to break down DNA appreciably.

A study on DNA stability in plant tissues (Chiter et al, 2000) showed that fresh maize and maize silage contained high molecular weight DNA that required relatively high temperatures and pressurised steam, or chemical expulsion and extrusion (in the case of oilseeds) to fully degrade. The authors commented, "These results imply that stringent conditions are needed in the processing of GM plant tissue for feedstuffs to eliminate the possibility of transmission of transgenes."

Straub and coworkers (1999) found that GM DNA of *Lactobacillus* in heat-treated fermented sausage could still be detected after 9 months of storage. Furthermore, the meat matrix protected DNA from degradation.

A paper *not* cited in the GM Science Report gave clear evidence of horizontal gene transfer in food. Bauer and coworkers (1999)[3] investigated the ability of a plasmid to transform *Escherichia coli* in 12 foods under conditions commonly found in processing and storage. Transformation was found in all foods with frequencies depending on the food and on temperature. Surprisingly, *E. coli* became transformed at temperatures below 5 degrees C, i.e. under conditions of storage of perishable foods. In soy drink this condition resulted in frequencies higher than those at 37 degrees C.

Some definitive experiments that could inform on the safety of GM food and crops

At a public meeting last November, Ho had submitted to the Advisory Committee for Novel Foods and Processes (ACNFP) a list of experiments that should be done to address areas of uncertainty, and these are reproduced below, in a slightly improved form.

1. Feeding experiments similar to those carried out by Pusztai's team, using well-characterized transgenic soya and/or maize meal feed, with appropriate, unbiased monitoring for transgenic DNA in the faeces, blood and blood cells, and post-mortem histological examinations that include tracking transfer of transgenic DNA into the genome of cells. As an added control, non-transgenic DNA from the same GM feed sample should also be monitored. In addition, the possible role of the CaMV 35 S promoter in producing the 'growth-factor-like' effects in young rats should be investigated.
2. Feeding trials on human volunteers using well-characterized transgenic soya and/or maize meal feed, with appropriate, unbiased monitoring for transgenic DNA and horizontal gene transfer in the mouth and in the faeces, blood and blood cells. As an added control, non-transgenic DNA from the same GM feed sample should also be monitored.
3. Investigation on the stability of transgenic plants in successive generations of growth, especially those containing the CaMV 35S promoter, using appropriate quantitative molecular techniques.
4. Full event specific molecular characterisation of all transgenic lines to establish uniformity and genetic stability of the transgenic DNA insert(s), and comparison with the original data supplied by the biotech company to gain approval for field trials or for commercial release.

[3] Bauer F, Hertel C, Hammes WP. Transformation of *Escherichia coli* in foodstuffs. *Syst Appl Microbiol*. 1999, 22, 161-8.

5. Tests on all transgenic plants created by the *Agrobacterium T-DNA* vector system for the persistence of the bacteria and the vectors. The soil in which the transgenic plants have been grown should be monitored for gene escape to soil bacteria. The potential for horizontal gene transfer to the next crop via the germinating seed and root system should be carefully monitored.

We reject the GM Science Review Report

The GM Science Review has failed to answer the charge that GM technology is inherently unsafe and unpredictable. We reject the conclusion that there is "no evidence" that GM crops pose a threat to health and the environment, and also reject the recommendation to effectively commercialise GM crops on a "case by case" basis.

There is no case for growing any GM crops in Britain (or anywhere else in the world). On the contrary, when all the creditable scientific evidence and concerns are accurately taken into account, there are many reasons to ban the environmental release of GM crops to make way for organic farming, agroecology and other forms of non-GM sustainable agriculture.

Dr. Vyvyan Howard

I have read the relevant sections of the Review. There is precious little science there to be read. It even manages to avoid citing, arguably, the sole independent hazard assessment of a GM food, published by Ewan & Pusztai in the *Lancet*, a highly reputable journal. So much for even-handedness. The Review continually repeats the mantra that there is 'no evidence' to suggest that anything untoward has happened or will happen in the future. Let us examine this more closely.

The US 'experiment' with GM food is held up as 'evidence' that GM foods are safe. While it does appear that acute toxic effects are not a problem, the Review acknowledges that long-term low-dose toxicity (the sort that most people are worried about) could be a problem, and that there are areas of uncertainty. It is therefore misleading to claim that there is 'no evidence' that there is a problem.

One cause of 'no evidence' is that you didn't bother to look. Another cause of 'no evidence' is that you did look but didn't find anything. There can be several reasons for that. There may truly be nothing to find. The study design might be bad, there is an effect to be found, but you miss it. The effect might be so diffuse that however good the study design, it couldn't pick up the effect. Which of these is likely to be the truth?

Certainly, with respect to population effects, the biotech industry didn't bother to look. If you don't want to find anything, that is quite an effective approach! How useful is epidemiology? It can be a very blunt tool if the background rate of very common conditions - such as allergy or cancer - are being affected. For example, if thalidomide had caused cleft palate (a common condition) rather than phocomelia (a very rare condition) it is likely that we would still not be aware of the connection. To have any chance of knowing if GM foods have non-acute toxic effects you would need to know

a) what the background conditions were before you introduced GM food;
b) the 'exposure' of individuals to GM food, i.e. what they were consuming.

Then any changes in the incidence of various conditions could be related to 'dose'. Virtually none of this information is available because none of it has been collected. GM foods were introduced piecemeal into the US diet. Nobody knows who is eating what. Apart from some cancers, there is very little background information about the starting condition for various conditions before the introduction of GM foods. Therefore, if there were effects occurring in, say, the background rate of allergy, there would be absolutely no way of knowing. The report interprets this as 'there is no evidence'.

The Review should at least be honest and make clear their statement that 'there is no evidence' is simply another way of saying 'we do not know and we cannot know'. And yet there is a considerable amount of scientific evidence from the animal and microbiological literature that there are matters of concern about the toxicology and allergenicity of GM foods. These appear to be under-represented in the Review.

Dr. Eva Novotny

Unrealistic Assumptions Regarding the Extent of Gene Flow

The section of the Report dealing with gene-flow is overly optimistic as to how rigorously cross-contamination of non-GM crops by GM crops can be limited (p. 202). It endorses the MAFF (Ministry of Agriculture, Fisheries and Food) study that set separation distances between GM crops and non-GM varieties, but that study plays down the effects of more unusual weather conditions. Recommendations on separation distances must take account of the fact that such conditions do occur in some seasons. Consumers who choose non-GM foods do not wish to have these foods only on average, in most seasons, while finding that they are eating several times the legal limit in other seasons. 'Whole-farm' averaging to obtain recommended separation distances is also suspect, as pollen flow over a receptor field is highly irregular. Maize to be sold as 'corn-on-the-cob' is especially a case for special monitoring, as each kernel is pollinated individually. A cob growing in a pocket of high-density pollen in a field that is 'on average' within the limit of contamination would have a high incidence of GM kernels. Practical experience in North America also suggests that the recommended separation distances are too small. The experience in North America is that contamination occurs easily and quickly: almost all seeds of non-GM varieties having GM counterparts are now contaminated by GM seeds, and in Saskatchewan, Canada, nearly all organic farming of oilseed rape (canola) has collapsed because of GM contamination.

There is no escaping the conclusion that there can be no co-existence of GM and non-GM agriculture.

Dr. Arpad Pusztai

[Dr. Pusztai's response is in the form of a letter to Dr Adrian Butt, Secretary of the GM Science Review, and an accompanying email to Mr Richard Pitts at the GM Science Review Secretariat.]

Dear Mr Richard Pitts,

As requested by your colleague I am now attaching an electronic copy of my previous letter in connection the First GM Science Report. I very much hope that you will also pass this on to Professor King.

The letter speaks for itself; it is detailing some of the shortcomings of the report and unlike the Report it is dealing with the problems from the viewpoint of a (still) practising scientist. The only point I want to add after reading the entire report is that it makes a skillful play with the principle of inclusiveness. The strategy was clear; quite a lot of comments and papers by GM-sceptics or anti-GM people are referred to in the reference list though, of course, your scientific panel could not bring themselves to refer to our *Lancet* paper (only Kuiper's comments on it!) or our scientific review on the potential health effects of GM foods (whose receipt was acknowledged by yourself). The panel obviously found that it was much simpler to deal with these views and papers by either dismissing them out of hand or just simply ignoring them. However, this way the result is excellent from your point of view and nobody can, therefore, say that the deliberations by the panel were not inclusive or the views which are critical of GM crops/foods were not discussed but alas, as they were unsuitable or not good enough, these views could not be amalgamated into the report. I thought that I might have to look up the precise meaning of the word "hypocrisy" but then I decided that, regretfully, the spirit behind this report is good enough for the definition of the word.

Hopefully for your next report we need not have to use the classical words: "could do better". Unfortunately, very few people will believe in this.

Yours sincerely

Arpad Pusztai

Dr Adrian Butt
Secretary, GM Science Review
Office of Science and Technology
Bay 484, 1 Victoria Street
London Sw1H 0ET

Dear Dr Butt,

As I understand there will be a follow up to the First Report that has just been released. Perhaps then comments by others than your panel of experts will also be taken into account. Although I do not want to comment on the full report I would like to make a few observations on Chapter 5, the part dealing with GM food/feed nutritional/toxicological safety, on which I am usually regarded as an expert, at least by a part of the scientific community.

I must say in advance that both the Executive Summary and most of the contents of Chapter 5 invariably disappointed and baffled me. However, after having had a look at the composition of the Panel in which plant molecular biologists were pretty well represented, it became obvious to me that, to say it politely, there was a striking shortage of nutritional scientists on the panel with relevant experience and track record. I am not going into details of the sometimes clearly obvious pro-GM bias amongst the panel members, I shall leave this to others. My comments will be on the science or, more precisely, the disappointing lack of it in the Report which was (at least in Chapter 5) unduly verbose, repetitive and short of experimentally established facts. Key references were missing which would have shown that the bland statements and reassurances in the text were in fact wrong. I shall give you a few examples:

P. 62. You approvingly quote Kuiper et al (2001) who say: "international concensus has been reached on the basic scientific principles presently used for the safety assessment of foods…" Apart from the fact that many people would question the validity of this statement which is an opinion rather than a fact, this is contradicted on your next page in the Report (see my next comment!) Incidentally, the report is full of such contradictions.

P. 63. It is stated that "very few traditional foodstuffs… have been subjected to systematic toxicological or nutritional safety assessment". Such a sentence could only be described by a panel whose members are not familiar with the scientific literature. Thus, soya, one of the major crops, which became prominent in nutritional practice, particularly in animal nutrition, has been tested *ad nauseam*, with hundreds if not thousands of papers (including something around 20 from my lab) having been published.

The Report is full of assertions unsupported by experimental evidence:
P. 65. "Bt proteins break down in sunlight (that is when Bt spores are sprayed on crops), in the latter (i.e. when these are expressed in transgenic crops) they are broken down during processing and /or in the gastrointestinal tract. In fact, the evidence is to the contrary, i.e. that Bt proteins (lectins!) not only do not break down in the gastrointestinal tract but that they bind to the surface of the mammalian gut and are also potent immunogens and immune adjuvants. There is no excuse for missing this information because in our review [A Pusztai, S Bardocz and SWB Ewen "Genetically Modified Foods: Potential Human Health Effects"**,** Chapter 16 in *Food Safety:*

Contaminants and Toxicants, JPF D'Mello (ed), CABI Publishing, 2003], the receipt of which you acknowledged in your letter, this is fully described and referenced.

It is further said in the Report which is full of such bland statements without references that "…it is also important to test the whole crop in feeding studies". In our review you had a reasonable but critical review of all (10 or so) of such studies in the literature but this is never mentioned.

P. 66. When it comes to other critical comments which are favourable to the views of the panel, there is no such reticence. Even though these criticisms are not backed up by science and uttered by politically motivated people, they are accepted as gospel truth in a "Science Review"? Since when is it that pontification by the Scottish Executive can be regarded as scientifically valid when they say that the HHCC report is fundamentally flawed (interesting use of the word, probably borrowed from the Royal Society!)? In this context one can also ask that since when the opinion of a former scientist (Dr Burke) carries such weight that on his word and without experimental evidence the results of a peer-reviewed paper on GM potatoes (which is incidentally never mentioned in the Report even though some of the comments on this very paper by Kuiper et al, 1999, are!) are rejected because a Chinese scientist had done some work on GM tomatoes and sweet peppers even though this has never been published?

It is also interesting that there are plenty of soothingly reassuring words and sentences in the Report that how important the safety testing of GM food is but when it comes to actually give an indication whether this is done in practice, instead of giving references to these works the Report refers to comforting reviews, such as Kuiper et al (2001). However, it is never stated that in Kuiper's review, which in many respects is not bad, there are only 10 refereed publications mentioned - hardly a huge number since the introduction of the first GM crop (FLAVR-SAVR tomato) in 1993 to enable us to form a consensus. Incidentally, our review also mentions these very same papers but, probably, from a more critical viewpoint.

Again, there are plenty more reassurances in the Report. For example on p. 68 it says that "and the new (transgenic) proteins are typically tested in animal models for acute toxicity". However there is again a reticence to give references to these studies. Could it be that the only acute toxicity study with Roundup Ready Soya and published in the *Journal of Nutrition* (1996) was not referred to in the Report because, to use the favourite word of the Royal Society, both the design and execution of this study were flawed?

More reassurances: Could insertion…lead to unintended effects? There is, however, no problem because "For this reason… the new GM variety is checked for compositional equivalence…phenotypic and agronomic equivalence, and *nutritional and toxicological equivalence".* I do not doubt that the majority of your panel sincerely believes in this. After all before Galileo and Copernicus people believed that the sun was circling round the earth and not the other way, but a scientific review should be based on and dominated by scientifically established facts and not beliefs and opinions.

At this stage I give up because there is not much mileage in pointing out glaring inconsistencies, half-truths not supported by evidence, bias, etc. On reading the Report it appeared to me that the panel members' views were most likely pre-formed and therefore they could not have been affected by evidence contrary to their beliefs placed in front of them. In many peoples' view the

most likely explanation for this was that some of the panel members were ideologically motivated. With the disproportionally high quota of biotech industry representatives and scientists on the panel who obviously firmly and unsurprisingly believe in the value of GM crops, the largely pro-GM bias of the Report was very much like that could have been expected. All the same, I would most charitably still like to believe against all odds that the explanation for the rather poor quality of the Report was that the knowledge and expertise of most of the panel members was not sufficient for and commensurate with the task. It would be interesting to find out that how many of these panellists actually read our review but, of course, we shall never find this out.

I very much hope that you will pass this letter on to Professor King and perhaps even to individual members of the panel. Although I would like to believe that reason and science will eventually prevail, unfortunately from personal experience I see not much hope for this.

Yours sincerely

Arpad Pusztai 31 July 2003

David Quist

The GM Review on Gene Flow: Throwing Caution to the Wind

Brief comments on Chapter 7: “Gene flow, detection and impact of GM crops” of the GM Science Review Panel, First Report

October 2, 2003

1. General Comment

First, I felt the report established a good working framework for outlining the issues at hand, especially the sections on “Gaps of Knowledge” and “Scientific uncertainties of importance”. These are important considerations in the adoption of any well-rounded risk assessment. It was, however, disappointing what the authors chose to do (or didn't do) with that framework.

The general shortcomings of the chapter were in two main areas: first, in the use of “absence of evidence is evidence of absence” fallacy, and two, inadequate accounts and significance in the “Gaps of Knowledge” and “Scientific uncertainties of importance” mentioned above. Lastly, the chapter as a whole is unrealistically optimistic about the potential to mitigate undesirable gene flow in agricultural systems. Evidence to date suggests that despite even the best of intentions, irreversible transgene introgression into conventional varieties WILL occur. Breakdowns in the system, both biogenic and anthropogenic have shown to be unavoidable with the current framework of GM crop management. Despite the lessons (economic, political, and ecological) of the U.S., Canada, and Mexico with unmitigated gene flow, it is disappointing that this assessment does not convey much of what can be learned from these very revealing experiences.

2. Response to statement that the results of Quist and Chapela were flawed: p. 204, p. 245

The criticisms levied against the Quist and Chapela publication (Quist and Chapela, 2001 *Nature* v.414: 541-543) centre on the secondary statement of transgene fragmentation after integration with local maize landraces. The first and main statement of the report, that transgenes had indeed introgressed into local varieties was not being challenged. The methodology used in generating data for the second statement was never demonstrated as flawed, as there was simply a disagreement in appropriate experimental design and valuation of the data presented. From the agronomic perspective of the paper’s critics, the data presented was of little merit or value, as it constituted “useless” information from the point of view of gene function. Conversely, viewed from an ecological perspective (as the study was designed for), the data generated are of acute interest for understanding how transgenes behave in natural systems. It is essential that these distinctions are clear. The evidence of transgene introgression has been further validated by independent research carried out by the Mexican government. The Quist and Chapela paper was not retracted from *Nature* and continues to be a valuable contribution within the citable scientific literature on transgenic gene flow.

3. Specific Comments (responses in bold)

p. 195

"However, the vast majority of this pollen will not result in successful cross-hybridisation for any number of reasons e.g. sexual incompatibility, it does not land on the female parts of the plant, it cannot successfully compete with other pollen grains or because it is unviable. "

This depends on the crop in question. Canola and corn are the big OPVs (Open Pollinated Varieties) to consider in cross contamination, but other crops may be significant in this regard as well.

p. 198

"Separation distances based on these predictions and agricultural practices that minimise seed-mediated gene flow have been employed to successfully minimise gene flow between non-GM crop varieties for economic (e.g. certified seed crops and identity preservation schemes for different types of maize)"

The use of Identity Preservation schemes and certification programmes are still in their infancy, and have not been reproduced on a scale that warrants a large degree of confidence. Scaling up these programs to cover complex distribution regimes effectively is suspect at best.

p. 199

"Genetic elements that are commonly used in GM technology may show that transgenic DNA is present but these will not identify its source."

Still, markers covering many specific events of GM crops (but not all) are available. Further analysis through molecular characterization of the transgenic construct would yield the varietal identity.

p. 200

"In a report for the then Ministry of Agriculture, Fisheries and Food, Ingram (2000) identified robust, representative data sets and applied them …"

The "robustness" of this report needs to be checked, if this is the basis of the assessment on pollen flow distances.

Comments from section 7.2.3…

Maintaining "safe" distances as a means of minimizing gene flow is reasonable if the management regime is actually followed in the first place. A recent report considers that such strategies are not failsafe. Recent USDA survey (http://www.usda.gov/nass) revealed that 20% (and this is probably a very conservative estimate) of farmers planting Bt maize do not follow rules for maintaining minimum distances.

It seems sensible that if GM pharmaceuticals DO find their way into commercial production, they should only be allowed in plants not used as food or not an Open Pollinated Variety (OPV). Despite this common sense, it is the two most highly out crossing OPVs food crops, maize and canola, that these drugs and industrial chemicals are being introduced into! Is this a deliberate attempt to smother the issue by making pandemic contamination a forgone conclusion?

Regulating crops on a case-by-case base would only be effective if there were SIGNIFICANT resource dedicated to oversight, which goes far and beyond what exists today!

In short, oversight and regulation of GM crops is going to be an extremely expensive endeavor. Such output in costs should be overcome by the benefits that the technology brings to consumers and the public at large. Are there benefits of GM technology to the consumer that justify the enormous cost of regulation? It is quite clear that the answer is no.

p. 207

"Screening for genetic elements commonly used in GM crops (e.g. the cauliflower mosaic virus [CaMV] 35S promoter) may identify unintended GM presence in some cases - however, this is not reliable since these elements are commonly found in nature (results in false positives because the DNA is derived from a source other than the crop)"

Research had demonstrated that Cauliflower mosaic virus (CaMV) is specific to the Mustard family (Brassacaeceae). Therefore, the possibility of false positives may be a concern for oilseed rape (*Brassica* spp.) of the crops that are in commercial production. Still, the CaMV promoter used in many recombinant DNA constructs is modified from the endogenous form in the virus, a distinction readily discernable with a complete molecular characterization of the transgenic construct, or identification of other commonly used transgenic elements.

p. 208

The authors explore apomixis as a technology for minimizing gene flow from transgenics to conventional crops or wild varieties. The research is still far off from commercial development. In my assessment, this "technology" has potentially disastrous consequences for maintaining genetic diversity and freedom of seed systems from the control of seed companies. Definitely it's a new form of GMO that hasn't been given much attention in the public or scientific arenas, and requires careful assessment of its proposed value.

Coupling genes to prevent hybrid offspring from competing with "pure" GMO crops? This would be categorically disastrous. As species loss through hybridization is one of the biggest problems that invasive species may pose to an ecosystem, it is not difficult to imagine the ramifications of technologies such as these!

p. 210

The authors correctly allude to the difficulty in extrapolating management regimes (e.g. safe minimum distance for segregating GM and non-GM varieties) from small scale plots to large fields.

But there is too much faith in management practices, too much faith in future genetic use restriction technologies (GURTs) and pollen flow limiting technologies in the report.

I like that they are asking: What types of uncertainties exist? But then why didn't they attend to this? The research proposed to study effects of gene flow need to be asking ecological and population biology-level questions.

p. 214

"More than two decades of experience with the technology indicates that in the context of gene flow transgenes behave exactly as resident naturally-occurring genes. The issue of gene flow from crops to wild relatives is not unique to GM, and there is no evidence that current transgenes are more likely to transfer or persist in the wild than other genes. However, each crop/gene combination is, and must continue to be, considered on a case-by-case basis. "

There is no sound, peer reviewed scientific basis that supports this assertion. This is the substantial equivalence argument in its most incredulous form! This should be challenged.

p. 215

"Consent to release a GM crop would not be given were any harm to human health or the environment envisaged from the transfer of a transgene by gene flow to wild relatives. "

As long as the burden of proof is on the producers of the variety to demonstrate scientifically the absence of harm in peer-reviewed studies might this be acceptable.

The concept of burden of proof on the producers should be stressed, especially if assessment is going to be on a "case by case" basis as this report strongly infers. Who is going to pay for all these assessments, anyhow? The taxpayers or the companies that want to introduce their technologies?

p. 215

The use of the term "introgression" is defined incorrectly. The term has different meaning depending on usage. As a general use term, as it was originally coined in the 1920s, was more or less equivalent to hybridization. Plant breeders then took the term to mean first hybridization, then backcrossing to the original population (not further hybridization as presented in the GM Review text).

p. 219

"Evidence that transgenes are inherited and transferred between individuals in a similar way to resident genes may be derived from more than a decade's experience with the technology. Genes inserted by recombinant DNA technology and selected for plant breeding programmes demonstrate Mendelian segregation and recombination and 'flow' from plant to plant exactly as resident genes"

If one carefully reads the current literature, you see that this is really not true. Many of the early studies reported [more or less] Mendelian inheritance of transgenes, but were based on crude methods of identification. A recent study that compares gene presence with gene expression finds that Mendelian inheritance is more uncommon than common. See Breiztger and Tonks, *Crop Sci.* 43:4–12 (2003).

p. 221

With respect to potential increased fitness in GM-wild hybrids, the positive fitness coefficient conveyed by a transgene could become negative in later generations if the expression of the transgene is lost, or effects endogenous genes in later populations. This point is not considered very often in the debate: that genes could go from producing an overall benefit to an individual plant for a time, but could through time turn into a cost! This would lead to bottlenecking of diversity.

p. 222

"Overall, the fact that genes for pest and disease resistance inserted into crops by conventional breeding have not produced invasions of wild relatives in semi-natural habitats, coupled with the evidence that transgenes behave as naturally-occurring genes, suggest that predictions based on the tenets of invasion biology are supported by genetic evidence."

This statement is only true by the flawed rationale "absence of evidence is evidence of absence" of gene flow impacts. There have not been sufficient studies, or sufficient exposure of experience of transgene flow, to determine whether this statement above is adequately true or false. The author has to make some very unsupportable assumptions in order to arrive at the conclusions she/he did.

p. 223

"There is currently no evidence to indicate that transgenes are more likely to transfer and persist in the wild than naturally-occurring genes."

Untrue. The work of Joy Bergelson et al. (*Nature* 1998 vol. 395 p 25) indicates that transgenic *Arabidopsis* have significantly higher (up to 20X) rates of out crossing compared to "naturally mutagenic" conventional *Arabidopsis*.

7.4.6 Gaps of knowledge and scientific uncertainties in HGT studies

The most glaring deficiencies in any research in the prokaryotic (bacterial) world are that almost all of our understanding comes from culturable bacteria, i.e. those that will grow on nutrient media under laboratory conditions. We know that these bacteria only represent a very small fraction of the entire bacterial community existing in a given ecosystem. Furthermore, the importance of different stages of metabolism and development of bacterial populations, especially under different nutrient regimes (e.g. artificial conditions of the lab) are not adequate mirrors of such bacterial states in the natural environment. Consequently, it is foolhardy to conclude that laboratory-based evidence of HGT in prokaryotes is representative of natural HGT processes over phylogenetic, developmental, or temporal gradients.

Up to 7.5…

Indeed there is not experimental evidence of viral transfer of GM DNA. This is exactly the kind of "gaps of knowledge" and important uncertainties that require greater weight (and understanding) in sound risk assessment of the ecological implications of GM crops.

p.245

"there is no evidence that the CaMV 35S promoter is mobile, unlike natural and widespread plant transposable elements. Quist and Chapela (2001) reported the fragmentation of the CaMV 35S promoter in maize landraces when transgenes were transferred from GM maize. However, the design of the experiments on which this particular conclusion was drawn was deeply flawed (Kaplinsky *et al*., 2002; Metz M. and Fütterer, 2002). "

See section 2 above for response on our *Nature* paper.

p. 245

"we eat large amounts of CaMV-infected crucifers (a 1980s study showed 10% of UK cauliflowers and cabbages were infected. Organically grown crops are likely to have even higher levels)."

A portion of a genetic construct, taken apart from its endogenous organization and regulation, cannot be assumed to behave similarly to the natural counterpart.