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The Precautionary Principle

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Date of publication: March 2002

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ISIS News 6, September 2000, ISSN: 1474-1547 (print), ISSN: 1474-1814 (online)

Use and Abuse of The Precautionary Principle

*Proponents of biotechnology have been busy attacking the precautionary principle lately. Why? Because it holds the key to protecting health and the environment and require the industry to prove beyond reasonable doubt that a technology or a product is safe before it can be adopted. **Peter Saunders**, Professor of Mathematics and co-Founder of ISIS shows how the precautionary principle is just codified common sense that people have accepted in courts of law as much as mathematicians have accepted in setting the burden of proof in statistics. But pro-biotech scientists have been abusing science as well as the precautionary principle. A version of this article has been submitted to the US Senate Committee on Biotechnology*

There has been a lot written and said about the precautionary principle recently, much of it misleading. Some have stated that if the principle were applied it would put an end to technological advance. Others argue that it fails to take science properly into account, though in fact it relies more heavily on scientific evidence than other approaches to the problem. Still others claim to be applying the principle when clearly they are not. From all the confusion, you might think that it is a deep philosophical idea that is very difficult for a lay person to grasp (1).

In fact, the precautionary principle is very simple. All it actually amounts to is a piece of common sense: if we are embarking on something new, we should think very carefully about whether it is safe or not, and we should not go ahead until we are convinced it is. It's also not a new idea; it already appears in national legislation in many countries (including the United States), and in international agreements such as the 1992 Rio Declaration and the Cartagena Biosafety Protocol agreed in Montreal in 2000.

Those who reject the precautionary principle are pushing forward with untested, inadequately researched technologies and insisting that it is up to the rest of us to prove that they are dangerous before they can be stopped. At the same time, they also refuse to accept liability, so if the technologies do turn out to be hazardous, as in many cases they already have, someone else will have to pay the costs of putting things right.

The precautionary principle is about the burden of proof, a concept that ordinary people have been expected to understand and accept in the law for many years. It is also the same reasoning that is used in most statistical testing. In fact, as a lot of work in biology depends on statistics, neglect or misuse of the precautionary principle often arises out of a misunderstanding and abuse of statistics.

The precautionary principle does not provide us with an algorithm for decision making. We still have to seek the best scientific evidence we can obtain and we still have to make judgements about what is in the best interest of ourselves and our environment. Indeed, one of the advantages of the principle is that it forces us to face these issues; we cannot ignore them in the hope that everything will turn out for the best whatever we do. The basic point, however, is that it places the burden of proof firmly on the advocates of new technology. It is for them to show that what they are proposing is safe. It is not for the rest of us to show that it is not.

The Burden of Proof

The precautionary principle states that if there are reasonable scientific grounds for believing that a new process or product may not be safe, it should not be introduced until we have convincing evidence that the risks are small and are outweighed by the benefits. It can also be applied to existing technologies when new evidence appears suggesting that they are more dangerous than we had thought, as in the cases of cigarettes, CFCs, lead petrol, greenhouse gasses and now genetically modified organisms (GMOs) (2). In such cases it requires that we carry out research to gain a better assessment of the risk and, in the meantime, that we should not expand our use of the technology but should put in train measures to reduce our dependence on it. If the dangers are considered serious enough, the principle may require us to withdraw the products or impose a ban or moratorium on further use.

The principle does not, as some critics claim, require industry to provide absolute proof that something new is safe. That would be an impossible demand and would indeed stop technology dead in its tracks, but it is not what is being demanded. The precautionary principle does not deal with absolute certainty. On the contrary, it is specifically intended for circumstances in which there is no absolute certainty. It simply puts the burden of proof where it belongs, with the innovator. The requirement is to demonstrate, not absolutely but beyond reasonable doubt, that what is being proposed is safe.

A similar principle applies in the criminal law, and for much the same reason. In the courtroom, the prosecution and the defence are not on equal terms. The defendant is not required to prove his innocence and the jury is not asked to decide merely whether they think it is more

likely than not that he committed the crime. The prosecution must establish, not absolutely but beyond reasonable doubt, that the defendant is guilty.

There is a good reason for this inequality, and it has to do with the uncertainty of the situation and the consequences of taking a wrong decision. The defendant may be guilty or not and he may be found guilty or not. If he is guilty and convicted, then justice has been done, as it has if he is innocent and found not guilty. But suppose the jury reaches the wrong verdict, what then?

That depends on which of the two possible errors was made. If the defendant actually committed the crime but is found not guilty, then a crime goes unpunished. The other possibility is that the defendant is wrongly convicted of a crime, in which case his whole life may be ruined. Neither of these outcomes is satisfactory, but society has decided that the second is so much worse than the first that we should do as much as we reasonably can to avoid it. It is better, so the saying goes, that a hundred guilty men should go free than that one innocent man should be convicted.

In any situation in which there is uncertainty, mistakes will occur. Our aim must be to minimise the damage that results when they do.

Just as society does not require a defendant to prove his innocence, so it should not require objectors to prove that a technology is harmful. It is up to those who want to introduce something new to prove, not with certainty but beyond reasonable doubt, that it is safe. Society balances the trial in favour of the defendant because we believe that convicting an innocent person is far worse than failing to convict someone who is actually guilty. In the same way, we should balance the decision on risks and hazards in favour of safety, especially in those cases where the damage, should it occur, is serious and irredeemable.

The objectors must bring forward evidence that stands up to scrutiny, but they do not have to prove there are serious dangers. The burden of proof is on the innovators.

The Misuse of Statistics

You have an antique coin that you want to use for deciding who will go first in a game, but you are worried that it might be biased in favour of heads. You toss it three times, and it comes down heads every time. Naturally, this does nothing to reassure you. Then along comes someone who claims to know about statistics. He carries out a short calculation and informs you that as the “p-value” is 0.125, you have nothing to worry about. The coin is not biased.

Now this must strike you as nonsense, even if you don’t understand statistics. Surely if a coin comes down heads three times in a row, that can’t prove it is unbiased? No, of course it can’t. But this sort of reasoning is being used to prove that GM technology is safe.

The fallacy, and it is a fallacy, comes about through either a misunderstanding of statistics or a total neglect of the precautionary principle – or, more likely, both. In brief, people are claiming to have proven that something is safe when what they have actually done is to fail to prove that it is unsafe. It’s the mathematical way of claiming that absence of evidence is the same as evidence of absence.

To see how this comes about, we have to appreciate the difference between biological and other kinds of scientific evidence. Most experiments in physics and chemistry are relatively clear cut. If we want to know what will happen if we mix copper and sulphuric acid, we really only have to try it once. We may repeat the experiment to make sure it worked properly, but we expect to get the same result, even to the amount of hydrogen that is produced from a given amount of copper and acid.

Organisms, however, vary considerably and don’t behave in closely predictable ways. If we spread fertiliser on a field, not every plant will increase its growth by the same amount, and if we cross two lines of maize, not all the resulting seeds will be the same. We often have to use some sort of statistical argument to tell us whether what we have observed represents a real effect or is merely due to chance.

The details of the argument will vary depending on exactly what it is we want to establish, but the standard ones follow a similar pattern.

Suppose that plant breeders have come up with a new variety of maize and we want to know if it gives a better yield than the old one. We plant one field with each of them, and we find that the new variety does actually produce more maize.

That’s encouraging, but it doesn’t prove anything. After all, even if we had planted both fields with the old strain, we wouldn’t have expected to get exactly the same yield in both. The apparent improvement might be just a chance fluctuation.

To help us decide whether the observed effect is real, we carry out the following calculation. We suppose that the new strain is actually no better than the old one. This is called the “null hypothesis” because we assume that nothing has changed. We then estimate as best we can

the probability that the new strain would perform as well as it did simply on account of chance. We call this probability the p-value.

Obviously, the smaller the p-value the more likely it is that the new strain really is better, though we can never be absolutely certain. What counts as a small enough value of p is arbitrary, but over the years statisticians have adopted the convention that if p is less than 5% we should reject the null hypothesis, i.e. we may infer that the new strain is better. Another way of saying this is that the increase in yields is 'significant'.

Why have statisticians fastened on such a small value? Wouldn't it be reasonable to say that if there is less than an even chance (i.e. $p=0.5$) of such a large increase then we should infer that the new strain is better?

No, and the reason why not is simple. It's a question of the burden of proof. Remember that statistics is about taking decisions in the face of uncertainty. It is a serious business advising a company to change the variety of seed it produces or a farmer to switch from one he has grown for years. There could be a lot to lose if we are wrong. We want to be sure beyond reasonable doubt that we are right, and that's usually taken to mean a p-value of 0.05 or less.

Suppose we obtain a p-value of greater than 0.05. What then? We have failed to prove that the new strain is better. We have not, however, proved that it is no better, any more than by finding a defendant not guilty we have proved that he is innocent.

In the example of the antique coin, the null hypothesis was that the coin was fair. If that were the case, then the probability of a head on any one throw would be 0.5 so the probability of three heads in a row would be $(0.5)^3=0.125$. This is greater than 0.05, so we cannot reject the null hypothesis. Thus we cannot claim that our experiment has shown the coin to be biased.

Up to that point, the reasoning was correct. Where it went wrong was in the claim that the experiment has shown the coin to be fair. It did no such thing.

Yet that is precisely the sort of argument that we see in scientific papers defending genetic engineering. A recent report "Absence of toxicity of *Bacillus thuringiensis* pollen to black swallowtails under field conditions" (3) claims by its title to have shown that there is no harmful effect. In the discussion however, the authors state only that there were "no significant weight differences among larvae as a function of distance from the corn field or pollen level." In other words, they have only failed to demonstrate that there is a harmful effect. They have not proven that there is none.

A second paper (4) claims to show that transgenes in wheat are stably inherited. The evidence for this is that the "transmission ratios were shown to be Mendelian in 8 out of 12 lines." In the accompanying table, however, six of the p-values are less than 0.5 and one is 0.1. That is not sufficient to prove that the genes are unstable and so inherited in a non-Mendelian way. But it does not prove they are, which is what was claimed.

The way to decide if the antique coin is biased is to toss it more times and see what happens. In the case of the safety and stability of GM crops, more and better experiments should be carried out.

The Anti-Precautionary Principle

The precautionary principle is so obviously common sense that we might expect it to be universally adopted. That would still leave room for debate about how big the risks and benefits are likely to be, especially when those who stand to gain if things go right and those who stand to lose if they do not are not the same. It is significant that the corporations are implacably opposed to proposals that they should be liable for any damage caused by the products of GM technology. They are demanding a one-way bet: they pocket any gains and someone else pays for any losses. It also gives us an idea of how confident they are about the safety of the technology.

What is harder to understand is why our regulators are still so reluctant to adopt the precautionary principle. They tend to rely instead on what we might call the anti-precautionary principle: When a new technology is proposed, it must be approved unless it can be shown conclusively to be dangerous. The burden of proof is not on the innovator; it is on the rest of us.

The most enthusiastic supporter of the anti-precautionary principle is the World Trade Organisation (WTO), the international body whose task it is to promote free trade. A country that wants to restrict or prohibit imports on grounds of safety has to provide definite proof of hazard, or else be accused of erecting artificial trade barriers. A recent example is the WTO's judgement that the European Union's ban on US growth-hormone injected beef is illegal.

By applying the anti-precautionary principle in the past, we have allowed corporations to damage our health and our environment through cigarette smoking, lead in petrol, and high levels of toxic and radioactive wastes that include hormone disrupters, carcinogens and mutagens. The

costs in human suffering and environmental degradation and in resources to attempt to put these right have been very high indeed. Politicians should bear this in mind.

Conclusion

There is nothing difficult or arcane about the precautionary principle. It is the same reasoning that is used every day in the courts and in statistics. More than that, it is just common sense. If we have genuine doubts about whether something is safe, then we should not use it until we are convinced it is. And how convinced we have to be depends on how much we really need it.

As far as GM crops are concerned, the situation is clear. The world is not short of food. Where people are going hungry it is because of poverty. Hardly anyone believes that there will be a real shortage within 25 years, and a recent FAO report predicts that improvements in conventional agriculture and reductions in the rate of increase of the world's population will mean we will continue to be able to feed ourselves indefinitely.

On the other side, there is both direct and indirect evidence that gene biotechnology may not be safe for health and the environment. The benefits of GM agriculture remain hypothetical.

We can easily afford a five-year moratorium to support further research into improving the safety of gene biotechnology and making it more precise and more effective. We should also use the time to develop better methods of sustainable farming, organic or low-input, which do not have the same potentially disastrous risks.

1. See, for example, S. Holm and J. Harris (*Nature*, 400 (1999) 398). Compare C.V. Howard & P.T. Saunders (*Nature* 401 (1999) 207) and C. Ruffensburger *et al.* (*Nature* 401 (1999) 207-208).
2. We are now told that in the case of tobacco and lead, many in the industry knew about the hazards long before the public did. It is not always wise to accept broad and unsupported assurances about safety from those who have a very strong interest in continuing the technology.
3. A.R. Wraight *et al* (2000), *Proceedings of the National Academy of Sciences* (early edition). Quite apart from the use of statistics, it generally requires considerable skill to design and carry out an experiment to provide a convincing demonstration that an effect does not occur. It is all too easy to fail to find something even when it is there.
4. M.E. Cannell *et al.* *Theoretical and applied Genetics* 99 (1999) 772-784.

(A slightly shorter version of the letter below was published in *Nature*, September 1999)

The Precautionary Principle

Holm and Harris (*Nature*, 29 July) strongly criticise the precautionary principle (PP) but they seem not to understand it. They complain that it is not valid for evaluating evidence, when that is not what it is for. It is a tool for decision making, and, like many such tools, deals in expectations rather than probabilities. The whole point is that it requires us to take into account not just the probability that a technology will be hazardous, but also both the benefits if it succeeds and the costs if things go wrong. There may only have been a very small probability that a large ship travelling at high speed in the North Atlantic would hit an iceberg, but the captain of the Titanic should have thought more about what could happen if it did -- and all the more so because it didn't really matter all that much if the voyage lasted a few hours more.

Holm and Harris also argue that the PP would have prevented us from proceeding towards the development of genetically modified (GM) plants because the greatest uncertainty about their possible harmfulness existed before anybody had yet produced one. But the PP does not demand that we halt research if we cannot be certain that the end result will be safe, though common sense surely suggests that it is not prudent to make large investments if the end result is likely to be dangerous. It is to be applied at each stage in the process, weighing the risks in going one step further against the likely benefits if the project as a whole is successful.

That is why we and many others are arguing not for a complete ban on research into GMOs but only for a five year moratorium on field trials and commercial planting. There is a lot more research to be carried out in the relative safety of a closed laboratory before we can go on to trials in the open. This is always good practice, but it is especially important in the case of GMOs because of the irreversibility that is inherent in the technology. If a new conventional drug proves to be harmful we can recall it and so limit the damage, but once genes have left the laboratory there is no calling them back. The recent experiments in which GM milkweed was found to be harmful to the Monarch butterfly were performed in contained conditions; had this been discovered in field trials, the gene might already be spreading through the environment.

Our objection to the current field trials of GM crops is based not on the question of whether commercial planting would be safe (though we are indeed concerned about that), but on whether

the trials themselves are safe and whether the experiments are sufficiently well designed that the information they may provide will be worth the risk that is associated with them. Neither has been shown to be the case. Hopefully, at the end of a moratorium we will be able to make a much better informed risk assessment.

C. Vyvyan Howard & Peter T. Saunders

ISIS News 3, December 1999, ISSN: 1474-1547 (print), ISSN: 1474-1814 (online)

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

If you want to know why our governments are failing to regulate toxic discharges, food additives, and GMOs to protect health and the environment, it is because they are not acting in accordance with the precautionary principle. Adopting such a principle will change our whole approach to environmental policies and to regulation. This book tells you the reasons why and more importantly, how the precautionary principle has been and can be implemented in practice.

In general terms, this principle calls for protective, preventative actions of harm even when scientific evidence is uncertain. More importantly, it shifts the burden of proof of *safety* to the perpetrators, instead of demanding regulators and civil society to provide scientific proof of *harm*. The WTO is operating against the precautionary principle when it judged the EU ban on US growth-hormone injected beef illegal. This is how the WTO undermines every single effort by citizens and governments all over the world to protect health and the environment (For a list of examples, read another important publication, *Invisible Government, The World Trade Organization: Global Government for the New Millenium?* by Debi Barker & Jerry Mander, International Forum on Globalization, San Francisco, 1999)

The present book is the collective effort of an impressive international panel of public health professionals, lawyers, academics, environmentalists and policy makers. It is replete with useful information and good examples. I learned how Sweden has the best environmental law in Europe based on the strongest version of the precautionary principle. In contrast, the UK, with a long tradition of “scientific corporatism and elitism”, prefers to adopt the “long pipes and tall chimneys” approach to make optimal use of the waste assimilative capacity of the environment. Even when pressed to adopt the precautionary principle, its role is limited as is clear from the statement given by the UK Government, which is worth quoting in full (see p. 30),

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

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

MWH

ISIS News 5, July 2000, ISSN: 1474-1547 (print), ISSN: 1474-1814 (online)

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 CryIAB 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.

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

Postscript:

The myth that swallowtails were unharmed by bt toxin continued to be perpetrated, especially in mainstream scientific journals. For example, it was reported in *Nature Biotechnology* 2000, 18, 701, under the headline, "Swallowtails unaffected by Bt toxin", where it stated the half-truth, "Although corn pollen accumulated on the leaves eaten by the larvae, there was no difference in butterfly health or mortality between the experimental and control groups."

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 hygrosopicus*, 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.

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ISIS News 7/8, February 2001, ISSN: 1474-1547 (print), ISSN: 1474-1814 (online)

The Precautionary Principle and Scientific Evidence

Peter Saunders and Mae-Wan Ho argue: *The precautionary principle is not an algorithm for making decisions, but a principle for making decisions based on available evidence. So let's look at the evidence.*

In a recent article, Comstock claims that the precautionary principle commits us at the same time to two contradictory courses of action: that we should develop GM crops and that we should not [1], and hence the principle is 'incoherent'.

Like so many other opponents of the precautionary principle, Comstock misunderstands its role. He assumes it is an algorithm for making decisions, which is why he writes of the principle as committing us to one or another course of action.

We want to emphasise that the precautionary principle is not an algorithm for making decisions. It does not make decisions for us, but it is a principle on which to base decisions. It is a principle for assigning the burden of proof, in much the same way that the defendant in a criminal court is assumed innocent until proven guilty 'beyond reasonable doubt' [2]. This important rule reflects society's view that convicting the innocent is far worse than acquitting the guilty. It has a profound effect on the outcome of many trials, but it still leaves the jury with a lot to do. They still have to weigh up the evidence, and they have to decide for themselves what constitutes 'reasonable doubt'.

In the same way, the precautionary principle requires us to assign the burden of proof to those who want to introduce a new technology, particularly in cases where there is little or no established need or benefit and where the hazards are serious and irreversible. It is up to the perpetrators to prove that the technology is safe 'beyond reasonable doubt'. We cannot expect the precautionary principle by itself to tell us what to do about GM crops or any other new technology. Like a jury, we have to weigh up the evidence, and like a jury we have to come to a decision.

So, what is the evidence on GM crops? There is practically no evidence that they are safe, of the kind that could stand up in a court of law. A survey published last June showed that there is less than a handful of papers on the subject of safety assessment published in peer-reviewed scientific journals [3]. The vast majority consists of unpublished reports submitted to regulatory bodies for product approval, and these, far from supporting claims of safety, actually provides evidence to the contrary [4].

The published papers from the industry are no better. For example, Monsanto's study on Roundup Ready soya was seriously flawed. Two papers [5, 6] showed, among other things, significant increases in milk fat in cows and lower weight gains in male rats fed GM soya. There was also a 26.7% increase in a major allergen and growth inhibitor, α -antitrypsin in the GM soya. Monsanto had failed to submit even more damning data indicating that another allergen, a soya lectin, was increased by 100% in retooasted soya beans [7].

On the other hand, there is already plenty of evidence of actual and suspected hazards from findings reported in the scientific literature.

We summarise some of the findings giving *direct* evidence of hazards, omitting those giving indirect evidence of hazards. These have been reviewed extensively [8,9] and only new references are cited below.

1. GM genes such as those coding for bt toxins are harmful to beneficial and endangered insect species. Several of the toxins are also known to be actual or potential allergens for human beings [10] and to be harmful for mice [11].
2. New, unexpected toxins and allergens have arisen from the inherently random, uncontrollable nature of the process whereby GMOs are made.
3. GM constructs in GM plants have spread to related species by cross pollination, and weeds and superweeds resistant to multiple herbicides have appeared.
4. GM constructs containing antibiotic resistance genes have spread to bacteria in the soil and in the gut of bees. These bacteria constitute a reservoir of antibiotic resistance genes, which may be passed on to pathogenic bacteria, making infections very difficult to treat.
5. DNA is found not to be readily broken down by most commercial processing or in the gut of mammals [12].
6. The gut of livestock and human beings contain bacteria that can take up foreign DNA containing antibiotic resistance genes.
7. Viral and plasmid DNA resist complete digestion in the gut of mice and transfer to blood, liver, spleen and kidney cells. In pregnant mice, the DNA passed through the placenta to end up in the cells of the fetus and newborn.
8. Many forms of cancer in humans and animals are associated with random insertion of invasive genetic elements into the cell's genome. Cancer risks are a major concern in human 'gene therapy'.
9. New viruses have been created in many GM plants with viral genes in the GM construct.
10. GM constructs and vectors used in 'gene therapy' generate live viruses in cells used to package them by recombining with dormant viruses in the cells' genome.
11. A deadly virus that killed all its victims has been created accidentally through genetic engineering in the laboratory [13].
12. GM lines are notorious unstable, do not breed true, and do not perform consistently in the field. Evidence is emerging on yield drag, increased use of herbicides, susceptibility to disease, and other failures.

Given the weight of evidence, it seems obvious to us that no GM crops should be planted in open fields, unless and until we can be convinced, by counter-evidence, that the risks are minimal.

But by being cautious, are we, as Comstock and others claim, running equal risks in the other direction, of losing potential benefits, or the ability to deal with needs that may appear in 50 years time? Not at all.

The biotech companies and their supporters say we need GM crops to increase yield to feed a growing world population. Norman Borlaug, father of the green revolution and prominent supporter of agricultural biotechnology, claims GM crops are needed to feed a projected 10 billion.

Again, let us look at the evidence. There is no scientific report documenting that yield has been increased in GMOs compared to non GMOs; quite the contrary is the case, as mentioned earlier, yield drags are frequently reported. What about population increase? According to the United Nations Population Division, world population growth had been slowing down since the 1960s. The estimate in 1998 was that total world population will peak at 7.7 billion in 2040, then go into long term decline to 3.6 billion by 2150, less than two-third of today's number. Similarly, a FAO report published in July 2000 [14] concludes that existing technologies, not counting GMOs, will produce enough and more than enough food to meet population growth. The real problem is one of distribution, as generally acknowledged. People are starving in the midst of plenty.

What about the possibility that at some time in the future we may have to make changes in the crops we grow and that genetic engineering may be needed? Or that with more research, gene biotechnologists will be able to produce new varieties that are indeed better and safer than the present ones? Even allowing for those possibilities does not mean we have to rush ahead with the present inadequately researched and tested technology. Nor does it mean we have to accept unsubstantiated promises that GM crops will provide the answer.

Looking at all the evidence and taking seriously the precautionary principle thus lead to the following conclusion. We should continue doing basic research in molecular genetics, including research relevant to the safety of GM constructs as well as making GM plants; for example, on how to modify existing genes precisely and safely, rather than to transfer in GM constructs haphazardly. But all that should be done in the laboratory and in the greenhouse under carefully contained conditions.

There should also be major effort devoted to developing better varieties of crops by conventional breeding and to research on organic, low-input farming methods. Agroecological farming methods which use crops and knowledge adapted to local conditions have been increasing yields two, three-fold since the 1980s. They provide social, environmental and health benefits in Latin America, Africa and Asia. There are good reasons to encourage farmers to grow and sell locally crops that are adapted to local conditions, and not to pressure them into growing national or international varieties for export. Export industrial agriculture is responsible for a great proportion of the fossil fuel consumption that contributes to climate change. Furthermore, there is incalculable health bonus to be gained in phasing out agrochemicals that are known to be linked to cancers and many other illnesses.

In that way, we can be confident about feeding the world today and for the foreseeable future, and we will still stand to gain from whatever benefits GM technology may bring. The only losers will be the biotech industry, because they cannot afford to wait. The rest of us can.

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5. Hammond et al, 1996, *Journal of Nutrition* 126, 717-26.
6. Padgett et al, 1996, *Journal of Nutrition* 126, 702-16.
7. "Buried data in Monsanto's study on Roundup Ready soybeans" by Barbara Keeler dooles@netins.net(Ericka).
8. Dr. Mae-Wan Ho's statement to public hearing on Chardon LL, October 26, 2000 www.maff.gov.uk, also www.i-sis.org
9. See World Scientists' Open Letter and other papers, www.i-sis.org
10. See Witness Brief by Prof. Joe Cummins to New Zealand Royal Commission on Genetic Engineering www.i-sis.org
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14. *Agriculture: Towards 2015/30*, FAO Global Perspectives Studies Unit, July 2000