OBJECTION TO MONSANTO'S APPLICATION FOR GENERAL RELEASE OF GM COTTON RR FLEX

SUBMITTED TO: NATIONAL DEPARTMENT OF AGRICULTURE, c/o REGISTRAR: GENETICALLY MODIFIED ORGANISMS ACT

DECEMBER 2005

SUMMARY

The application is for a general release permit to allow the commercial sale and growing of a new transformation event MON88913, also known as Roundup Ready Flex cotton. The new RR Flex variety ostensibly provides increased tolerance to glyphosate compared to the current product, Roundup Ready cotton line 1445. Use of MON 88913 will enable the application of Roundup agricultural herbicide over the top of the cotton crop at later stages of development than is possible with line 1445.

Monsanto intends to release the new variety, RR Flex during October/November 2006, in Mpumalanga/Limpopo provinces, and will include both irrigated and dryland cotton plantings.

1. Upon examination of Monsanto's previous application for commercial release of line 1445, we found an admission by Monsanto that they were applying for the approval without being in compliance with the Plant Quality Control Act with regard to field trials, a requirement for permission for varietal registration of the Roundup Ready herbicide. Although some sort of field trials were submitted, these were not adequate because the commercial permit was needed by Monsanto, on its own version, to import a fairly large quantity of GM seeds (2000 bags/50 tons), for multiplication purposes and large scale user;
2. Monsanto is now seeking a commercial permit based on field trials conducted for only one growing season 2004-5 in respect only of efficacy tests and phytotoxicity characteristics of RR Flex. Despite this, Monsanto makes wide ranging claims of benefits, including: effective weed control, convenience and simplicity, increased grower income, increased adoption of reduced tillage practises, compatibility with integrated pest management, etc., based on assessments conducted in the US;
3. Monsanto anticipates that 5000 bags of the RR Flex cotton will be available for planting in South Africa, these "would be used by farmers as a refuge plantings as their preference is to plant "stacked" variety (BGRR). We find this extremely disconcerting, in the light that even in Monsanto's own literature, a compulsory refugia of 20% is supposed to be planted with non-transgenic cotton;
4. We are concerned about the implications arising from the use of RR Flex and the stacked varieties involving herbicide tolerant crops for agricultural workers and small scale farmers in terms of food and job security, particularly in view of there being no socio-economic studies available that addresses these concerns;
5. Genetic modification by the application of recombinant DNA technology is characterised by scientific uncertainty. This stems from several factors including the inherent imprecision of currently employed recombinant DNA techniques, the use of powerful promoter sequences in genetic constructs and the generation, as a result of genetic modification, of novel proteins to which humans and animals have never previously been exposed;
6. The transfer of the herbicide-tolerant trait to weeds could result in increased herbicide application;
7. The potential for economically important weeds developing herbicide tolerance is a cause for concern;
8. Glyphosate use has resulted in several unwanted effects on aquatic systems and terrestrial organisms and ecosystems;
9. RR Cotton was denied regulatory approval by the European Commission in 1999 because of concerns about the *aad* resistance marker;
10. The US experience of Roundup Ready field trials has shown a marked increase in herbicide usage, particularly glyphosate; and
11. In the Argentinean experience, the large- scale uptake of Roundup Ready Soya has had devastating impacts on food security and the environment.

It is our respectful submission that the Executive Council (EC) is obliged to refuse the approval sought by the Applicant because the EC has a duty to do so in terms of section 24 of the Constitution, in order to protect the environment.

ALTERNATIVELY, the Minister of Environment must call for an environmental impact assessment (EIA) in terms of section 78 of the Environmental Management Biodiversity Act, 2004 (NEMBA, Biodiversity Act), which came into effect on the 1 September 2004.

BACKGROUND

CONCERNS REGARDING GENETICALLY MODIFIED PLANTS

INTRODUCTION

There is a great deal that is not known about genetically modified plants. The main concerns related to food safety and environmental issues. Further, there are concerns that there is great potential for ecological harm and negative impacts on biodiversity should genetically modified plants be introduced into the natural environment without adequate testing and review. Specific concerns include:

- The transfer of allergens or the unintentional creation of new allergens
- The build up and spread of herbicide resistant and pesticide genes to surrounding weeds, creating "superweeds"
- The loss of biological diversity resulting from competition between genetically modified plants and natural species
- The potential for harm to wildlife species dependent on native plants species for food
- The potential for harm to threatened or endangered species

ANTIBIOTIC RESISTANCE GENES AND THE SAFETY THEREOF

Horizontal Gene Transfer (HGT)

Horizontal gene transfer (HGT) is the transfer of genetic material between organisms, outside the context of parent to offspring reproduction.[i,ii] It is most commonly recognized as infectious transfer.[iii] HGT frequencies are now known to be much higher than originally thought. The evolution of antibiotic resistance, for example, is an indicator of the frequency of gene transfer, given that antibiotics have been used in medicine only for about 50 years.iii The intentional modification of plants could through horizontal gene transfer result in the unintentional modification of other organisms. What the possible impacts of such gene transfer might be is not known.

Use of Antibiotic Resistance Markers

Antibiotic resistance marker genes are used often in the development of transgenic crops as selectable markers. Selectable markers allow the modified form to be selectively amplified while unmodified forms are eliminated. The use of antibiotic resistance markers has application in development of the transgenic line allowing for selection of modified plants in the laboratory. The transgenic crop line however, will retain the marker gene for its lifetime in each of its cells.ii

Potential for HGT of Antibiotic Resistance Marker Genes (ARMG)

The significance of any potential gene transfer is dependent on the marker being transferred and what its existing or future therapeutic application is or might be. Where there are antibiotic resistant marker genes, there is a potential for gene transfer of these markers to

pathogenic organisms. Kanamycin, contrary to popular belief, is still used in medical applications, e.g. prior to endoscopy of the colon and rectum[iv] and to treat ocular infections. [v] It is well known that there is cross resistance between antibiotics of a particular type.ii Neomycin was found to cross react with kanamycin B in inhibiting RNAse P ribozyme 16s ribosomal RNA and tRNA maturation.[vi] Other aminoglycoside antibiotics including streptomycin, gentamycin and tobramycin, which are used to treat human disease, have exhibited cross-resistance.ii The possibility of transfer of the marker by HGT, and subsequent adverse effects on human and animal health, cannot be ruled out in those cases where these antibiotics are still being used.

Resistance of DNA to Digestion

Monsanto argue that gene transfer is unlikely as the protein is rapidly degraded under conditions with simulate mammalian digestion. There are however several reported cases in the literature of both the persistence and transfer of gene sequences after ingestion of GM products. Polymerase chain reaction (PCR) has been used to demonstrate the presence of large fragments of M13 phage DNA, which had been fed to mice, in the faeces and bloodstream and in white blood cells.[vii]. Research published by the UK government in 2002 has shown that bacteria in human intestines had in fact taken up a novel gene from processed food containing GM Soya.[viii] It has been reported that people with ileostomies (i.e. who make use of a colostomy bag) are capable of acquiring and harbouring DNA sequences from GM plants in the small intestine.[ix] Recombinant DNA fragments and Cry1Ab protein was also found in the gastrointestinal contents of pigs fed genetically modified corn.[x]

The CaMV Promoter

The cauliflower mosaic virus (CaMV) is a DNA-containing para-retrovirus replicating by means of reverse transcription. It contains within its genome a viral promoter called 35S, a general strong plant promoter, which has been used to secure expression of transgenes in a large proportion of commercialised GMOs. There are several studies indicating the potential for transcriptional activation of the 35S CaMV promoter in mammalian systems.[xi,xii]

The CaMV 35S promoter has been found to have a recombination hotspot where it tends to fragment and join with other double stranded DNA in a very non-specific manner.[xiii] These hotspots are flanked by multiple motifs involved in recombination and functions efficiently in all plants, green algae, yeast and Escherichia coli. The potential exists for the viral genes to recombine with other viruses to generate new infectious viruses,[xiv] carcinogens and mutagens as well as to reactivate dormant viruses.

Detractors claim that virus infected cabbages and cauliflowers have been consumed for years with no ill effects and that similar pararetroviral sequences occur widely in plants, causing no apparent harm.[xv] That the intact virus causes no obvious harm in the natural host is related to the fact that its integrity is maintained and that it is adaptive to the host biology. This is unlike the fragments of naked DNA as in the transformed plant where the natural regulatory mechanisms are not present.xiv A call has been made that the use of the CaMV promoter in transgenic plants be phased out due to the structural instability arising out of its use.[xvi] The presence of the 35S CaMV promoter, which is known to be active in micro-organisms,[xvii] could facilitate the transfer of an antibiotic resistance marker from the plant to bacteria in the intestines of humans and livestock.

International Concerns Regarding HGT and theARGMs

Several European countries including Austria, Luxembourg, France, Norway and the United Kingdom expressed grave concerns about the presence of antibiotic genes in GM products and the EU as a result, decided to prohibit GMOs with antibiotic resistance genes after the 31st December 2004 (directive 2001/18EC and Revising Directive 90/220/CEE).[xviii]

COTTON

THE IMPORTANCE OF COTTON

Cotton is more widely used than any other fibre and in the United States alone, annual business revenue stimulated by cotton production and processing exceeds US$120 Billion. No part of the cotton plant is wasted during processing. Cotton fibre is used in making cloth. The linter i.e., the short fuzz on the seed provides cellulose for making plastics, explosives, batting for padding mattresses and furniture and is incorporated into high quality paper.

Cottonseed yields oil, meal and hulls. Oil is used for shortening, as a cooking oil and for salad dressing. Cotton meal and hulls are used as livestock, poultry and fish feeds and as fertilizer. The cotton plant stalks and leaves are used as soil conditioners and ploughed back into the ground.[xix]

In West Africa alone, up to 16 million people are involved in different aspects of cotton production and processing. The combined contribution of West and Central Africa to cotton production has placed these regions as the world's second largest exporter of cotton after the United States.[xx]

ROUNDUP - READY COTTON

DESCRIPTION AND MAIN FEATURES

All plants have an *epsps* (5-synthase) gene. The EPSPS enzyme is involved in the synthesis of the aromatic amino acids, tyrosine, phenylalanine and tryptophan. The herbicide glyphosate (Roundup) specifically binds to and inactivates EPSPS. Cotton lines 1445 and 1698 were produced to allow for the use of Glyphosate as a weed control measure. These novel plants express a glyphosate tolerant version of the *epsps* gene[xxi] and are therefore referred to as being Roundup-Ready. Fields sprayed with glyphosate will kill off weeds without impacting on the fitness of the transgenic plants. Events 1445 and 1698 contain two antibiotic resistance marker genes viz., aad conferring resistance to streptomycin and spectomycin, inserted after the epsps gene cassette; followed by a kanamycin resistance gene driven by the CaMV promoter. Reference: [xxi]

FIELD TESTING AND PERVASIVENESS OF COTTON LINES 1445 AND 1698

GLYPHOSATE

Herbicide Tolerance and Effects on Non-target Species

The main environmental concern related to introducing herbicide resistance into transgenic plants is the development of weed populations that are resistant to particular herbicides, the so-called superweeds.[xxii] These weeds may then be able to successfully outcompete other non-herbicide –resistant weeds.[xxiii] This may result in increased use of herbicides in greater volumes and varieties with possible negative impacts on soil and groundwater.[xxiv] Increased herbicide use may also result from less restrained herbicide application arising from producer confidence that the desirable plant will be unaffected.

Country	Environ.	Food and/or Feed	Food	Feed	Marketing
Argentina	1999		2001	2001	
Australia	2000		2000		
Canada			1996	1996	
China					2004
Japan	1997		1997	1998	
Philippines			2003	2003	
South Africa	2000				
United States	1995	1995			

Glyphosate is a broad spectrum herbicide and its usage may result in harmless plant species being destroyed. The large scale cultivation of glyphosate resistant crops will result in an increase in the use of, glyphosate with concomitant negative environmental impacts. The full impact of glyphosate on groundwater can only really be determined by long-term monitoring programmes. In terms of impacts on human health, glyphosate is acutely toxic to humans and in California has been reported to be the third most commonly reported pesticide related illness amongst agricultural workers.[xxv]

Increased Glyphosate Use Impacts on other Plant Species

The dramatic increase in the use of glyphosate over the past decade has resulted in weedy morning glories in the South-eastern United States developing tolerance to glyphosate. The repeated use of herbicides exerting strong selection pressure on crop weeds has led to more than 250 documented cases of herbicide resistance, a process that is 'likely to accelerate with increased reliance on herbicides'.[xxvi] A strong positive directional selection in the presence of glyphosate and strong negative directional selection in its absence was observed.[xxvii]

Common ragweed found in a 22 acre patch of north-central Arkansas dryland has survived heavy, and repeated, shots of Roundup.[xxviii] Laboratory studies are still in progress, but preliminary indications are that resistance to glyphosate (Roundup) has developed in these plants. The presence of resistant ragweed is unlikely to cause major waves amongst agriculturalists as ragweed is not a threat to any major crop and there are herbicides besides Roundup to control the weed. The larger issue is the potential for agriculturally important weeds such as pigweed, tall waterhemp or lambsquarter to develop resistance. Monsanto is well aware of the problem ragweed and is evaluating sample plants in St. Louis.xxviii

Health and Environmental Effects of Glyphosate and Glyphosate-tolerant GMOs

There is a paucity of experimental studies devoted to health or environmental effects of glyphosate-tolerant GMOs or glyphosate itself. A study on mice fed GM soybean suggested that epsps-transgenic soybean intake was impacting on the morphology, particularly the nuclear features of liver cells, in both adult and young mice.[xxix] The mechanism for this effect is still to be determined.[xxx]. Glyphosate use, an integral part of planting Roundup Ready crops, has indicated several unwanted effects on aquatic[xxxi] systems, terrestrial [xxxii] organisms and ecosystems[xxxiii]. Negative impacts on human [xxxiv,xxxv], rodent [xxxvi] and fish [xxxvii] health have also been observed.

MONSANTO'S PREVIOUS COMMERCIAL RELEASE APPLICATION FOR RR COTTON

An application was made to the South African National Department of Agriculture on 29/06/2000 for authorization for conditional general release of Roundup Ready cotton lines 1445 and 1698. The table above summarises the regulatory approvals in each of the listed countries. RR Cotton was denied regulatory approval by the European Commission in 1999 because of concerns about the *aad* resistance marker.[xxxviii]

Monsanto stated in their application that they are applying for the approval without being in compliance with the Plant Quality Control Act with regard to field trials, a

requirement for permission for varietal registration of the Roundup Ready herbicide. Although some sort of field trials were submitted, these were not adequate because the commercial permit was needed by Monsanto, on its own version, to import a fairly large quantity of GM seeds (2000 bags/50 tons), for multiplication purposes and large scale user.

The ACB has brought this irregularity to the attention of the Registrar, Ms Vosges as well as to Dr Julian Japhta requesting an explanation. None has to date, been forthcoming.

THE CURRENT APPLICATION FOR COMMERCIAL GENERAL RELEASE AUTHORISATION: ROUNDUP READY FLEX

The application is for a general release permit to allow the commercial sale and growing of a new transformation event MON88913, also known as Roundup Ready Flex cotton. According to Monsanto's application, it appears that one of the driving forces behind the production of this new variety is "the necessity of making special adjustments and going to additional expense to be able to conform with the label requirements that state that 'over the cotton' application of Roundup can only be applied from the ground cracking stage up to the 4th true lead/node cotton growth stage….broadcast application after this time could result in boll loss, delayed maturity and/or yield loss." The new RR Flex variety ostensibly provides increased tolerance to glyphosate compared to the current product, Roundup Ready cotton line 1445. Use of MON 88913 will enable the application of Roundup agricultural herbicide over the top of the cotton crop at later stages of development than is possible with line 1445.

Monsanto intends to release the new variety, RR Flex during October/November 2006, in Mpumalanga/Limpopo provinces, and will include both irrigated and dryland cotton plantings.

Although Monsanto anticipates that 5000 bags of the RR Flex cotton will be available for planting in South Africa, these "would be used by farmers as a refuge plantings as their preference is to plant "stacked" variety (BGRR). As soon as general release approval has been obtained for Roundup Ready Flex (88913) an application will be submitted for stacked product containing Bollgard II (15985) Conditional *General Release 17/3(5/03/225) and Roundup Ready Flex (88913).*" We find this extremely disconcerting, in the light that even in Monsanto's own literature ("Your pocket sized user guide for Bollgard with Roundup Ready cotton), a compulsory refugia of 20% is supposed to be planted with non-transgenic cotton.

INADEQUECY OF FIELD TRIALS

Field trials of the RR Flex were apparently conducted in South Africa for only one season-namely, 2004-2005. However, these trials were conducted only to establish the efficacy and phytotoxicity characteristics of RR Flex. Yet, it on the basis on just this one season of tests, that Monsanto is now seeking a commercial permit. In support of such application, Monsanto makes wide ranging claims of benefits, including: effective weed control, convenience and simplicity, increased grower income, increased adoption of reduced tillage practises, compatibility with integrated pest management. An examination of the 'field inspection reports' of the National Department of Agriculture (NDA) appear to be nothing more than tick lists, as they do not provide any analysis of the inspection, let alone, verification of the claims made by Monsanto. Indeed, the bulk of Monsanto's application deals with testing on GM cotton line 1445, and tests that it has conducted in the USA. We believe that extensive field trials are required to be conducted under South African conditions, to especially investigate the possibility of the transfer of the herbicide-tolerant trait to weeds as a result in increased herbicide application. The potential for economically important weeds developing herbicide

tolerance is a cause for great concern to us as well as the scientific community in South Africa.

EXPERIMENTAL DUMPING GROUNDS

We have raised our extreme disquiet on a number of occasions that the South African legislation allows multinational companies to use our country as an experimental dumping ground and for seed bulking purposes, and thereby defeating the objectives of biosafety regulation. We repeat these concerns and point out the Monsanto in its application says the following "Delta and Pinelands have for several years imported genetically modified cottonseed, including Bollgard, Bollgard II, Roundup Ready and Roundup Ready Flex and in the combined BGRR varieties, for local evaluation, multiplication, selection and bulking up for the American cotton market. This was done under permits from the Directorate Plant Quality Control initially and subsequently in terms of the GMO Act."

SOCIO-ECONOMIC IMPACTS

Monsanto argues that the introduction of RR Flex and then the combination of Bollgard II x RR Flex is scale neutral benefiting both small and large scale commercial farms. Monsanto goes so far as to say that "RR Flex will be even more beneficial to the small scale farmers who spend an enormous amount of time weeding cotton fields by hand."

We are concerned about the implications arising from the use of RR Flex and the stacked varieties involving herbicide tolerant crops for agricultural workers and small scale farmers in terms of food and job security. These issues need to be urgently investigated by the Executive Council both in terms of the GMO Act and the Biosafety Protocol.

ROUNDUP READY SOYA: A CASE STUDY

EXPERIENCE OF OTHER GM CROPS: ROUNDUP READY SOYA IN THE USA

More research has been carried out on the nature and extent of herbicide applications with Roundup Ready soya. Roundup Ready Soya bean went from comprising only a small fraction of soya bean planted in the USA in 1996 to more than half of all soya bean planted in 1999, an uptake all the more remarkable given the yield-drag associated with engineered varieties.[xxxix] In a report reviewing the results of 8200 university-based soybean varietal trials it was found that RR soybean yield drag could result in perhaps a 2.0 to 2.5 percent reduction in national average soybean yields compared to what they might have been had seed companies not forced crop production focus on herbicide tolerance. Further, the dependence of RR systems on herbicides resulted in 2 to 5 times more herbicide being applied compared to other popular weed management systems.[xxxix]

ROUNDUP READY CROPS: THE ARGENTINEAN EXPERIENCE

Argentina was one of the first countries to authorise GM crops with the cultivation of Monsanto's Roundup Ready soya in 1997.[xliii,xl] Large areas of Argentina's most fertile farming region in the Pampas had been suffering from serious soil erosion. Farmers experimenting with a no-tilling approach to alleviate the problem saw the introduction of a herbicide tolerant crop as a heaven-sent solution.[xl] Impoverished smallholders, largely peasant farmers, leased their land out to soya farmers and by 2002 almost half of Argentina's arable land -11.6 million hectares was planted with soya, almost all of it GM, compared with just 37,700 hectares of soya in 1971.[xl,xli] The demand for arable land for planting soya saw cultivation extending into more environmentally fragile areas; Argentina has lost three-quarters of its native forest to farming over the past century.[xlii]

In 2001, Benbrook reported that Argentinean Roundup Ready soya growers were using more than twice as much herbicide as conventional soya farmers, largely because of unexpected

problems with tolerant weeds.[xl,xli] His warning of shifts in the composition of weed species, the emergence of resistant superweeds, and changes in soil microbiology under the existing herbicide application regime went unheeded. The outcome is the emergence of several previously uncommon species of glyphosate tolerant weed, a decline in soil bacteria, changes in soil structure and fitness with soil becoming inert thereby inhibiting the usual process of decomposition.[xl] On top of all of this is a proliferation of volunteer soya. Rival's to Monsanto in the agrochemical industry are promoting their products to eradicate these volunteers with Syngenta advocating the use of Paraquat and atrazine.[xl,xliii] and Dow AgroSciences recommending a mixture of glyphosate with metsulfuron and clopyralid.[xl,xliii.]

Spraying of RR soya crops has resulted in devastating impacts on the health of local populations and on their environment, livestock and food crops. Studies carried out by the University of Formosa Province reported serious health problems in peasant communities arising from such fumigation on RR soya fields.[xliii,xl] The Argentinean experience also raises issues of food security. Argentina has gone from being known as one of the world's best beef producer and the breadbasket of the world to an economy dependent on near monoculture.[xli] The proliferation of soya has provoked an exodus of people from the rural areas to the cities and into extreme poverty since they cannot produce their own food.[xl,xli] RR soya has also won out against traditionally grown crops such as sweet potatoes, sweet maize, lentils (a staple), peas and cotton. Argentina used to produce food sufficient to feed eight times its population, now it imports milk. 'Now, in beef country, the poor are being fed with crops used for animal feed in the first world'.[xli]

LEGAL ISSUES

EC HAS A CONSTITUTIONAL AND STATUTORY DUTY TO PROTECT THE ENVIRONMENT

It is our respectful submission that the Executive Council (EC) is obliged to refuse the approval sought by the Applicant because the EC has a duty to do so in terms of section 24 of the Constitution, in order to protect the environment. Indeed, the application must be refused because the statutory framework obliges the EC to *inter alia* adopt a risk averse approach in assessing environment hazards and to evaluate the environmental impacts of the proposed activities and to have regard to the cumulative potential impacts of such activities on the environment.

MINISTER OF ENVIRONMENT MUST CALL FOR AN EIA ITO BIODIVERSITY ACT

The South African government has to date, never called for an environmental impact assessment (EIA) to be conducted. However, the National Environmental Management Biodiversity Act, 2004 (NEMBA, Biodiversity Act), which came into effect on the 1 September 2004 (section 78) creates the possibility that where the Minister is of the belief that the release of a GMO may pose risks to the environment, to order that an EIA be conducted. We call on the Minister to exercise his powers in terms of section 78 and call for and arrange for an EIA to be conducted. Whilst we are aware that the Department of Environmental Affairs and Tourism (DEAT) are in the process of developing tools to implement section 78, the failure of the DEAT to have such tools ready cannot be an excuse to do nothing, and therefore, flout our rights under the Constitution.

MINISTER OF ENVIRONMENT MUST CALL FOR A SCOPING REPORT ITO ECA

Monsanto is obliged to obliged to submit a Scoping Report in terms of the Regulations to the Environment Conservation Act (Regulations governing activities identified under section 21(1) of the ECA were promulgated in Government Notice R1183, Government Gazette of 5 September 1997) which include *inter alia*, the employment of an independent consultant;

identification of environmental issues and full details regarding alternatives, in the said Scoping Report, as required by the ECA Regulations.

In this regard, we point out that the in terms of section 6(1) of the ECA Regulations, the Applicant must submit in such Scoping report, the following information:

a brief project description;

a brief description of how the environment may be affected;

a description of all alternatives; and

an appendix containing a description and public participation process followed, including a list of interested parties and their comments.

We have thoroughly perused the information furnished to us, and have not found any evidence to show that the Applicant had complied with these provisions. It is our contention that the Applicant has failed to comply with subsections (c) and (d) above. Indeed, to date, Monsanto has never conducted any public participation process in terms of the ECA and has relied on the 'notice and comment' procedures of the GMO Act. We ask that the Minister comply with the provisions of the ECA, as a necessary pre-requisite, and natural precursor to the implementation of section 78 of the Biodiversity Act.

REFERENCES

[i] Heinemann, J. A. (2003) *Bioscience*. 12, 51 cited in [ii].

[ii] European Communities: Measures Affecting the Approval and Marketing of Biotech Products (DS291, DS292, DS293). (2004) Third Party Submission by Norway.

[iii] Heinemann, J. A. Gene Ecology Guide to: Measuring Horizontal Gene Transfer. Condensed version of paper published in Nature Biotechnology in September 2004. *Personal Communication*.

[iv] Ishikawa, H. Akedo, I., Minami, T., Shinomura, Y., Tojo, H. & Otani, T. (1999) Prevention of infectious complications subsequent to endoscopic treatment of the colon and rectum. *Journal Infect. Chemother.* **5**, 86.

[v] Hehl, E. M., Beck, R., Luthard, K., Guthoff, R. & Drewelow, B. (1999) Improved oenetration of aminoglycosides and fluorozuinolones into the aqueous humour of patients by means of Acuvue contact lenses. *European Journal of Pharmacology.* **55(4)**, 317.

[vi] Mikkelsen, N. E., Brannvall, M., Virtanen, A. & Kirsebom, L. A.l (1999) Inhibition of RNase P RNA cleavage by aminoglycosides. *National Academy of Sciences*, *USA*. **96**, 6155.

[vii] Schubbert, R., Lettmann, C. Doerfle, W. (1994) Ingested foreign (phage M13) DNA survives transiently in the gastrointestinal tract and enters the bloodstream of mice. *Mol. Gen Genet.* **242**, 495.

[viii] Netherwood, T., Matin-Orue, S. M., O'Donnell, A. G., Gockling, S., Gilbert, H. J. & Mathers, J. C. (2002) Transgenes in genetically modified Soya survive passage through the human small bowel but are completely degraded in the colon. UK Food Standards Agency. *Research Report G01008: Evaluating the risks associated with using GMO in human foods.*

[ix] Heritage, J. (2004) The fate of transgenes in the human gut. *Nature Biotechnology.* **22(2)**, 170. http://www.nature.com/cgi-taf/DynaPage.taf?

[x] Chowdhury, E. H., Kuribara, H., Hino, A., Sultana, P. and Mikami, O. (2003) Detection of corn intrinsic and recombinant DNA fragments and Cry1Ab protein in the gastrointestinal contents of pigs fed genetically modified corn. *Journal of Animal Science.* **81**, 2546.

[xi] Ryabova, L. A. & Hohn, T. (2000) Ribosome shunting in the cauliflower mosaic virus 35S RNa leader is a special case of reinitiation of translation functioning in plant and animal systems. *Genes & Development*. **14**:817

[xii] Ho, M-W. et al. (2000) Hazardous CaMV promoter? *Nature Biotechnology*. **18(4)**, 363

[xiii] Kohli, A., Griffiths, S., Plcios, N., Twyman, R. M., Vain, P., Laurie, D. A., Christou, P. (1999) Molecular characterization of transforming plasmid rearrangements in transgenic rice reveals a recombination hotspot in the CaMV 35S promoter and confirms the predominance of microhomology mediated recombination. *The Plant Journal*. **17**, 591.

[xiv] Ho, M-W. A brief history of the CaMV 35S promoter controversy. http://www.i-sis.org.uk

[xv] Hull, R., Covey, S. N. & Dale, P. (2000) Genetically modified plants and the 35S promoter: assessing the risks and enhancing the debate. *Microbial Ecology in Health and Disease*. **12**, 1.

[xvi] Christou, P., Kohli, A., Syoger, E., Twyman, R. M. Agrawal, P., Gu, X., Xiong, J., Wegel, E., Keen, D., Tuck, H., Wright, M., Abranches, R. & Shaw, P. (2000) Transgenic plants: a tool for fundamental genomics research. *John Innes Centre & Sainsbury Laboratory Annual Report 1999/2000*. p29.

[xvii] Pobjecky, N., Rosenberg, G. H., Dintergottlieb, G. & Kaufer, N. F. (1990) Expression o f the beta-glucuronidase gene under the control of the CaMV-35S promoter in *Schizosaccharomyces-pombe*. *Molecular and General Genetics*. **220(3)**, 517.

[xviii] African Centre for Biosafety, the South African Freeze Alliance on Genetic Engineering, Biowatch, and the Safe Food Coalition (2004) Demand for a ban on imports of bt176 and for a public enquiry into safety of food derived from genetically modified crops. May 2004.

[xix] The Story of Cotton. The importance of Cotton. http://www.cotton.org/pubs/cottoncounts/story/importance.cfm

[xx] Economic and Social Importance of Cotton Production in West Africa: Role of Cotton in Regional Development, Trade and Livelihoods. Sahel And West Africa Club Secretariat / OECD. Draft for Discussion and Comment. January 2005. http://www.Hnoc.Org/Fabric.Htm

[xxi] MON-Ø1445-2 (MON1445/1698). Agbios Databse. http://www.agbios.com/dbase.php?action=ShowProd&data=MON1445%2F1698&frmat=LONG

[xxii] Heritage, J. (2004) The fate of transgenes in the human gut. *Nature Biotechnology.* **22(2)**, 170. http://www.nature.com/cgi-taf/DynaPage.taf?

[xxiii] Ervin, D. E., Welsh, R., Batie, S. S. and Carpenter, C. L. (2003) Towards n ecological systems approach in public research for environmental regulation of transgenic crops. *Agriculture Ecosystems and Environment.* **99**, 1.

[xxiv] Greenpeace (1997) Glufosinate and genetic engineering. economic and environmental implications of herbicide resistance. *Greenpeace, International Genetic Engineering Campaign, Background Information*. 04/97.

[xxv] Greenpeace (2000) Genetically engineered crops: Soya, maize, oilseed rape and potatoes. *Greenpeace Briefing. Genetic Engineering Briefing Pack*. January 2000.

[xxvi] Williams, P. (2004) Morning glories creeping their way around popular herbicide, new UGA research reports. http://www.uga.edu/news/artman/publish/040823baucom.shtml

[xxvii] Baucom, R. S. & Mauricio, R. (2004) Fitness costs and benefits of novel herbicide tolerance in a noxious weed. *Proc Natl Acad Sci U S A*, **101(36)**:13386-90 http://www.pnas.org/cgi/reprint/0404306101v1?ck=nck

[xxviii] Bennett, D. (2004) 'Highly suspicious' plants found in north-central Arkansas. Delta Farm Press. http://deltafarmpress.com/news/083004resistant-ragweed/

[xxix] Malatesta et al. (2002) Ultrastructural Morphometrical and Immunocytochemical Analysis of Hepatocyte Nuclei from Mice fed on Genetically Modified Soy Bean. *Cell Structure and Function,* **27**: 173-180

[xxx] European Communities – Measures Affecting the Approval and Marketing of Biotech Products, (DS291, DS292, DS293), Third Party Submission by Norway, Geneva 24 May 2004

[xxxi] Solomon and Thompson (2003) Ecological risk assessment for aquatic organisms from over-water uses of glyphosate. *J Toxicol Environ Health B Crit Rev*., May-Jun, **6(3)**:289-324

[xxxii] Ono et al. (2002) Inhibition of *Paracoccidioides brasiliensis* by pesticides: is this a partial explanation for the difficulty in isolating this fungus from the soil?" *Med Mycol*., **40(5)**:493-9

[xxxiii] Blackburn and Boutin (2003) Subtle Effects of Herbicide Use in the Context of Genetically Modified Crops: A Case Study with Glyphosate (Roundup). *Ecotoxicology*, **12**:271-285

[xxxiv] Marc et al. (2002) Pesticide Roundup provokes cell division dysfunction at the level of CDK1/Cyklin B Activation. *Chem. Res. Toxicol*., **15**:326-331

[xxxv] Axelrod et al. (2003) The effect of acute pesticide exposure on neuroblastoma cells chronically exposed to diazinon. *Toxicology,* **185**:67-78

[xxxvi] Dallegrave et al. (2003) The teracogenic potential of the herbicide glyphosate Roundup in Wistar rats. *Toxicology Letters,* **142:**45-52

[xxxvii] Jiraungkoorskul et al. (2003) Biochemical and histopathological effects of glyphosate herbicide on Nile tilapia. *Environ Toxicol*., **18(4)**:260-7

[xxxviii] GM Cotton that People Forgot. ISIS. http://www.i-sis.org.uk/GMCTPF.php

[xxxix] Benbrook, C. (1999) Evidence of the magnitude and consequences of the Roundup Ready Soybean yield drag from university-based varietal trials in 1998. *AgBioTech InfoNet Technical Paper Number 1*. Benbrook Consulting Services, Sandpoint, Idaho.

[xl] Branford, S. (2004) Argentina's bitter harvest. *New Scientist*, April 20, pp40-43.

[xli] Joensen, L & Semino, S. (2004) Argentina: The Last Roundup. *The Ram's Horn*, February, Canada. **218** Grupo de Reflexión Rural, Argentina

[xlii] Farming in Argentina - The green desert. *The Economist.* http://www.economist.com/printedition/displayStory.cfm?Story

[xliii] Ching, L. L. (2004) How GM Crops Destroy the Third World (Case studies from Argentina, Indonesia and India), ISP Briefing, 29 April, House of Commons, London