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Report:

From Seattle to MontrealWorld Scientists Calling for GM Moratorium Swell to Over 230

Seattle was a truly inspiring event for the global civil society, every sector was represented from all over the world: labour, family farmers, indigenous peoples, professionals, consumer organisations, citizen action groups, environmentalists. Suddenly, everyone realizes we are all struggling against the same thing: corporate rule under a globalised economy that has created massive poverty and brought the earth to the edge of extinction. And still, our governments in the industrialized North are bent on negotiating agreements behind closed doors at the WTO that will effectively sacrifice environmental protection, labour and safety standards, and even basic human rights to trade and financial imperatives. Fortunately for everyone, governments from the Third World and other non-industrialized countries have united to say a resounding 'No!' on our behalf. Our Open Letter from World Scientists to All Governments, calling for a GM moratorium, a ban on biopatents and a public enquiry into the future of food security (see ISIS website) was successfully delivered to the Heads of Delegation to the WTO, thanks to the Third World Network. In the event, 144 scientists from 27 countries were included. Our letter was particularly timely as Canada and Japan proposed to set up a Biotechnology Working Group in the WTO to deal with GMOs and biotechnology, while the United States called for improvements to rules and disciplines of the WTO to ensure that trade in agricultural biotechnology products is based on "transparent, predictable and timely processes". The aim of the proposals, as pointed out by Mathew Stilwell of the Center for International Environmental Law and Martin Khor of

the Third World Network, is to limit the ability of importing countries to regulate GM products and to subordinate the International Biosafety Protocol, currently being negotiated under the Convention on Biological Diversity, to the WTO. The proposals were a blatant attempt to undermine the Biosafety Protocol and to force trade of GMOs in the face of serious threats to health and biodiversity. They were strongly opposed by the like-minded group which included the African region, the Caribbean and most countries in the Third World.

In the event, an estimated 35 000 to 50 000 took part in peaceful demonstrations in the city. Yes, it was overwhelmingly peaceful despite aggressive tear-gassing, pepper sprays, rubber bullets and other tactics employed by the Seattle police, and a few shop windows broken as a consequence. Michael Meacher, UK Minister for the Environment, gave an accurate account in his diary for the *Independent on Sunday*, and definitely blames the Seattle police. The police chief has resigned amid calls for a public enquiry.

The official WTO negotiations collapsed – to great jubilation in the streets – after the government delegations of the developing nations united in protesting against the lack of transparency and democracy in the proceedings. The rich industrialized nations again tried to impose their corporate agenda on the poor countries, and failed. It was a decisive victory for the developing countries and for all citizens of civil society in their collective struggles against corporate feudalism.



From left to right: Angela Ryan, Julian Haffegge, Chris Ririe, Mae-Wan Ho.

But, beware of the next round: the upcoming Biosafety Protocol meeting in Montreal, starting 25 January 2000, when GMOs and products thereof will take centre stage. We shall be submitting our letter to the official delegations there. Since Seattle, the number of scientists who have signed on has jumped to over 230, thanks to Jaan Surkuula, Director of Physicians and Scientists for Responsible Assessment of Science and Technology (PSRAST) and signatories to their statement who have joined forces with us, plus others who have signed on independently. Please help collect more signatures for Montreal! It will be a very crucial meeting, and we must make sure that the arguments of real scientists who adopt the ecological perspective and the precautionary approach are heard loud and clear.

At least ten scientists on our list were active in Seattle, in the teach-ins, workshops as well as the street demonstrations (none got arrested, fortunately): Dr. Phil Bereano of Council for Responsible Genetics USA; Dr. Tewelde Egziabher of Ministry of the Environment, Ethiopia and Spokesperson for the African Region and Like-minded Group on Biosafety; Dr. Michael Fox of Council for Responsible Genetics USA; Dr. Mae-Wan Ho of ISIS and Open University UK; Dr. Jonathan King, Molecular Biologist, MIT, USA; Dr. Peter M. Rosset of Institute for Food and Development Policy, USA; Devinder Sharma of Forum for Biotechnology and Food Security India; Dr. Vandana Shiva, Research Foundation for Science and Ecology India; Dr. David Suzuki of the Suzuki Foundation and University of British Columbia Canada; and Dr. Christine von Weisaeker, Ecoropa Germany. (M.W.H.)

Lead Stories

Pusztai Publishes Amidst Fresh Storm of Attack The Sorry State of 'Sound Science'

Pusztai has published amidst a fresh storm of attack, and even reported threats to the Editor of The Lancet (see Ewen, S. and Pusztai, A. (1999). Effect of diets containing genetically modified potatoes expressing Galanthus nivalis lectin on rat small intestine. The Lancet 354, 1353-4; also <http://plab.ku.dk/tcbh/PusztaiPusztai.htm> for Pusztai's full rebuttal to his critics). The controversy reveals the

sorry state of the so-called 'sound science' which his critics purports to defend, and highlights the general disregard for the precautionary principle in current 'risk assessment'.

GM potatoes expressing a snowdrop lectin (GNA) under the cauliflower mosaic viral (CaMV) 35S promoter have been developed to increase insect and nematode resistance. GNA was chosen because previous studies by the authors showed the effects of the lectin on the rat small bowel have been 'minimal', at least when fed on large amounts of the lectin for ten days or less. Pusztai's collaborator, Stanley Ewen, examined the microscopic structure of the lining of different parts of the rat gut in groups of animals fed for ten days, respectively, on non-GM potatoes, GM-potatoes and non-GM potatoes spiked with the GNA protein. All the diets had the same protein and energy content.

Variable effects were found in different parts of the gut. In the stomach, a highly significant proliferation of the lining was found in both rats fed GM potatoes and those fed non-GM potatoes spiked with lectin. It was reasonable to conclude, therefore, that the effect on the stomach lining was mainly due to the expression of the GNA transgene. However, significant changes in the lining of the small intestine and parts of the large intestine were found only in the group of rats fed GM potatoes. Ewen and Pusztai conclude that "other parts of the construct or the genetic transformation (or both) could also have contributed to the overall biological effects of the GNA-GM potatoes." In addition, rats fed GM potatoes also had significantly increased lymphocytes (white blood cells) in the gut lining, which indicates damage to the intestine.

The explosive claim is that "other parts of the construct or the genetic transformation process" may be toxic. If that were the case, *all* GM crops may not be safe. Elsewhere, Pusztai has questioned the safety of the cauliflower mosaic viral promoter in the transgenic potatoes which is in practically all current GM crops. Could the signs of damage to the intestine be due to viral infection? That was a claim made in Pusztai's earlier communications, though not in the present publication. If so, might the cauliflower mosaic viral promoter have anything to do with it? (see Viral Gene Switch – A Recipe for Disaster? This issue)

Neither Pusztai nor Ewen regards their research as definitive proof that GM potatoes, or GM food in general is

harmful. Pusztai has repeatedly stressed the need for further research. However, the results do throw into serious doubt the claim of the biotech industry and regulatory authorities that GM food is *safe.* According to a leading British statistician, one should be worried about safety if even a single rat had been affected.

The attacks on Pusztai say more about the sorry state of the so-called 'sound science' that lies behind current risk assessment, whether it be for radioactive discharge, industrial chemicals, toxic wastes or GMO. It is a reductionist, mechanistic science that ignores the complexity and interdependence of living systems, that has, furthermore, been thoroughly discredited by recent scientific findings (see *Genetic Engineering Dream or Nightmare?* Featured in Book Briefs, this issue). More importantly, it is directly in conflict with the precautionary principle that has been accepted in several international conventions including the Convention of Biological Diversity and the EU (see an excellent recent publication, *Protecting Public Health & the Environment*, featured in Book Briefs, this issue).

As applied to GMOs, the principle may be stated as follows: where there is scientific evidence to suspect serious irreversible harm, lack of scientific certainty or consensus should not be used as justification for taking preventative measures. This is based on that offered in another important recent publication, *An Orphan in Science: Environment Risks of Genetic Engineered Vaccines*, (see Book Briefs, this issue), and in line with that adopted by Swedish law for hazardous and chemical products.

Risk assessment based on what Pusztai's critics refer to as 'sound science' not only ignores the complexity and interdependence of real living systems and reasonable suspicion of harm based on scientific evidence, it also places the onus on regulators and civil society to demonstrate that something is definitely harmful before it can be refused approval, withdrawn or banned. It is such systematic misuse and abuse of scientific evidence that has continued to allow corporations to endanger human health, destroy wildlife and our planet with impunity. No wonder there is a debate on whether risk assessment should be 'science-based' at all.

We believe that risk-assessment should be science-based, but it should be based on real, reliable science whose goal is to enable us to live

sustainably with nature. In contrast to his critics, Pusztai has behaved with integrity and social responsibility as a scientist, which is fully in accordance with the precautionary principle. (M.W.H.)

Viral Gene Switch – A Recipe for Disaster?

This story highlights the hazardous nature of the genetic engineering process as well as the new gene constructs created and released into the environment.

A scientific paper on the cauliflower mosaic viral promoter (CaMV promoter) has attracted at least nine attacks, including one from Monsanto, before it is actually published. The attacks and rebuttals have been ricocheting around the web, but what is it all about? (Please visit ISIS website for the paper, Ho, M.W., Ryan, A. and Cummins, J. (1999). The cauliflower mosaic viral promoter – a recipe for disaster? *Microbial Ecology in Health and Disease* (in press), and the official author's reply to critiques.)

Prof. Joe Cummins of the University of Western Ontario was the first scientist to question the safety of the cauliflower mosaic viral (CaMV) promoter, which is in practically all GM crops currently grown commercially or undergoing field trials. He pointed out that the promoter could recombine with other viruses to generate new disease-causing viruses. In our joint paper, we review some recent findings which give further grounds for concern, and recommend the immediate withdrawal of all crops and products containing the CaMV promoter, which effectively means all commercial and field tested GM crops, and products with incompletely degraded DNA.

The story begins with the 'promoter'. A 'promoter' is a stretch of genetic material that acts as a switch for turning genes on. Every gene needs a promoter in order to work, or to become expressed. But the promoter is not a simple switch like that for an electric light, for example, which has only two positions, either fully on or fully off. Instead, the gene promoter has many different parts or modules that act as sensors, to enable it to respond, in ways we do not yet fully understand, to signals from other genes and from the environment. These signals tell it when and where to switch on, by how much and for how long. And under certain circumstances, the promoter may be silenced, so that it is off all the time.

The role of the promoter of a normal gene in an organism is to enable the gene to work appropriately in the extremely complex regulatory circuits of the organism as a whole. The promoter associated with each of the organism's own genes is adapted to its gene, while the totality of all the genes of the organism have been adapted to stay and work together for millions, if not hundreds of millions of years. The genome of each organism is organized in a particular way which is more or less constant across the species, so individuals within a species can freely interbreed. Each species protects its integrity and remains genetically stable because there are biological barriers which prevent distant species from interbreeding or otherwise exchanging genetic material. Foreign DNA is generally broken down or put out of action. Genetic engineering attempts to overcome these biological barriers so genes can be arbitrarily transferred between species that would never interbreed in nature. In order to do so, special tricks are needed.

When genetic engineers transfer foreign genes into an organism to make a GMO, they also have to put a promoter in front of each of the genes transferred, otherwise it would not work. The promoter plus the gene it switches on make up a 'gene-expression cassette'. Many of the genes are from bacteria and viruses, and the most commonly used promoter is from the cauliflower mosaic virus. Several gene-expression cassettes are usually stacked, or linked in series, one or more of them will be genes that code for antibiotic resistance, which will enable those cells that have taken up the foreign genes to be selected with antibiotics. The stacked cassettes are then spliced in turn into an artificial gene carrier or 'vector'. The vector itself is generally made by joining together parts of viruses and other infectious genetic parasites (plasmids and transposons) that cause diseases or spread antibiotic and drug resistance genes. In the case of plants, the most widely used vector is the 'T-DNA' which is part of the tumour-inducing plasmid ('Ti plasmid') of *Agrobacterium*, a soil bacterium that infects plants and give rise to plant tumours or galls.

The role of the vector is to smuggle genes into cells that would otherwise exclude them. And more importantly, the vector can jump into the cell's genome and so enable the gene-expression cassettes it carries to become incorporated into the genetic material of the cell. The genetic engineer cannot control where and in

what form the vector jumps into the genetic material of the cell, however. And this is where the first unpredictable effects can arise. Each transgenic line or GMO is unique, and gives rise to different unintended effects. In the case of food, this can mean unexpected toxins and allergens (see GM Soya & Increased Soya Allergy in Science Notes, this issue).

The foreign genetic material in the GMO – referred to as the 'transgenic DNA' or the 'construct' – is quite complicated. It consists of new genes and new combinations of genes - from diverse species and their genetic parasites - that have never existed in nature. Such chimaeric constructs are already known to be structurally unstable, that is, they have a tendency to break and join up and rearrange. It is to be expected that such structural instability can only increase when the construct is introduced, by a hit or miss process, into a new genome. The instability of GMOs is a big problem for the industry. GMOs often do not breed true (Terminator in New Guises, this issue).

Why use a promoter from a virus such as the CaMV? Like all viruses, CaMV is a genetic parasite that has the capability to infect cells and hi-jack the cell to make many copies of itself in a short period of time. Its promoter is therefore very aggressive, and is also found to be active in *all* plants, monocots, dicots, algae, and the *E. coli* bacteria that live in the gut of all mammals. Hence, the CaMV promoter is very popular with genetic engineers. It effectively makes the gene placed next to it turn on full blast in any plant genome, at perhaps a thousand times the volume of any of the organism's own gene. Having it in the genome is rather like having the loudest phrase of a heavy-metal piece, played with the most powerful amplifier, over and over again, throughout a live performance of a Mozart concerto. What the CaMV promoter does is to place the foreign gene outside the normal regulatory circuits of the host organism, subjecting the host organism to unremitting metabolic stress. This will multiply the unintended, unpredictable effects in the GMO. It may also be another reason why GMOs are notoriously unstable (Finnegan, J. & McElroy, D. 1994, *Bio/Technology* 12, 883). The organism generally reacts to the presence of foreign genetic material by breaking it down or putting it out of action in other ways. Even after the genetic material is incorporated into the genome, it can silence the foreign genes so they are no longer expressed

(see Terminator in New Guises, this issue).

The key recent finding, which provoked us to write our paper, was the report by Kohli *et al*, (1999) *The Plant Journal* 17, 591, that the CaMV promoter contains a 'recombination hotspot' – a site where the DNA tends to break and join up with other DNA, thus changing the combination and arrangement of genes. Around the hotspot are several short stretches, or modules, for binding various enzymes, all of which are also involved in recombination, ie, breaking and joining DNA. Furthermore, the CaMV promoter recombination hotspot strongly resembles the borders of the T-DNA vector carrying the transgenes, which are also known to be prone to recombination. It is that which enables the vector to invade the cell's genome in the first place.

The aim of our original paper, restated explicitly in our official rebuttal, was to review the relevant findings and, in particular, to point out the *implications* which the researchers themselves are unwilling or unable to draw. The findings that transgenic DNA has the tendency to break and join in several places imply that parts or all of it may be more likely than the plant's own DNA to jump out of the genome and successfully transfer horizontally to unrelated species. Horizontal gene transfer, in this context, means the transfer of the genetic material directly by infection to the genetic material of unrelated species, in principle to all species interacting with the GMO: bacteria, fungi, earthworms, nematodes, protozoa, insects, small mammals and human beings. This process is uncontrollable and cannot be recalled. Transgenic DNA has been designed to be invasive and to overcome species barriers; once released, it will invade different organisms especially bacteria which are in all environments, where it will multiply, mutate and recombine.

There are additional findings which suggest an increased potential for transgenic DNA to spread horizontally. For example, the enzymes in the cell that insert the transgenic DNA into the genome can also make it jump out again. DNA released from both dead or live cells can survive without being degraded in all environments, including the mouth and gut of mammals. DNA can be readily taken up into cells. And *all* cells can take up naked or free DNA. A recent finding suggests that integrated viral sequences are preferentially taken up and incorporated into the cell's genome (see Reusable DNA Alert, this issue). The instability of transgenic DNA may

also be enhanced as the result of the metabolic stress inflicted on the organism by the CaMV promoter which gives rise to continuous over-expression of transgenes.

The major consequences of the horizontal transfer of transgenic DNA are the spread of antibiotic resistance marker genes among bacteria and the generation of new bacteria and new viruses that cause diseases from the many bacterial and viral genes used. The generation of new viruses could occur by recombination with live or dormant viruses which we now know to be present in all genomes, plants and animals included. Recombination with defective, dormant animal viral promoters may also occur, as we know that there are modules which are interchangeable between plant and animal promoters. Recombination of CaMV promoter modules with defective promoters of animal viruses may result in recombinant promoters that are active in animal cells. This may reactivate the virus, generate new viruses or give functional viral promoters causing over-expression of one or another of dozens of cellular genes which are now believed to be associated with cancer.

In conclusion, there is sufficient scientific evidence to support well-founded suspicion of serious, irreversible harm to justify the immediate withdrawal of all GM crops and products containing the CaMV promoter from environmental release. This is fully in accord with the precautionary principle. (M.W.H)

Terminator Technology In New Guises

The terminator technology, which genetic engineers harvested seeds not to germinate, was vigorously opposed by farmers and consumers all over the world. One of the claimed benefits is that it prevents the spread of transgenes, but its real purpose is to protect corporate patents on seed. It offers no benefit to farmers or consumers. In response to widespread opposition, Monsanto has recently announced that it will not commercialize terminator seeds, if only because such seeds are not yet available. But research is continuing.

In fact, terminator technology has continued to be developed under a number of different guises. The main one is 'Genetic Use Restriction Technologies' (GURT) (see Traitor Tech. The Terminator's Wider Implications. *RAFI Communique*, January/February, 1999). Newer

versions make seeds dependent on the application of a chemical for germination, or for expressing the desired transgenic trait – the chemical being exclusively manufactured by the company selling the seeds, so the end result is again to protect corporate patents.

Genetic engineering is not a precise technology. On the contrary, it is uncontrollable, unreliable and unpredictable (see Viral Gene Switch – A Recipe for Disaster?). The GURT technologies are worse. They depend on 'site-specific recombination' – breaking and joining DNA at two specific sites recognised by a recombinase enzyme, which then snips out the DNA between the two sites. The two sites might flank a blocking sequence within a promoter, so removal of the blocking sequence will enable a gene to be expressed which makes a poison to prevent the seed from germinating, for example. Or it may do the opposite, the sites may flank the promoter itself which is necessary for expressing the gene, so when it is removed, the gene will no longer be expressed, and the seed will germinate. The gene coding for the recombinase enzyme is engineered to be under the control of the external stimulus, ie, the chemical manufactured exclusively by the company, so the recombinase will be active only when the chemical is applied.

Thus, GURT technologies involve multiple feats of precise gene stacking, inserting the gene stacks into plants in exactly the configurations constructed, and subsequent to that, precise regulation in the transgenic plant(s), and exactly predictable response of the recombinase to the external chemical stimulus. However, those requirements for precision are beyond the capability of the genetic engineer. The hazards of the transgenic DNA resulting from GURT technologies are much greater, because the imprecisions of inserting multiple gene-constructs are multiplied, and also because of the site-specific recombination mechanisms deliberately introduced. Recombination creates new combinations of genes and has the potential to scramble genes and genomes when it is imprecise. It is already known that recognition between designated recombination sites and their enzymes (recombinases) are far from exact (see Kohli *et al*, 1999, *The Plant Journal* 17, 591) and many mistakes are anticipated. These genes – the recombinase and the recombination sites - once engineered into the plants, will spread both by ordinary cross-

pollination and by horizontal gene transfer, multiplying the opportunities for scrambling or rearranging genes and genomes.

Now, a new report claims to have used site-specific recombination to solve one problem of imprecision in genetic engineering plants, which is that multiple copies of the foreign genes tend to be inserted at each site (Srivastava, V., Anderson, O.D. and Ow, D.W. (1999). Single-copy transgenic wheat generated through the resolution of complex integration patterns. *Proc. Nat. Acad. Sci, USA* 96, 11117-21). As pointed out by the authors, multiple copies are undesirable because it often leads to transgene instability, either on account of gene-silencing by the host organism, or structural instability such as recombination between multiple copies which result in the loss of the transgene.

To solve the problem, the researchers constructed vectors consisting of transgenes flanked by recombination sites that are *inverted* (so they are not recognized by the recombinase). When the transgene is integrated into the wheat genome in a repeated configuration, the recombinase will only snip out the block of genes between sites that are in the same orientation, so ultimately, only one single copy of the transgene will be left at each site, at least in theory. However, it is clear that many unexpected results were also obtained alongside the expected, including the inversion of genes (literally genes turned around), scrambled transgene configuration and scrambled host genome, often arising from the imprecise action of the site-specific recombinase. The authors admit the possibility of scrambling and removing host genome DNA in their procedure, and recommends obtaining single-copy transgenic lines from several different progenitor lines.

In our view, genes and constructs involving site-specific recombination systems should not be approved for release into the environment in any form. (M.W.H.)

Biopatents

Biopiracy Exposed

Eleven indigenous peoples' organisations, collectively known as the Council of Indigenous Traditional Midwives and Healers of Chiapas, are demanding that a US Govt. funded bioprospecting programme suspend its

activities in Chiapas, Mexico, and are asking other indigenous people in Chiapas to refuse to cooperate with the researchers (RAFI 1/12/99 news release). But U. Georgia (US), cooperating with a Mexican university research centre, El Colegio de la Frontera Sur (ECOSUR), and Molecular Nature Ltd., a biotech company based in Wales, UK, refuse to halt the five-year project which aims to collect and evaluate thousands of plants and microorganisms used in traditional medicine by Mayan communities.

Sebastian Luna, an indigenous Tzeltal spokesperson, refers to the project as a robbery of traditional indigenous knowledge and resources. It explicitly proposes to patent and privatize resources and knowledge that have always been collectively owned. It create conflicts within the communities as some individuals are collaborating with the researchers for a few pesos or tools.

Dr. Alejandro Nadal, researcher at Colegio de Mexico has denounced another biodiversity contract in Mexico signed by the Universidad Autonoma de Mexico (UNAM) between Diversa Corporation (US) in which researchers are obliged to provide samples of unique micro-organisms from natural protected areas of Mexico to Diversa for a mere \$50 per sample.

Our governments and academic institutions should stop these immoral, unlawful acts of biopiracy and respect indigenous communities' rights over their collective knowledge and biological resources. (M.W.H.)

Biopiracy Patents Revoked

An important victory was won by indigenous peoples from nine South American countries as US Patent and Trademark Office announced the cancellation of a US patent for the "ayahuasca" vine, *Banisteriopsis caapi*, which is native to the Amazonian rainforest (Center for International Environmental Law (CIEL) press release, 4.11.99). Thousands of indigenous peoples in the region use the vine in traditional religious and healing ceremonies. PTO's decision came in response to a request for re-examination of the patent filed in March by Coordinating Body for the Indigenous Organization of the Amazon Basin (COICA), the coalition of Amazonian Peoples and Their Environment, and lawyers at CIEL. The PTO based its rejection of the patent on the fact that publications describing *Banisteriopsis caapi* were

"known and available" prior to the filing of the patent application. This will set the precedent for revoking other similar patents which have been awarded. In a separate proceeding at the PTO, the three groups have called for changes in the PTO rules that allow patent claims based on traditional knowledge and use by indigenous peoples. Applicants should identify all biological resources and traditional knowledge that they used in developing the claimed invention, and should disclose the geographical origin, and provide evidence that the source country and indigenous community consented to its use. (M.W.H.)

EU Biopatents Directive Opposed

German Minister of Justice Herta Daeubler-Gmelin stated in letter to Greenpeace that the European Patents Office's decision last June to implement the EU Directive on patenting was illegal, according to a Greenpeace Germany press release (1.12.99). Since Sept. 1, the EPO is allowing patents on plants and animals, as well as patents on human genes and parts of the human body. The German Ministry at first approved the decision in June, only to withdraw in October. The latest German decision was in accord with that taken by France, who had voted against the implementing regulations in June.

The unexpected decision by the EPO last June was the initiative of the President of the Office, Ingo Kober, who in doing so, fulfilled the wishes of the genetic engineering industry. The implementation will enable private corporations to sequence and patent the human genome. Scientist who have recently sequenced the human chromosome 22, had to publish their results promptly in order to prevent a commercial company from patenting the whole chromosome patented. But particular genes on chromosome 22 may already have been patented.

(M.W.H. & A.R.)

Gene Patents Stall Cures and Research

Medical research aimed at developing screening methods and cures for congenital diseases are being stifled by corporate patents on human genes, according to a front page report in the Guardian (15.12.99). A survey of US laboratories found that a quarter of American research laboratories have received letters from lawyers acting on

behalf of biotech companies demanding that they stop carrying out clinical tests for Alzheimer's disease, breast cancer and other disorders, because their patents are infringed. Companies holding patents are demanding high fees for testing, or for licensing the tests. Half of the laboratories surveyed have stopped work on developing screening because they know a patent had been licensed or is pending.

A group of American doctors and scientists have issued a protest that these patents and exorbitant licensing fees are limiting "access to medical care, jeopardizing the quality of medical care and unreasonably raising its cost".

Jonathan King, genetic researcher at MIT (and signatory to our World Scientists Statement), points out that research is being stifled also because of the culture of secrecy that now surrounds scientific research; "It's a common experience at scientific meetings for people to withhold information because they have a patent pending. Progress is being slowed down." (M.W.H.)

Science Notes

Reusable DNA Alert

The genetic material of dead cells is scavenged by other cells. It is taken up by *phagocytosis* – a kind of eating response in which the cell envelops the material – and is then either metabolised to generate energy and raw materials for building the cell, or it may be incorporated into the genome of the cell. Integrated viral sequences may be preferentially incorporated.

Researchers used DNA from killed human lymphoid cell lines with integrated Epstein-Barr virus (EBV) as marker to follow the fate and expression pattern of the DNA taken up by various other cell lines. The lymphoid cells were killed by an irradiation procedure or a drug that fragmented DNA, and then added to cultures of human fibroblasts, macrophages, or bovine aortic endothelial cells. They found that all the living cells took up the DNA from the killed lymphoid cells, but only DNA from lymphoid cell lines with integrated EBV resulted in expression of viral genes and incorporation of DNA containing viral sequences into the cells' genome. DNA from killed lymphoid cell-lines with non-integrated EBV (existing as episomes) did not result in expression of viral genes,

suggesting that viral sequences were not incorporated into the living cells' genome.

The researchers also found that the frequency of horizontal transfer of human DNA to the genome of bovine cells was greatly increased in DNA from lymphoid lines with integrated EBV compared with the same lymphoid lines without any integrated EBV; furthermore, almost all of the transferred DNA was associated with the integrated EBV. It suggests that the integrated EBV may be preferentially transferred and incorporated. The authors conclude, "we speculate that similar mechanisms of horizontal DNA transfer may be of importance in conditions characterized by high levels of apoptosis [ie, cell death], eg, in tumours treated with irradiation or chemotherapy".

Ref. Holmgren, L., Szeles, A., Rajnavolgyi, E., Foldman, J., Klein, G., Ernberg, I. and Falk, K.I. (1999). Horizontal transfer of DNA by the uptake of apoptotic bodies. *Blood* 93, 3956-63.

Our comment: The results suggest that integrated viral sequences may be more invasive than other parts of the genetic material. This is in line with our suggestion that transgenic DNA may be more prone to transfer horizontally (see *Viral Gene Switch – A Recipe for Disaster?* This issue). Also, the authors' speculation that similar mechanisms of horizontal DNA transfer may occur in tumours treated with irradiation or chemotherapy raises questions on the possibility that such treatments may spread cancer to other cells, assuming that the EBV is an important causal agent of tumour-formation. (M.W.H.)

GM Soya and Increased Soya-associated Allergy

Scientists at the York Nutritional Laboratory have announced that soya food allergy among the British public have unexpectedly risen 50% between 1998 and 1999. Soya is now in 9th position on the list of top serum reactive (test for allergenicity) foods, up from 14th place in 1997. This finding coincides with the large increase in imported foods from the US containing GM soya.

Monsanto's GM soya, approved in 1996, was found to contain a 26.7% increase in a major allergen, trypsin-inhibitor, which is also a growth inhibitor. Consistent with this result, the growth rate of male rats was found to be inhibited by the GM soya. Monsanto has not tested all possible

allergens. These results warrant a complete withdrawal of GM soya, at least until evidence that it is safe is obtained.

Reference : Personal Communication, Mark Varey, York Nutritional Laboratories.

Padgett S.R. et al (1996) The composition of glyphosate-tolerant soybean seeds is equivalent to that of conventional soybeans. *Journal of Nutrition* 126, 702-16 (A.R.)

Troubled GM Soya Not Substantially Equivalent

Once again, Monsanto's Roundup Ready GM soya is shown up to be not 'substantially equivalent' to non GM counterparts. Bill Vencill of the University of Georgia in Athens examined the effects of heat on GM soya in laboratory growth chambers. In soil temperatures of 25 C or less during the day, both GM and non GM varieties grew the same. But in warmer soils, the GM beans had stunted growth and in soils reaching 45 C the differences were marked - lower heights, yields and weights, and the stems cracked and split open in every GM soya bean plant. This phenomenon exposes the plant to secondary fungal infections and explains what may have happened to crops during the two hottest growing seasons in southern states, when there were substantial crop losses by farmers growing GM soya.

These results indicate changes in plant physiology caused by the insertion of transgenes, which make the plant resistant to glyphosate - Monsanto's Roundup. It has been shown that GM plants carrying these genetic alterations produce 20 per cent more lignin, which is the tough, woody form of cellulose. The bacterial enzyme that imparts resistance to glyphosate affects a major metabolic pathway in the plant, which sends lignin production 'into overdrive' says Vencill. This unexpected 'side effect' may have been what caused the GM plants to be more brittle. Resistance to gluphosinate, by contrast, uses a gene that enables plants to break down the herbicide, and such GM plants were not effected by heat in this way. Monsanto declined to comment but said that farmers could avoid the problem by choosing a variety of GM soya that is better suited to hot conditions.

Reference: NewScientist, News, November 20, 1999, "Splitting Headache" by Andy Coghlan.

Our comment: These physiological problems with Monsanto's Roundup Ready GM soya beans clearly demonstrate the inadequacy of the principle of substantial equivalence. In our 2nd update of concerns on the WSS, we report Marc Lappe's findings that Monsanto's GM soya is non-substantially equivalent in having a reduced phytoestrogen content compared to its non GM counterparts. The insertion of transgenes into a plant cell causes major unpredictable, unintended, which cannot be detected by current tests purporting to establish 'substantial equivalence' and hence gain regulatory approval as being safe for human consumption.(A.R. & M.W.H.)

Promiscuous Transposons in Over-drive Alert

A new marker system has been designed to follow gene transfer in arthropods and many other phyla. It is thought to enable better control strategies against agricultural pests and disease vectors. It relies on a transposon-based transformation technique, which has been used extensively to study insects. One of the major obstacles in the use of transposons has been the difficulty in obtaining marker genes that will allow easy and reliable identification of transgenic animals. The green fluorescent protein (GFP) from the jellyfish *Aequorea victoria* is a universal marker and has been shown to be active in both plant and animal kingdoms. A strong artificial promoter has now been found that is hyperactive, regionally restricted and universal. It contains three binding sites for Pax-6 homodimers in front of a TATA box (3xP3), and has been shown to drive expression of an enhanced GFP variant in the eye of fruitfly and in flour beetle. The evolutionary conservation of Pax-6 in the eye development of insects and vertebrates means that the 3xP3 promoter may be active in any photoreceptor cell. It has been described as a 'master regulator' in terms of function, and when mediated by transposons, provides a powerful new technique for generating transgenic organisms and studying a large group of pest species. The construct is artificial in origin, universal in function and does not require any other host-specific factors. It may therefore essentially function in all animals that have eyes. It has been suggested that, should it be coupled

with a set of promiscuous transposon vectors, such a system could be used to study almost any species. It is thought the system can be applied to competitive wild-type strains, making it suitable for pest-management programmes.

Reference: Genetic Techniques: A universal marker for transgenic insects. *Nature* 402, 370-371 (1999).

Our comment: This system is a useful research tool that should be scrupulously contained within the laboratory. **On no account should it be released into the wild.** The artificial promoter may be expressed in all organisms that have eyes. Such a powerful universal promoter coupled with promiscuous transposon vectors will transfer horizontally with disastrous consequences. (A.R.)

New Ways to Silence Transgenes

Researchers at the John Innes Center in Norwich finds a new species of small antisense RNA molecule involved in post transcriptional gene silencing (PTGS) in plants. PTGS represents a natural antiviral defense mechanism, which works against any invasive foreign genetic element that finds expression. Transgenic RNA in GM plants are frequently targeted by PTGS mechanisms and this strongly suggests that transgenes are perceived as viruses by their host cell.

This study has detected antisense RNA that is uniform in length - approx. 25 nt (nucleotides) and complementary to the targeted mRNA. It has been term 'spoiler RNA' for it forms a duplex with the target RNA and promotes degradation as well as interfering with translation. It has been shown to accumulate in cells, either when transgene transcription or RNA virus replication is taking place. The size of the spoiler RNA is also significant - it is small enough to move through the plasmodesmata (pores between cells) and has been shown to spread into nearby cells and activate PTGS elsewhere in the plant. The precise role of the 25nt RNAs in PTGS is yet to be elucidated, but it is suggested these are components of a systemic signal and specificity determinant in PTGS. Reference: Hamilton A.J, Baulcombe D.C (1999). *Science* 286, 950-952 also see "Silent Saboteurs" *NewScientist*, 6.11.99 p 25.

Our comments: This new discovery shows that GM plants respond to transgenes in the same way they do viruses. Transgenic RNA transcripts are produced at a very high copy

number in GM plants and are under the control of powerful promoters like the CaMV 35S promoter. Viral infection causes metabolic stress in cells and can lead to PTGS. The same can now be said of transgenic constructs in GM plants. Furthermore, the size and migratory nature of the RNAs reveal how small neucleotides have very important biological functions in cells.

This calls for regulation of all naked or free nucleic acids used in genetic engineering biotechnology, a point made forefully by Traavik (1999). *Too Early May be Too Late: Ecological Risks of Naked DNA*, Report to Directorate of Nature Management, Trondheim, Norway. (A.R.)

Sleeping Viruses Lurk in Plant Genomes

A new study provides evidence of repeated integration of pararetroviral-like sequences into the genome of tobacco at a copy number of approx 10 000. Therefore, plant pararetroviruses may integrate much more commonly into host chromosomes than has been previously thought. Furthermore, the insertions are thought to have occurred by illegitimate recombination. Plant viral sequences were thought to integrate rarely, if at all, into host genomes and this new evidence calls for a reconsideration of this view.

This has considerable implications for plant genome evolution as integrated pararetroviral DNA could act as an insertional mutagen or contribute strong constitutive promoters to neighboring plant genes or could accumulate to generate a new repetitive sequence family.

Reference; Jakowitsch J et al (1999) Integrated pararetroviral sequences define a unique class of dispersed repetitive DNA in plants. *PNAS* Vol 96 No23 pp 13241-13246

Our comment: This paper provides evidence that dormant viral DNA may be much more widespread in plant genomes than previously thought. It highlights the need for more extensive research in this area and it also has a bearing on the ecological impact of GM plants - although the authors of this paper fail to mention this. The CaMV 35S promoter is a pararetroviral-derived sequence used in most transgenic constructs, where it is integrated at random into the host genome. Furthermore, it contains an independent recombination hotspot and may therefore recombine with dormant viral sequences, which are in some instances integrated at extraordinarily

high copy numbers and are also highly recombinogenic - as shown by the amount of illegitimate recombination events detected in this study. This may result in the reactivation of dormant viral sequences, novel epigenetic effects and other genetic disruptions, all of which are potentially hazardous and unpredictable (see *Viral Gene Switch – A Recipe for Disaster?* This issue). (A.R.)

More on Bt-Toxin

A new study shows that Bt toxin is exuded from Bt-corn and remains active in the soil, where it binds rapidly and tightly to clays and humic acids. It also retains insecticidal properties and is protected against microbial degradation by being bound to soil particles. This research shows that the Bt toxin persists in various soils for at least 234 days (the longest time studied). Unlike the bacterium, which produces the toxin in a precursor form, Bt corn contains an inserted truncated cry1Ab gene that encodes the active toxin. Larva of the tobacco hornworm were used to verify that the toxin was active and when placed on a medium containing exudates from Bt corn, stopped feeding and began to die after 2 to 3 days, and had a mortality of 90 to 95 percent after 5 days.

The authors point out that 15 million acres of Bt corn were planted in the US in 1998. Bt toxin that is released into soil from roots would add to the amount of toxin introduced into soil from pollen and as a result of incorporating plant residues into the soil after harvesting the crop. Bt toxin in the rhizosphere will kill target pest but may also promote the emergence of toxin-resistant target insects.

Moreover, receptors for the toxin can be found on beneficial non-target insects which will also be killed, and this will have an impact on other organisms in higher trophic levels, in other words, a major impact on biodiversity.

Reference: Deepak Saxena, Saul Flores, G. Stotzky (1999) *Nature* 402, 480, p 480.

Our comment: The ecological impacts of GM plants producing bt toxins are now clearly predictable, based on existing scientific evidence. The immediate withdrawal of all bt-crops is the only responsible course of action. (A.R.)

Book Briefs

Against the Grain. Biotechnology

***and the Corporate Takeover of Your Food* by Marc Lappe and Britt Bailey**, Common Courage Press, Monroe, Maine, 1998.

This is the book that Monsanto tried to suppress. It is extremely well researched and reveals a great deal of vital information. It is clear and carefully constructed, appealing to both scientist and non scientist alike. It tackles every level of the GM debate: from the farm to the plate; onto the laboratory bench and into the scientific literature; from the global market place to the corruption of our food chain; and reveals the real issues at the heart of world hunger. It presents strong evidence, which is carried through with logical argument and reasoning. It captures the far reaching ramifications, and demonstrates that the GM debate is probably the most important debate of our time. It should be compulsory reading for all undergraduates of the life sciences. (A.R.)

***An Orphan in Science: Environmental Risks of Genetically Engineered Vaccines*, by Terje Traavik**, Report to Directorate for Nature Management, Trondheim, Norway, 1999.

This Report follows close at the heels of an earlier one by the same author, *Too Early May Be Too Late, The Ecological Risks of Naked DNA*, also written for the Directorate of Nature Management of the Norwegian Government, both of which count as the most significant contributions to risk assessment of genetic engineering biotechnology.

Genetically engineered vaccines are a major route for environmental release of GMOs, and yet ecological risk assessment has never been contemplated. The vaccines are used not only for human beings, but also in veterinary medicine and fish farming. Traavik identifies the possible risks and hazards, which, in his view and in accordance with the precautionary principle, should demand preventative measures. In practice, however, the risks are "considered non-existent from the medical and scientific points of view" simply because no investigations addressing them have ever been done. It also betrays the deplorable lack of ecological thinking in mainstream science and medicine, as well as a disregard for the precautionary principle.

Traavik begins by describing the history of vaccination, the immune response and the different kinds of vaccines used traditionally and their relative efficacy. Then he goes on to examine the entire range of genetic

engineered vaccines currently being developed, which include naked recombinant DNA and RNA containing viral sequences. He reviews the literature on the trials of vaccines in animal models, then identifies the possible hazards involved. Particularly revealing are a couple of more detailed case studies, as for example, on the anti-rabies vaccine made with the vaccinia virus, which had been widely used in anti-small pox immunizations earlier this century.

His conclusion is that, "from an ecological and environmental point of view many first generation live, genetically engineered vaccines are inherently unpredictable, possibly dangerous" and should not be used on a large scale until the problems identified have been addressed and clarified. Some of the main problems are as follows: the generation of new viruses by horizontal gene transfer and recombination, the unpredictable changes in host range of genetically engineered viruses and viral genomes, the infectious nature and long persistence of naked nucleic acids used as vaccines.

Changes to the genetic material of viruses are known to alter their infectivity and host range in unpredictable ways, so that previously non-susceptible species become susceptible. Recombinant viruses have already been isolated from wild-life and human beings as the result of the mass immunization programmes with the vaccinia virus against small-pox. The genetically engineered anti-rabies vaccine made from the vaccinia virus was released in the early 1990s in food baits intended for wild foxes, against the advice of a substantial number of scientists. These baits have obviously been taken up by many, if not all, species of wild mammals. All of these will be reservoirs for recombination and generation of new viruses. Naked DNA and RNA are now known to be protected from degradation in all environments and to be readily taken up by all cells (see *Viral Gene Switch – A Recipe for Disaster?* This issue), and according to a very recent report, viral sequences appear to be preferentially incorporated into the cells' genome (see *Reusable DNA Alert*, Science Notes). Cells taking up naked DNA include germ cells, so people receiving vaccinations may be receiving germ-line genetic modification at the same time. The safest vaccines, according to Terje, are those consisting of purified viral proteins only; and he believes their efficacy can be improved.

Terje fully acknowledges that the imperative to save lives is very strong,

especially in the short-term. However, the long term negative ecological and health impacts may far outweigh short-term gains. One could add that other measures have proven far more effective for preventing and ameliorating infectious diseases. These measures are improvements in nutrition, hygiene, and living conditions, clean drinking water, unpolluted environment, and the eradication of poverty.

This is an authoritative account by a world-class virologist and cancer researcher who is also sensitive to the need for alleviating human suffering and protecting the environment. He sets a fine example for us all. I especially urge all our regulators on biosafety to read this book and take its message to heart. (M.W.H.)

Protecting Public Health & the Environment, Implementing the Precautionary Principle, edited by Carolyn Raffensperger and Joel Tickner, Island Press, Washington, D.C., 1999.

If you want to know why our governments are failing to regulate toxic discharges, food additives, and GMOs to protect health and the environment, it is because they are not acting in accordance with the precautionary principle. Adopting such a principle will change our whole approach to environmental policies and to regulation. This book tells you the reasons why and more importantly, how the precautionary principle has been and can be implemented in practice. In general terms, this principle calls for protective, preventative actions of harm even when scientific evidence is uncertain. More importantly, it shifts the burden of proof of *safety* to the perpetrators, instead of demanding regulators and civil society to provide scientific proof of *harm*. The WTO is operating against the precautionary principle when it judged the EU ban on US growth-hormone injected beef illegal. This is how the WTO undermines every single effort by citizens and governments all over the world to protect health and the environment (For a list of examples, read another important publication, *Invisible Government, The World Trade Organization: Global Government for the New Millennium?* by Debi Barker & Jerry Mander, International Forum on Globalization, San Francisco, 1999)

The present book is the collective effort of an impressive international panel of public health professionals, lawyers, academics, environmentalists and policy makers. It is replete with useful information and good examples.

I learned how Sweden has the best environmental law in Europe based on the strongest version of the precautionary principle. In contrast, the UK, with a long tradition of "scientific corporatism and elitism", prefers to adopt the "long pipes and tall chimneys" approach to make optimal use of the waste assimilative capacity of the environment. Even when pressed to adopt the precautionary principle, its role is limited as is clear from the statement given by the UK Government, which is worth quoting in full (see p. 30),

"Where there are significant risks of damage to the environment, [we] will be prepared to take precautionary action to limit the use of potentially dangerous materials or the spread of potentially dangerous pollutants, even where scientific knowledge is not conclusive, if the balance of likely costs and benefits justifies it. The precautionary principle applies particularly where there are *good grounds* for judging either that action taken *promptly at comparatively low cost* may avoid more costly damage later, or that irreversible effects may follow if action is delayed (emphasis added)"

This *is* scientific corporatism, an admission that scientific evidence must bow to the profit motive. Everyone, but everyone should read this book and agitate for the adoption of the strongest form of the precautionary principle at all cost. Our life and the life of our planet depend on it. (M.W.H.)

Genetic Engineering Dream or Nightmare? Turning the Tide on The Brave New World of Bad Science and Big Business, by Mae-Wan Ho, New Leaf and Gateway Books, Dublin, 1999.

This is an updated and revised edition of a book of almost the same title (missing the phrase, "Turning the Tide on") published in 1998, which was widely reviewed and sold out. Please see ISIS website. It is one of the very few books that offers a complete perspective and critique on all areas of genetic engineering biotechnology, the social and political implications, and especially the discredited scientific paradigm driving and promoting the technology. It is written for the whole range of general readers from ordinary citizens to policy-makers. The science behind the technology is made sufficiently accessible so readers can make up their own minds, in particular, with regard to the dangers posed. The new edition has a lot of additional

scientific information and is improved for easier reading. (M.W.H.)

Imagine a World without the Monarch Butterflies. Awakening to the Hazards of Genetically Altered Foods, by Alex Jack, One Peaceful World Press, Becket, Mass, 2000
This little book is like a mini encyclopedia on the GM debate over the past few years. It contains all the important arguments and references and even manages to put over a 'who's who' within the circles of active resistance against GM foods and those on the opposing side. It is undoubtedly at the cutting edge of the debate and is an essential reference book, useful for anyone wanting to grasp hold of the issues quickly. (A.R.)

New Papers on ISIS website:

Cauliflower Mosaic Viral Promoter – A Recipe for Disaster? Ho, M.W., Ryan, A. and Cummins, J. *Microbial Ecology in Health and Disease* (in press)

Authors reply to critiques of the above

The Biotechnology Debate Has United the World Against Corporate Rule (M.W.H.'s teach-in at International Forum on Globalisation, 27 Nov. Seattle)

GM foods and the Science War (M.W.H.'s talk in Consumer Choice Council conference, 1 December, Seattle)