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GM FOOD SAFETY: Scientific and Institutional Issues

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LECTIN STUDY

In 1995 the then Scottish Office of Agriculture, Environment and Fisheries Department (SOAEFD) advertised a research programme on safety aspects of GM crops. Until then, there was not a single publication in peer-reviewed journals on the safety of GM food. Not surprisingly, this was of great public and scientific concern, so it was thought that a research programme ought to be commissioned. SOAEFD solicited project proposals to look at all possible angles of GM food crops: environmental aspects, effects on soil, effects on animals directly or indirectly, and on risks for human consumers.

Peer review of our proposal

To obtain funding for experiments to test GM food safety, we had to write a detailed proposal, something like 50 pages. It had to specify what we wanted to do and how, detailing the design of all the experiments, what we were going to deliver and when, etc.

Originally there were 28 proposals which were whittled down to eight, and all these went for peer-review to the BBSRC (Biological and Biotechnological Sciences Research Council). Ours was chosen as the most sound proposal. Within the BBSRC there were a few Royal Society Fellows who had a look at our proposal and passed it in their peer-review. Nobody gives £1.6 million for a research proposal only on the basis of the opinion of a few scientists within the Scientific Advisory Unit (SAU) advising SOAEFD.

In this project there were three research units involved—the Scottish Crop Research Institute (SCRI), University of Durham, Department of Biology and ourselves at the Rowett Institute in Aberdeen. We divided the work tasks among ourselves. At the

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request of the scientists participating in the programme, I co-ordinated it.

The GM potatoes which we used had been created in Durham by scientists financed by Axis Genetics, a Cambridge biotechnology company. They were field-grown at Rothamstead Experimental Station for 2 years, so they were coming from field trials beyond the laboratory stage of development. We used these GM potatoes as a model in our studies, aiming to find suitable methods for the risk assessment of GM crops.

At the Rowett, we even had a profit-sharing agreement with the company which developed the potatoes: should they be commercially released, the Rowett would share the profits of the enterprise with Axis Genetics. So this was good academic work aimed to help a project of commercial significance. When critics claimed, 'These were academic studies', this claim was to belittle their significance.

Unexpected results

The idea was to use the gene of snowdrop bulb lectin, GNA, because we knew that it would not pose major health problems for the animals, according to our previous studies (Pusztai *et al.*, 1990). We had done extensive nutritional–physiological studies for 6 years and published them before the genetic transformation was carried out. In these studies we incorporated the gene product, GNA, into the rats' diet at different concentrations; we went up to something like 800-fold the level that we were expecting to be expressed in the potatoes. The rats still had no major health problems. So we had the assurance that this was a safe lectin and therefore a safe gene.

Moreover, from studies at Durham and SCRI, we also knew that the gene product, GNA, expressed in the potatoes did interfere with both the development and mortality of one of their main pests, the potato aphid. One can test for this effect in artificial feeding trials with aphids, and they had done this. So we started off with a gene which appeared to be doing the job of controlling insect damage but which wouldn't do any harm to the rat.

Nevertheless problems with our research appeared from the start, firstly in the insect-control part of the work, which we discussed extensively at our regular project meetings (confidential minutes of flexible research project 818). There appeared to be no correlation

between the expression level of GNA in the potato plant and the protection it afforded against the aphids. This lack of quantitative correlation was very worrying. Sometimes the expression level of the GNA was low but the protection was high, and sometimes vice versa. No results were ever published.

Now this result was very difficult to understand. And the scientist who persevered with this line of research, the co-ordinator at SCRI (Walter Robertson), was suddenly offered early retirement. With some arm-twisting, he accepted it.

In science we are very good at achieving the primary objectives of genetic modification, e.g. controlling aphid damage. We selected a gene which would achieve this objective, then did the genetic transformation and finally we checked in the laboratory whether or not we had achieved it. However, in the environment there are always other things which will also be affected. In this world nothing stands in isolation; when one changes something, there are also consequences for other things around.

Some of my colleagues found disturbing indications that the GM potatoes, in addition to harming potato pests, also damaged non-target and potentially beneficial insects. Nick Birch (1997) at SCRI, together with other members of the group, published a paper on how GNA expression in the potato affected aphids. They also looked at the two-spotted ladybirds which, in nature, feed on aphids and so control their population (Birch *et al.*, 1999).

At the same time we at the Rowett were also beginning to obtain nutritional data which somehow did not fit into our ideas. Somehow the gene product was safe when one used GNA sprinkled on to the diet, but it was less safe when expressed by the GM potatoes—in fact, expressed at a lower level than in the GNA-supplemented control diet. We couldn't understand how.

So, these two strands of our experimentation were yielding unexpected results. At that time we were beginning to think that there must be something wrong with this supposedly precise technology, for which it has been claimed that one can change the phenotype by simply inserting one gene in a particular way. We had two successful lines of GM potatoes, both coming from the same transformation event, done at the same time and in the same vessel; yet they were different.

Now how can one understand this difference? We were beginning

to suspect that the problems were likely to come from the position where the genes had been inserted because they could have interfered with the plant's own gene expression. If the transferred genes landed in different parts of the genome, they could have differently affected the expression level of the potato's own genes. I would guess that this is the most likely explanation for the unexpected problems.

Wrong experiment?

Some people said to me, 'You're a controversial scientist and your results have been criticized'. Fine, there is nothing wrong with that view, provided that it involves legitimate scientific criticism. In science we do experiments, then write them up, submit them to a journal where it is going to be peer-reviewed, if the work is good enough, it will eventually be published.

The people who criticized us said that 'These are the wrong results, wrong data, wrong experiments', etc. Top scientific committees, including the Royal Society of London, told us, 'You are only telling us about your uncensored, non-peer-reviewed results which had been obtained by poor experimentation, bad design and wrong conclusions'. Supposedly in my previous 270 papers, some 40 of them with the same design and methodology, I was scientifically alright, but then suddenly I had a mental breakdown.

Incidentally, the Royal Society never had the design of our experiments or the methods used by us. The only thing they had was some of the edited internal Rowett Institute reports which, against my wishes, had been passed on to them by the Director of the Rowett. Our successful, peer-reviewed 1995 project proposal was not amongst those listed by them for their so-called 'peer review'. So apparently the Royal Society never asked to see the design of our experiments.

The Royal Society has never before publicly conducted a peer-review of controversial scientific results. Moreover, against all natural justice, the Royal Society did not publish our data but only their criticism of it. *The Lancet* in its Editorial called this 'breathtaking impertinence' against a senior scientist.

In science the only thing acceptable as a counter-claim is when other scientists, preferably in several other laboratories, do similar work and go through exactly the same process as we have done with

our *Lancet* article; they get it peer-reviewed and published. This is the way science progresses. It doesn't really matter whether the President of the Royal Society voices his opinion, because it is merely an opinion and as such has no scientific validity.

■ *THE LANCET* VERSUS ROYAL SOCIETY

After our paper was published in *The Lancet* (Ewen and Pusztai, 1999), some people in the scientific establishment maligned it. Under normal conditions the peer-review is done by two referees. Ours had six referees. Indeed, I have all the referees' comments because the author communicates with them via the Editor.

True, there were criticisms, but we dealt with them. When we thought that the criticisms were fair, we amended the manuscript. However, when we did not accept the referees' criticism, we countered their argument with our point of view.

There is nothing unusual about this procedure; it is the normal course in journal publication. Because it is good to have your colleagues' opinion, I have done this many times before with other publications. But the opinion of your colleagues may not be better than yours; after all, you've done the work. So you accept some criticisms but reject others.

In such a way, our paper had been revised three times. Despite this, there are no substantial alterations in the paper. The changes were more about the format than substance. Because of the sensitivity of the whole business, the referees insisted that we should give all the data, regardless of whether they were significantly different or not. Thus, we had a huge table in the paper containing all statistical analyses, which incidentally were done by my wife, Dr Susan Bardocz, with the help of one of the referees.

The original purpose of the refereeing system is to improve papers. I am very grateful for those referees who did contribute to the paper in this helpful way. Most importantly, when the refereeing process was finished, our paper was accepted on both scientific merit and public interest, as explained by Richard Horton, *The Lancet* Editor. As he went on: in view of the clear evidence of support, i.e. that five of the six referees accepted it, he could not refuse to publish it.

☐ *Publication delay*

At the time, the Rowett still had the right to scrutinize our papers but had no right to change them. Thus, we thought that it would be best if we sent by fax the galley proofs to the Director of the Rowett just before it would be published on Saturday, 1 October 1999. So we faxed it to him late Friday afternoon, and then we went away, as we were sure it would be published in that form.

But then the Editors looked at it and they said that the table was not in the right format for *The Lancet* because the statistical significances were marked with stars, and not by the actual p (significance) values. Unfortunately, they couldn't get in touch with us; Dr Ewen was at his time-share flat and we were in Hungary. So the publication was held up for 2 weeks.

This delay gave the pro-GM brigade a fortnight in which they tried to stop the publication. The Director of the Rowett straight-away faxed it on to the Scottish Office, and to the Royal Society. It came as a bombshell to them that the paper was going to be published after all.

According to *The Guardian*, Professor Peter Lachmann phoned Richard Horton and threatened him. Unfortunately for Lachmann, *The Guardian* journalists found out that he cannot be regarded as impartial because he was involved with the biotech industry. He was also involved with a previous report of the Royal Society (1998), which did not recommend the need for future research into the possible health effects of GM food. Funnily enough, when his threats became common knowledge, the Royal Society washed their hands of the whole affair; they said that they did not know anything about this phone call.

☐ *False claims*

The scientific establishment had to find some reason for rubbishing the paper to justify their original rejection of our work. So that was probably the reason why the President of the Royal Society said, 'We still cannot accept this publication because Dr Pusztai did not use the right low protein controls'. Surely the six referees could not have missed something as important as this. You needn't be a Nobel Prize winner to read our paper and see that all diets contained the same amount of protein and energy.

But the journalists did not question the judgement of the President of the Royal Society. They assumed that he gave a proper scientific judgement on the paper, so they accepted his words at face value. In making such an untrue claim, was he scientifically incompetent? Or did he knowingly misrepresent our experiment?

As regards the comments made by Professor Pickett, FRS, the referee who opposed the publication of our paper, the story becomes even more curious. He told the *Independent* that Richard Horton (*The Lancet* Editor) must have had some political motivation for publishing the paper, because 'the referees' did not accept it. Significantly, he did not say 'one referee', but 'the referees'. And this claim was repeated many times at the OECD conference in February 2000. A senior scientist involved in the present field trials of GM crops, Nigel Halford, said, 'We should not spend time on Pusztai's paper here because it had been rejected by the referees'.

And one can go on with this story. Professor Pickett, for example, said that the design of my experiment was terrible: if it was presented by one of his students, he would fail the student 'because what we did was wrong, by changing horses in mid-stream'. That is to say, we supposedly changed the experimental design in the middle of the experiment: we started by feeding the rats with the control diet and then we switched to GM and vice versa.

It was absolutely clear in our paper that we did nothing like this. The design of the experiment was described in a clear-cut way. And Professor Pickett was one of the referees. If he actually read the paper, then why would he misrepresent our experiment? And if he did not read the paper, then how could he reject it? I don't know which one is the worst of these two explanations. It appears that peoples' attitude profoundly changes when their interests are jeopardized, contradicted or threatened by some scientific findings.

■ PROXY ADVICE

Nowadays ethics unfortunately is not much involved in science. When one looks at pronouncements from the Nuffield Council on Bioethics, and from other powerful scientific committees, one finds that they generally take the side of the establishment. When I was in

front of the Science and Technology Committee of the House of Commons, I made the point that most of the important decisions are taken by the wrong people. These are often has-beens, people who have long retired from active scientific work, though I don't want to be unkind to these people.

For example, Professor James was the nutrition expert on the ACNFP (Advisory Committee for Novel Foods and Processes). Undoubtedly he has worked in a scientific environment as the Director of the Rowett, the premier nutrition institute of this country. But I wouldn't regard his expertise to be based on his direct scientific experience. He does not do any experimental work and, unfortunately, people like him seldom listen to scientists still working at the bench. There is a huge difference between doing something or just reading or hearing about it.

In contrast, my previous Director, Sir Kenneth Blaxter, was a great man. Although he was very busy, he always spent at least a day each month in the lab of every senior bench-scientist. He came in and asked, 'What are you doing? Show me'.

This is the minimum that a top scientific administrator should do—to come into the lab and see for himself what is happening, to see what are the problems and to experience them on this level. Ours is an experimental science. You can't simply read about it and learn it that way.

Unfortunately, with some scientific administrators nowadays, this experience is reduced to a once-a-year occasion. At best they call the working scientists in to their office, where they are supposed to tell him about the work done in the last year. When one goes up together with the whole group of something like 18 people to the Director's office and tries to explain to him in an hour the progress we have made in the previous year, he faces an almost impossible task to take in all this. The most he can possibly learn is that we are working with lectins and that some of this work is done with GM crops.

I was responsible for eight research programmes, four of which were core-funded from the public purse. Another two (including our GM potato work) were financed by the Scottish Office (SOAEFD), in addition to another two commercially funded research programmes. Even I, as an active scientist, had real difficulties keeping abreast with all the work and the people carrying out the work.

☐ *'Best scientific advice'?*

Scientific administrators have no time to properly read anything. I personally know that all the papers and the submissions by the biotech companies to the ACNFP usually end up with people like us to read them. Unfortunately, most of the time the committee members cannot even wait to ask for our advice because they are so busy. Many times I was told, 'You just phone the guy at the Ministry and tell him what your advice is'. These 12 committee members sit around a table, have a nice meal together and then make momentous judgements about whether the government should approve a novel food.

That is the reality of the situation, even though they may put a scientific gloss on it. This is what is meant when the ministers say, 'We get the best scientific advice'. But if you are out of the lab and only have this superficial contact with science, your ideas can be worse than to have no science at all. It is likely that whatever common sense they may have had disappeared some time ago. They think that they know, when in fact they do not. These guys have insufficient knowledge or time; they are on other committees and fly all over the world.

For example, our Director seldom spent more than a week per month at the Rowett. Eventually he was criticized for that. As he did not spend long enough at the Institute, he could not possibly know what was going on. So I told the Science and Technology Committee that these important committees must have proper working scientists as members, or they should contract out some matters to working scientists. They must bring in real scientific advice, not just to the Ministers but to the members of the scientific committees because they're not working scientists themselves.

For example, in some of the Rowett press releases, it was said that Dr Pusztai had this very important work and that his results had been passed onto the appropriate committees, such as the ACNFP. This was in the days when everything seemed to go well for the Rowett, and they were trying to take credit for it. But in fact my papers had never been passed onto any of the committees. Indeed, it became apparent that the members were totally unaware of our research.

Moreover, they didn't know about other relevant pieces of research. As became clear from Granada's 'World in Action' TV

programme, Professor Janet Bainbridge was totally unaware of Professor Doerfler's work, which showed that some pieces of DNA could escape digestion, get into the circulation, even pass on to the next generation through the placenta.[1] When she was quizzed about it, she said, 'There are thousands of papers, I cannot be aware of them all'.

Professor Bainbridge is the chairperson of ACNFP, the committee which is responsible for advising government on whether or not to approve novel foods. Yet she didn't know anything about this paper. What sort of impression does this create?

These committees must be made broader by bringing in consumer representatives, ethicists, representatives of the social sciences—but also active experimental scientists. And then one should get up-to-date professional advice which is based on actual experimental work. It should not be based on third-hand knowledge which seeps through the system.

MAFF in the dark

Our work was commissioned by SOAEFD, Scotland's equivalent of MAFF (Ministry of Agriculture, Food and Fisheries), which was responsible for regulating the safety of GM foods. Nevertheless, on the day of my TV interview on 'World in Action', a guy from MAFF kept phoning me to complain that he had been kept in the dark: 'Why is it that I had not been told about this work? There are reporters queuing outside my office and demanding information on your work, but I have no information to give'.

He kept asking me to send him a letter pronto, so that he would know what it was all about. The TV company put out a press release the night before, so reporters naturally assumed that they could go to the right department of MAFF and would get everything explained. This poor guy kept saying to me 'I haven't got the faintest idea'. He never talked to anyone at SOAEFD about this work.

If all our results had been passed on to the appropriate committees, as Professor James asserted, then why had MAFF never heard about our work? So the Science and Technology Committee should have listened to my advice. If the ministers really want to act on the 'best scientific advice', then they should appoint some real working scientists to these committees—not just those whom they presume to

be scientists. Then perhaps in future we could avoid these embarrassing happenings.

SCIENCE AS PROSTITUTION

Commercialization of scientific research has come gradually since the middle of the 20th century.[2] It accelerated with the Conservative government of Prime Minister Thatcher. She managed to destroy true British science. The research institutes and the universities became more and more commercially orientated. In fact, we prostituted ourselves.

Customer science

In the 1980s the Cabinet Office established a 'think tank' which suggested that the only good science is that which can be exchanged for money at the end of the day. For example, then knowledge could be regarded as good science if it meant that electronics was understood better—and thus led to the production of better TV sets, more money and more profit.

Now, there is nothing wrong with such applications and I would not be against them. Technology is important and needs to be underpinned with science. However, when the whole relationship is turned the other way round, then the commercial product (e.g. the TV set) becomes far more important than its inside (e.g. the circuitry), the science that made it possible. When commercially orientated science is regarded as the only good science, then I disagree.

This mission- and product-oriented science ruled supreme until the beginning of the 1990s. Then Mrs Thatcher said: this good science should be supported by industry, not by public funds. Now, there is nothing wrong with industry support, but substantial funds which used to come from the government were now to come entirely from industry. As a result, we had to prostitute ourselves to commerce.

Industrial involvement in science and commercial funding of research is not wrong *per se*, but it must be done in a balanced way, so that we are not selling our soul to industry. Commercial research must be only a part of the whole scene. From the following example it will be easier to understand the situation.

☐ *Exclusive contract*

At the Rowett Institute we had a major research programme with a pharmaceutical company. Through our contract, the company bought all our research on lectins in the human gut context, even those parts which they have not financed at all. So, everything which we did in this field belonged to them. The Rowett sold us because it was in their financial interest. They drew up a contract, which was signed on our behalf.

This is prostitution. I have no other word for it. This was a clever way for the government to reduce scientific expenditure. But in the process they left us at the mercy of the commercial companies.

For example, the money from this company was for a specific part of our work which interested them. This was to use lectins for the prevention of gut damage in chemo-radiation therapy. We co-own a patent with the company on this technique; it's still in our name.

Although we were very successful with this project, any progress to capitalize on our work was totally dependent on the company. If they wanted to push the project forward, they could do it either with or without us; but equally, if they wanted to drop it, we could not do anything about it. They bought everything in advance, so that we could not even initiate our own research without their agreement.

Moreover, all the research work we did with lectins in a gut context belonged to this company, so the GM potato project also belonged to this company. They financed only our work using lectins for the prevention of radiation- and chemotherapy-induced mucositis damage, yet they could have claimed all of our results and could have stopped the publication of everything else. I still cannot publish the results. The company could take me to court if we published it, because the Rowett signed an exclusive agreement with them. In a sense we were sold to them—lock, stock and barrel. And that's not exceptional in government-funded research institutes.

Professor James said I was suspended for something like 12 days from GM work only, not from the other work. Yet I was suspended from all my research, including what was financed by this pharmaceutical company. The company in fact disowned us, in order to avoid bad publicity which could affect their other investments too. The patent was in our name, yet we were not allowed to do any more work for them. Although this mucositis work had nothing to do with

GM food, my dismissal meant the end of our project, because all the decisions were up to the company, which had the legal right to shut us out of our own invention and work.

☐ *Invention shelved*

In order to put our invention into medical practice, one has to go through a number of regulatory steps, culminating in human clinical trials. As the Rowett Institute obviously does not have money to develop our idea, the only way open was to sell us and our idea to this company. For this contractual arrangement, the company should have assured us that this noble objective of alleviating human suffering was going to be achieved through their financing.

But now all the work has gone into the company's files. The invention has been neither developed, nor published. And we can't do anything about it. Our contract says that the company has the right to postpone publication for up to 5 years. Clearly it would have benefited the public for the work to be published, but we cannot legally do it.

Obviously, we can understand that inventions need to be protected, especially when a company spends about half a million pounds. We even understand that they ought to have some return for their investment. But are they going about it in the right way? And is it right to shelve a valuable invention? In some instances it may even be in the interest of the company to publish the results because of their PR value and because they may help them to raise extra funds for developing the invention.

However, the decision is entirely for the company and we have no say in the matter. If the interests of the scientists and the company go hand in hand, that's fine. The problem arises when we are shut out of our own invention.

Unfortunately, nowadays this is a general problem in science. The cards are stacked against the scientist. It's the company which has all the aces, because they have the money and the lawyers. Which scientist can afford to go to litigation? Even research institutes cannot do it because they haven't got enough money to finance the expensive, risky business of legal litigation. So I think that there ought to be some form of adjudication. It's unreasonable for a

company to delay something for 5 years. This is against the public interest and against the scientists' interest.

UNCRITICAL VIEWS

In the debate on the safety of GM food, two opposing sides are running in parallel. Although I'm told the two extremes will meet in infinity, in reality we are really just taking up positions, and these two parallel lines don't seem to meet.

The pro-GM scientists say that the issue has been hijacked by the mass media, as if the public concerns were based on journalistic sensationalism. Of course, newspapers are in the business of selling newspapers, not in the pursuit of scientific enlightenment. However, the scientific truth usually asserts itself after a time.

Far more serious is that the scientific establishment is going over the top. In some instances they are not just economical with the truth, but in fact they are lying. Such behaviour is far more serious because it's not just distorting science, but it is also taking the debate in a wrong direction.

At issue is not just whether GM food is good or bad, but whether scientific debate is conducted in an ethical manner. This is a very important issue. We can all make mistakes, but deliberate ones are far more serious than anything that the *Daily Mail* may write about the scientific issues. I'm afraid that this is what characterizes this whole debate.

The scientific establishment is not willing to concede that there are points which need to be clarified, which could be done only by further research. There are many issues on which the scientific establishment says something which is manifestly untrue. This is not the way to conduct a serious scientific debate. They may not like the experiments that we did, but that's beside the point.

In my TV interview I said that genetic modification technology—if it is properly developed—may be a good thing. I am not against it. What I am against is this uncritical view. And it is not just uncritical, but it is being used to make safety claims for products which have not been properly tested. Now surely there cannot be anything wrong with that statement, but you see how the scientific establishment responded to our concerns.

Differences denied

It is often said, for example, 'Genetic engineering is just the same thing as was done in the past; it's a faster and more precise method of conventional breeding'. They know perfectly well that this is not true. Genetic modification may be better or worse, but it is different, and there is no doubt about that difference. And those who make claims for similarity, usually from the scientific or political elite, know perfectly well that it is untrue. So I don't really understand why they say it.

Again it is said, 'We eat tons of cauliflower mosaic virus (CaMV) during our lifetime. It is therefore inconceivable that using the DNA part of this virus—the CaMV 35s promoter, as a molecular switch to turn on the transferred gene in the genome of the plant—should present any safety problems in GM foods'.

As they know perfectly well, however, what we normally eat is the full virus, which has a protein coat that covers the DNA. This is what our immune system already recognizes. If you take off this coat, which determines the species specificity of the virus, then it is a different matter again. It could be better or worse for safety, but it is different. Therefore the associated risks ought to be investigated.

Likewise it is said, 'DNA is all degraded in the gut', when they know perfectly well that 0.1% does not break down, as documented in publications. (That figure may be higher for vegetarians.) The intact DNA should be of great concern to us. However, the associated risks have not been investigated either.

Indeed, the top scientific establishment ignore these uncertainties, perhaps because they are reluctant to fund research to investigate them. We have methods to investigate them, so why don't we? That's the crux of the issue.

Whatever the daily newspapers say, by tomorrow that's yesterday's story. But when prominent scientists speak, their statements may carry real weight. These two types of statement cannot be put on the same scale.

Missing evidence

I take a practical scientific point of view. In the few instances when these uncertainties were investigated by independent scientists, potentially serious problems surfaced. We don't know whether these

problems can occur generally, whether they are irreversible and whether they have any pathological significance.

Another problem is that we have very few data on the safety of GM foods. Our data base is extremely limited. In my TV interview I always limited my comments to GM potatoes and did not draw any general conclusions about GM food. However, we must admit that our results have a relevance to the general debate on GM food safety.

If you want to challenge existing data or concepts, the only way in experimental science is to do more experiments. But if we don't do this, then the lack of evidence cannot be taken to support a contrary point of view, i.e. safety claims. According to Sir John Krebs, drawing conclusions from the February 2000 Edinburgh OECD conference, there was no evidence that GM food poses any health risk.[3] This may be true, empirically speaking, but unfortunately there has never been any attempt to study the question, so the converse claim may also be true: that there is no meaningful evidence of safety.

If the head of our Food Standards Agency talks about 'no evidence of risk', then what conclusions can we draw? Is he omniscient? Clearly he has expressed an unscientific view. When such views are publicly announced by top scientists, then one always has this uneasy feeling that they may have some political agenda, because it cannot be regarded as a scientific agenda.

After a friend pestered Sir Robert May about the issue of testing of GM food on humans, eventually he admitted that there has never been any human testing. Nevertheless, we are told, 'But millions of Americans are eating it, and nobody has died'. Now, for a start, how do we know that nobody died? We don't know who is eating what, when, and how much. No records are kept, no post-market monitoring has been done, and GM crops are not segregated from non-GM crops. Therefore we have no way of knowing any of the effects of GM food.

Science makes quantitative comparisons. When we create something new, we compare it with something old which we think we do know. And the comparison must be quantitative. Take the principle to extremes: it does matter how much potassium cyanide one swallows. With a microgram, nothing will happen to you. But when one swallows a milligram, something lethal will happen. One cannot assume that quantities are irrelevant. So, when not

even qualitative comparisons are made, how can one draw any conclusions?

These are very serious issues. No glossing over them, or being economical with the truth, or even lying, will make these issues go away. They will still be there. If you do science and you don't stick to the truth as you see it, then the whole business of science loses its main reason. If I know in advance what result I will get, then why should I do an experiment?

For me a great attraction of science is that it's unpredictable; you don't know what result you're going to get. You may have your pet ideas, as we had in our group when we started. We thought that GM potatoes would be OK because it's a great idea. But scientists must be able and free to make up their minds on the basis of the experimental evidence obtained.

LIMITS OF PREDICTABILITY

Phenotypic variability of food

The US Food and Drug Administration (FDA) don't like natural products to be used in medical applications. According to the FDA, such products are too variable and not homogenous. If you use genetic modification technology, however, the FDA would look at the products more favourably. There are several genuine scientific problems with their safety assumption, but most regulators haven't a clue about them.

Genetic modification usually produces new proteins in *E. coli*. If one transfers DNA from a higher plant to a prokaryote like *E. coli*, they are billions of years apart on an evolutionary scale, though the same genetic code still applies. So the DNA sequence will still be transcribed and eventually expressed the same way, regardless of whether it comes from a prokaryote or from the eukaryote.

But there are possibly major differences too in what happens after the gene is transcribed. One of the best examples is glycosylation, the covalent attachment of carbohydrate residues to the peptide chain. This doesn't occur in prokaryotes like *E. coli*. Therefore if the gene product is a glycoprotein, it cannot be reproduced in a prokaryote. Even in two different plants, the glycosylated products of the same gene will be different.

Many other differences exist. In 1996 the Monsanto GM cotton

became unstable in the Southern states of the USA, probably because of the high temperatures, yet the similar Novartis GM cotton didn't. Some people say that the GM technology is not a proper technology because its products should be precise and predictable, repeatable and reproducible—which they are not. For example, one of our GM potatoes—that was derived from the same transformation and grown on the same plot—still contained 20% less protein than its parent line or the second GM line.

It is claimed that we know all the factors which control this process. I have just read a big review article on the role of transposons. These are highly mobile pieces of DNA within the plant's own genome which are responsible for producing phenotypic variability. It is said that we know all about the human genome, but we only know about 5% of it; we don't know anything about the other 95%, the in-between bits.

There are particular sequences, usually inverse repeats in the genome, which are very prone to transposition. In this sequence there is also a DNA sequence which codes for a transposing enzyme which excises bits of the sequence and shifts them along. As a result, the elements which control the regulation of the gene are moved over, leading to the establishment of a different regulatory network. There is no way that we can truly predict this change.

GM technology—the transfer of genes with viral promoters—destabilizes the genome. This gives more scope for transpositions, one of the main mechanisms for creating biological diversity. Once the new forms are created, then biological competition and natural development will decide whether that species is good or bad, whether or not it will be viable.

The genetic instability due to GM technology is a nightmare because one can't really predict what is going to happen. If one adds the possibility of intentionally creating new DNA sequences by recombination, i.e. a new life form, then the outcome will be even more uncertain. If this new DNA codes for something possibly harmful, then our immune system wouldn't recognize this new life form, so it could go on the rampage, by creating new incurable diseases.

We are being told, 'But there is no evidence for this scenario'. However, and more importantly, neither have we any evidence that this could not happen.

Environmental risks

For predicting environmental risks, too, the initial research had great limitations. Further research has simulated a tri-trophic interaction, where one looks beyond the behaviour of the selected pest that needs to be eliminated, towards the next thing in the chain of events. Tri-trophic interactions involve a plant toxin, pest and predator. Such interactions have not been extensively explored in GM research, although they may have huge ecological importance. Indeed, there are only three pieces of such research published in the scientific literature.

A Swiss study showed that Bt toxin-expressing maize could also harm beneficial lacewings. Although these were mainly laboratory/semi-field studies, they indicated potential harm (Hilbeck *et al.*, 1998a,b). These tri-trophic interactions could also occur under field conditions. So these studies should have at least stimulated further research.

There is the classic case of the Bt toxin-expressing GM maize developed to control the European corn borer, a main pest of maize. Unfortunately, it has been shown that the pollen of this GM maize can also potentially harm the Monarch butterfly (Losey *et al.*, 1999). This study has now been taken a step further by scientists at Iowa University who demonstrated that this can also occur in semi-field conditions (Hansen and Obrycki, 1999).

QUICK FIX AS PROGRESS

If I understood Prince Charles correctly, he said that science has become a way to get a quick fix for outstanding problems. I certainly agree with that. For example, if one wants to get rid of aphids which harm potatoes, we can create GM insecticides. There are a number of genes whose protein products can do that job, so that the problem can be fixed.

But the real problem comes when you try to put this 'fix' into its real-life context. It is often said that such views are 'anti-science', but I think this is rubbish. Successful scientists used to look at the problem in its context, rather than take it out of context and artificially boost a part which appeared desirable to them. Formerly, the main criterion for funding a piece of work was its scientific merit,

rather than its perceived or supposed merit for the public good. Science now is highly directed, driven by tasks and products.

In my opinion, the main criterion for good science is not how useful it is, but how well it is done. It is often said that one must promote the public good. But the road to hell is paved with the best intentions, and if your intentions are not even the best, then you get to hell very quickly.

So I think this whole business has been twisted out of context. Science ought to be done for finding out. It's not for fixes. I listened to the Reith lecture, particularly what Prince Charles said. Although he's not a scientist and knows that he's not a scientist, he spoke a lot of sense. Strangely, in this democratic age, he speaks for most of the people—the common people.

Science ought to aim at finding out. Science should be the pursuit of truth, without any financial advantage. That is the definition of science—the scientific enquiry.

Unfortunately for all of us, this has been twisted out of its original meaning. Now they say that science must not be pursued just to please the scientific mind: it's not the truth that is important, but the truth for a particular social context. The context is set by government and the scientific establishment because they have a preconceived idea of what is good for us all. So we have moved away from academic freedom.

This agenda is anathema to science. If you know in advance all the things which you are going to find, then there is not much point in doing it, is there? You are told this is what you must do and what you must find. If you are sceptical, then you are branded a Luddite, as if you want to stop progress.

When I was not taking the 'official line', many times I was told, 'You are proposing an anti-science agenda'. Quite the opposite: I want more science, not less. But I want science to be objective, as much as possible—not what the establishment have in mind. And not because science gives you a financial advantage.

SOCIO-ETHICAL ASPECTS OF SCIENCE

I have recently lectured at a liberal arts college in the USA. In this college they are trying to get the students to understand that everything in our society is always done in a social context. Courses in

government science and ecology and so on are intended to help the students to absorb this basic philosophy. Even students whose primary education is in science are made to see that their scientific activities will be done in a social context.

Some people voice the opinion, quite rightly, that the direction that science research takes should be influenced not only by scientists but also by non-scientists who bring different perspectives and values. I think this is very important. For me, the last 2 years I was on a real learning curve. Although in life our opinions are formed by all our life experiences, a great deal of these come from our own profession. However, for most people, life and professional experiences seem to be running on separate lines.

Like others, I had some basic ideas about what my life ought to be like. Early in my life I vowed never to be involved with any biological project which had obvious warfare implications. I have never wanted my science to be used against people. Had I been a physicist, I would have never considered taking part in the Manhattan Project to build an atom bomb.

However, even with these philosophical commitments, one does not always anticipate what are the potential outcomes, implications and consequences of our work. One has very little free time to do so. If you are a successful scientist, you have enough problems keeping up with your scientific activities. So if anything is not very obvious at the beginning, you don't start to question its implications.

☐ *Intolerance*

When we started with this genetic modification work in 1995, we thought that it was a great idea. For example, we accepted claims that GM crops would enable society to reduce the application of agrochemicals to the land. Clearly, this is a noble aim, but we didn't have the knowledge or the data to question its validity. In fact, we thought it was more than likely alright.

However, as we went through the whole process of research and our doubts were beginning to emerge, the realization also came that perhaps these doubts have implications which go beyond science. After all, I'm not just a scientist but also a member of the public who wants to live in a clean environment. So I started to look at GM from a different point of view, a much broader perspective.

Then, when I voiced my doubts over the safety of GM in public, what followed was a true eye-opener. To my cost, I found out just how far the establishment would go to try to destroy someone who brought into the open his concern, which was based on his own experimental work. My message was obviously uncomfortable to the scientific–political establishment with vested interests in the success of the GM technology.

Even scepticism is not tolerated by them. For them this is almost like a religious crusade. The establishment must crush anyone who appears to be standing in their way. If this had happened 500 years ago, I would have probably been put to the stake and burnt. They did to me the equivalent—what they could do in our age. They certainly went out of their way to destroy me, both as a person and definitely as a scientist.

☐ *Social consent*

I think that ethical and social considerations must come into scientific issues, both for the individual scientist and also for the scientific–political establishment. The scientist may think that he must have an absolute right to do anything, but he has no such right. For example, human cloning is reprehensible, both for me and many other scientists. I think that this questions and jeopardizes all our basic moral values; it is also unsettling for the whole structure of society and human existence.

Moreover, we have no right at all to subject people to the results of our work without consulting the public about this and securing their consent. Indeed, we have no justification to do experiments in which there is a human involvement without their consenting to this role. Moreover, we should have a strong enough ethical stance to self-regulate our research activities whose results might jeopardize the long-term future and development of the human race. Even if some people consent to such experiments, the responsible scientist should draw the line somewhere.

If scientists cannot draw this line, then others in society must do it for them. Scientists are sometimes too close to their subject to be able to make rational long-term decisions which take the whole human race into consideration. Scientists must not be allowed to do

experiments with human eugenics, for example. I thought that we fought a world war against that.

There must be a strong involvement with the public, though obviously 7.5 billion people cannot be sitting around a table to discuss the issues. We have to find the best ways to involve people in discussing issues which may affect them. There has also to be involvement from other sciences, liberal arts, social sciences, environmentalists, philosophers, religious representatives, etc.—people who may legitimately hold different viewpoints.

And the debate has to be done beforehand, not just after a technology has been developed, as with GM technology now. The damage might have been done already, and we might not know.

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□ *NOTES*

1. See scientific papers by Doerfler *et al.* (1997), Doerfler and Schubbert (1998) and Schubbert *et al.* (1994, 1998). See also the review article by Traavik (2000).
2. According to a major report, government departments 'do not require scientific support, but [rather] applied R&D, to achieve specific predetermined objectives'. Moreover, applied research should be subject to the 'customer-contract' principle (Rothschild, 1971). For public sector research institutes, initially the main 'customers' were government departments, which made contracts for specific policy-relevant research projects. In retrospect, this shift can be seen as a step towards commercializing public-sector research. Corporate influences on public-sector research have been widely analysed, e.g. Harvey (1998).
3. 'Worldwide, many people are eating GM foods (especially in North America and China) with no adverse effects on human health being reported in the peer-reviewed scientific literature', declared John Krebs (2000).

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