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Contents

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Reports

World Scientists Go Sustainable

World Scientists' Open Letter welcomed by all except industry

World Scientists' Open Letter was signed by more than 310 scientists from 38 countries when presented to the United Nations Convention on Sustainable Development (CSD), April 24 to 5 May 2000, New York. It was warmly welcomed and given much prominence in the official as well as unofficial proceedings because it speaks for the overwhelming majority of the participants and stakeholder groups. They share our concerns on the hazards of GMOs and strongly favour a moratorium on environmental releases. They are opposed to growing GM crops in developing countries, especially to patents on seeds and other life-forms and living processes, which threaten food security, sanction biopiracy of indigenous knowledge and genetic resources, and violate basic human rights and dignity. Most of all, there is a chorus of support for sustainable agriculture involving holistic approaches that integrate indigenous and western scientific knowledge and are adapted to local ecological conditions. Representatives of the G77 (the developing countries) and China repeatedly called for a holistic approach to sustainable development that is compatible with the diverse cultural traditions of countries within the group.

It was clear that industry and the industry-friendly governments of the Miami Group – US, Canada, Australia, Argentina, Uraguay and Chile – were isolated. Farmers across the developed and the developing world, indigenous peoples, trade unions, consumer groups, public interest organizations, the majority of government delegates and scientists (those not sitting with industry), were all speaking as with one voice.

Martin Khor, Director of Third World Network and Prof. Miguel Altieri, a well-known proponent of agroecology were invited to speak in the formal sessions, to much acclaim. Martin attacked the globalized economy for exacerbating the gap between the poor and the rich, as the superpowers continue to legislate unsustainable and unfair treaties in the World Trade Organization that disadvantage the Third World; perpetrating neo-colonial exploitation and worsening the global ecological crisis. Miguel gave a detailed documentation of the successes of agroecology in Latin America and elsewhere, which have doubled and tripled yields within the past 10-15 years and reversing the social and environmental devastation of corporate agriculture. Among other contributors to the stakeholders dialogue were Dr. Peter Rosset of Food First Institute, Chee Yokeling and Victoria Corpus of Third World Network and myself from ISIS. Third World Network also organized workshops and a special seminar chaired by Colombian delegate Juan Mayr, the official Chair of the CSD session, who also chaired the Cartegena Biosafety Protocol meetings in Cartegena last year and in Montreal this January.

Thanks to Lim Li Lin of Third World Network, our Open Letter was subsequently presented to the UN Conference on Biological Diversity held in Nairobi later in May where some 60 countries signed the Cartegena Biosafety Protocol. The Letter was given prominent press coverage amidst calls for moratorium on releases of GMOs in Africa.

Prof. Oscar Zamora has reported earlier that our Open Letter was presented to the Congress in the Philippines, which helped to secure a moratorium on GMO imports in that country.

Many thanks to Sandro Puetz of the Gene-ethics network in Berlin for translating our Open Letter into German, and posting it on their website http://www.gen-ethisches-netzwerk.de

So, please, scientists please stand up for your convictions and join us. Sign on at our website. We are taking our letter next to Washington D.C. in the US for a special forum on June 29, "Can biotechnology help fight world hunger?" organized by Congressman Tony Hall. MWH

Scientists, Don't Forget the Social Context!

Prominent UK Member of Parliament lashes out at scientists

Dr. Ian Gibson, MP for Norwich North, chairs the Parliamentary and Scientific Committee and is also a Member of the House of Commons Select Committee on Science and Technology. He was criticised by the scientific establishment as "anti-science" when he raised the issue of genetic discrimination in connection with the increasing number of diagnostic tests made available by the human genome project. His reply is the strongest statement yet that scientists have to be socially accountable for what they do. This is a breath of fresh air. Finally, someone of influence has spoken out for the public as well as the vast majority of scientists who are not genetic engineers. Doctors, lawyers, teachers, even corporations, have been called to account, so why not scientists?

"Why should the issue of genetically modified organisms be raised in its social context by the green movement, for example, and not first in a strong manner by scientists?" he writes in the April issue of the publication of the British Association for the Advancement of Science, *Science & Public Policy*.

He challenges scientists to answer "why they are allowed to spend their time doing 'blue skies' research and are paid for indulging their talents without having to answer for the social consequences of their research." He also called for a full dialogue involving legislators, lawyers, scientists and the public. "Without a proper discourse", he writes, "science will move backwards and fail to capture public support and scientists will continue to be portrayed as dysfunctional and arrogant."

Dr. Ian Gibson cannot be accused of not understanding science, as he has a Ph. D. in Biochemistry and has been a full-time academic until he got elected to Parliament in 1997. MWH

Announcing Sustainable Science Audit

Joint ISIS and TWN Project

ISIS believes that science as much as scientists should be socially and ecologically accountable, and has launched a sustainable science audit project jointly with the Third World Network (Penang). The first audit is on the 'golden rice' – a GM rice engineered to produce pro-Vitamin A – which is being offered to the Third World as cure for widespread vitamin A deficiency.

The audit uncovers fundamental deficiencies in all aspects, from the scientific/social rationale to the science and technology involved. It is being promoted in order to salvage a morally as well as financially bankrupt agricultural biotech industry.

The scientific / social rationalization for the project exposes a reductionist self-serving scientific paradigm that fails to see the world beyond its own narrow confines. The 'golden rice' is a useless application. Some 70 patents have already been filed on the GM genes and constructs used in making the 'golden rice'. It is a drain on public resources and a major obstruction to the implementation of sustainable agriculture that can provide the real solutions to world hunger and malnutrition.

'Golden rice' is not a 'second generation' GM crop as has been claimed. It involves standard first generation technology, and carries some of the worst features in terms of hazards to health and biodiversity. Rockefeller Foundation, the major funder of the project by far is reported to have withdrawn support from it, although this is still to be confirmed. Our own recommendation is that the project should be abandoned altogether.

The Report, "The 'Golden Rice' – An Exercise in How Not to Do Science" is available on ISIS' website.

MWH

Science behind Closed Doors

Corporate science engineering 'consensus'

At the World Economic Forum in Davos early this year, Bruce Alberts, President of the US National Academy of Sciences (NAS), gathered behind the scenes with a group of a dozen other presidents of national science academies to create an International Academy Council (IAC) to provide "impartial scientific advice" to governments and international organizations on issues such as genetic engineering, threatened ecosystems, and biodiversity.

Bruce Alberts also chairs The National Research Council (NRC), which has a full-time staff of 1000 and a $200 million annual budget. Through the NRC, the NAS conducts studies and prepares about 200 reports annually, largely under contract to federal agencies. In flagrant violation of the rules of open government - the 1972 Federal Advisory Committee Act - which Alberts still vehemently opposes, NRC committees and panels meet secretly in closed sessions. They do not disclose their minutes or conflict of interest statements, and fail to require that their membership reflects balanced representation of divergent interests and viewpoints.

The NRC committee which issued the 1996 report on "Carcinogens and Anti-carcinogens in the Human Diet" dismissed concerns on cancer risks to infants and children from food contaminated with carcinogenic pesticides, alleging that these "occur at levels far too low to have any adverse effects on health." Dr. Sam Epstein, acting on behalf of an *ad hoc* coalition of about 100 leading independent experts in public health and cancer prevention, and representatives of a wide range of labor and citizen groups, warned Alberts that the committee was grossly unbalanced, being disproportionately weighted with industry consultants, and pointed out further that no pediatrician had been invited to serve on the Committee. Alberts responded by admitting "that some of the committee members have performed some consulting for industry," but dismissed the concerns on grounds that "the same members have also advised or consulted for regulatory agencies"!

A more blatant conflict of interest arose in the composition of the NRC biotechnology panel set up in March, 1999, with disproportionate representation of experts directly linked to industry. It transpired that the panel's executive director, Dr. Michael Phillips, was secretly negotiating for a senior position in the Biotechnology Industry Organization, and joined the industry some 3 months later.

As federal support is beginning to shrink, the NAS plans to increase funding from non-federal sources, which currently account for some 15% of its budget. The NAS is also planning to extend its influence to major national policy concerns. Alberts has refused to release a pending report recommending reorganization of NAS policies and procedures.

All this was revealed in a letter submitted to *Science* magazine, co-signed by Samuel S. Epstein, M.D., School of Public Health, University of Illinois at Chicago and Chairman of Cancer Prevention Coalition, Edward

Goldsmith, Editor and Founder of *The Ecologist* and Dr. Mae-Wan Ho of ISIS. The letter was rejected, despite repeated requests for reconsideration from Sam Epstein.

This is not the first time that magazines such as *Science*, *Nature* and *New Scientist* have refused to give voice to scientists dissenting from the corporate view, and they may be plumbing new depths in the current debate in genetic engineering, when undue and apparently unlimited access to their pages is granted to pro-biotech scientists and other supporters of the industry.

Nature Biotechnology (Jan. 2000) published a long report that attempted to discredit a (now published) paper on the potential hazards of the cauliflower mosaic viral promoter in the worst style of gutter journalism; and only gave the authors a very grudging right to reply after a delay of three to four months (see ISIS News #4) when the same offending journalist was allowed to have yet another go (see *Nature Biotchnology* April, 2000). I have long cancelled my personal subscriptions to these magazines.

There is still no open public debate on the abundant scientific evidence of actual and potential hazards of genetic engineering, nor on how scientific evidence ought to be used in the context of the precautionary principle. Some scientists have had their lives and work ruined, not the least by having to read boring scientific papers and reports no one would ever have volunteered to read, if they didn't think it is so important for the public to be informed as to what corporate science has in store for us.

We can have no confidence in any group of scientific advisors who have not been through the open democratic process. The US National Academy of Science report on GM crops was released in April this year amidst fresh controversy. While the Biotechnology Industry Organization (BIO) – the industry's lobby - was delighted by the report, claiming in a press release that GM foods "are thoroughly tested and safe", critics have rejected the report. US Senator Dennis Kucinich called for the study to be scraped because the panel was "tainted by pervasive conflicts of interest". Many scientists in the US are among the critics, though *Science* magazine refers to us all as 'activists' (*Science*, 14 April, 2000). We have repeatedly invited and challenged those scientists who are still claiming that GM crops pose no special risks to open debate and discussions *in terms that the public can understand*, instead of hiding behind jargon words that defeat even most other scientists. They have turned us down again and again. MWH

Corporate Science on the Offensive

ISIS targeted

Dr. C. S. Prakash, Director of the Center for Plant Biotechnology Research at Tuskegee University (USA), is the latest corporate recruit to counter the worldwide rejection of GM crops. I first came across him in a pro-GM 'documentary' I was tricked into taking part by Equinox, the science series of Channel 4 TV in the UK (see ISIS NEWs #4). I met Prakash again at the multi-stakeholders dialogue at the 8th session of the United Nation's Commission on Sustainable Development (April 24-May 4, New York), where he sat with, and spoke for the biotech industry. On June 1, I encountered him for the third time in a debate in London, organized by the US Embassy. I was told Prakash has been sent over by the US State Department. Unlike his predecessor Val Giddings, Prakash oozes charm and bonhomie. He said he has already been touring Europe "to prevent other Mae-Wan Hos from springing up" and London, UK, was his last stop.

The debate, held in The School of Oriental and African Studies, was on the motion, "Agricultural biotechnology is vital for the developing world", with Prakash and Matt Ridley, speaking for, and myself and John Vidal speaking against. Ridley and Vidal are both well-known journalists on opposite ends of the political spectrum. To my surprise and dismay, it was not an open debate as only 'stakeholders' were invited. Judging by comments from the floor, the majority were from industry or pro-biotech pressure groups. The Monsanto 'science outreach' representative came out smelling like roses compared to two molecular geneticists associated with Cropgen, a new pressure-group of scientists funded by industry, members of which have been very prominent in the media recently, and appearing to be targeting ISIS in particular.

A few days later, one of the Cropgen scientists, Conrad Lichtenstein, wrote a pompous article in *The Guardian* newspaper ("A misguided media swarm" June 6) where he dismissed all the scientific studies that cast any doubt on the safety of GM crops, especially those that have been given a lot of press coverage: Arpad Pusztai's work that GM potatoes adversely affecting young rats and John Losey's finding that GM pollen is lethal to Monarch butterflies. In anticipation of the as yet unpublished report from Jena University in Germany - that GM genes have transferred from GM pollen to the bacteria and yeasts of baby bees - he argued that, if so, it must be occurring all the time. (Not so long ago, these scientists have denied that such horizontal gene transfer can occur.) And, he claims, it doesn't matter, because neo-Darwinian natural selection will select them out: the organisms to which the foreign genes have transferred will die out either immediately or in the long run, by the principle of the survival of the fittest. He failed to notice that neo-Darwinian natural selection operating on human beings to whom GM genes and constructs have spread won't be very good for health. The article ended with an attack on me.

He was "alarmed to hear an anti-GM university biologist state that GM genes are more resistant to the natural processes by which enzymes break down other DNA and that GM genes, as they are designed to "invade" genomes, are also more unstable and can more easily move around, dangerously spreading". He claimed that when he asked for direct experimental evidence, he was given "the techno-babble which puts fear into the hearts of the scientifically uneducated".

I wrote a letter to *The Guardian* (June 8) answering his attacks, and inviting him yet again to visit the ISIS website where all the evidence has been presented with detailed citations of the scientific papers. *The Guardian* then published another attack from him in the same tone (June 12) , demanding actual references to the scientific literature. I again submitted my reply.

But *The Guardian* did not publish my letter the next day, nor the next after I made a polite enquiry. Finally, when I threatened to complain to the Independent Press Commission, they agreed to publish a much shorter version without the references because their spokesperson said they simply cannot engage in detailed scientific debates of that kind. Why did they allow Lichtenstein to demand the references knowing that they won't allow me to supply them?

Lichtenstein and others like him are the reason why the public continue to perceive scientists as "arrogant and dysfunctional", as UK Member of Parliament Dr. Ian Gibson wrote (See "Scientists, Don't Forget the Social context!", this issue). They are also guilty of abuse of scientific evidence (as well as abuse of scientists) and acting against the precautionary principle.

The text of my talk, "GM Crops – How Corporations Rule and Ruin the

World" can be found on the ISIS website. My first reply to Lichtenstein was published in the letters section of *The Guardian* (8 June) with the last two sentences omitted. The second reply published (16 June) was much shorter than what I had originally submitted, but makes the key point that the best kept secret of the biotech industry is that there is no evidence for the long term stability of the GM inserts in both structure and location in the plant genome for any GM line already commercialized or undergoing field trials.

Both original letters are reproduced at the end of this report. Lichtenstein's comments on horizontal gene transfer and natural selection are typical of GM proponents adhering to the discredited, reductionist neo-Darwinian paradigm (see "An End to Bad Science and Beginning with Life Again" www.i-sis.org on how the new genetics makes neo-Darwinian theory untenable). MWH

Ho Replies to Lichtenstein 1

I am the "anti-GM university biologist" that Conrad Lichtenstein referred to in his article on the GM controversy (6 June). The debate he described was arranged by the US Embassy for biotechnologist, Dr. C.S. Prakash, sent by the US State Department to promote GM agriculture in Europe. I agreed to participate because I believe in promoting critical public understanding of science and to draw attention to well-known and relevant scientific knowledge that is being ignored.

Almost by definition, genetic engineering organisms involves designing GM-constructs which invade genomes and overcome natural processes that break down foreign genetic material. Due to their highly mixed origins, however, GM-constructs are more unstable than natural genetic material as well as more invasive; and may therefore be more likely to spread to unrelated species. Those points were not challenged by Prakash because these basic principles and observations of genetic engineering are covered in text books and are also areas of active research. I answered Lichtenstein's questions in full and referred him to our website <www.i-sis.org> where the relevant scientific papers are cited and where more than 300 scientists from 39 countries, including many molecular geneticists who share my concerns, are demanding a moratorium on releases of GM organisms.

There is genuine scientific dissent among scientists and the public are not served by those who continue to misrepresent the GM debate as science *versus* anti-science. In demanding a moratorium, we are not trying to stop research into molecular genetics. On the contrary, we are arguing for more basic research that can tell us how and if GM technology can be safely used. More than that, we need open, wide-ranging and inclusive debates on the kind of science and technology that can best serve society.

Ho replies to Lichtenstein 2

Conrad Lichtenstein (Letters, 12 June) demands references on the invasiveness and instability of GM constructs in genetic engineering. There are many; here are just a few.

For designing GM constructs to overcome being broken down, and to increase invasiveness and stability, read Kumpatla *et al*, *Trends in Plant Sciences* 3, 96, 1998.

A major class of GM constructs are artificial vectors for transferring genes, made from the most invasive natural viruses and genetic parasites; their instability is highlighted in a text book, *Principles of gene manipulation*, by Old and Primrose, Blackwell Science, 5th ed, 1994.

There are many articles on the instability of GM plants, a recognized problem area. The most actively investigated are mechanisms silencing integrated GM genes, but loss of part or all of the GM construct has also been observed, even during later generations of propagation (see for example, Register *et al*, *Plant Molecular Biology* 25, 951, 1994).

Finally, a GM gene in *Arabidopsis* was found to be up to 30 times more likely to spread than the same gene created by conventional induction of mutation (Bergelson *et al*, *Nature* 395, 25, 1998). But no investigations were done to determine if this was associated with instability of the GM construct.

The instability and invasiveness of GM constructs are supported by direct and indirect evidence, while no evidence exists for the long term stability of the GM inserts with regard to structure and location in the plant genome. On grounds of safety and efficacy, such evidence should have been provided before approvals for releases were granted.

Articles

Swallowing the Tale of the Swallowtail

No "absence of toxicity" of Bt pollen

The paper which claims "absence of toxicity" of Bt-pollen under field conditions is faulty in experimental design and actually demonstrates that Bt-pollen is toxic in the laboratory.

A study in Cornell University last year (1) prompted widespread concern that pollen from Bt-corn may be harmful to the Monarch butterfly. Researchers from the University of Illinois now claims that a field study on the black swallowtail, *Papilio polyxenes*, shows that Bt-pollen is not toxic to this species (2).

The black swallowtail feeds on host plants found in narrow strips between roads and crop fields in midwestern USA. A day after the start of Bt-pollen release, researchers set up five rows of five potted host-plant beside a field of Bt-corn (Pioneer variety 34R07 expressing the CrylAB gene in its pollen), at various distances from the edge of the field. Pollen traps consisting of a microscope slide coated with vaseline was placed with each plant to measure total pollen deposited. A second set of potted plants were placed behind the first set three days later. Ten first instar larvae were put on each plant, and the number of live larvae on each plant recorded daily for 7 days.

However, no control experiments were set up. A proper control experiment would have consisted of a replicate set of potted host plants and larvae placed next to a non-GM corn field.

It rained during the 5th and 7th day of the first experiment, and during the 2nd, 4th and 5th day of the second experiment. Would that not have washed away the pollen from the surface of the leaves? If so, what relevance would the pollen counts - on greasy pollen traps - have on actual pollen ingested by the larvae?

Pollen counts decreased sharply with distance from the field as expected; but there was no correlation between pollen counts and mortality. Even though the larvae were counted everyday for seven days, the detailed counts were not given. Instead, the aggregate percentage mortality was presented. Not only were the mortalities high, they were also highly variable. The means ranged from 45 to 82%, and in many cases, the standard deviation in each direction was almost as large as the mean. It was obviously impossible to draw any conclusion from such an experiment. But they stated, "No significant relationships between larval survivorship or mass were detected either as a function of distance from the edge of the field or as a function of pollen deposition." That was true, but the main reason may be that it was a bad experiment. They suggested that the high mortalities might be due to predation. If so, would mortality not be correlated with "larval mass"? Yet no such correlation was reported.

Back in the laboratory, they deposited different amounts of Bt and non Bt pollen on leaf-discs and fed

each in a single dose to a first instar larva which was observed over the next three days. They found no effect with the Bt-pollen collected from the field, even at the highest dosage. But exactly how much Bt toxin did each larva consume? From the figures presented, it can be calculated that at the highest dose used - 10 000 pollen grains – the larva would have consumed only 1 picogram of Bt protein, ie, 1/1 000 000 000 000 or one trillionth of a gram, over the three days.

With another Bt-corn pollen - Novartis Max 454 - which expresses 40 times as much Bt protein, ie, 40 picograms, a highly significant increase in mortality was found on the third day: 80% compared with about 10% for the rest.

As the laboratory experiments involved feeding a single dose over three days, it gave no information as to the effects on mortality of cumulative doses over the entire life-cycle of the butterfly, such as it may experience in the field.

The claim of "absence of toxicity" in the title of this paper is thus misleading to say the least. It will be an abuse of science if this report were to be accepted as evidence that Bt-pollen is safe for black swallowtails.

References and Notes

1. Losey, J.E., Rayor, L.S. and Carter, M.E. (1999). Transgenic pollen harms monarch larvae. *Nature* 399, 214.
2. Wraight, C.L., Zangeri, A.R., Carroll, M.H. and Berenbaum, M.R. (2000). Absence of toxicity of *Bacillus thuringiensis* pollen to black swallowtails under field conditions. PNAS early Ed. MWH

To Bt or Not to Bt

How sound science makes the case

Since the publication of Losey's study in the journal *Nature* showing that Bt-corn pollen harms monarch butterflies, things have gone into a downward spiral for Bt-crops. Bt-corn is now banned in Austria, France and Germany, and Monsanto's Bt-potato division has been closed down by its new parent company, Pharmacia.

'Bt' is short for *Bacillus thuringiensis*, the soil bacterium providing the genes for making toxins that kill insects; different forms of which are incorporated into GM crops. The adverse environmental impacts of Bt crops are now well documented in the scientific literature, ranging from harm to non target organisms to the evolution of resistance in insect pests, making it necessary to plant a high proportion of non-Bt crop for 'resistance management'. Aberrant gene expression in the field results in low-dose varieties which are ineffective in pest control and foster resistance. Cross pollination with non GM varieties creates Bt-weeds, and the Bt-plants themselves cause major problems as volunteers. Active Bt toxin leaks from plant roots into the soil where it is not biodegradable and accumulates over time. This will have major impacts on soil health, with knock-on effects on all other trophic levels of the ecosystem. The recent report that a GM gene has transferred from GM pollen to microbes in the gut of bee larvae underlines the fact that Bt toxin genes, like all other GM genes, will spread out of control. The case for withdrawing all Bt-crops is now compelling.

The way the case has been built is exemplary of the power of good independent science, which is indispensable for sound policy decisions.

No less than eighteen Bt crops were approved for field testing by the US Dept. of Agriculture between 1987 and 1997 (1). Bt cotton was the first to be approved for commercial use (USA 1995), followed by corn, potato and tomato.

The first specific concerns on the safety of Bt crops were raised from within the scientific community in 1997 when Angelicka Hilbeck and colleagues (2) showed that lacewings fed on pests that have eaten Bt-maize took longer to develop and were two to three times more likely to die.

Organic farmers also started to voice their fears - they have been using the spores of *Bacillus thuringiensis* as an occasional insecticide spray. Their fear was founded in the rapid development of resistance to Bt toxin in pest populations continuously exposed throughout the GM plant's growing season, with the potential loss of their only organic insecticide. They were also worried about GM contamination via cross-pollination - now admitted as unavoidable by our regulators.

Bt toxins are active against insects in the Order of Coleoptera (beetles, weevils and styloplids) which contains some 28,600 species

Then came Losey's famous Monarch butterfly study (3), which was confirmed by another from the University of Iowa (4), showing that milkweed in and at varying distances from Bt crops in the field does cause an increase in mortality to Monarch butterflies. Milkweed samples were taken from within and at the edge of the Bt corn field and were used to assess mortality of first instar monarch, *D. plexippus* exposed to Bt and non-Bt corn pollen. Within 48 hours, there was 19% mortality in the Bt corn pollen treatment, compared to 0% on non Bt-corn pollen exposed plants and 3% in the no pollen controls.

In a desperate recent attempt to counter this evidence, the pro-biotech lobby has just released a story claiming that pollen from Bt corn does not harm the black swallowtail. This story has been thoroughly deconstructed (see "Swallowing the Tale of the Swallowtail", this issue).

The biotech industry is fully prepared to misreport research results in order to confuse and mislead the public. On Nov 2nd 1999, a scientific meeting took place in Rosemount, Illinois, to discuss Bt corn and monarchs. That same morning, all the major news desks round the US received a fax carrying a News article about the meeting - which had only just begun at that point - headlining 'Researchers conclude Bt corn poses little risk to Monarchs'.

Luckily, Carol Yoon of the NY Times was at the meeting and received word from her editor in New York. She asked the participants if they agreed with what was obviously a press release from industry. The answer from the floor was a resounding "No" - her report was the only accurate account of the meeting, but unfortunately, the majority of US citizens got the industries' take on it (5).

After months of heated debate on the effects of Bt on non-target insects, the US Environmental Protection Agency (EPA) convened a Scientific Advisory Panel (SAP) meeting in Dec 1999 and asked the panel to review EPA's non-target organism testing requirement, applicable to Bt crops. The panel found EPA requirements inadequate and urged the agency to substantially expand the scope and quality of the studies that it relies upon (6).

Plans for managing the development of Bt-resistance in insect pests have been actively debated in the scientific literature, and earlier this year, the EPA revised their original mandate and ruled for larger refuges of non GM crop planted with the GM crop. This was hailed as a step in the

right direction and now refuges have to be at least 20%. But major controversies remain as to whether or not the refuges should be sprayed by conventional insecticides (7). A study in the University of Arizona (8) showed that boll worm larva fed on GM and non GM develop at different rates and it is highly unlikely that they will interbreed, dashing any hopes of diluting out or slowing down the evolution of resistance. These moths mate within three days of hatching and the males only live for a week. Also, dilution only works if the Bt-resistance is recessive, ie, requiring two copies of the resistance gene, and the EPA's resistance management program relies on the trait being recessive. Unfortunately, studies on the inheritance of Bt resistance showed that it is a dominant trait (9) as insects with only one copy of the resistance gene survive exposure to Bt. Low levels of Bt expression in Bt crops has also been documented and also serves to foster resistance.

In June1999, Monsanto applied for the first Experimental Use Permit on CRY3Bb transgenic corn, another Bt corn line aimed at corn rootworm. The application has been thoroughly assessed by an alliance of four independent non profit organizations (10), who report the most astonishing findings. The technical study submitted by Monsanto in July 1999 contained no molecular data, nor data on the breeding regime, for three different Bt lines. Data on the levels of protein expression in different tissues was included. But 300 corn plants were produced for two of the transformation experiments, and some of the critical measurements of expression levels were done on only two plants. Despite this, the data clearly indicate that different transformations led to significantly different levels and patterns of protein expression. Such differences are of crucial important in assessing efficacy, resistance management and non-target impacts, as well as changes in the microflora of the digestive systems of livestock and humans using the crop for food.

Monsanto then submitted its application in full in August 1999, moving from greenhouse-scale research to unrestricted field use within one year. In the covering letter they wrote; "Please note that approval of this registration by May 2000 would reduce the need for additional submissions and reviews for year 2000 field trials". This statement makes it blatantly obvious that Monsanto has no intention of investigating their findings any further with respect to health and environmental impacts. To date, the full application is still pending in the US, but has been granted commercial approval in Puerto Rico and Hawaii for this growing season.

In Dec 1999, Gunther Stotsky and colleagues (11) reported that Bt toxin is released into the rhizosphere – the area around the plant roots in the soil - in exudates from the roots of Bt corn, where the toxin is protected from biodegradation and accumulates. This raised, for the first time, the question of what is happening underground? A total of 15 million acres of Bt corn were planted in the US in 1998, 20% of the total acreage. The leaked toxin enters the soil in an activated form - Bt transgenes are truncated to produce active toxin, unlike the precursor-form produced in the bacterium, which has to be cleaved in the gut of susceptible insect pests. Moreover, the toxin is expressed continuously, and hence exuded for extended periods of time.

In organic farming the toxin is sprayed sporadically in an inactive precursor form, only becoming active in the gut of the target insects once ingested. Furthermore, it is sprayed onto the surface of plants where it is readily biodegraded. Stotsky suggests that the widespread planting of Bt crops is equivalent to adding large doses of active toxin to the soil, not only from the plant root but also from the plant residues ploughed in, as well as from pollen. There is at present no clear indication as to how soil communities might be affected by Bt toxin from root exudates. It may promote evolution of toxin resistant target insects. But receptors for Bt toxins are present in both target and non-target insects, therefore both will be affected. Bt toxins are active against insects in the Order of Coleoptera (beetles, weevils and styloplids) which contains some 28,600 species, far more than any other Order (12). The widespread use of Bt genes in crops and the build up of active toxin in the soil will have long term ecologically risks to non-target species and organisms in higher trophic levels, such as birds.

Simultaneously, it was reported that Novartis had filed a patent for another insecticide to be used in conjunction with Bt crops (13). It turns out that the pest-control spectrum of Bt toxins is limited, and other pesticides have to be used, that have been shown to be very damaging to health. This discredits industry's claim that Bt is essential for reducing harmful pesticide use.

This April brought further reports on pockets of Bt-resistance among pests in GM fields, and of GM cotton plants turning up as weeds in other crops (14). The cotton boll weevil may make a come back if such volunteers are ignored. An entomologist at Clemson Univ. said, "I could look across soybean fields and see hundreds of these Bt cotton plants". A return of the cotton boll weevil to parts of the American Cotton Belt would be a disaster, considering it cost $1.3 million to eradicate them by 1995.

The ecological interaction between organisms is complex and scientifically challenging. The behaviour of insects with regard to choice, of food can have important impacts. This aspect has been overlooked completely in environmental risk assessments of GM crops. Researchers at Rothamstead in the UK (15) have pointed out that killing non-target species is a risk not unique to GM technology, as conventional regimes actually kill insects in an indiscriminate manner that is equally unsustainable. They highlight the need to find alternatives to conventional practices and suggest that management and good husbandry of bio-control agents should act in an integrated manner to eliminate caterpillars.

The health assessment of Bt crops relies totally on past experiences with Bt sprays in organic farming. It is wrong to assume that Bt toxin in GM crops is the equivalent to what has been used for over thirty years on organic produce with no deleterious effects. As with all GM crops, comprehensive feeding trials have yet to be conducted and therefore there are no data supporting the safety of eating Bt crops. Furthermore, there is a general lack of scientific transparency with all GMOs and Bt-crops are no exception. Crucial data are withheld from the public domain under various confidentiality statements made by the biotech companies in their applications for license.

Leading US agronomist Charles Benbrook has just completed a comprehensive review on EPA's management of Bt-corn (16). It provides important insights into the structural and legal shortcomings in the approval process, the major among which was the failure to adhere to the precautionary principle.

The summary of findings reported by independent scientists investigating or evaluating environmental risks are sufficiently compelling to warrant the immediate withdrawal of all Bt crops from use.

Notes and references

1. ISB Environmental Releases Database for USDA APHIS website : www.aphis.usda.gov/bbep/bp/index.html

2. Hilbeck, A., Baumgartner, M., Fried, P.M. abd Bigler, F. (1997). Effects of transgenic Bacillus thuringiensis-corn-fed prey on mortality and development time of immature Chrysoperla carnew (Neuroptera: Chrysopidae) Enivronmental Entomology 27, 480-487
3. Losey. J., Raynor. L., & Carter. M. E., (1999) *Nature* 399,214
4.See:http://www.ent.iastate.edu/entsoc/ncb99/prog/abs/D81.html
[Non-target effects of Bt corn pollen on the Monarch butterfly (Lepidoptera:Danaidae) *L. Hansen, Iowa State University, Ames , IA 50011
and J. Obrycki, Iowa State University, Ames, IA 50011. Contact e-mail: lrahnsen@iastate.edu]
5. First Hand Account ^ Industry manipulation of Bt research, by Beck Goldburg, Environmental Defense Fund. Forwarded to Biotech Activists 11/05/99
6. The final report of the SAP panel is accessible at <http://www.epa.gov/scipoly/sap/1999/december/report.pdf>
7. Shelton, A.M., Tang, J., Roush, R.T., and E. Earle. (2000) "Field tests on managing resistance to Bt-engineered plants, *Nature Biotechnology*, Vol 18;399-342
8. Liu, Y-B., Tabashnik, B.E., Dennehy, T.J.,Patin, A.J., & Bartlett, A.C.
(1999) *Nature* 400:519.
9. Huang, F., et al. (1999) *Science* 284, 965-967
10. Comments Submitted to Docket No OPP-30487a: Registration application for CRY3BB transgenic corn modified to control the corn rootworm March 20 2000. On behalf of Environmental Defense, the Institute of Agriculture and Trade Policy, the Science and Environmental Helath Network, the Center for Food Safety, and the Consumer Policy Institute/Consumer Union.
11. Deepak Saxena, Saul Flores, G. Stotzky (1999) Insecticidal toxin in root exudates from Bt corn. *Nature* Vol 402 pp 480
12. Arnett, R.H., and R.L. Jacques. Guide to Insects, Simon and Schuster. 1981.
13. Genetically modified plants may still need pesticides, By Andy Coghlan and Barry Fox, *New Scientist*, 18.12.99
14. Pockets of resistance : A pest might make a comeback thanks to engineered weeds. *New Scientist*, By Andy Coghlan April 15 2000.
15. Poppy, G. (2000) GM crops:environmental risks and non-target effects, *Trends in Plant Scienc* 5 , 4-6.
16. Benbrook, C. and Suppen, S. (2000) Applying the Precautionary Principle in Assessing Transgenic Corn Technologies in the US <www.biotech-info.net/case_studies>
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Horizontal Gene Transfer Happens

A practical exercise in applying the precautionary principle

At first, they said horizontal transfer of genes to unrelated species couldn't happen, then they said "just because it happens in the laboratory doesn't mean it happens in nature". Recently, Prof. Kaatz of Jena University found in field studies that GM genes may have transferred from GM pollen to bacteria and yeast in the gut of baby bees (*The Observer*, 28 May, 2000). That study is not yet published.

But, researchers have earlier found evidence of horizontal gene transfer of GM genes to soil bacteria in the field where GM sugar beet was planted, and this has been reported in the scientific literature (1). Readers of ISIS News will note that there have already been several studies documenting the horizontal transfer of GM genes from GM plants to soil fungi and bacteria in the laboratory (2).

In this article, I shall review the published study to show how the precautionary principle can be applied in practice to interpret and use scientific evidence responsibly and in accordance with sound science.

German geneticists Frank Gebhard and Kornelia Smalla began a series of experiments in 1993 to monitor field releases of GM rizomania-resistant sugar beet (*Beta vulgaris*) for persistence of the GM construct in the soil and for horizontal gene transfer. They found that the GM construct has persisted in the soil for at least two years after the plants were grown and harvested, and different parts of the GM construct may have transferred to unknown soil bacteria.

The researchers are exemplary in documenting clearly their experimental material as well as the procedure, and I take pleasure in reporting their research in some detail. The GM sugar beet contained the following genes.

- *BNYYV cp* (the coat protein of Beet Necrotic Yellow Vein Virus) with CaMV 35S promoter (from the cauliflower mosaic virus) and *3'nos* terminator (from soil bacterium *Agrobacterium tumefaciens*). A promoter is a gene switch required to turn the gene on, ie, to transcribe the gene; a terminator, in this context, is a genetic signal to ensure that the gene transcript will be translated into protein.
- Marker genes *nptII* (neomycin/kanamycin phosphotransferase (from Tn 5, a bacterial transposon) with terminator *3'ocs* (from *A. tumefaciens*) and *bar* (phosphinotricin acetyltransferase (from *Streptomyces hygroscopicus*, another soil bacterium) with terminator 3'g7 (source unspecified) both under the control of the bidirectional TR1/2 promoter (from *A. tumefaciens*). These two marker genes confer resistance, respectively, to the antibiotic kanamycin (Km) and the herbicide glufosinate ammonium.

In order to detect the GM construct, PCR (Polymerase Chain Reaction) was carried out with three different sets of primers - short DNA sequences complementary to and hence specific for different parts of the construct. This allowed the amplification and detection of even trace amounts of GM construct.

Bacteria in the soil samples were cultivated in media with, and without kanamycin, in order to detect the proportion that is kanamycin-resistant. Individual kanamycin resistant colonies were probed for the GM construct. To detect GM construct independently of cultivation, total soil DNA was extracted and amplified by PCR with the three different primer sets.

The GM construct or parts of it was found to have persisted for up to 2 years under field conditions and in soil microcosms with introduced GM plant DNA for up to six months. Let us look at the findings regarding horizontal gene transfer.

GM sugar beet litter introduced into the soil led to an increase in both the Km resistant and total bacterial populations. Most of the kanamycin resistant bacteria are those that already exist in the soil, as antibiotic resistance is widespread. Though the authors did not comment on it, the proportion of resistant bacteria did increase significantly between 1.5 and 2 years, suggesting that this increase may be due to the transfer of kanamycin resistance marker genes from the GM construct to soil bacteria. It takes time for litter to rot and the DNA contained to be released.

A total of 4000 isolates of Km resistant bacterial colonies were individually screened with a "dot blot" technique to identify sequences that bind to, or "hybridize with" GM –specific probes. This technique is more direct, but much less sensitive than PCR. "A few isolates giving weak hybridization signals ….were detected". These were checked with

the PCR technique, but none gave PCR products, and hence the authors dismissed the results as false positives. There are obvious limitations to this experiment. First, 4000 is a small number of isolates, and most of them are probably from bacteria already carrying pre-existing kanamycin resistance. Second, the failure to obtain PCR products can be due to the fact that only fragments of the GM constructs or rearranged versions of the GM construct have been transferred. In order to rule out those possibilities, it is necessary to do more extensive molecular analyses.

Construct-specific DNA was found in practically all soil samples 6 months after GM sugar beet litter was introduced into the soil, while no GM–specific DNA was present in the soil with young GM plants. GM-specific DNA persisted for up to 2 years in the field. This suggests that GM-DNA is released mainly after the plant litter has disintegrated.

When total bacteria from soil were isolated, treated with DNAase (enzyme which break down DNA) to remove free DNA, two out of seven samples were found to contain GM construct after 18 months. This again suggests that horizontal gene transfer has occurred. The authors were careful not to rule out the possibility that GM-DNA may simply have "adsorbed" onto the external surfaces of the bacteria.

Soil microcosm studies to which free DNA from the GM sugar-beet was added showed that the intensity of the signal for GM construct decreased during the first days and subsequently increased (strongest at 23 days). This suggests that the GM-DNA may have been taken up by soil bacteria and have replicated with the multiplication of the bacteria. But the authors did not state this explicitly, nor offer any other explanation for the observation.

Bacterial lawns were grown up from soil samples in the microcosm experiments. After four days, the bacteria were harvested, treated with DNAse and the DNA released from the bacteria by boiling and freezing. PCR amplification with all three primer sets resulted in several positive signals, "which might indicate uptake of transgenic [GM] DNA by competent bacteria". But, "Because the isolates carrying the construct-specific DNA sequences were not accessible, an interpretation of the signals remains inconclusive."

The authors are scrupulously careful not to interpret the results as *proof* that horizontal gene transfer has taken place. The results, however, *are* prima facie evidence of horizontal gene transfer. The failure to isolate the bacteria which have taken up the GM construct is not surprising, as over 99 percent of soil bacteria cannot be isolated by current culture techniques, and this is one major limitation to detecting horizontal gene transfer in the field. The authors further state, "The presence of bacterial genes, promoters, terminators, or origins of vegetative replication in transgenic plants will enhance the probability of stable integration of DNA stretches based on recombination events [should transgenic DNA be taken up by the bacteria]." (pp. 270-1).

The precautionary principle states that where there is reasonable suspicion of harm, scientific uncertainty or lack of scientific consensus must not be used to postpone preventative action. The precautionary principle also requires us to interpret scientific evidence appropriately, to allow for uncertainty. Uncertainty is the hallmark of any *active* knowledge system, which is what science is, as opposed to religious fundamentalism. And this is ultimately why the precautionary principle must be part and parcel of sound science. The valid use of scientific evidence is to set precaution, and not to set permissive standards for scientists and corporations to continue to treat life and our life-support system as one vast laboratory, as has been the case for the past 50 years.

Gebhard and Smalla's paper does not provide positive *proof*, by itself, of horizontal gene transfer, but it does provide *reasonable suspicion* that horizontal gene transfer has occurred, especially as it corroborates previous laboratory investigations demonstrating horizontal gene transfer. There is already overwhelming evidence that horizontal gene transfer and recombination have created new bacterial and viral pathogens and spread drug and antibiotic resistance among the pathogens. GM constructs consist predominantly of bacterial and viral genetic material as well as antibiotic resistance marker genes. To persist in ignoring horizontal gene transfer in risk assessment not only violates the precautionary principle, it violates all the tenets of sound science and responsible governance.

References

1. Gebhard, F. and Smalla, K. (1999). Monitoring field releases of genetically modified sugar beets for persistence of transgenic plant DNA and horizontal gene transfer. *FEMS Microbiology Ecology* 28, 261-272.
2. For a more recent review, read "Horizontal Gene Transfer – Hidden Hazards of Genetic Engineering" by Mae-Wan Ho, to be posted on ISIS website. MWH

Can Viruses Cross from Plants to Animals?

The CaMV debate continues…

The question of whether viruses can cross from plants to animals was raised in the course of the debate on the hazards of the cauliflower mosaic virus (CaMV) promoter used in practically all GM crops.

There is indeed evidence that viruses may have crossed from plants to animals. Also, similar viral sequences have integrated into the genomes of both plants and animals, which suggests that sequences may have moved from animals to plants. Transposons (jumping genes related to viruses) and endogenous viruses are now found in the genomes of all higher organisms, plants and animals included. All these recent findings have important implications for the ecological and health impacts of GM crops, which have not been adequately addressed by our regulatory authorities.

The *circoviruses* are small single stranded DNA viruses that cause serious infections of the digestive systems of humans and other animals, particularly pigs and chickens. They also cause infections in clover, banana and coconut. There is evidence that vertebrates may have acquired circovirus from exposure to plant sap (1). The similarity between plant and animal circoviruses was noted earlier (2,3). As the virus group is quite recently discovered, it is not known when the shift from plants to animals may have occurred, nor whether the virus may still migrate between plants and animals at present. Plant and animal circoviruses are related to the plant geminiviruses (4) which have been used in genetic engineering but not commercially.

The soya genome contains several hundred copies of a large retroviral sequence called SIRE (Short Interspersed Repetitive Element), which is related to retrotransposons called *copia* in the fruitfly and *Ty1* in yeast (5, 6). Retroviruses are RNA viruses that replicate via reverse transcription, ie, making a complementary copy of DNA from the RNA. A retrotransposon is a jumping gene that uses reverse transcription to spread itself around the genome. In other words, SIRE is a plant retrovirus related to the retrotransposons of fruit flies and their food, yeast.

Plant pararetroviruses, which include the cauliflower mosaic virus, have also been found to be integrated into plant chromosomes at high copy numbers (7), and virus infection may result from endogenous pararetrovirus in plants (8,9). Pararetroviruses are DNA viruses which use reverse transcription to multiply itself.

Foamy viruses are found in animals including human beings, which are integrated into the chromosomes during each cycle of replication. These resemble plant pararetroviruses in that they infect as double stranded DNA (10, 11). Foamy virus is associated with human thyroid infection leading to Graves disease (12). The foamy virus and plant endogenous pararetrovirus are very similar, and possibly related. Switching of such viruses between plants and mammals took place some time in our evolutionary past, but whether or not it can still take place is not known, and should be investigated.

The use of pararetrovirus promoter sequences from cauliflower mosaic virus (CaMV) in essentially all commercial GM crops and those undergoing field trials has not been subject to risk assessment in the light of all these and other recent findings suggesting it may be unsafe (13, 14, 15). Government agencies such as USDA, and scientists advising the UK government argue there is no risk from the CaMV promoter because the virus has been eaten with infected cabbages (16). Furthermore, they also imply that as so many copies of retrotransposons and pararetroviral sequences are already in the plant genomes, each of which has a promoter, then adding a few copies of CaMV promoter will not make any difference (17). These arguments have been answered in full (see ref. 15 in particular). Some key points are summarized here.

The CaMV promoter in the intact virus and the intact viral genome is a stable integral part of the virus and is very different from the isolated CaMV promoter in GM constructs, which are notoriously unstable and prone to break and join with other genetic material. This increases their propensity for horizontal gene transfer. A *prima facie* case that the CaMV promoter in the intact virus is not the same as the one in GM construct is that while the intact virus is specific for plants in the cabbage family, the latter is promiscuous, and works in many, if not all species (look out for the next episode soon!).

The integrated viral and retrotransposon sequences may have intact promoters, but again the promoter is a stable integral part of the element; furthermore, most of the elements are inactive, which means that their promoters are chemically modified to be non-functional.

The CaMV promoter has a recombination hotspot (18) a site at which it is likely to break and join with other genetic material. Consequently, GM constructs with CaMV promoter(s) will be more prone to horizontal gene transfer and recombination

The CaMV promoter is promiscuous in function, and is active in all plants, algae, yeast and *E. coli.* Thus, any gene linked to it will be expressed continuously at high levels in all these species to which it is transferred.

The CaMV promoter has a modular structure, and is interchangeable in part or in whole with the promoter of other viruses to give infectious viruses.

Adding a CaMV promoter, prone to recombination, to genomes laden with sleeping pararetroviruses and retrotransposons can only increase the chances of re-activating infectious viruses and creating new viruses that may cross from plants to animals.

References

1.Gibs,M., and Weiler, G. (1999). Evidence that a plant virus switched hosts to infect a vertebrate and then recombined with a vertebrate infecting virus. *Proc. Natnl. Acad. Sci. USA* 96,8022-7..

2. .Meehan,B.,Creelan,J.,McNulty,M. and Todd,D. (1997). Sequence of porcine circovirus DNA affinities with plant circovirus" *J.GenVirol.* 78,221-7.

3 Bassami,M., Berryman,D.,Wilcox,G., and Raidal S. (1998). Psittacine beak and feather disease virus nucleotide sequence analysis and its relationship to porcine circovirus, plant circoviruses and chicken anaemia virus. *Virology* 249,453-9.

4.Niagro,F.,Forshoegfel,A.,Lawther,R. ,Kamalanathan,L.,Ritchie,B.,Latimer,K .,and Luckert,P. (1998). Beak and feather disease virus and porcine circovirus genomes intermediates between the geminivirus and plant circovirus. *Arch Virol* 143,1723-44,1998

5.Laten,H.,Majundar,A. and Gaucher,E. (1998). SIRE-1 a copia/Ty1-like retroelement from soybean encodes a retoviral envelope-like protein. *Proc. Natnl.Acad Sci USA* 95,6897-902.

6.Bi,Y and Laten,H. (1996). Sequence analysis of a cDNA containing the gag and pol regions of the soybean reteovirus like element. *Plant. Mol. Biol*. 30,1315-9,1996.

7.Jakowitsch,J.,Mette,M.,van der Winden,J.,Matzke,M. and Matzke,A. (1999). Integrated pararetroviral sequences define a unique class of dispersed repetitive DNA in plants" *Proc. Natnl. Acad. Sci. USA* 13241-6.

8.Ndowora,T.,Dahal.G.,LaFleur,D.,Har per,G.,Hull.R.,Olszwewski,N. and Lockhart,B. (1999). Evidence that badnavirus in Musa can originate from integrated pararetroviral sequences. *Virology* 255,214-20.

9.Harper,G.,Osuji,J.,Heslop-Harrison,J and Hull,R. (1999). Integration of banana streak badnavirus into the Musa genome:molecular and cytogenetic evidence. *Virology* 255,207-13.

10.Enssle,J.,Moebes,A.,Heinkelein,M., Panhusen,M.,Mauer,B.,Schweitzer,M., and Neumann-Haeflin,D. (1999). An active foamy virus integrase is required for virus replication" *J. Gen Virol* 80,1445-52.

11. Yu,S.,Sullivan,M., and Linial,M. (1999). Evidence that the human foamy virus genome is DNA *J. Virol*. 73,1565-72.

12. Lee,H.,Kim,S.,Kang,M.,Kim,W.,and Cho.B (1998). Prevalence of foamy virus related sequences in the Korean population. *J.Biomed SCI.*5,267-73,1998

13. Ho, M.W., Ryan, A. and Cummins, J. (1999). Cauliflower mosaic viral promoter – a recipe for disaster? *Microbial Ecology in Health and Disease* 11, 194-197.

14. Cummins, J., Ho, M.W. and Ryan, A. (2000). Hazards of CaMV promoter? *Nature Biotechnology* 18, 363.

15. Ho, M.W., Ryan, A. and Cummins, J. (2000). Hazards of transgenic plants with the cauliflower mosaic viral promoter. *Microbial Ecology in Health and Disease* (in press).

16. Hull R, Covey SN, Dale P. Genetically Modified Plants and the 35S Promoter: Assessing the Risks and Enchancing the Debate. *Microbial Ecology in Health and Disease* (in press).

17. Matzke, M.A., Mette, M.F., Aufsatz, W., Jakowitsch, J. and Matzke, A.J.M. (2000). *Nature Biotechnology* (in press).

18.Kohli,A.,Griffiths,S.,Palacios,N.,Twy man,R.,Vain,P., Laurie,D. and Christou,P. (1999). Molecular characterization of transforming plasmid rearrangements in transgenic rice reveals a recombination hot spot in the CaMV 35S promoter and confirms the predominance of microhomology mediated recombination" *Plant.J.* 17,591-601.

MWH

Major Victory – Neem Patent Revoked

May 10th 2000 – The Opposition Division of the European Patent Office (EPO) revoked a controversial patent, which had been granted to the US multinational corporation W.R. Grace for a fungicide derived from seed of the Neem tree. The legal opposition to the patent was filed five years ago and spearheaded by Indian scientist Vandana Shiva. IFOAM President Linda Bullard said " This is a great day not only for us but for all people throughout the world, especially from the Third World, who have been fighting to take back control of their resources and knowledge systems from the patent regimes of the North. We are gratified about the decision's recognition of the intellectual achievements of the South and urge the patent office to reject the 11 Neem patent applications still under examination. We hope that our victory will mark a turning point in the struggle against biopiracy". On the day of the hearing the EPO was presented with a petition signed by 500,000 Indian citizens demanding that all the patents on the Neem tree be revoked and banned.

Shortly after the victory, Murli Manohar Joshi, the Minister for Science in India announced new plans to create a digital database for Indian plants that will be included in the patent application system of the Geneva-based World Intellectual Property Organisation. The new database will be available to patent offices world wide, so data can be obtained before issuing patents for non-original inventions that belong to traditional Indian systems. AR

Source: The Edmonds Institute. See http://www.edmonds-institute.org & Jarayaman K.S May 18th 2000, '…As India pushes ahead with plant database', *Nature* 405, 267

Terminator is back!

Seven new terminator patents were filed in 1999 and beyond these, at least 43 patents have been issued for inducible gene control systems, or genetic trait control technology. The patentees include virtually all the gene giants or their subsidiaries; Aventis, Bayer, Dupont, Monsanto, Novartis and Zeneca, amongst others. Recent take over events may render corporate commitments to disavow terminator meaningless. Both Monsanto and Astra Zeneca have each merged with other companies since pledging not to commercialise suicide seeds. Whilst Astra Zeneca claims its policy on terminator remains the same, it could not say what might happen in light of its merger with Novartis. Astra Zeneca also holds a minority stake in a company, ExSeed Genetics, that won a terminator patent last year.

At the CBD meeting in Nairobi the biotech industry and US government regulators were arguing that seed sterility could be used to mitigate the problem of horizontal gene transfer from GMOs, offering a built in safety system. But surely this is an admission that GMOs are not environmentally safe? Besides, horizontal gene transfer cannot be prevented by this technology, and it is not clear that the technology can 'mitigate' the effects of horizontal gene transfer (see "Terminator in new Guises" ISIS News #3). Silvia Ribeiro from RAFI says " If the CBD doesn't have the intestinal fortitude to ban this technology then they won't have the guts to enforce the Biosafety Protocol". AR

Source: Terminator on Trial. News release 12 May 2000. RAFI. 'Nairobi Biodiversity meeting Must Ban Terminator or the Precautionary Principle will become a 'Post Mortem' critics warn.'

Battle Ground of Rice Research

The International Rice Research Institute (IRRI) is pushing Asian farmers to accept intellectual property rights (IPR) on rice, that include plant variety protection (PVP) systems or 'terminator technology'. IRRI has also just won a handsome $5M grant from the US senate to develop 'Vit A rice' for Asia. There are currently 160 rice patents world wide, held by 13 companies in the industrial north. Huge investments have gone in, and IRRI has its own trademark on rice varieties and are very proactive with rice patents. How else can wealthy corporations capture and control the huge rice markets of Asia?

IRRI should be supporting the African region and other developing world countries in the struggle to reform the WTO agreement on Trade Related Aspects of Intellectual Property (TRIPS), to promote equity and sustainable development, as well as the implementation of provisions under the Convention on Biological Diversity (CBD).

Peasant movements, NGOs and independent farmer-scientist networks from Southeast Asia are all calling for a complete restructuring of agricultural rice research. They want to see it go into the hands of those who genuinely wish to benefit the poor, instead of transnational corporations.

The initiative of Asian rice farmers must be supported internationally and all patents on rice varieties should be revoked and banned. These measures alone will protect the interests of the poor. For more details see ISIS Sustainable Science Audit 'Vit A rice – An exercise in how not to do science' this issue. AR

Source: See GRAIN news and analysis 31 March 2000 http://www.grain.org
Letter to President Bill Clinton on behalf of Institute for Agriculture and Trade Policy, ActionAid, and Centre for International Environmental Law.
Press Release, 2 June, BIOTHAI, KMP and MASIPAG in co-operation with VIA CAMPESINA and GRAIN

Biopiracy in Japan

Pesticide Action Network (PAN) Indonesia launched a boycott campaign (April 2000) against the Japanese manufacturing company Shiseido Co Ltd. Shiseido have stolen and patented nine Indonesian herbs that originate from tribal indigenous peoples in Indonesia. The herbs have been passed down through their ancestors and used for healing since ancient times. They include remedies for anti-ageing agents, hair tonics and skin preparations. Shiseido even has the audacity to cultivate the herbs on plantations in Indonesia, for they will not grow in Japan. They are manufacturing various skin and hair care products and have given no consideration whatsoever to the people who rightfully own the intellectual property. This is a clear case of Biopiracy.

During last month's meeting at the World Intellectual Property Organisation the United States pressured Colombia and other developing countries to weaken and finally withdraw a proposal seeking to promote the interests of indigenous communities by protecting their traditional knowledge. The proposal was to register the genetic resources of patents under an access contract, thus implementing Article 8 (j) of the CBD ensuring these communities share in the benefits of their genetic resources. AR

Source: PAN Indonesia, email biotani@rad.net.id & Letter to President Bill Clinton on behalf of Institute for Agriculture and Trade Policy, ActionAid, and Centre for International Environmental Law.

CIMMYT Cop-out over patents

The International Maize and Wheat Improvement Centre (CIMMYT) – one of the world's most influential green revolution institutes, under the umbrella of the Consultative Group on International Agricultural Research (CGIAR) – has always been one of the most honourable and transparent of all the CGIAR institutes. Their position on patents has until recently been unreservedly hostile. Therefore, it came as a disappointing blow when they announced April 2000 that they had amended their policy on intellectual property and will now adopt a case-by case evaluation system, which will accept patents and other intellectual property options. The rationale is that selective patenting will ensure farmers and researchers in the South have free access to CIMMYT's inventions – 'preventative patenting' in other words. They believe the decision will keep profiteers at bay, and allow CIMMYT to collaborate with Gene Giants on cutting-edge biotech research. They claim they are making the best of a bad situation and their decision sounds a 'reality check' for other public- research institutions trying to find their way through the patent pandemic.

But patents are governed by civil law and cost thousands of dollars to obtain. CIMMYT will also have to invest scarce resources in new monitoring mechanisms to police its intellectual property. Moreover, patents are extremely expensive to defend – on average, it costs well over a quarter of a million dollars in patent litigation, per litigant. Will donors allow their foreign aid money to be used to pay for lawyers fighting patent violation in various parts of the world?

An alternative strategy could achieve the same goal and cost CIMMYT nothing; they could file 'non-patent patents', which legally entrench the invention in the public domain so that patent examiners and applicants must take its claims into account when considering new claims. CIMMYT can also simply publish its research. Theoretically, either or both mechanisms can be used and will prohibit others from making patent claims on the same information. Publicity is another powerful weapon against predatory patentees and several patent claims have been dropped in recent years simply because the abuse of the system was so obvious. By taking those options instead, CIMMYT would not be participating in a system which it claims to despise. Their present decision is a cop-out and will be politically painful to review and harder still to reverse.

AR

Source: Rural Advancement Foundation International article 'RAFI GENO-TYPES', 12th April 2000 see http://www.rafi.org

Pioneer Hi-Bred wins Federal Lawsuit

As part of a $100 million settlement in a federal lawsuit, Cargill admitted to growing Pioneer Hi-bred International Inc.'s seed corn in order to isolate unique genetic material for its own use. Pioneer sued Cargill as well as two other competitors - Asgrow and DeKalb - in October 1998 after it found Pioneer 'genetics' in these other companies' products.

Cargill's executive vice president Fritz Corrigan said "This has been a painful period for Cargill; we were shocked that our investigation into Pioneer's allegations revealed that our seed business hadn't always lived up to our high ethical standards". The investigation resulted in Cargill pulling 11 hybrid varieties from the market. Pioneer's president and chief executive applauded Cargill for "doing a thorough job of investigating and eradicating problem areas it found in its seed business".

The outcome of this federal lawsuit demonstrates that biotech companies are prepared to go to any lengths to get GM products into the market, included stealing from one another.

AR

Source: 'Cargill Settles Gene-Theft Lawsuit' By Susan Stocum, Associated Press Writer

More Challenges for USPTO

The Council for Responsible Genetics (CRG) is challenging the USPTO to further amend its revised Guidelines before they are final. CRG notes US patent law excludes "Products of nature" from patentable subject matter [35 USC 112; Diamond v Chakrabarty 100 S. Ct 2204, 2206]. It further notes that the 'essential goal' of the description of an invention requires that applicants clearly convey the information that they have invented the subject matter. It is clear that human genes are products of nature for they are derived from our progenitors through the human germ line. In order to qualify as 'invention', 'description' of a gene would have to establish that the gene does not occur in nature. CRG maintains the original US Patent Acts, as written 200 year ago under the supervision of Thomas Jefferson, remain as valid today as they have always been.

NIH officials backed by groups such as the Association of American Medical Colleges (AAMC) is also challenging the USPTO over homologous sequences or sequences with similar genetic codes. They claim the difference in a single base pair in a gene sequence can have important functional implications and that it is extremely difficult to make an accurate prediction on utility based on similarity. The National Advisory Council for Human Genome Research puts it even more bluntly, "Finding partial sequence similarity is an obvious and non-inventive step". Patent holders currently do not need to continue with a full characterisation of their genes, for they can eventually claim rights over others hard won results.

AR

Source : David Dickson. May 4 2000, NIH opposes plans for patenting 'similar' gene sequences. Nature, Vol 405 p3. & Council for Responsible Genetics Open letter, distributed by Philip L Bereano Department of Technical Communication,, College of Engineering, University of Washington.

Patenting Smelling Genes

Oakland's DigiScents announced that it has filed a patent covering 125 of the genes that allow us to recognise smells. Ambryx Inc. in San Diego is on the same trail. Smell is one of our six senses that evolved so as we can sense nutrients. We have some 300 to 400 receptors in our nasal cavity, in a region called the olfactory epithelium and a different gene regulates each one. Odours react with lots of different receptors and humans can recognise 10,000 separate smells. Moreover, two people bent over the same rose use differing receptors to register the scent. This complexity could complicate the patenting of olfactory genes. DigiScents is being very quiet about its patent claim, other than to say it covers a large percentage of the smell receptor universe. About 150 smell receptors are already safely in the public domain, put there by government funded research. The companies point to a variety of uses, including creating 'corrective lenses for the nose'.

AR

Source; BioScope. Tom Abate. Patenting Scent. Email, abates@gate.com

Human Gene Patenting Unfair Say Researchers

AIDS research scientists have found four errors in the gene and protein sequence of a patent issued by US PTO (Feb. 2000) to Human Genome Sciences Inc. The company isolated the gene using automated computers

to sequences it and software to determine it belonged to a class of cell membrane receptors, chemokine receptors, which pick up chemical signals in the body. They could not claim the sequence as the invention, only a copy of the actual gene, which they deposited in the American Type Culture Collection in Virginia.

A few months later, scientists at the Aaron Diamond AIDS research centre in New York discovered HIV requires the receptor to enter cells. A drug that can block the receptor would be a new weapon against AIDS. The question now stands – who deserves to profit from this discovery?

The AIDS research scientists claim that it is simply not fair to award ownership rights to gene to a company that had no idea of its function in disease and that did not even spell out the sequence correctly in its patent. Tanya Dragic of Aaron Diamond said "They use sophisticated equipment…it isn't innovative work. It's not fair for others to have to pay licensing fees just because they got lucky". Automation of gene sequencing has meant that tens of thousands of genes and gene fragments have been patented this way. There are more than three million patents pending in the US on human genetic material alone. AR

Source: Errors found in patent for Aids genes, scientists say. Los Angeles Times, 03/21/00 By Paul Jacobs, Peter G Gosselin & RAFI GENOTYPES April 12 2000. & David Dickson. May 4 2000, NIH opposes plans for patenting 'similar' gene sequences. *Nature* Vol 405 p3.

Human Genome 2000 – Taking Bets

At the Cold Spring Harbor genome meeting (May 2000) biologists were literally taking bets on the number of genes in the human genome. One person told *Nature*, "Sequencing is like digging a gold mine - how much gold is there to find???"

Companies use gene-hunting software programs to find genes but Tim Habbard of Britains Sanger centre has doubts "Automatic annotation over-predicts the number of genes due to false positives and cases where multiple genes are annotated when there is really only one." Extrapolation methods have weaknesses too. Chromosome 22 and 21 – whose sequences have just been published - are similar in size; but Chromosome 21 has 225 genes, compared to 545 on chromosome 22.

The Sanger Centre in Cambridge UK is determined to ensure the human genome will not be privatised. A preliminary 'First Draft' will be jointly published shortly by Sanger and Celera; Venter has abandoned the race and will concentrate on follow-up research.

However, in the wake of the Clinton Blair announcement Todd Dickinson, the Commissioner of Patents and Trademarks made a mockery of it and said "genes and genomic inventions that were patentable before the announcement, still continue to be patentable under the same set of rules". It appears the announcement did nothing to slow or stop the privatisation and exclusive monopoly control of human genetic material but rather served to take the political heat off human gene patenting. AR

Source: Researchers take a gamble on the human genome. By Paul Saglik, *Nature* Vol 405 p 264 & RAFI – GENO-TYPES 26 March 2000. DeCoding the Clinton/Blair Announcement. See <www.rafi.org>

Genetics Scandal in Iceland

The Icelandic government is suspected of receiving $250, 000 from deCODE Genetics, a biotech firm, whilst it was working on trying to pass a genetics bill. The genetic database was approved by the Icelandic parliament through the Icelandic Health Sector Database Act in 1998. In Jan 00. Parliament granted deCODE an exclusive licence to the database for 12 years, including the ability to sell any discoveries. But Icelanders are inflamed and strongly oppose the plans. Icelanders make attractive subjects for geneticists because of the homogenous nature of the population - the island is remote, has a small population and the people have remained, relatively racially 'pure'. The database has been widely criticised by several groups including the World Medical Association and the Iceland Psychiatric Human Rights group. A major concern is privacy, the database contains the genetic information of practically all Icelanders, and citizens are assumed to agree to participate unless they opt out - 17,240 people out of 275,000 so far targeted have done exactly that. AR

Source: Genetics Scandal Inflames Iceland, by Kristen Philipkoski See < http://www.wired.com/news/politics/o.1283.35024.00.html> Wired Digtital Inc, a Lycos Network site.

Science Bytes

Defence Against Genome Invaders

Plants have a wide-range of defences against genome invaders – foreign genetic material. That's why GM plants are often unstable. A review of the processes is presented by researchers.

"The widespread occurrence of transgene inactivation in plants and classical cases of silencing of duplicated sequences in fungi suggest that all genomes contain defense systems that are capable of monitoring and manipulating intrusive DNA. Such DNA might be recognized by its structure, its sequence composition relative to that of its genomic environment and possibly by its disruption of normal biochemical functions."

Although methylation, especially of repeated sequences, is widely associated with gene inactivation, other mechanisms may be involved, including modification of chromatin structure. Elimination of inactivated intrusive DNA (presently best documented for filamentous fungi) may also contribute to genomic defense mechanisms in plants. " It is likely that, like viral and other infectious RNAs, alien RNA is also recognized by cellular defense systems."

Most of the knowledge of defence mechanisms against foreign genetic material came originally from observations in bacteria. But over the years, similar mechanisms are uncovered in higher organisms. These include:

- Cytoplasmic nucleases (enzymes) which break down invading genetic material
- DNA methylation for inactivating the foreign genes
- Modification of histones (proteins) bound to foreign genes
- Genomic surveillance systems capable of searching and debilitating repeated sequences or foreign sequences which are out of place
- Gene-silencing mechanisms which pick out genes that have similar or homologous sequences
- Post-transcriptional gene silencing which breaks down the transcripts of foreign genes
- Selective elimination of duplicated sequences, including integrated viral sequences in mammalian transformed cells

The three major events postulated to occur in response to invading DNA or RNA are "detection, inactivation and elimination". These

events work against the stability of transgenes.

This review covers interesting aspects of genome 'architecture' and the structure of 'chromatin' (the association of DNA with histones and other proteins involved in packaging the DNA into chromosome) which affect the fate of the integrated foreign genes. Most transposition and viral integration intermediates share certain structural features that may be prime targets for DNA methylation. Genomes appear to be made up of isochores – very long stretches of DNA with high compositional homogeneity, either GC rich or AT rich. This makes it possible to detect inserted genes that are compositionally different.

Stable integration and expression of introduced genes are essential for genetically engineered crops, and thus "transformation constructs must be designed to avoid host surveillance processes." The review outlines some design strategies for avoiding host surveillance suitable for *Agrobacterium*-mediated transformation methods as well as for biolistics and other direct DNA-mediated procedures, "provided that conditions for obtaining plants with few transgene copies can be established."

These design strategies include introducing gene sequences that are different from those in the plant to avoid gene-silencing which work on duplicated sequences, and adding either GC rich or AT rich flanking sequences to direct it to the appropriate isochore.

Reference: Kumpatla, S.P., Chandrasekharan, M.B., Iyer, L.M., Li, G. and Hall, T.C. (1998). Genome intruder scanning and modulation systems and transgene silencing. *Trends in Plant Sciences* 3, 96-104.

Our Comments: This review explicitly acknowledges the problem of transgene instability in plant genetic engineering and suggests design strategies to overcome different mechanisms that break down, search out, inactivate and eliminate invading genetic material. It deals realistically with the fact that transgenes are recognized to be invaders by crop plants (see also "Transgenes are Genome Invaders", this issue), which is denied by Conrad Lichtenstein, a pro-biotech molecular biologist (see "Corporate Science on the Offensive", this issue).

Transgene instability not only compromises the agronomic performance of GM lines, it has important ecological and health consequences. Structural instability of GM-inserts, due to excision mechanisms or the instability of GM constructs - not explicitly covered in this review - will also give recombinations and rearrangements within the host plant genome that may alter the plant's metabolism towards the production of harmful metabolites. It makes unintended, secondary horizontal spread of transgenes more likely.

Transgenes *are* Genome-invaders

Transgenes are recognized as genome-invaders by the host plant. The host plant mounts defence mechanisms against transgenes which are normally used against viruses.

'Post-transcriptional gene silencing' is a defense mechanism in plants similar to 'quelling' in fungi and RNA interference in animals. It silences foreign genes (ie, inactivates it) after the gene is transcribed into RNA, by preventing the RNA being translated into protein. Four genes are found to be required for post-transcriptional gene silencing in *Arabidopsis*. One of these, *SDE1*, is a plant homolog of *QDE-1* in the fungi, *Neurospora crassa* that codes for an RNA-dependent RNA polymerase (an enzyme which makes a complementary copy of an existing RNA). The researchers propose that SDE1 polymerase synthesizes a double-stranded RNA which initiates post-transcriptional gene-silencing. According to this idea, when a virus induces post-transcriptional gene silencing, the virus-encoded RNA polymerase will produce the double-stranded RNA, and therefore has no need for plant *SDE1*.

Plants defend themselves from invading DNA or RNA primarily by inactivating the RNA messages of the invader. Virus RNA is recognized during replication because it is double stranded, and double-stranded RNA is otherwise unusual in plant cells. The double-stranded RNA is destroyed by another plant enzyme (RNAse). To be successful, a virus must have a gene that inactivates the plant gene coding for the enzyme that destroys the replicating virus. Transgenes (GM-constructs) are recognized by the plant cell as foreign invaders because the plant cell has an RNA dependent RNA polymerase (resembling the virus replication enzyme) that converts the messenger RNA of the transgene into double stranded RNA. The double-stranded RNA is then attacked and destroyed by the same cellular defence mechanisms that work against replicating viruses.

To be successful, the transgene must evade the plant's defences against invading foreign nucleic acid.

Reference: Dalmay, T., Hamilton, A., Rudd, S., Angell,S., and Baulcombe, D.C. (2000). An RNA-dependent RNA polymerase gene in *Arabidopsis* is required for posttranscriptional gene silencing mediated by a transgene but not by a virus. *Cell* 101, 543-553.

Our Comment: Transgene silencing and the defense against foreign nucleic acid illustrate a fundamental aspect of the organisms in that they must defend their genetic identity and integrity against a multitude of foreign nucleic acids. As transgene constructs become better designed to overcome host defence mechanisms, they will be more powerful genome invaders. Their potential for successful horizontal gene transfer and recombination will concomitantly increase, and so will their ecological and health hazards. It is time to pause and reflect. JC & MWH

No Vaccines in Food Plants!

A recent review considers the development of plants expressing antigens of bacteria and viruses a particularly promising approach to vaccine development. The first human clinical trial for an edible plant vaccine was approved (by the US Food and Drug Administration) and carried out in 1997. GM potatoes expressing an *E. coli* diarrhea toxin gene (the B subunit of *E.coli* heat-labile toxin LT-B) constitutively (ie, continuously and in all parts of the plant) were taken orally by human volunteers in Phase I/II clinical trials.

Each received raw potato cubes from a random sample of non-GM control tubers or GM tubers. Eleven received 50 -100 g of GM potato while three received 50 g of non-GM potato. Ten of the 11 who ate the GM potatoes showed a significant rise in LT-B antibodies, whereas no LT-B specific antibodies were detected in the controls. The serum antibody levels induced by ingestion of the GM potatoes were comparable to those measured when volunteers were challenged with 10^6 virulent enterotoxigenic *E.coli* (ETEC) bacteria.

Thus, GM potatoes expressing the recombinant LT-B protein proved capable of inducing an immune response in humans when taken orally. Phase I and II trials are currently in progress with GM potatoes expressing hepatitis B surface antigen (HBsAg) as a booster for the commercial hepatits B vaccine, and GM potatoes with Norwalk virus virus-like particles (VLPs) as a vaccine against viral diarrhea. All three trials successfully induced systemic and mucosal immune responses without the aid of adjuvants (additional agents that stimulate immune response), and there were no adverse effects observed.

Reference: Amanda M Walmsley, A.M. and Arntzen, C.J. (2000). Plants for

delivery of edible vaccines. *Current Opinion in Biotechnology* 11:126-129.

Our Comments: Food crops should not be used for vaccine production. First of all, they will readily contaminate crops that are used as food. This point has been made previously (Ho, M.W. and Steinbrecher, R. (1998). Fatal Flaws in Food Safety Assessment, *Environmental & Nutritional Interactions* 2, 51-84). For example, it is assumed potatoes do not spread by pollination or by over-wintering tubers. Actually, both modes of transfer are known. Genes for the vaccines may also spread horizontally by sucking insects and by transfer to soil microbes. The genes and proteins may be released during plant wounding or breakdown of roots and rootlets and pollute surface and ground water. The vaccines may provoke allergic responses if humans or other mammals or birds are repeatedly exposed to the allergen.

In addition, many instances of recombination between viral transgenes and viruses have already been reported (reviewed in Ho *et al* (2000). *Microbial Ecology in Health and Disease* (in press)). Have these plants been assessed for their ability to generate recombinant viruses? When genes of viruses infecting human beings are incorporated into plants, are we not increasing the potential for generating new recombinant viruses that may cross from plants to human beings? (see "Can viruses cross from plants to animals?" This issue).

Vaccine production in plants may be a good idea. *But it should be done in plant tissue culture under strictly contained conditions and not in crops grown in the open field*. JC & MWH

Bacterial Genes and Autoimmune Responses

Bacterial DNA can trigger autoimmune responses, and so can synthetic oligonucleotides.

Over the past few years, it has become recognized that along with structural components and products of bacteria, bacterial DNA is also capable of signaling danger of infection to cells of the immune system. Particular DNA sequences (CpG motifs), which are abundant in prokaryotic (bacterial) but not in mammalian DNA, cause the activation and stimulation of immune cells. Research has been catalyzed by the finding that certain synthetic oligodeoxynucleotides mimic the action of bacterial DNA (see ISIS News#2, "Gene therapy and naked DNA vaccines can trigger autoimmune reactions"). Immuno-stimulation induced by bacterial DNA or synthetic oligonucleotides is being used therapeutically to condition or modify ongoing immune responses.

For example, CpG motifs have been used as vaccine adjuvants as well as instructing agents to selectively induce primary (Th1) immune responses involving T- helper cells, inflammation and cellular immunity. Hence, CpG motifs might be used in future as adjuvants and/or immunomodulatory agents in an attempt to treat or prevent undesired humoural cell response including allergy (associated with IgE antibodies).*

Reference: Heeg K and Zimmermann S (2000). CpG DNA as a Th1 Trigger. *Int Arch Allergy Immunol*. 121, 87-97.

Our Comments: Practically all transgenic crops have bacterial genes. Not much thought has been given to the potential impact of these bacterial DNA sequences in crop plants as they are digested by mammals or taken up in through wounds as plant juices or breathed in as pollen or crop dust. Recent research in gene therapy and DNA vaccines show that DNA can indeed be delivered into cells by oral ingestion, skin application or nasal inhalation (Reviewed in Unregulated Hazards: 'Naked' and 'Free' Nucleic Acids, ISIS and TWN Report, Jan. 2000 www.i-sis.org). Bacterial DNA not only produces immunity but stimulates inflammation and autoimmune responses. Autoimmune diseases include diabetes, Lupus , arthritis and multiple sclerosis.

It may be supposed that people and animals have bacteria in their guts but these bacteria normally pass through the digestive system protected by their thick cell walls. Bacterial DNA incorporated into the cells of the food crops is not so protected, and will be subject to digestive breakdown to generate fragments that may trigger autoimmune reactions. Whether these bacterial DNA danger signals are good or bad for mammals is something that should be known before we expose the world a to an avalanche of transgenic crops.

JC

Note added by Editor

The following was posted to ISIS by Bili Goldberg (BiGoldberg@aol.com)

Apparently, according to an abstract in a recent FASEB Journal, the use of synthetic CpG oligonucleotides (ODNs) as DNA vaccine adjuvants and in plasmid vectors (including HIV vaccines) may be fraught with problems with the finding of inhibitory CpG ODNs.

Ashman *et al*. *FASEB Journal* 2000, 14:A963 (Abstract 46.6) state:

"These results imply that the design of CpG-based vaccine adjuvants and plasmid vectors for DNA immunization must not only include stimulatory ODN sequences but avoid inhibitory ones."

GM Crops and the Ecology of Microbes

The widespread horizontal gene trafficking among bacteria makes it highly likely that GM constructs in GM crops will spread to microbial populations in all environments.

Eukaryotes ('higher' organisms which sequester their genomes in a nucleus) evolve principally through the modification of existing genetic information passed on in normal reproduction. Bacteria, however, have obtained a significant proportion of their genetic diversity through the acquisition of genetic material from distantly related organisms. Such horizontal gene transfer produces extremely dynamic genomes in which substantial amounts of DNA are introduced into and deleted from the chromosome. These lateral transfers have effectively changed the ecological and pathogenic character of bacterial species.

Large blocs of DNA are acquired by bacteria by taking up naked DNA molecules, by mating, by plasmid exchange and by virus (the transduction process). For example the disease causing genes for both cholera and anthrax are located on transferable plasmids and can also be spread by bacterial viruses in nature. The evolutionary biology of bacteria is dominated by horizontal gene transfer.

Reference: Ochman, H., Lawrence, J.G. and Groisman, E.A. (2000). Lateral gene transfer and the nature of bacterial innovation. *Nature* 405, 299 - 304

Our Comments: Large blocs of bacterial/viral DNA are introduced into all transgenic crops now released to the environment in field tests or commercial production. The bacterial genes include antibiotic resistance markers, replication origins (of plasmids), expressed genes for herbicide or insect resistance and other bacterial plasmid genes. Such genes are released back into the bacterial *milieu* during digestion in the gut of predators from human to insect, and as crop residues in the soil. The ecological and health impacts of such gene releases from the millions of acres of GM crops have largely been ignored by those charged with protecting health and the environment.

JC

Plastic Gene-activators

Plastic gene activators have been synthesized in the laboratory. Ken and Barbie may be due for incarnation.

Genes need activator proteins to

turn them on, called transcription factors. Transcription factors typically consist of a DNA binding domain and a separable activation domain; most activator proteins are also dimers – consisting of two subunits or modules. Researchers have replaced these protein modules with synthetic counterparts to create artificial transcription factors. One of these, molecular weight 4.2 kD, gives high levels of DNA site-specific l activation of transcription *in vitro* (in the test-tube). This molecule contains a sequence-specific DNA-binding polyamide in place of the typical DNA-binding region and a nonprotein linker in place of the peptide involved in forming the dimer. The activating region is a designed peptide. Because synthetic polyamides can, in principle, be designed to recognize any specific sequence, these results represent a key step towards the design of small molecules that can up-regulate any specified gene.

Reference: Mapp, A.K., Ansari, A.Z., Ptashne, M., and Dervan, P.B. (2000). Activation of gene expression by small molecule transcription factors. *Proc. Natl. Acad. Sci. USA*, Vol. 97, Issue 8, 3930-3935

Our Comments: Polyamide polymers include nylon along with a range of versatile plastics such as bar code holders. It is truly a step to the "new world" of genetic technology to design plastics that replace proteins (and biology) as gene regulators. This should throw the world of gene patents into turmoil. It should further stimulate a new genetic engineering industry that provides for biodegradation of plastic cell components (in the interim incineration may have to suffice). Presently there are no genetic code words for polyamide monomer but such words may not be far off.

These synthetic gene activators will have many applications. But they should only be used *in vitro* under well-contained conditions. Perhaps plastic genes and wholly plastic beings are not far off (they may be named Barbie and Ken). JC

Book Briefs

Exploding the Food Myths in the GM debate

The Multiple Functions and Benefits of Small Farm Agriculture in the Context of Global Trade Negotiations by Peter M. Rosset, September 1999
Cultivating Havana: Urban Agriculture and Food Security in the Years of Crisis by Catherine Murphy, May 1999
The Potential of Agroecology to Combat Hunger in the Developing World by Miguel Altieri, Peter Rosset and Lori Ann Thrupp, October 1998
Food First Publications, Food First Institute for Food and Development Policy <www.foodfirst.org>

These three excellent concise reports are just a sampling from the Food First Institute. Together, they explode all the myths currently used to promote GM crops and at the same time clearly identifying the problems as well as the opportunities that must be brought into the GM debate.

The Multiple Functions and Benefits of Small Farms challenges the conventional wisdom that small farms are backward and unproductive. Evidence drawn from both North and South shows that small farms are more productive, more efficient and contribute more to economic and social development than large farms. Small farmers are better stewards of natural resources; they conserve biodiversity and safeguard the future sustainability of agricultural production.

This report also shows that trade liberalization and corporate export agriculture have had a significantly negative impact on small farmers and this will be exacerbated by agreements negotiated at the World Trade Organization (WTO). The Agreement on Agriculture is likely to further undermine the already fragile viability of small farms, which will be devastating for rural economies and environments worldwide.

Small farms encourage a diversity of cropping systems, landscapes, local cultures and traditions, creating an aesthetically pleasing rural landscape and open space. They also encourage responsible management of soil, water and wildlife. Farmers and consumers are brought into more direct contact, fostering friendly, accountable relationships. Most importantly, small farms mean more equitable distribution of land and other resources as well as economic opportunities, empowering both farmers and local communities.

Small integrated farms are far more productive than monocultures. Figures from the US Agricultural Census in 1992 depicts a sharp decline of net income, from $1400 to $12/acre, as farm size increased from 4 to 6709 acres. Similar trends are found in at least ten other countries in the Third World. In some Third World countries the smallest farms are not the most productive, but the most productive farms are still small, of ten hectares or less.

As the result of trade liberalization, corporations have been able to flood the Third World and the world market in general with cheap food which is heavily subsidized by the state, both directly and indirectly. This has driven food prices down to below the cost of production. Local farmers are undercut, and at the same time, the minimum acreage needed to support a family goes up. The end result is the disappearance of small farmers and the concentration of farm land in ever fewer hands. This has been happening not just in the Third World but everywhere in the industrialized world as well.

Large farmers, meanwhile, turn increasingly to mechanized monocultures, replacing human labour in order to keep production costs down, to be 'competitive'. The major drive to export grain from America, which began in the 1970s contributed to a 40 percent increase in soil erosion in the corn and soybean belts. Today, about 90% of US cropland is losing topsoil faster than can be replaced. But large farmers have not benefited at all.

When the huge agricultural export 'boom' took off in the US in the 1970s, the farmer's income actually *declined*, and remained almost level between 1975 and 1995. "[T]he average American farmer has not benefited from the export boom at all. Rather the profit have accrued to the grain cartels." The US drive to dominate global grain markets has destroyed family farmers and damaged rural ecosystems both at home and abroad.

The greatest myth perpetrated in the world today is the need to be 'competitive' in everything, from food production to the mobile phone and education, even. For far too long, this ideology has pitched farmers and sweat-shop labourers in the South against their counterparts in the North. All the while, it is the corporate bosses that have been growing obscenely rich at their expense. University academics and scientists have been willing instruments and accomplices in this corporate takeover. By and large, they have been too self-engrossed, too comfortable or too timid to do otherwise, or to tell us the truth. It has been a continuing revelation for me just how much of the most important and innovative work has been done outside of our academic institutions. It is no wonder that the National Farmers Coalition in the US are demanding that the land grant universities stop agricultural biotechnology research which benefit the corporations at their expense.

Cultivating Havana is a unique documentation of the period immediately following the breakup of the Soviet Bloc in 1989, which plunged Cuba into the worst economic crisis in its history. It lost 85% of its trade, including both food and agricultural inputs. The conventional system of agriculture was highly dependent on imports of agrochemicals and farming equipment, and without those inputs, domestic production fell, leading to a

30% reduction in caloric intake in the early 1990s. Cuba was faced with a dual challenge of doubling food production with half the previous inputs.

The way Cuba responded was an inspiration to the rest of the world. It began with a nation-wide call to increase food production by restructuring agriculture. This involved converting from conventional largescale, high input mono-crop systems to smaller scale, organic and semi-organic farming systems. The focus was on using low cost and environmentally safe inputs, and relocating production closer to consumption in order to cut down on transportation costs.

Urban agriculture has been a key part of this effort. A spontaneous, decentralized movement had arisen in the cities. People responded enthusiastically to government initiative, and by 1994, more than 8000 city farms were created in Havana alone. Front lawns of municipal buildings were dug up to grow vegetables. Offices and schools cultivated their own food. Many of the gardeners were retired men in their 50s and 60s, and urban women played a much larger role in agriculture than their rural counterparts.

By 1998, an estimated 541 000 tons of food were produced in Havana for local consumption. Food quality has also improved as people now have access to a greater variety of fresh fruits and vegetables. Although the program still faces many challenges, urban gardens continue to grow and some neighbourhoods are producing as much as 30 percent of their own needs.

The growth of urban agriculture is largely due to the State's commitment to make unused urban and suburban land and resources available to aspiring urban farmers. The issue of land grants in the city has converted hundreds of vacant lots into food producing plots, and new planning laws place the highest land use priority on food production.

Another key to success was opening farmers markets and legalising direct sales from farmers to consumers. Deregulation of prices combined with high demand for fresh produce in the cities allowed urban farmers to make two to three times as much as professionals.

The government also encourages gardeners through an extensive support system including extension agents and horticultural groups that offer assistance and advice. Seed houses throughout the city sell seeds, gardening tools, compost and distribute biofertilizers and other biological control agents at low costs.

New biological products and organic gardening techniques are developed and produced by Cuba's agricultural research sector, which had already begun exploring organic alternatives to chemical controls, enabling Cuba's urban farms to become completely organic. In fact, a new law prohibits the use of any pesticides for agricultural purposes anywhere within city limits.

Many believed that when the economy recovered, urban agriculture would disappear. But quite the opposite has occurred. The urban agricultural movement is stronger than ever and growing, and both public and private sectors are investing.

The big surprise is that Cuba did not invent urban agriculture. It has been a world-wide movement since the 1970s, and today an estimated 14 percent of the world's food is produced in urban areas. This is perhaps one of the most important aspect of sustainable development, as more and more of the populations worldwide are becoming urbanized. It presents both a challenge and an opportunity for town-planning and design to transform the concrete jungle into habitats surrounded by open fields and gardens which can attract and support wild-life at the same time. Just imagine growing up in cities with urban agriculture instead of existing slums and soulless housing estates.

The *Potential of Agroecology to Combat Hunger in the Developing World* presents a convincing case. Agroecology is a special blend of indigenous and western scientific knowledge and practices "to arrive at environmentally and socially sensitive approaches to agriculture, encompassing not only production goals, but also social equity and ecological sustainability of the system." Despite this obviously political-sounding description, it is intensely practical, and has already a lot to show for it in farms around the world: Africa, Asia, and Latin America.

For example, a programme in Honduras started in the 1980s by World Neighbours introduced soil conservation practices to control erosion by drainage, contour ditches, grass barriers and rock walls and to restore soil fertility with chicken manure and intercropping with legumes. Yields tripled or quadrupled from 400 to 1 200-1 600 kilograms per hectare for the 1 200 families involved in the programme. The use of grain legumes as green manure has been particularly successful. The velvet beans (*Mucuna pruriens*), planted by hundreds of farmers in the northern coast of Honduras have boosted corn yields to 3 000kg/hectare, more than double the national average. Taking advantage of well-established farmer to farmer networks such as the campesino a campesino movement in Nicaragua and elsewhere, this simple practice spread rapidly. In a single year, more than 1 000 peasants recovered degraded land in the Nicaraguan San Juan watershed. Farmers adopting cover cropping have lowered their use of chemical fertilizers from 1900 to 400kg/ha, while increasing yields from 700 to 2000 kg/ha, and lowering their production costs by 22 percent.

In Peru, pre-Columbian technologies have been revived. One of these is the raised fields system that evolved on the high plains of the Andes some 3 000 years ago. According to archaeological evidence, these 'waru-warus', or platforms of soil surrounded by ditches filled with water, were able to produce bumper crops despite floods, droughts and killing frosts common at altitudes of nearly 4 000 meters. Reconstructing these systems showed that the combination of raised beds and ditches had a temperature modulating effect , extending the growing season and giving higher productivity. In the Huatta district, sustained potato yields of 8-14 tonnes/ha compare very favourably with the average yields for the area of 1-4 tonnes/ha. Similar successes are repeated in Bolivia, Chile and Cuba.

In Africa, agroecological practices have succeeded in regenerating soil for subsistence farmers suffering from soil degradation. In Senegal, millet and groundnut are planted in rotation and legumes are intercropped with cereals. Compost is used to restore soil fertility and manure from cows, goats and sheep are added to the compost. Yield increases in millet of more than 400 kg/ha were achieved by applying at least 2 tonnes of compost. In Tanzania, a soil erosion and agroforestry project began in 1980 in the Lushoto district. Perennial grass is planted along contours as well as contour strips of trees, shrubs and creeping legumes. Erosion was reduced by an average of 25 percent. Total yields increased by 64 - 87 % and gross marginal income for the hundreds of people adopting these practices was 74% higher compared to conventional approaches.

The tremendous advantages of agroecological approaches are clear. It relies on local knowledge and are adapted to local ecological and cultural practices. It offers the only practical way to actually restore degraded agricultural land. It is environmentally sound and affordable, and can be used to recover marginal lands which cannot be used by green-revolution crop. Finally, it empowers the farmers and frees them from the control of corporate monopolies. It is an

approach that is likely to increase equality as well as sustainability.

Why, then, are these approaches not more widely adopted? Mostly because "powerful economic/corporate and institutional interests have backed research and development (R&D) for the conventional GR [Green Revolution] agroindustrial approach, while R&D for agroecology and sustainable approaches has[sic] been largely ignored or even ostracized."

MWH

Farmageddon by **Brewster Kneen**, New Society Publishers, British Columbia, Canada, 1999.

I once saw a French film about the tragi-comic musings of a teenage girl who imagined how she was conceived by artificial insemination (AI). The sperm-donor was her father, married to her mother at the time, but mother couldn't bear to have sex with father. In today's world, where not only AI, but *in vitro* fertilization, pre-implantation diagnosis, germline gene therapy, human embryo cloning and human stem cell organogenesis are threatening to become routine, that film has lost much of its irony. But how did we get here, and what was the problem?

That is the question asked by Brewster Kneen. In his opening gambit, he wondered if the apparently innocuous step of getting rid of the bull and using AI to breed cows was the first step down the road to the current biotechnology, which he aptly defines as "the application of technology to life and the practice of treating life as technology". It occurred to him that in agriculture, the problem was farm consolidation and the consequent disappearance of small diversified family farms. What Kneen has to say about agriculture exactly parallels other aspects of our life. Farm consolidation was referred to as rationalization then.

Rationalization is the term used when they get rid of human labour, in the farm, as in the manufacturing and other industries. Rational philosophy is grounded in the science of mechanics and informs the mechanistic science that has dominated much of the twentieth century. Rationalization is a gradual replacement of human beings, animals and life with machines in the drive for efficiency, for competitiveness. It is the substitution and the subjugation of life by machines and ultimately the transformation of life into machines.

'Farmageddon' is defined by Kneen as the 'late twentieth-century conflict apparently over control of crops and food, with prospects of turning into the final struggle between the forces of life and the forces of death early in the twenty-first century'. Despite the apocalyptic-sounding title, it is a very readable yet thoughtful analysis of how we got here in agriculture, and why we must and can resist the corporate takeover. Right from the first, it exposes the moral blackmail implicit in the demand created by the biotech propaganda machine, to "feed the world and save the environment".

"There is also the subtle and pernicious assumption that it is *we* who must feed the world. There is no suggestion that this moral imperative is itself immoral, and that the people of the world might well be able to feed themselves if we would leave them alone and not demand that they produce luxury foods for us." (p.18) And if we don't keep dumping heavily subsidised surplus foods on the world to destroy the livelihoods of family farmers.

For decades, pundits have been issuing dire warnings of the population explosion that will cause hundreds of millions to starve to death, and population control was seen to be the only way out of the impending catastrophe. Since the push for biotechnology, however, no one mentions population control any longer. Instead, the *Times* magazine, several years ago, assures us that even though the population will hit 10 billion, farmers can meet the challenge with "modern biotechnology and a little bit of ancient wisdom." And that has been the message ever since.

Norman Borlaug, father of the Green Revolution, at first a sceptic, soon turned fervent convert. He roundly condemns "misinformed environmentalists" for claiming that the consumer is being poisoned by monoculture crops and stopping "scientific progress" by objecting to GM crops, which he believes can feed a population of 10 billion.

The figure of 10 billion happens to have no basis whatsoever. It is a wild exaggeration. The United Nations' world population figures have had to be revised downwards several times in the late 1990s. By mid-1998, the projection was that world population will peak at 7.7 billion in about 2040, then go into long-term decline, dropping to 3.6 billion by 2150, or less than two-third of present world population. That changes the complexion on the 'feeding the world' argument.

This book is a mine of valuable information. It goes behind the veil of secrecy into the dark culture that permeates corporate biotechnology, to identify those who stands to benefit from this dangerous experiment with life and our life-support system. It is also liberally annotated with quotations from books that one would like to read and does not have time for.

MWH

New Postings on ISIS website

ISIS Sustainable Science Audit #1: The 'Golden Rice" - An Exercise in How Not to Do Science

GM Crops – How Corporations Rule and Ruin the World
(MWH's debate with C.S. Prakash)

The Prince Speaks for the People, and for Scientists Too
(MWH on Prince Charles' Reith Lecture)

Biotech Breakdown
(good popular article on genetic engineering by Susan Borowitz)

World Scientists Open Letter to All Governments
Submitted to US Congress 29 June, 2000

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