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Dr. STANLEY EWEN • Second speech

This paper is available online at www.gmfreeireland.org/conference/trans/S.Ewen2.pdf



Dr. Stanley Ewen is a Consultant Histopathologist with **Grampian University Hospitals Trust** in the UK. He is also a member of the **Independent Science Panel** (www.indsp.org), an international transdisciplinary network of scientists working for the public good. He and **Dr. Arpad Pusztai** co-authored a landmark paper on the health risks of GM food published in **The Lancet** in 1998.

This is the verbatim transcript of a video recording of the second of Dr. Ewen's two speeches at this conference which incorporates all of the tables and photos from his PowerPoint presentation entitled **3 Key papers on GMOs in the last 6 months**. One can download the PowerPoint presentation separately as a 60kb ppt file from www.gmfreeireland.org/conference/PPT/Ewen2.ppt

Numbers in the text refer to the endnotes, which begin on page 8. These endnotes, (together with the notes between round brackets in the main text) have been provided by the conference chair Michael O'Callaghan. Dr. Ewen's first speech may be found at www.gmfreeireland.org/conference/trans/sewen1.php.

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Michael O'Callaghan:

It's my great pleasure now to introduce Dr. Stanley Ewen, who has come all the way from Scotland. He's a member of the Independent Science Panel on GM [1].

Dr. Ewen:

Thank you very much. Nice to be with you, as I said before. We are enjoying ourselves enormously in this part of Ireland, thank you very much!

This is the second part of a talk that started yesterday [2]. And if I can summarise it very quickly, what I said yesterday, what we were able to show – Pusztai and myself [3] were able to show that there is a very definite growth factor effect of GM food – the sort of GM food that

we had fed to the rats. And the finger of suspicion pointed to the promoter – that is to say, the little engine driver (CaMV gene) [4] that's inserted with the genetic information that's shot into the genome of the recipient plant.

The second point I tried to make is that many of these food products most certainly bind to the gut cells. Now for example, Bacillus thuringiensis toxin [5] will certainly bind to any animal intestine, and most certainly will bind, therefore, to the human gut as well.

So problems may follow, I believe – and this is an opinion – other people will have different opinions of course. But in my opinion, anything that's a growth factor and that is absorbed into cells in the gut may have consequences [6].

Slide 1: 3 key papers on GMOs in the last 6 months

By Dr. Stanley Ewen

Independent Science Panel on GM.

But I'd like to present to you very quickly – I've been told I must do it quickly – three recent pieces of information that have occurred over the past 6 months that I think are highly interesting and highly relevant to this whole debate on safety and GM food. So without any more ado, I'll just press on. And if I use a forbidden word or a word that you don't understand, you must challenge me immediately and say "I don't understand that, can you express it in layman's English?"

Slide 2: GM technology

- Gene of new protein + β -glucuronidase gene + antibiotic gene (ampicillin) are inserted somewhere into host genome.
- The cassette also includes CaMV promoter inserted adjacent to transgene to drive the new genes into maximum expression.
- Can the CaMV promoter survive digestion?

Well GM technology, of course, was explained by Deborah Garcia's presentation in the film [7]. But just to remind you: of course, it's a gene of a new protein, plus beta glucuronidase [8] as a marker gene [9] – the GUS gene, anti-biotic (resistance) gene [10] which is usually Ampicillin [11] but could be Kanamycin [12], and some inserted – this lot – is then inserted somewhere into the host genome, we don't know where [13]. The cassette also – this whole business of the new protein gene, and the beta glucuronidase and the antibiotic gene is a "cassette" – that's what the technical term is. And this cassette also includes, of course, cauliflower mosaic virus (CaMV) promoter [14], and that is inserted adjacent to the trans-gene to drive the new genes into maximum expression in the plant recipient.

Slide 3: Regulatory Committees

- Regulation uses simple analysis of GMO crops to claim substantial equivalence [15].
- Regulation accepts biotechnology industry claims derived from chemical evidence (HCl + pepsin) that bacterial recombinant proteins are digested in stomach - but transgenic crop proteins have never been tested.

Slide 4: Plant DNA and the human GI tract ('04)

- First human study of GM soya ingestion (Netherwood et al.).
- 3 of 7 ileostomy patients contained CaMV 35S promoter before study had started.
- All 7 passed excreta containing GM DNA after test meal ("surprised that any could survive").
- Faeces of 12 volunteer controls contained no CaMV (were they age and sex matched?).

The question is, can the cauliflower mosaic virus promoter survive digestion? Because this was one of the key issues: what was causing the growth effect that I had observed in the rats? [16] And of course it brings up the study that was done in England with GM soya [17]. And just to say – I'm going to go through this even more quickly than usual if you don't mind – but just to say that I did present this one yesterday; it was interesting to note that three of the seven people who were tested actually contained the (CaMV) promoter before the study started. That was very interesting, because as far as we knew there was no possibility of GM food in England or Scotland. However, they did contain it, and one can speculate it might have come from soya or whatever [18].

Slide 5: CaMV promoter is active in human Caco cells

- Traavik et al have shown that CaMV accesses human colon cells in culture (Eur. Food Res. Technol 222, 185 2006) and can drive expression of green fluorescent protein as well as luciferase in Caco cells in vitro.
- CaMV is weaker than the strong promoters of EBV or CMV.

So the question then is, "is the cauliflower mosaic virus promoter active in human cells?" And this word here (i.e. Caco) stands for cancer colon – it's a sort of acronym.

And these are cells derived from a human cancer, and then they're going to be exposed to the cauliflower mosaic promoter. Because the paper is a very interesting one indeed, and is fundamental to understanding what can happen.

Terje Traavik, from Tromso in North Norway [19], has shown in January this year (2006) [20] that cauliflower mosaic virus can access these human colon cells in culture; and they can drive the expression of a green fluorescent protein – it's just a marker, the words don't really mean very much – but the point is that this promoter can drive the expression: it gets into the cells of the body!

Now the cauliflower mosaic virus was selected because it was a plant promoter, and it was thought therefore that it wouldn't be harmful to human tissue and wouldn't or couldn't involve human tissue whatsoever. And Terje Traavik had a sort of positive control – Epstein-Barr virus or the cytomegalic virus – and these were much more powerful in promoting; but still, cauliflower mosaic virus entered the cells and had this weak promotion effect. It was really support for the fact that this growth effect that we had noted was most likely to be due to the cauliflower mosaic virus. A very exciting, observation, and fully published in a well-refereed journal. [21]

Slide 6: The safety threat of glyphosate

- Glyphosate is similar to glutamic acid and the number of glutamate receptors in rat pup brain can be reduced by glyphosate. 70% of all GM crops are engineered to produce glyphosate resistance (rye grass for golf courses).
- Spraying of glyphosate causes build up of N-acetyl glyphosinate (NAG) in plant tissues.
- Colonic bacteria can retoxify NAG (33% goat colon, human?).

The other thing I'd like to bring to your attention is the safety threat of glyphosate [22]. Of course, it is similar to glutamic acid, which is a neurotransmitter in the brain, and 70% of all GM crops are engineered to produce glyphosate resistance. And it's been suggested that GM ryegrass should be used in the future for golf courses [23].

Michael O'Callaghan:

Glyphosate is what is in Roundup (weedkiller), which is already spread all over Irish (conventional non-organic) farms.

Dr. Ewen:

Yes.

Now the spraying of glyphosate then causes... because the way in which the resistance operates is that the Roundup-ready (GMO) plant contains an enzyme which acetylates [24] glyphosinate and produces N-acetyl-glyphosinate or gluphosinate, depending on the formulation, which I'm going to call NAG from now on, in plant tissues.

Now the key question is, once the plant has detoxified it, it stores it in all its tissues – make no mistake: can colonic bacteria [25] re-toxify the NAG?

Now it does occur. In fact 33% of the active glyphosate can occur in the goat colon: this has been recorded. But what about the bacteria in the human colon? Is that a possibility?

I think it possibly is, but nobody has shown it.

Slide 7: Glyphosate toxicity

- Overdose produces respiratory distress, fits eventually coma.
- Smaller doses may influence behaviour.
- In humans GM corn or GM soya will contain NAG, hence glyphosate is likely to be deacetylated in human gut mainly colon.

And just to say that of course glyphosate toxicity, overdose produces respiratory distress, fits, and eventually, coma. Smaller doses may influence behaviour.

But in humans, GM corn (maize) and GM soya will contain NAG, hence glyphosate is likely to be de-acetylated in the human gut, mainly in the colon.

Slide 8: GM crop herbicide safety

- Formulations may cause synergistic, and dose dependent, delay of cells into M-phase.
- S. Richard June 2005 (Env. health perspect 113, 716) has shown that glyphosate is very toxic to cytotrophoblast (JEG3 cells from choriocarcinoma) at levels "100 times" lower than agricultural levels. Those housed next to fields are at great danger from abortion (farmers should be obliged to identify pregnant women nearby).

Formulations (of Roundup weedkiller) may be synergistic (i.e. the health risks of the whole mixture may not be predicted by knowledge of the health risks of the various components taken separately) [26]. And it's a dose-dependent effect.

Now the important second paper of this trio of interesting papers is from Sophie Richard; it's a paper in a French journal – Environmental Health Perspectives – in June, exactly last year [27]. And she showed that glyphosate is very toxic indeed to the cytotrophoblast. Now the cytotrophoblast is one of the layers of the human placenta. Simple glyphosate was toxic at levels 100 times lower than agricultural levels! But interestingly enough, Roundup was twice as effective as that; so it was toxic at 200 times lower than agricultural levels!

So we have noticed in the past, as doctors, that people, ladies, next to a field that's been sprayed (with Roundup) often presented with abortion (miscarriage). My suggestion is that if you're going to be spraying a field with glyphosate, the farmer should be obliged to identify any ladies who may be pregnant next door to the field and give them warning. Because I do believe that there is a risk to the placenta. [28]

Slide 9: Survival of rat pups fed on GM soya (Dr. Ermakova, Moscow)

- Female rats fed GM soya (5-7g per day) 2 weeks before mating, during pregnancy and during lactation (New journal - ECOSInform 1, 4-10).
- 55% mortality in pups and 36% weighed < 20g (average normal wt 30g).
- Control group (normal soya and no soya) was 6.7% and 6% respectively.
- Could the GM soya contain high levels of glyphosate?

To follow on from that quite neatly, I suppose, is the survival of rat pups fed on GM soya. And this is the paper by (Dr. Irina Ermakova) [29], from Moscow, that was written up in a brand new Russian journal called ECOSInform [30], and it was in the first issue, and of course she was feeding female rats with GM soya. There's the dose, and then two weeks before mating, also during pregnancy, and later, during lactation.

There was a 55% mortality in the pups, 36% weighed less than 20 grammes, and that was compared to normal. The control group, fed on normal soya and no soya, was 6.7% and 6% respectively. So there was an eight times increase in mortality in the rat pups.

Could the GM soya contain high levels of glyphosate? This was never measured, but could it?

Slide 10: Cassette beta-glucuronidase

- Steroids, toxins and drugs are detoxified by liver to glucuronide.
- Normal small intestine almost sterile thus bacterial deglucuronidation limited.
- But GUS gene-derived β -glucuronidase could amplify deglucuronidation in the small intestine resulting in higher circulating levels of toxins, steroid and drugs (M. Hill personal commun.)

The other thing I'd like to mention, and this is going to be quite quick, is the way in which the body handles steroids [31] – that's to say the natural steroids which we produce -, toxins and drugs: they're detoxified by the liver of course, by converting to a glucuronide [32]. It's simply something that is added on to the drug to make it soluble and harmless, and then it's passed out in the bile [33]. Now the normal small intestine in the human is almost but not quite sterile; thus bacterial de-glucuronidation is limited. But, the GUS gene [34] which I mentioned already in the beginning, in the cassette is gene-derived and it produces beta-glucuronidase, that's its effect. That could break down the glucuronide back into the active steroid or active toxin. And therefore if that's absorbed from the small intestine you could get higher levels of steroid than normal.

Now this is a question I'm asking: is this part of the explanation of the increasing frequency of human breast cancer and human prostate cancer? [35] Those two cancers are definitely endocrine-dependent [36] – in other words, steroid-dependent.

That was from a chap called Hill [37], in Puerto Rico.

Slide 11: Transgenic pea makes mice ill (NHMRC Australia Nov 2005)

- Bean α -amylase inhibitor inserted into pea.
- Fed to mice 2x/wk for 4 wks.
- Specific circulating IgG at 2 wks and at significant level at 4 wks.
- DTH response in footpad.
- Eosinophils in challenged lung lavage fluid.
- Thus transgenic expression of non-native proteins can lead to altered immunogenicity.
- No GM crop tested like this before but must be.

The other key paper is (on) the transgenic pea that makes mice ill [38]. And that was a report from Australia, and what they did was to put the bean alpha-amylase inhibitor [39] into the pea. It was fed to mice two times a week for four weeks, and they measured the circulating IgG [40] – that's just a particular type of antibody – and they noticed a response. It's far too difficult for me to explain what this is, but just to say that there is a response when you inject – it's like getting a tuberculin test [41] in your skin: when you inject a tiny amount of the Tuberculosis bacillus and you get a reaction. Well in the same way, when they injected a tiny amount of the amylase inhibitor, they got this reaction in the foot-pad of the mouse. They found the inflammatory cells were present in the challenged lung - you give a little bit into the lung – and they found that they got an inflammatory cell response [42]. The assumption then was that transgenic expression of non-native proteins can lead to altered immunogenicity [43].

Now no GM crop has ever been tested in this way before, but I demand that all GM crops in future be tested in this way, looking for allergy, and in particular anything new that's coming along should be tested.

Slide 12: GM corrupts truth

4 ways to hide the truth:

1. Shape research by control of funding and discredit critical voices.
2. Market GMOs as the answer to hunger in Africa.
3. Promote the biotech industry by manipulating regulatory frameworks.
4. Prevent labelling food containing GMO.

In summary, you'll be glad to hear, Michael, there are four ways to hide the truth:

One: you can shape research by control of funding and discredit critical voices.
Two: you can market GMOs as the answer to hunger in Africa.
You can promote the biotech industry by manipulating regulatory frameworks.
And you can prevent labeling of food containing GMOs [44].

Now it's not me who said that. It was the World Council of Churches report in December 2005 [45].

Slide 13: Knowledge privatisation

- In August 2005 Syngenta filed 15 global patents on 30,000 gene sequences from rice.
- If granted then Syngenta would have a monopoly over rice, wheat, rye, fruits and vegetables.
- Syngenta would be able to determine price, access, research and re-use of seeds in the near future.

Slide 14: GM in Europe

- Austria (Joseph Proell) will re-open the GM debate at Brussels on 09.03.06.
- His question is "why should GMOs be approved when there is no qualified majority?".
- Austria, Greece, Luxembourg, Hungary and Poland oppose GM food.
- McConnell wants a U-turn if contamination of crops can be prevented.
- Director of Scot FSA (Paterson) fast tracked Monsanto crops in Canada.

Thank you.

ENDNOTES:

1. The Independent Science Panel (<http://www.indsp.org>) is an international transdisciplinary network of scientists committed to science for the public good. Its many publications include the excellent report *The Case for a GM-free Sustainable World*, which explains how the biotech lobby's pseudo-scientific claims that GMOs are safe are based on the outdated reductionist paradigm which ignores 30 years of new scientific insights in molecular biology, ecology, complexity theory, and the emergent properties of complex systems. There is no need for "new scientific evidence" to prove the health and environmental risks of releasing GMOs. You can download the report as a 408kb pdf file from [www.gmfrireland.org/documents/science/A GM-Free Sustainable World.pdf](http://www.gmfrireland.org/documents/science/A%20GM-Free%20Sustainable%20World.pdf) .
2. For Dr. Ewen's first speech see www.gmfrireland.org/conference/trans/sewen1.php .
3. Dr. Arpad Pusztai and Dr. Stanley Ewen published a study about the potential dangers of genetically modified potatoes in *The Lancet* in 1998: *Ewen SWB, Pusztai A (1999): Effect of diets containing genetically modified potatoes expressing Galanthus nivalis lectin on rat small intestine. Lancet 354:1353-1354*. According to *The Lancet* editor, Richard Horton, the former Vice-President and Biological Secretary of The Royal Society and President of the Academy of Medical Sciences Professor Lachmann phoned him during the peer review process threatening that his job would be at risk if he published Pusztai's paper, and called Horton "immoral" for publishing something he knew to be "untrue". After the article was published, the biotechnology industry and The Royal Society again attacked Horton and *The Lancet*. But 24 independent scientists later confirmed the accuracy of Pusztai's research. See www.gmwatch.org/archive2.asp?arcid=1132 and Dr. Pusztai's homepage at <http://www.freenetpages.co.uk/hp/a.pusztai> for details.
4. The 35S CaMV promoter gene (taken from the Cauliflower Mosaic virus) is closely related to human hepatitis B virus, and less closely, to retroviruses such as the AIDS virus. It is used in most GM crops to boost very high levels of expression of the other foreign genes with the desired traits which are introduced as the genetically modified "gene expression cassette." The CaMV promoter can drive the synthesis of related viruses. It is active in all living systems from bacteria to higher plants. Two kinds of potential hazards exist: the reactivation of dormant viruses, and recombination between the CaMV promoter and other viruses, dormant or otherwise, to generate new, super-infectious viruses or viruses with broadened host-range. It has been claimed that the 35S promoter is plant-specific and would not be active in mammalian cells, and hence would not pose risks linked to the consumption of GE food and feed in the event that plant DNA fragments are taken up from the mammalian gastrointestinal tract. However, this claim has not been supported by experimental data.

On the contrary, there have already been published reports indicating that this assumption might be incorrect, for example, previous research has indicated the potential of the 35S promoter to be active in mammalian systems. More recently, direct evidence that the 35S promoter is active in mammalian cell cultures has been presented.

Of particular importance are the cells lining the intestinal wall, given that the gastrointestinal tract will be the first site of exposure to GE food and feed.

In a recently published paper, scientists have demonstrated that the 35S CaMV promoter was able to drive the expression of two reporter genes (gfp and luc) in the human cell line Caco-2, which share a number of characteristics with human enterocytes (cells lining the intestinal wall).

While the protein expression levels were modest compared to results obtained with strong mammalian promoters, the significant observation remains that the 35S CaMV promoter, generally assumed to be plant specific, initiated significant protein expression levels in host cells that share important characteristics with those lining parts of the human gastrointestinal tract.

These results, taken together with other published papers, leads the scientists to conclude that the 35S CaMV promoter is capable of initiating gene expression in some mammalian cell lines under a range of different conditions and circumstances. Computer based searches further indicate that transcriptional activation by the 35S promoter may be stronger in other human and animal cell types than those investigated so far.

This research clearly warrants further serious investigation, including by in vivo means.

Whether there are GE food safety implications would be linked to the process of foreign DNA uptake from the human gastrointestinal tract. The uptake of food-derived DNA fragments from the intestines into the blood stream and some organs has already been demonstrated in various animal species and recently also in humans.

Given the potential for the 35S promoter to initiate gene expression in some mammalian cells, if the intact 35S promoter is taken up, the biological consequences are potentially great (for example, inappropriate expression of genes may occur).

For more information see: <http://www.gmwatch.org/archive2.asp?arcid=5945> .

See also: *The 35S CaMV plant virus promoter is active in human enterocyte-like cells European Food Research and Technology (2005), DOI 10.1007/s00217-005-0154-3* Marit R. Myhre (2, 4), Kristin A. Fenton (4), Julia Eggert (3), Kaare M. Nielsen (3) and Terje Traavik (1, 2)

5. The so-called Bt crops are modified with genes from the soil bacterium *Bacillus thuringiensis* so as to produce their own pesticides. These include Bt maize, Bt cotton etc. and account for 18% of GM crops currently being grown. 71% of GM crops are resistant to weedkillers (including "Roundup-Ready" crops patented by Monsanto. The remaining 11% of GM crops are both resistant to weedkillers and produce their own pesticides. Virtually no currently-grown GM crops are designed to increase yields, boost nutrition or survive harsh environmental conditions (e.g. drought).

Specific strains of *Bacillus thuringiensis* produce slightly different types of Bt toxin which are damaging to certain species of insects including the European corn borer, southwestern corn borer, tobacco budworm, cotton bollworm, pink bollworm and the Colorado potato beetle. *Bacillus thuringiensis* is also used as a biological control agent by organic farmers.

Genetically modified Bt crops including Bt cotton, Bt corn, and Bt potatoes are being grown in the United States, Canada, Argentina, South Africa, France, and Spain.

See *Possible Health Hazards of Genetically Engineered Bt Crops: Comments on the human health and product characterization sections of EPA's Bt Plant-Pesticides Biopesticides Registration Action Document*, by Michael Hansen, Ph.D., Consumer Policy Institute/Consumers Union, Presented to the EPA Science Advisory Panel Arlington, VA, USA, October 20, 2000: <http://www.organicconsumers.org/ge/btcomments.cfm> .

In India, Bt cotton has lead to massive crop failures, including 68% lower incomes for farmers (<http://www.gmwatch.org/archive2.asp?arcid=6444>), thousands of farmer suicides: <http://www.hindu.com/thehindu/holnus/002200609070310.htm>, and reports of sheep deaths.

In May 2005, an illegal shipment of 2,546 tonnes of illegal genetically modified Bt10 maize was unloaded at Greenore, Co. Louth. For details see <http://www.gmfreeireland.org/scandal> .

In September 2006, leading scientists issued the following statement on the potential allergenicity of the Bt toxin, Cry1AC:

Scientists' statement from
Professor Ian F. Pryme
Professor Gilles-Eric Seralini
Dr. Christian Velot

5 September 2006

We, the undersigned, note with concern the recent discoveries of contamination of rice [1] and rice products, including baby food [2], with an experimental genetically engineered (GE) rice. The GE rice contains a gene for the Cry1Ac protein, or possibly for a fusion Cry1Ab/Cry1Ac protein with similar immunogenic properties to Cry1Ac3. Cry1Ac has not been approved for human consumption in any food crop and there is concern over its potential allergenicity.

Research [4] into the gene for Cry1Ac has found that

1. Cry1Ac protoxin is a potent immunogen.
2. The protoxin is immunogenic by both the intraperitoneal (injected) and intragastric (ingested) route.
3. The immune response to the protoxin is both systemic and mucosal.
4. Cry1Ac protoxin binds to surface proteins in the mouse small intestine, and this could induce mid or long-term effects on mammalian health.

Therefore, we urge the developers and regulatory authorities of this GE rice to proceed with caution with the use of the gene for the Cry1Ac in any part of the genetic construct within the GE rice. It is possible that humans, in particular sub-populations such as infants and small children could be exposed to immunogenically-significant amounts of Cry proteins contained in foods.

A thorough evaluation of its food safety prior to any import, consumption, approval or further development of this GE rice would be necessary as rice is a staple food crop. Studies following the steps recommended by the FAO/WHO expert consultation [5] to evaluate allergenicity should be conducted by independent scientists, and their results published in peer-reviewed journals to allow evaluation of food safety. In addition, further studies into the potential allergenicity of Cry1Ac and other Bt proteins should be undertaken as a matter of the utmost urgency.

Signed

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Notes:

1. Zi, X. (2005) GM rice forges ahead in China amid concerns over illegal planting. *Nature Biotechnology* 23: 637.
2. <http://www.greenpeace.org/china/en/press/releases/20060314-heinz-rice-cereal>.

3. Tu, J., Zhang, G., Datta, K., Xu, C., He, Y. Zhang, O., Khush, G. & Datta, S.K. (2000) Field performance of transgenic elite commercial hybrid rice expressing *Bacillus thuringiensis*-endotoxin. *Nature Biotechnology* 18: 1101-1104.

4 Moreno-Fierros, L. Garcia, N. Gutierrez, R. Lopez-Revilla, & R. Vazquez-Padron, R.I.(2000) Intranasal, rectal and intraperitoneal immunization with protoxin Cry1Ac from *Bacillus thuringiensis* induces compartmentalized serum, intestinal, vaginal and pulmonary immune responses in Balb/c mice. *Microbes Infect* 2: 885-90; Vazquez-Padron, R.I, Moreno-Fierros, L. Neri-Bazan, L, de la Riva, G.A & Lopez-Revilla, R. (1999) *Bacillus thuringiensis* Cry1Ac protoxin is a potent systemic and mucosal adjuvant. *Scand J Immunol* 49: 578-584; Vazquez-Padron, R.I Moreno-Fierros, L. Neri-Bazan, L, de la Riva, G.A & Lopez-Revilla, R. (1999) Intragastric and intraperitoneal administration of Cry1Ac protoxin from *Bacillus thuringiensis* induces systemic and mucosal antibody responses in mice. *Life Sciences* 64: 1897-1912; Vazquez-Padron, R. I., Moreno-Fierros, L. Neri-Bazan. L. Martínez-Gil, A.F., de la Riva, G.A. & Lopez-Revilla, R. (2000) Characterization of the mucosal and systemic immune response induced by Cry1Ac protein from *Bacillus thuringiensis* HD 73 in mice. *Braz J Med Biol Res* 33: 147-155; Vazquez-Padron, R. I., Gonzales-Cabrera, J., Garcia-Tovar, C. Neri-Bazan, L., Lopez-Revilla, R., Hernandez, M., Moreno-Fierros, L. & de la Riva.G.A. (2000) Cry1Ac protoxin from *Bacillus thuringiensis* sp. kurstaki HD73 binds to surface proteins in the mouse small intestine. *Biochem Biophys Res Comms* 271: 54-58. Guerrero, G. G., Dean, D.H. & Moreno-Fierros, L. (2004) Structural implication of the induced immune response by *Bacillus thuringiensis* Cry proteins: role of the N-terminal region. *Molecular Immunology* 41: 1177-1183.

5. FAO/WHO 2001. Evaluation of allergenicity of genetically modified foods. Report of a joint FAO/WHO expert consultation on allergenicity of foods derived from biotechnology, 22 - 25 January 2001. Rome, Italy.

6. Consequences may include cancer. Article 14 of European food safety legislation (EC/178/2002) calls for the assessment of the long term effects of GMOs and effects of subsequent generations. However, to date the long term effects of eating or growing GM foods seem to be completely ignored. A leaked European Commission document submitted to the World Trade Organisation admits "there is no unique, absolute, scientific cut-off threshold available to decide whether a GM product is safe or not". For details, download the report *Hidden uncertainties - What the European Commission doesn't want us to know about the risks of GMOs*, Friends of the Earth Europe and Greenpeace, April 2006: http://www.foeeurope.org/publications/2006/hidden_uncertainties.pdf .
7. *The Future of Food* is a documentary film produced and directed by Deborah Koons Garcia, who spoke at the Green Ireland conference (for transcript of her speech see <http://www.gmfreeireland.org/conference/trans/dkoonsgarcia.php>). Her film provides an in-depth look at the genetically modified foods controversy, and is an excellent community organising tool. Shot on location in the U.S., Canada and Mexico, the film examines the complex web of market and political forces that are changing what we eat as huge multinational corporations seek to control the world's food system through patented GM crops which invade conventional and organic crops and require contaminated farmers to pay annual patent royalties or face patent-infringement lawsuits. The film explores alternatives to large-scale industrial agribusiness, placing organic and sustainable agriculture as solutions to the global farm crisis. Running time: 90 minutes. Order the DVD for €25 from GM-free Ireland on (0404) 43 885, or contact us to arrange a screening, cinema release or TV broadcast in your community.
8. Glucuronidases are glycoside hydrolases that cleave glucuronic acid glycosides (glucuronides). Human glucuronidase is a lysosomal glycosidase, and hydrolyzes the glucuronide groups from proteins. Glucuronidase exhibits both endo-glycosidase and exo-glycosidase activities, meaning that it can cleave monosaccharides from the middle of a chain or from the end.

Glycosylation is an interesting phenomenon that occurs in the endoplasmic reticulum (where carbohydrates are added to arginine groups via a process called N-linked glycosylation) and in the Golgi apparatus (where carbohydrates are added to

serine/threonine groups via a process called O-linked glycosylation). This process is required for the appropriate folding of most proteins. Errors in glycosylation prevent many proteins from functioning properly.

Glucuronidase fits well into the lysosome's role as a recycling center for the cell.

An assay with beta-Glucuronidase (GUS assay) can find out, when and where a certain gene is transcribed.

Preparations of beta-Glucuronidase from the snail *Helix pomatia*, historically referred to by the trademark Glusulase, are used to digest the ascus of the yeast *Saccharomyces cerevisiae* after sporulation. *E. coli* is among the few bacteria that can synthesize glucuronidase and therefore this trait is used to identify it.

9. A marker gene is a gene or short sequence of DNA that can be identified and tracked which acts as a tag for another, closely linked, gene on the same chromosome (the target gene). It is then used to check for the presence of the target gene. Most GMO crops contain anti-biotic resistance marker genes. Following the random insertion of the foreign DNA cassette, the target recipient organisms are soaked in a related antibiotic; those organisms which survive must therefore have been successfully modified with the anti-biotic resistance gene along with the intended transgenic DNA.
10. Anti-biotic resistance gene: see note 9 above.
11. Ampicillin is a beta-lactam antibiotic that has been used extensively to treat bacterial infections since 1961. It can sometimes result in allergic reactions that range in severity from a rash to potentially lethal anaphylaxis. Belonging to the group of beta-lactam antibiotics, ampicillin is able to penetrate Gram-negative bacteria. It inhibits the third and final stage of bacterial cell wall synthesis, which ultimately leads to cell lysis. Ampicillin is closely related to amoxicillin, another type of penicillin, and both are used to treat urinary tract infections, otitis media, uncomplicated community-acquired pneumonia, *Haemophilus influenzae*, salmonellosis and *Listeria meningitis*. It is used with flucloxacillin in the combination antibiotic co-fluampicil for empiric treatment of cellulitis; providing cover against Group A streptococcal infection whilst the flucloxacillin acts against the *Staphylococcus aureus* bacterium. Ampicillin is often used in molecular biology as a test for the uptake of genes (e.g., by plasmids) by bacteria (e.g., *E. coli*). A gene that is to be inserted into a bacterium is coupled to a gene coding for an ampicillin resistance (in *E. coli*, usually the *bla* gene, coding for β -lactamase). The treated bacteria are then grown on a medium containing ampicillin. Only the bacteria that successfully take up the desired genes become ampicillin resistant, and therefore contain the other desired gene as well.
12. Kanamycin (marketed under the brand name Kantrex®) is an aminoglycoside antibiotic, available in both oral and intravenous forms, and used to treat a wide variety of infections. Kanamycin works by affecting an unknown aspect of translocation (part of the translation process in which the mRNA is shifted one codon in relation to the ribosome), and by causing messenger RNA (mRNA) to be misread by the ribosome, causing a lethal level of translational errors. Common side effects include changes in hearing (either hearing loss or ringing in the ears), toxicity to kidneys, and allergic reactions to the drug.
13. The "cassette" of transgenic DNA that is inserted into a GMO crop ends up in an unknown location in the recipient plant's genome when the method of insertion is random. Current crop plant transformation methods typically require tissue culture (i.e. regeneration of an intact plant from a single cell that has been treated with hormones and antibiotics and forced to undergo abnormal developmental changes) and either (a) infection with a pathogenic organism (*A. tumefaciens*), (b) bombardment with a "gene gun" which blasts tiny particles of gold or tungsten coated with the modified DNA into the recipient organism (like a microscopic shotgun) or (c) when the process of insertion is made by

zapping the recipient organism with electricity to create holes in its surface, through which the transgenic DNA penetrates.

It would therefore not be surprising if plant transformation resulted in significant genetic consequences which were unrelated to the nature of the specific transgene. Indeed, both tissue culture and transgene insertion have been used as mutagenic agents (Jain 2001, Krysan *et al.* 1999).

In theory, plant transformation could result in exact insertion of a single transgene without further genomic disruption. In practice, this rarely, if ever, occurs. In addition to the transgene, each transformed plant genome contains a unique spectrum of mutations resulting from (a) tissue culture procedures, (b) gene transfer methods such as *Agrobacterium*-mediated or particle bombardment transfer, (c) transgene insertion and (d) superfluous DNA insertion. These transformation-induced mutations can be separated into two types: those introduced at the site of transgene insertion, i.e. *insertion-site mutations* and those introduced at other random locations, i.e. *genome-wide mutations*.

For details see *Genome Scrambling – Myth or Reality? Transformation-Induced Mutations in Transgenic Crop Plants*. By Allison Wilson, PdD, Jonathan Latham, PdD, and Ricarda Steinbrecher, Phd. EcoNexus Technical Report, October 2004:

Summary: <http://www.econexus.info/pdf/ENx-Genome-Scrambling-Summary.pdf> .

Full report: <http://www.econexus.info/pdf/ENx-Genome-Scrambling-Report.pdf> .

14. CaMV promoter – see note 4 above.
15. The economic argument that GM foods are “substantially equivalent” to their conventional counterparts is used by the agbiotech industry in their global strategy to try to force countries to open up their markets to GM food and farming. That’s because governments which sign the WTO’s World Trade Agreement must agree in principle to avoid any impediments to trade in so-called “like products” — regardless of differences in the process and production methods used to produce them. But from scientific point of view, GM crops and food are substantially *different* from their conventional counterparts because they are, by definition, transgenic — i.e. they are modified to contain mixtures of genetic material from various species which could not possibly occur in nature. Moreover, the controversial patents on GMO seeds and crops — which provide the legal means for the GMO patent owners to demand crop patent royalties and to file patent infringement lawsuits against contaminated farmers — are specifically based on the transgenic genes they contain.

The transgenic DNA in GM crops results in novel proteins which have never existed before in nature, and which our immune systems may be unable deal with or unable to recognise. This causes one class of health risks posed by GM foods.

In May 2003, the US, supported by Canada and Argentina, launched a WTO trade dispute against the EU concerning the EU authorisation regime for GMOs, alleging the EU’s *de facto* moratorium on approvals of GM foods between 1999-2003 violated the requirement that GMO authorization requests be processed without “undue delay” under the WTO’s Agreement on Sanitary and Phytosanitary Measures (SPS Agreement). The WTO also agreed with the co-complainants that marketing or import bans on GMO products in six EU member states — France, Germany, Austria, Italy, Luxembourg, and Greece — were in violation of WTO rules. The WTO’s secretive and undemocratic trade dispute panel, however, said the co-complainants failed to prove that the EU’s assessment procedures were not appropriate in relation to the actual risk posed by GM products, that there was insufficient scientific evidence to justify its assessment procedures, and that the EU failed to apply its procedures in a consistent manner by subjecting biotech products and products produced using biotech processing aids to different approval requirements. The panel also refused to rule on whether GM foods are generally safe or not. For details see <http://www.gmfreeireland.org/WTO> .

16. Ewen SWB, Pusztai A (1999): Effect of diets containing genetically modified potatoes expressing *Galanthus nivalis* lectin on rat small intestine. *Lancet* 354:1353-1354. See also Dr. Stanley Ewen's first speech at the Green Ireland conference at <http://www.gmfreeireland.org/conference/trans/sewen1.php> .

17. The Newcastle feeding study by Netherwood et. Al. (published 2003) involved a small portion of GM soya fed to just seven ileostomy patients:
www.foodstandards.gov.uk/news/newsarchive/statement .

See also <http://www.gmwatch.org/archive2.asp?arcid=990> and comments by Dr Michael Antoniou (Senior Lecturer in Molecular Genetics, GKT School of Medicine, King's College London) at <http://www.gmwatch.org/print-archive2.asp?arcid=143> .

18. See Dr. Stanley Ewen's first speech at the Green Ireland conference at <http://www.gmfreeireland.org/conference/trans/sewen1.php> .

19. Terje Traavic is Professor in Gene Ecology at the Department of Microbiology and Virology, School of Medicine, University of Tromso, and also Scientific Director of the Norwegian Institute of Gene Ecology (www.genok.org) at the University of Tromso, where he directs a GM food research programme funded by the Norwegian Research Council.

20. European Food Research and Technology, 222, 185 2006.

It has been claimed that the 35S promoter is plant-specific and would not be active in mammalian cells, and hence would not pose risks linked to the consumption of GM food and feed in the event that plant DNA fragments are taken up from the mammalian gastrointestinal tract. However, this claim has not been supported by experimental data. Previous research has indicated the potential of the 35S promoter to be active in mammalian systems. The new research provides direct evidence that the 35S promoter is active in mammalian cell cultures.

See also: *The 35S CaMV plant virus promoter is active in human enterocyte-like cells, European Food Research and Technology (2005), DOI 10.1007/s00217-005-0154-3, Marit R. Myhre (2, 4), Kristin A. Fenton (4), Julia Eggert (3), Kaare M. Nielsen (3) and Terje Traavik (1, 2).*

21. European Food Research and Technology, 222, 185 2006.

22. Glyphosate — the principal active ingredient in Roundup weedkiller manufactured by Monsanto — is 100 times more toxic than previously thought. See *Differential Effects of Glyphosate and Roundup on Human Placental Cells and Aromatase*, by Sophie Richard, Safa Moslemi, Herbert Sipahutar, Nora Benachour, and Gilles-Eric Seralini of the Laboratoire de Biochimie et Biologie Moléculaire, USC-INCRE, Université de Caen, Caen, France, published in *Environmental Health Perspectives* Volume 113, Number 6, June 2005. The paper shows that glyphosate acts as a disruptor of mammalian cytochrome P450 aromatase activity from concentrations 100 times lower than the recommended use in agriculture; this is noticeable on human placental cells after only 18 hr, and it can also affect aromatase gene expression. It also partially disrupts the ubiquitous reductase activity but at higher concentrations. Its effects are allowed and amplified by at least 0.02% of the adjuvants present in Roundup, known to facilitate cell penetration, and this should be carefully taken into account in pesticide evaluation. The dilution of glyphosate in Roundup formulation may multiply its endocrine effect. Roundup may be thus considered as a potential endocrine disruptor. Moreover, at higher doses still below the classical agricultural dilutions, its toxicity on placental cells could induce some reproduction problems. See <http://ehp.niehs.nih.gov/members/2005/7728/7728.html>

23. GM Roundup-resistant ryegrass and bentgrass being marketed for golf courses present a high risk of contaminating surrounding areas with GM superweeds. In a seminal study of

gene contamination from genetically engineered creeping bentgrass, the U.S. Environmental Protection Agency found evidence of "multiple instances at numerous locations of long-distance viable pollen movement from multiple source fields of GM (genetically modified) creeping bentgrass." The bentgrass being studied is engineered to resist Monsanto's Roundup herbicide and is the subject of a lawsuit filed by Center for Food Safety (CFS) and others seeking to halt open-air trials of the turf grass. "The EPA has just shown that genetically engineered bentgrass will contaminate numerous related species over vast areas and prove to be completely uncontrollable," said Joseph Mendelson, legal director at Center for Food Safety. "The only prudent course of action at this point is for the USDA to halt all new bentgrass field trials until it undertakes a full environmental impact statement for each field test."

http://www.centerforfoodsafety.org/press_release9_20_2004.cfm

See also: *Immediate Injunction Sought on Field Tests of Genetically Engineered Turf Grass* at http://www.centerforfoodsafety.org/press_release10_5_2004.cfm.

24. Acetylation (or ethanoylation) describes a reaction that introduces an acetyl functional group into an organic compound. Moreover, it is that process of introducing an acetyl group into a compound, specifically, the substitution of an acetyl group for an active hydrogen atom. A reaction involving the replacement of the hydrogen atom of an hydroxyl group with an acetyl group (CH₃ CO) yields a specific ester, the acetate. Acetic anhydride is commonly used as an acetylating agent reacting with free hydroxyl groups. In living cells, acetylation occurs as a post-translational modification of proteins. For example, histones are acetylated and deacetylated on lysine residues in the N-terminal tail as part of gene regulation. Typically, these reactions are catalyzed by enzymes with "histone acetyltransferase" (HAT) or "histone deacetylase" (HDAC) activity. The source of the acetyl group in histone acetylation is Acetyl-Coenzyme A, and in histone deacetylation the acetyl group is transferred to Coenzyme A.

Acetylated histones and nucleosomes represent a type of epigenetic tag within chromatin. Acetylation brings in a negative charge and neutralizes the interaction of the N termini of histones with the phosphate groups of DNA. As a consequence, the condensed chromatin is transformed into a transiently relaxed structure which allows genes to be transcribed. Acetylated chromatin is thought to be more "relaxed" and is called euchromatin. Methylated chromatin is more condensed (tightly packed), and referred to as heterochromatin.

25. Colonic bacteria are those which live inside the colon (large intestine).
26. Synergistic effect of Roundup ingredients – see note 22 above.
27. Differential Effects of Glyphosate and Roundup on Human Placental Cells and Aromatase, by Sophie Richard, Safa Moslemi, Herbert Sipahutar, Nora Benachour, and Gilles-Eric Seralini of the Laboratoire de Biochimie et Biologie Moleculaire, USC-INCRA, Université de Caen, Caen, France, published in *Environmental Health Perspectives* Volume 113, Number 6, June 2005. See also note 22 above.
28. Roundup is widely used in Ireland with no warnings about risks to pregnant women.
29. New scientific evidence of the health risks of eating Monsanto's Roundup Ready GM soy beans was announced by the Russian Academy of Sciences in October 2005. The astounding result may threaten the multi-billion dollar biotech industry. Irina Ermakova, a leading scientist at the Institute of Higher Nervous Activity and Neurophysiology of the Russian Academy of Sciences (RAS), added GM soy flour (5-7 grams) to the diet of female rats. The experimental diet began two weeks before the rats conceived and continued through pregnancy and nursing. Ermakova's first surprise came when her pregnant rats started giving birth. Some pups from GM-fed mothers were quite a bit smaller. After 2 weeks, 36% of them weighed less than 20 grams compared to about 6% from the other groups.

But the real shock came when the rats started dying. Within three weeks, 25 of the 45 (55.6%) rats from the GM soy group died compared to only 3 of 33 (9%) from the non-GM soy group and 3 of 44 (6.8%) from the non-soy controls. On October 27, 2005, the American Academy of Environmental Medicine (AAEM) board passed a resolution asking the US National Institutes of Health (NIH) to sponsor an immediate, independent follow-up of the study. Dr. Jim Willoughby, the Academy's president, said, "Genetically modified soy, corn, canola (oilseed rape), and cottonseed oil are being consumed daily by a significant proportion of our population. We need rigorous, independent and long-term studies to evaluate if these foods put the population at risk. For details see <http://www.gmfreeireland.org/downloads/Deadrats.pdf>.

30. This study, which was published in the Russian journal ECOSInform in 2006, is small in size and preliminary. The implications, however, are severe. The American Academy of Environmental Medicine agrees and in November 2005, they called on the U.S. National Institutes of Health to immediately replicate it.
31. A steroid is a lipid characterized by a carbon skeleton with four fused rings. All steroids are derived from the acetyl CoA biosynthetic pathway. Hundreds of distinct steroids have been identified in plants, animals, and fungi. Their most important role in most living systems is as hormones. Steroid hormones produce their physiological effects by binding to steroid hormone receptor proteins. The binding of steroid hormones to their receptors causes changes in gene transcription and cell function.

In human physiology and medicine, the most important steroids are cholesterol, the steroid hormones, and their precursors and metabolites. In the bloodstream steroids are bound to carrier proteins.

Cholesterol is an important steroid alcohol, being a common component of animal cell membranes. However, a high level of it can cause various conditions and diseases, such as atherosclerosis. Most other steroids are synthesized from cholesterol. Also, various hormones, including vertebrate sex hormones, are steroids created from cholesterol.

32. A glucuronide, also known as glucuronoside, is any substance produced by linking glucuronic acid to another substance via a glycosidic bond. The glucuronides belong to the glycosides. Toxic substances can be removed from the body in this manner - glucuronic acid forms a glycosidic bond with the toxic substance, and the resulting glucuronide, which has a much higher water solubility than the toxin alone, is eventually excreted.
33. Bile (or gall) is a bitter, greenish-yellow alkaline fluid secreted by hepatocytes from the liver of most vertebrates. In many species, it is stored in the gallbladder between meals and upon eating is discharged into the duodenum where it aids the process of digestion. Bile acts to some extent as a detergent, helping to emulsify fats (increasing surface area to help enzyme action), and thus aid in their absorption in the small intestine.
34. GUS gene, see note 8 above.
35. In some Western countries, such as the USA and the UK, cancer is overtaking cardiovascular disease as the leading cause of death.
36. The endocrine system is a control system of ductless glands that secrete chemical "instant messengers" called hormones that circulate within the body via the bloodstream to affect distant cells within specific organs. Endocrine glands secrete their products immediately into the blood or interstitial fluid, without storage of the chemical. Hormones act as "messengers," and are carried by the bloodstream to different cells in the body, which interpret these messages and act on them. Typical endocrine glands are pituitary, thyroid, and adrenal glands, but not exocrine glands such as salivary glands, sweat glands and glands within the gastrointestinal tract.

37. Personal communication from M. Hill to Dr. Stanley Ewen.
38. Study conducted by the Commonwealth Scientific and Industrial Research Organisation. <http://pubs.acs.org/cgi-bin/abstract.cgi/jafcau/2005/53/i23/abs/jf050594v.html>. See also related New Scientist article: <http://www.newscientist.com/article.ns?id=dn8347>. The study showed that the introduction of genes from a bean variety into a GM pea led to the creation of a novel protein which caused inflammation of the lung tissue of mice. So serious was the damage that the research was halted, and stocks of the GM pea were destroyed. The developers made a commitment that the "rogue" variety will never be marketed.
39. Amylase is a digestive enzyme classified as a saccharidase (an enzyme that cleaves polysaccharides). It is a constituent of human pancreatic juice and saliva, where it acts to breakdown long-chain carbohydrates (such as starch) into maltose which is then subsequently degraded by maltase, an enzyme, to glucose.

Amylase is also synthesized by many plants during the ripening of fruit and during the germination of cereal grains. Grain amylase is key to the production of malt. Many microbes also produce amylase to degrade extracellular starches. Beta-amylase is present in germinating seeds prior to germination whereas α -amylase and proteases appear once germination has begun.

40. An antibody or immunoglobulin is a large Y-shaped protein used by the immune system to identify and neutralize foreign objects like bacteria and viruses. Each antibody recognizes a specific antigen unique to its target. This is because at the two tips of its "Y", it has structures akin to locks. Every lock only has one key, in this case, its own antigen. When the key is inserted into the lock, the antibody attaches, tagging the microbe or an infected cell for attack by other parts of the immune system or by directly neutralizing its target (i.e. blocking a part of the microbe that is essential for its invasion and survival). The production of antibodies is the main function of the humoral immune system.

In mammals there are five types of antibody: IgA, IgD, IgE, IgG, and IgM, with 4 IgG and 2 IgA subtypes present in humans. (Ig stands for immunoglobulin, which is another name for antibody). These are classified according to differences in their heavy chain constant domains (see below for more information regarding the structural features of antibodies). Each immunoglobulin class differs in its biological properties and has evolved to deal with different antigens. IgA can be found in areas containing mucus (e.g. in the gut, in the respiratory tract or in the urinogenital tract) and prevents the colonization of mucosal areas by pathogens. IgD functions mainly as an antigen receptor on B cells. IgE binds to allergens and triggers histamine release from mast cells (the underlying mechanism of allergy) and also provides protection against helminths (worms). IgG (in its four forms) provides the majority of antibody-based immunity against invading pathogens. IgM is expressed on the surface of B cells and also in a secreted form with very high affinity for eliminating pathogens in the early stages of B cell mediated immunity (i.e. before there is sufficient IgG to do the job).

Immature B cells express only IgM on their cell surface (this is the surface bound form not the secreted form of immunoglobulin). Once the naive B cell reaches maturity, it can express both IgM and IgD on its surface - it is the co-expression of both these immunoglobulin isotypes that renders the B cell 'mature' and ready to respond to antigen. Following an engagement of the immunoglobulin molecule with an antigen, the B cell becomes activated, and begins to divide and differentiate into an antibody producing cell (sometimes called a plasma cell). In this activated form, the B cell will produce its immunoglobulin in a secreted form rather than a membrane-bound form. Some of the daughter cells of the activated B cells will undergo isotype switching, a mechanism by which the B cell begins to express the other heavy chains and thus produce IgD, IgA or (more commonly) IgG.

IgG is a monomeric immunoglobulin, built of two heavy chains γ and two light chains. Each molecule has two antigen binding sites. This is the most abundant immunoglobulin and is approximately equally distributed in blood and in tissue liquids. This is the only isotype that can pass through the placenta, thereby providing protection to the fetus in its first weeks of life before its own immune system has developed. It can bind to many kinds of pathogens, for example viruses, bacteria, and fungi, and protects the body against them by complement activation (classic pathway), opsonization for phagocytosis and neutralisation of their toxins. There are 4 subclasses: IgG1 (66%), IgG2 (23%), IgG3 (7%) and IgG4 (4%).

- * IgG1, IgG3 and IgG4 cross the placenta easily.
- * IgG3 is the most effective complement activator, followed by IgG1 and then IgG2.
- * IgG4 does not activate complement.
- * IgG1 and IgG3 bind with high affinity to Fc receptors on phagocytic cells. IgG4 has intermediate affinity and IgG2 affinity is extremely low.

41. The tuberculin skin test involves the injection of tuberculin antigen used to aid in the diagnosis of tuberculosis infection. An infection with the bacterium that causes tuberculosis frequently leads to a sensitivity to these antigens.
42. Inflammation is the first response of the immune system to infection or irritation and may be referred to as the innate cascade. Inflammation is characterised by the following quintet: redness (rubor), heat (calor), swelling (tumor), pain (dolor) and dysfunction of the organs involved (functio laesa).
43. Immunogenicity is the ability of a particular substance to provoke an immune response.
44. GM food remains unlabelled in the USA and Canada. EU law requires that any food or animal feed containing more than 0.9% of GM ingredients be labeled as such, even though the minimum detection threshold is 0.1%. So food and feed contaminated with under 0.9% levels does not require a label in the EU. A giant loophole in EU law allows meat and dairy produce from animals whose diet includes GM ingredients to remain unlabelled. Most non-organic Irish meat and dairy produce — which comes from animals fed on GM maize gluten, GM soya and GM oilseed rape — remains unlabelled, even though buyers in Italy and other leading export markets are demanding a completely GM-free food chain and offering premia for Irish beef and dairy produce from animals that have not been fed on GM ingredients. See <http://www.gmfreeireland.org/feed>.
45. See *Caring for Life: Genetics, Agriculture and Human Life; Discussion Document by the Working Group on Genetic Engineering, World Council of Churches, Geneva, June 2005*: <http://www.wcc-coe.org/wcc/what/jpc/geneticengineering.pdf> .

A short discussion of biotechnology on the World Council of Churches website is at: <http://www.wcc-coe.org/wcc/what/jpc/eearth-biotech.html> . Excerpt:

“In the light of our work on genetic engineering agriculture we therefore call upon the WCC, member Churches, individual Christians and people of good will to embark on the following six forms of action:

1. To build partnerships with civil society, people's movements, small scale farmer groups and Indigenous Peoples in opposing the science, philosophy and practice of genetic engineering in agriculture.
2. To challenge Christians in the employ of those promoting genetic engineering to reflect upon the implications of their work in the light of the Gospel's concern for truth and justice, and to consider the possibility of being whistle-blowers and conscientious objectors.
3. To encourage Christian theological reflection to shift from issues of food security to issues of food sovereignty so that our concerns for justice, freedom and participation are not compromised.

4. To encourage Christians involved in medical research to continue to investigate the impact of genetic engineering in agriculture upon human health, as called for by the European Commission.
5. To stand in solidarity with those working in local communities to promote healthy food and good nutrition amongst the deprived, especially in a time of HIV/AIDS.
6. To recognize in our work and reflection the way in which access to food stands on the interface between ecology and economy in the struggle for life against commodification and control.
7. To engage biblically and theologically in reflection on food, faith and freedom, and especially to consider the possibility that the agape meal at the heart of Christian worship - the Lord's Supper or Eucharist - could be envisaged as a sacrament of resistance against those who seek to control food. In doing these things, we stand in continuity with the AGAPE document, and particularly section 3.3., 'from food security to food sovereignty':

'We believe that God's economy of solidarity and justice for the household of creation includes the promise that the people of the world have the right to produce their own food and control the resources belonging to their livelihoods, including biodiversity. It is therefore the right and responsibility of governments to support the livelihoods of small farmers in the South and in the North. It is their right to refuse the demands of agribusinesses that seek to control every aspect of the cycle of life. Such an approach requires respect for indigenous spiritual relationships to land and the bounties of mother earth.'