ANNEX I-3

COMMENTS BY ARGENTINA ON THE REPLIES BY THE SCIENTIFIC EXPERTS TO THE QUESTIONS POSED BY THE PANEL 31 JANUARY 2005

COMMENT ON REPLIES TO QUESTIONS BY DR. ANDOW

Question 3

3. On the basis of the information before the Panel, is there any scientific evidence to support the hypothesis that wide-spread cultivation of Bt crops such as biotech maize of the Bt variety adversely affects non-target organisms which may be exposed to such crops under typical agricultural practice? (See, inter alia, EC-149, EC-150, EC-151, EC-152) If so, how does this risk compare with risks to non-target organisms arising from non-biotech applications for Bt toxins (i.e., the use of Bt toxin as an insecticide in conventional and organic farming)? What risk management options are available to mitigate any resulting risks and what is their efficacy?

Scientific evidence

03.01. In the answer to this question, I will concentrate on Bt maize and Bt cotton. Yes. there is some scientific evidence to support the hypothesis that wide-spread cultivation of Bt crops adversely affects non-target organisms which may be exposed to such crops under typical agricultural practice. However, this evidence is insufficient to establish the hypothesis that such adverse effects are expected to occur.

Comments by Argentina

This statement starts mentioning that there is "*some* (sic) scientific evidence to support the *hypothesis"…*, of non-target effects on organisms, "*which may be exposed",* and ends that "*this evidence* (sic) *is insufficient to establish the hypothesis that such adverse are expected to occur"*. It is clear from this wording that there is no *solid evidence* to support *the fact* that the organisms *will actually be exposed* in a way which may be of concern about the safety of the Bt crops mentioned.

03.02. The review of non-target effects of Bt plants in **EC-149** covered 13 laboratory studies evaluating potential hazard, and 14 field studies aimed at evaluating potential risk. Of the 13 lab studies reviewed, I conclude that five studies did not expose the test organisms properly and therefore are irrelevant hazard evaluations (an organism must be exposed to evaluate hazard). In two additional studies, four of eight test species were not properly exposed. Of the remaining, seven species were studied.[1] Of these seven, six were on Bt maize and none were on Bt cotton. Bt toxin had significant adverse effects on two of these six species, the collembolan *Folsomia candida* (a soil organism) and the lacewing *Chrysoperla carnea*. In neither case would adverse effects on these species been predicted based on the known spectrum of toxicity of the Cry toxin. There have been no studies to follow up the result with *F. candida*. Hence, I conclude that **there is a possible hazard (adverse effect) to collembola** from Cry1Ab Bt maize, but until this is confirmed, I cannot conclude that there is a potential risk to collembola. There have been numerous studies that

confirm that *C. carnea* is somehow adversely affected by Cry1Ab toxin. Hence, I conclude that **there is a potential risk to *C. carnea*** from Cry1Ab Bt maize.

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[1] *Folsomia candida*, *Coleomegilla maculata*, honey bee adults, *Hippodamia convergens* adults, 2 parasitoid species, *Crysoperla carnea*.

Comments by Argentina

Footnote 1 is not quoting literature, and therefore is not an argument.

On the phrase: "There have been no studies to follow up the result with F. candida. Hence, I conclude that there is a possible hazard (adverse effect) to collembola from Cry1Ab Bt maize, but until this is confirmed, I cannot conclude that there is a potential risk to collembola", we observe the following:

1. it states "to follow up the results", but it does not quote or mention to which results is the Expert referring to;

2. it is not easy to understand how, if there have been no studies, hence, the Expert concludes that there is a possible hazard;

3. how from the above, it can be concluded that there is a potential risk .

03.03. Of the 14 field studies reviewed in **EC-149**, six used plot sizes larger than 0.1 ha. Because most of the study organisms are mobile at spatial scales much larger than the plot sizes used, it is necessary to have larger plot sizes and to tailor the sampling methods to detect possible transient differences in population sizes between treatments. Otherwise, false negatives become problematic. The observed lack of significant differences between Bt and non-Bt treatments in nearly all the studies with small plot sizes is difficult to interpret, because the absence of an observed difference in these kinds of experiments is not a good indication that there were no differences. The only differences detected in these small plot studies were in the potato experiment, which will not be discussed here. Of the remaining six, two studies had insufficient replication. This low level of replication might allow the researchers to detect only differences larger than an order of magnitude. This detection threshold is much larger than what would be considered an adverse effect, so it is possible that some adverse effects were not detected. The remaining four studies had an equivalent of eight replications in each of two years. No adverse effects were observed. Unfortunately, the sampling methods were not sufficiently tailored to detect differences in population size. Taken as a whole, excepting the results on Bt potato, the other 13 studies would indicate that very large, order of magnitude adverse effects on non-target species are unlikely. However, the data do not address the likelihood of other large adverse effects on non-target organisms. Additional research would be needed before claims about safety can be supported with scientific evidence. In particular, the **cited field studies do not enable an evaluation of the likelihood of risk to *C. carnea***.

Comments by Argentina

The above paragraph is somewhat confusing. We observe:

1. Sentence 1 states that six studies were done on plot sizes larger than 0.1 ha. Sentence 2 indicates studies should be done on much larger than the plot sized used; it is not clear how much larger than 0.1 ha is needed;

2. Sentence 1 mentions six of 14 studies. Sentence 6 states "the remaining six" and only the potato experiment is mentioned before.

3. The number of studies-problem shows again when the Expert states : "the other 13 studies", excluding only the potato one. It is assumed that the Expert is referring "as a whole" to the (initially) mentioned 14 studies.

Other comments:

4. The Expert admits that "Taken as whole" the (other) 13 studies "would indicate that very large … adverse effects on non-target organisms are unlikely". In the next sentence, it is said that "the data do not address the likelihood of …other adverse effects on non-target organisms", and later on that "the cited field studies do not enable an evaluation of the likelihood of risk to *C. carnea*", and that "additional research would be needed". Not only the above shows some ambiguity, but also poses a question which is of a general validity in Science: there would always be the need for additional studies to prove something. Scientific knowledge is knowledge that has been validated through experiment, and its validity is not questioned just because future experiments (which there will always be) *may or may not* confirm its validity. Moreover, the need of additional knowledge is always one of the last sentences in a scientific paper.

Recent studies, however, have revealed a higher toxicity of Bt pollen and anthers than found in previous studies:

Anderson, P.L., Hellmich, R.L., Sears, M.K., Sumerford, D.V. & Lewis, L.C. (2004). Effects of Cry1Ab-expressing corn anthers on monarch butterfly larvae. Environ. Entomol., 33, 1109-1115.

Dively, G.P., Rose, R., Sears, M.K., Hellmich, R.L., Stanley-Horn, D.E., Calvin, D.D., Russo, J.M. & Anderson, P.L. (2004). Effects on monarch butterfly larvae (Lepidoptera: Danaidae) after continuous exposure to Cry1Ab-expressing corn during anthesis. Environ. Entomol., 33, 1116-1125.

Jesse, L.C.H. & Obrycki, J.J. (2004). Survival of experimental cohorts of monarch larvae following exposure to transgenic Bt corn pollen and anthers. In: The monarch butterfly. biology and conservation (eds. Oberhauser, K.S., Solensky, M.J.). Cornell University Press, Ithaca, pp. 69-75.

1. On the paper by Anderson et al, we reproduce here the abstract: (italics and underlined are ours. In capital letters, we indicated the relevant findings which contradict the contention that Bt toxin is a significant risk for monarca butterfly):

> **Previous studies suggest that exposure to corn, *Zea mays* L., anthers expressing *Bacillus thuringiensis* (Bt)-derived protein may have adverse effects on the larvae of monarch butterfly, *Danaus plexippus* (L.). To examine the potential effects of Bt anthers on monarch butterflies, studies were designed to test toxicity *in the laboratory*; examine anther distribution in space and time;**

compare distributions of anthers, pollen, and larval feeding; and *measure effects of long-term exposure in the field*. In the laboratory, monarch butterfly larvae fed on whole corn anthers, but anther feeding was sporadic. Larvae exposed to *0.3 ANTHER/CM^2* fed and weighed less after 4 d compared with larvae exposed to non-Bt anthers. Adverse effects increased with increasing anther density. Monarch butterfly larvae exposed to *0.9 ANTHER/CM^2* had reduced feeding, weight, and survival and increased developmental time compared with larvae exposed to non-Bt anthers. Later instars were more tolerant of Bt toxin. For all studies, *laboratory testing probably magnified effects because larvae were confined to petri dishes. Field studies showed toxic anther densities are uncommon on milkweed (Asclepias) leaves in and near cornfields during anthesis. Mean anther densities on milkweed leaves in cornfields during peak anthesis were between 0.06 AND 0.1 ANTHER/CM^2 (3–5 ANTHERS PER LEAF). When exposure to a density OF FIVE ANTHERS PER LEAF WAS TESTED IN FIELD-CAGE STUDIES, no effects on growth, development, or survival were detected. Based on probability of exposure to toxic densities, BT ANTHERS ALONE ARE NOT LIKELY TO POSE A SIGNIFICANT RISK TO MONARCH BUTTERFLIES IN IOWA.*

2. On the paper by Dively et al, we reproduce here some excerpts: (italics and underlined are ours. In capital letters, we indicated the relevant findings which contradict the contention that Bt toxin is a significant risk for monarca butterfly):

The potential non-target risks to monarch butterfly, *danaus plexippus* l., of transgenic corn transformed with a gene from the bacterium *Bacillus thuringiensis* (Bt) have been the focus of much scientific research and debate after a laboratory study by Losey et al. (1999) revealed toxicity to monarch butterfly larvae consuming Bt corn pollen deposited on milkweed plants (*Asclepias* spp.). *SUBSEQUENT STUDIES INDICATED THAT THE ACUTE EFFECT OF BT CORN POLLEN EXPRESSING LEPIDOPTERAN-ACTIVE CRY PROTEIN ON MONARCH BUTTERFLY POPULATIONS WAS NEGLIGIBLE (SEARS ET AL.2001). LARVAL EXPOSURE TO POLLEN ON A POPULATION-WIDE BASIS IS LOW, GIVEN THE PROPORTION OF LARVAE IN CORNFIELDS DURING POLLEN SHED, THE PROPORTION OF FIELDS PLANTED IN BT CORN, AND THE LEVELS OF POLLEN WITHIN AND AROUND CORNFIELDS THAT EXCEED THE TOXICITY THRESHOLD (OBERHAUSER ET AL. 2001, PLEASANTS ET AL.2001).CONSERVATIVELY, THE PROPORTION OF THE MONARCH BUTTERFLY POPULATION EXPONED TO BT CORN POLLEN WAS ESTIMATED TO BE 0.8% (SEARS ET AL.2001).LABORATORY BIOASSAYS ALSO SHOWED THAT ACUTE TOXIC AND SUBLETHAL EFFECTS OF POLLEN FROM THE MOST WIDELY PLANTED BT CORN HYBRIDS (EVENTS MON810 AND BT11) ARE UNLIKELY, EVEN AT PEAK LEVELS OF POLLEN SHED (HELLMICH ET AL.2001).THE ONLY TRANSGENIC CORN POLLEN THAT CONSISTENTLY AFFECTED MONARCH BUTTERFLY LARVAE WAS FROM THE CRY1AB EVENT 176 HYBRIDS, WHICH HAVE BEEN PHASED OUT OF COMMERCIAL USE IN THE UNITED STATES. FURTHERMORE, FIELD STUDIES PERFORMED IN IOWA, MARYLAND, NEW YORK, AND ONTARIO, CANADA, REPORTED THAT GROWTH TO ADULTHOOD OR SURVIVAL OF MONARCH BUTTERFLY LARVAE WAS UNAFFECTED AFTER EXPOSURES FOR 4-5 D TO MILKWEED LEAVES WITH NATURAL DEPOSITS OF*

CRY1AB EXPRESSING (EVENTS BT11 AND MON810) CORN POLLEN (STANLEY-HORN ET AL.2001).THESE RESULTS INDICATED NEGLIGIBLE EFFECTS OF BT POLLEN TO MONARCH BUTTERFLY LARVAE FROM SHORT-DURATION EXPOSURES IN FIELD SETTINGS. ALL SCIENTIFIC INFORMATION ON ACUTE TOXICITY AND EXPOSURE SUPPORTS THE ONCLUSION THAT BT CORN POSES A LIMITED RISK TO MONARCH BUTTERFLY POPULATIONS (SEARS ET AL.2001).WHAT RISK EXISTS IS CAUSED BY THE LIMITED EXPOSURE OF MONARCH BUTTERFLY POPULATIONS TO BT POLLEN IN NATURE. NEVERTHELESS, THE STUDIES TO DATE EXAMINED ACUTE AND SUBLETHAL EFFECTS AFTER 4-5 D OF EXPOSURE OF DEVELOPING LARVAE TO BT POLLEN.IN CORNFIELDS, LARVAE HATCHING AT THE ONSET OF ANTHESIS MAY BE EXPONED TO BIOLOGICALLY ACTIVE CRY1AB PROTEIN FOR PERIODS OF 12 D OR MORE (RUSSELL AND HALLAUER 1980).THIS WORST-CASE SCENARIO COULD POTENTIALLY IMPACT THE 0.8% OF THE MONARCH BUTTERFLY POPULATION EXPOSED TO BT …

Long-term exposure of monarch butterfly larvae throughout their development to Bt corn pollen is detrimental to only a fraction of the breeding population because *THE RISK OF EXPOSURE IS LOW*. When this impact is considered over the entire range of the Corn Belt, *THE ECOLOGICAL OUTCOME IS VERY SMALL.* Moreover, *BT CORN ADOPTION IS ASSOCIATED WITH LOWER INSECTICIDE USE AGAINST TARGET LEPIDOPTERA (PILCHER ET AL.2002), AND MOST INSECTICIDES ARE ACUTELY TOXIC TO LARVAE OCCURRING IN CORN OR IN OTHER CROPS THAT PROVIDE HABITAT FOR MONARCH BUTTERFLY POPULATIONS*. In field bioassays, larvae died within hours after feeding on milkweeds exposed to a single application of a pyrethroid insecticide (Stanley-Horn et al.2001) … .

… IT IS LIKELY THAT BT CORN WILL NOT AFFECT THE SUSTAINABILITY OF MONARCH BUTTERFLY POPULATIONS IN NORTH AMERICA … .

(Note of this reviewer) The above shows that Bt corn could be considered a protection to monarca butterfly, as its use would decrease the use of chemical insecticides, which are acutely toxic to larvae.

3. On the paper by *Jesse and Obrycki (2004)*, we reproduce here some excerpts from the abstract:

1. We present THE FIRST EVIDENCE that transgenic Bacillus thuringiensis (Bt) corn pollen naturally deposited on Asclepias syriaca; common milkweed, in a corn field causes significant mortality of Danaus plexippus L. (Lepidoptera: Danaidae) larvae. Larvae feeding for 48 h on A. syriaca plants naturally dusted with pollen from Bt corn plants suffered significantly higher rates of mortality at 48 h (20±3%) compared to larvae feeding on leaves with no pollen (3±3%), or feeding on leaves with non-Bt pollen (0%). Mortality at 120 h of D. plexippus larvae exposed to 135 pollen grains/cm2 of transgenic pollen for 48 h ranged from 37 to 70%. … We conclude that the ecological effects of transgenic insecticidal crops NEED TO BE EVALUATED MORE FULLY before they are planted over extensive areas.

We agree that the results shown here are the first evidence of an effect, but they should be validated by further research, as the authors recognized.

> 03.04. **EC-150** is a scientific paper that evaluated the effects of Bt maize litter (Bt11) on the earthworm *Lumbricus terrestris* in laboratory and semi-field experiments. There were no effects on survival or growth of immature earthworms in the semi-field experiment. There were no difference in adult survival or growth during the first 160 days in the laboratory experiment. Adults were about 20% smaller with Bt litter than non-Bt litter at 200 days. In total and compared with other published results, the results of this study indicate that adverse effects on *L. terrestris*, if they exist, are likely to be subtle. In addition, they suggest that **there is a possible hazard to earthworms** from Cry1Ab Bt maize litter, but until this is confirmed, I cannot conclude that there is a potential risk to earthworms.

Comments by Argentina

Again, the statements are confusing, starting with an "approval" sentence ("… adverse effects…, *if they exist*…") followed by a "disapproval" one ("… they suggest that *there is a possible hazard*…"). Adding to this, the statement ends with the impossibility to "… conclude that there is a potential risk". One ends being not sure about the resulting opinion.

> 03.05. **EC-151** documents a novel route of exposure of soil organisms to Cry1Ab toxin from Bt maize. Cry1Ab toxin is exuded from living maize roots. There has been some controversy as to whether the exudates are from damaged root cells or from a process involving living root cells, however, the evidence suggests that there is a process involving living root cells. This result was not anticipated. Theoretically, the Cry1Ab protein was considered too large to be exuded from living plant roots. **This study does not document a possible adverse effect of Bt maize**, however, it demonstrates that species inhabiting the maize root rhizosphere can be exposed to Cry toxin. This is significant because these species had been considered not at risk previously, and opens the possibility that unanticipated adverse effects to rhizoshere species might be identified.

Comments by Argentina

From the statement "This study does not document a possible adverse effect of Bt maize," it cannot be concluded (or even just "… opens the possibility that") "unanticipated adverse effects … might be identified". This sequence of premises is equivalent to the following logic: "If the occurrence of a fact is not documented, it follows that this fact might occur". This cannot be posed as an argument in the above context.

> 03.06. **EC-152** demonstrates that Cry toxins persist, accumulate and remain insecticidal in soil by binding to humic acids in soils. Previous work had demonstrated similar results in binding to clay in soils. Moreover, the toxins maintain toxicity for at least 234 days (the longest time examined). Together these studies demonstrate that Cry toxins will persist in soils much longer than previously believed, and that the mechanism of persistence is related to adsorption to clay particles and humic acids in the soil. Together with EC-151, these studies demonstrate that soil organisms are likely to be exposed to Cry toxin via root exudates and litter. **None of these studies document a possible adverse effect of Bt maize**. Together, however, they suggest that more species in the soil may be at risk

than previously expected. These results suggest that additional studies may be needed to evaluate these possibilities.

Comments by Argentina

We observe in this answer the same kind of reasoning as before (see above): From "None of these studies document a possible adverse effect…", it follows (suggests?) "that more species in the soil may be at risk…". Moreover, the adsorption to clay and humic acids of macromolecules and phosphorous compounds used as fertilizers, is a well known phenomenon. However, *persistence* is not equivalent to *availability*. In the case of plasmid DNA or phosphorous compounds used as fertilizers, it was demonstrated that laboratory treatments are needed to release them from the adsorbed complexes. Of course, there are microorganisms able to promote this release (*Penicillium bilanyi*, for example). Then, we are led through a never ending process in which, the last word, is always that risk can be (sic) "expected" and "that additional studies may be needed".

As an example of the consequences of extrapolating this reasoning, consider the anti-nutritional factors present in non-biotech crops. Some of them exhibit a strong deleterious action (e.g., ribosome inactivating proteins, or rips, which are present in many plants). They are present in crops at concentrations close to the newly expressed proteins in biotech crops. Persistence in soil (by the same mechanisms as before) can be predicted in these cases, but subsequent toxic effects to other organisms has been found to be very specific in the field (e.g., as defence mechanisms), or in *in vitro*, laboratory conditions. These factors may be of much higher concern, as it should be admitted in the context of the answer above, and are present in non-biotech crops. If the same reasoning is applied, one is to expect "that more species in the soil may be at risk than previously expected", and "that additional studies may be needed" before any regular, familiar crop is sowed again.

03.07. During 1999, concerns were expressed that monarch butterflies would be adversely affected by Bt maize pollen falling on their host plant, common milkweed. This result was followed up with a series of studies to assess the risk to monarchs. The authors of these follow-up studies concluded that the risk to monarch populations was insignificant for Mon810 and Bt11, because only a small proportion of butterflies would be exposed to these and the toxicity of pollen was low. The events and findings associated with these studies are summarized in an excellent review. Recent studies, however, have revealed a higher toxicity of Bt pollen and anthers than found in previous studies. Although some suggested that the risk to monarchs remains insignificant, a close reanalysis of the issues may allow other interpretations of risk to monarchs.

Comments by Argentina

Same as before: it is said that "Although some suggested that the risk to monarchs *remains insignificant* (studies quoted support that), a close *reanalysis* of the issues *may allow* other interpretations of risk to monarchs". Again, the succession of approval and disapproval sentences conducting to a need for more studies, seems to be recurrent. Again, one is left with the impression that, although risks are not proven or remain insignificant, further analysis would be needed. In other words, one is caught in the logic of "if a proof exists, further analysis may show that the proof does not exist". We observe that this should not be considered valid in the present context.

03.08. Most these same papers also addressed the potential risk to monarchs from Event 176 BT maize. Although they concluded that there was no risk to monarchs from Event 176, this was based largely on the assumption that Event 176 would not be used very much in production. Had Event 176 gained greater market share, it would likely have put monarchs at risk.

Comments by Argentina

See above.

03.09. As mentioned in paragraph 03.02, *C. carnea* is under a potential risk from Bt maize. Although this has not yet been studied in the field, I expect that the actual risk to *C. carnea* would not be large. In maize in temperate regions, this species feeds primarily on aphids, mites, thrips, and lepidopteran eggs and larvae. Previous studies have shown that the main aphid on maize does not contain any Cry toxin when feeding on Bt maize, and that mites contain the Cry toxin, but they do not adversely affect *C. carnea*. It is not known if thrips or Lepidopteran eggs contain Cry toxin. Adverse effects on *C. carnea* have been documented only when it feeds on diets containing Cry toxin or on Lepidopteran larvae that had fed on Bt maize. Any adverse effect from Lepidopteran larvae and possibly thrips and eggs would be diluted by feeding on aphids and mites. Consequently, I believe that any adverse effect on *C. carnea* in the field will be subtle and difficult to detect in the field.

Comments by Argentina

After saying that *C.carnea* is at risk, it is admitted above that the adverse non-target effects in the field (the Expert expects that) "*will not be large*". Studies are quoted in support of that, and it is concluded that, *if any*, these effects will be *subtle and difficult to detect in the field*. It is hard to find here a conclusive statement, when proven evidence is towards "approval" of the biotech crop. Not being large, or being difficult to detect, are expressions which seem to be addressed at avoiding to give a relevant answer, i.e., that not risk has been proved.

03.10. Relatively few non-target studies have been conducted on Bt cotton. This limits discussion of potential risks.

Comments by Argentina

Approval requirements always call for non-target effects studies. These must include foreign and local data.

03.11. It has been argued that the experience in using Bt maize and Bt cotton in the US provides evidence that there are no adverse effects on non-target organisms. It is true that Bt maize and Bt cotton have been used widely in the US, and it is also true that no adverse effects to non-target species have been reported and confirmed. However, these two facts do not imply that there have been no adverse effects on non-target organisms, because there is virtually no monitoring for such adverse effects. If such effects are not looked for, it is unlikely that they will be found, even if they exist. It can be reliably argued that the US experience with these crops suggests that there have been no immediate catastrophic adverse effects to non-target species. Such catastrophes would have become noticeable even if they were not actively looked for. However, it is more likely that adverse effects, if they exist, will

be more subtle, and would not be readily noticed. Hence, **the US experience does not imply that there are no adverse effects on non-target species**.

Comments by Argentina

See comments below 03.02 and 03.09 and others.

03.12. In any event, Cry toxins are unlikely to adversely affect mammals through direct toxicity. They exert their toxic effect by binding first with specific glycolipids in the gut. These protein-glycolipid complexes then bind to specific receptors (cadherin-like receptors) on the wall of the gut. The entire family of the specific glycolipid and receptor molecules are absent from mammals, thus Cry toxins cannot act in their normal way in mammals.

Comments by Argentina

A clear answer to the question is not provided above. By stating that "Cry toxins cannot act in their *normal way* in mammals", omission is made of the fact that, considering the mode of action of Cry toxins, an adverse effect on mammals is unlikely to occur.

03.13. Conclusion. Possible hazards have been identified and potential risks are evident, however, it cannot be concluded that an actual non-target risk of Bt maize or Bt cotton has been fully characterized. However, it is likely that if the analysis is completed, that there will be a documented risk of some Bt maize events to monarch butterflies.

Comments by Argentina

The Expert mentions that "possible hazards" have been identified (but not proven), and that "potential risks are evident ", but it cannot be concluded that they exist. Consequently, any conclusion referring to any existence of risks would be entirely speculative. Moreover, we consider that the last sentence, ending "it is likely that if the analysis is completed, there will be a documented risk of some Bt maize events to monarch butterflies" is an anticipated judgement, not a scientifically based argument.

Comparison with Bt insecticides

03.14. There are significant differences in exposure probability and exposure routes. Bt insecticides have low likelihood of a non-target risk because they do not persist very long after application. The Cry toxin is degraded rapidly under UV light, and efficacy of the insecticide is lost usually within a few days. This contrasts with Bt crops, which produce Cry toxin constitutively over the entire growing season at high concentrations throughout the plant tissue, and as noted above, can persist in the soil.

Comments by Argentina

Following the "likely to occur" reasoning, its follows that Bt formulated insecticides can probably persist in soil by similar mechanisms as plant-expressed Bt toxins. Also, "high concentrations" tends to ignore the fact that these concentrations are of the order of 0.001 % total protein, or lower.

03.15. It is theoretically possible that hazards will be different, but this depends on the protein structure of the Cry toxin in the plant compared with the insecticide. For example, Event 176 Cry1Ab is significantly smaller than Cry1Ab toxin in the bacterium, *Bacillus thuringiensis*. The full protein in the bacterium must be shortened to a form that shows active toxicity. Event 176 protein is already in an active form. Thus, if the shortening process affects hazards, then Event 176 protein may exhibit a different spectrum of hazards than the bacterium protein. However, it has not been scientifically demonstrated that this difference in structure actually affects hazard. There are also differences between Mon810 and Bt11 Cry1Ab and the Cry1Ab in the bacterium. There appears to be little difference between Event 1507 Cry1F and the Cry1F in the bacterium.

Comments by Argentina

We consider that this is a speculative reasoning. The expert calls for theoretically possible hazards, involving, for example, the protoxin-toxin processing in the insects gut, and the different structure (produced by plant vs. bacterium) which can affect hazard. But then, the Expert surprisingly omits to mention the only case of the latter (which will work in favour of his stand), that is, the modified Cry 9C protein in CBH 351 event. In this case, the different structure was an intended change, and its effects on mammals digestive process was quickly recognized by specific and mandatory tests in the GM crop review process. As the safety of this event was not being satisfactorily proven, this event was not approved or partially approved (for feed purposes only). This example is brought here to show the strictness of the regulatory systems in place in the countries which are part in this Panel. (As a further comment, this structure difference was anyway later proved to have no adverse effects on mammals).

03.16. Both are unlikely to adversely affect mammals. The Bt insecticides have undergone significant number of studies on mammalian toxicity, and none have been found to be toxic to any of the mammals studied. Coupled with paragraph 03.12, it is unlikely that either Bt crops or Bt insecticides will adversely effect mammals through direct toxicity.

Comments by Argentina

Although this point is favourable to an approval of the Bt events, we note that the Expert refers to "direct" toxicity, suggesting the possible existence of other, *indirect* toxicity, which is entirely speculative but cast doubt in the mind of laypersons.

Risk management options

03.17. Risk management measures should be commensurate to the risk.

03.18. One risk management option is to prohibit the use of the Bt crop. If this option is considered, it should be necessary to provide a worst-case risk assessment to provide a basis for concluding that a prohibition is commensurate to the risk. For example, what would be the harms if all earthworms were 20% smaller after feeding on Bt maize litter for more than 160 days (see paragraph 03.04)?

Comments by Argentina

See our comments under 03.04.

03.19. Another approach would be to limit the area of the transgenic crop until a reasonable assessment of the possible hazards and potential risks are completed. As the information is gathered, the risk management measure can be modified consistent with the principle of "modification."

03.20. For actual risks, such as the presumed risk to monarchs, geographic restrictions in use of the Bt crop could be considered. Incentives to use alternatives to the Bt crop can be provided. Disincentives for the use of the Bt crop could be imposed. Monitoring of the population at risk could be required, although this would likely be more expensive than restricting or managing use, and may be difficult to justify based on the principle of equivalence.

Comments by Argentina

We agree on geographic restrictions when proven to be necessary. This is not the case with monarchs, as geographic (and other) factors are against the existence of adverse effects (as the Expert states in the pertinent points). Incentives to use alternatives should always exist, for biotech as well for non-biotech crops, because maximising the benefits/risks ratio should always be pursued. We disagree with the concept of disincentives for any particular way agriculture is practiced, being traditional, biotech or organic; we rather promote co-existence, determined by overall benefits.

03.21. Efforts to improve risk assessment procedures could be viewed as a form of risk management. Improved procedures would be more effective at identifying potential risk, reducing uncertainty and allowing risk assessment to proceed more rapidly.

03.22. Another option would be to have no risk management. Here it seems necessary to have a risk assessment that concludes that there are no significant non-target risks and that unanticipated effects will be either absent or insignificant.

03.23. By no means should the Panel assume that this is an exhaustive list of possible management options. These are suggestions of approaches to risk management emphasizing avoiding risk. Approaches that emphasize mitigation of risk or tolerance of risk could also be considered.

Question 4

4. On the basis of the information before the Panel, is there any scientific evidence to support the hypothesis that the wide-spread cultivation of Bt maize or other, non-biotech applications of Bt toxins, leads to the emergence of Bt-resistant target organisms under field conditions? If so, what risk management options exist to mitigate any resulting risks and what is their efficacy?

Evidence for resistance

04.01. Widespread non-biotech applications of Bt toxins have resulted in the Bt-resistant target pest organisms under field conditions. Probably the best studied example is diamondback moth on cabbage, which has developed field resistance to Bt insecticide applications in several countries, including the US (Hawaii), Japan, Philippines and elsewhere.

04.02. There is strong evidence that resistance will develop in the field to any insecticide applied uniformly over wide areas for a long enough period of time. This has been a scientific consensus since the 1980s.

Comments by Argentina

We agree. Moreover, any selective pressure in the field will result in resistant individuals. It is evolution.

04.03. Bt-resistant target organisms have been found – pink bollworm (*Pectinophora gossypiella*) to Bt cotton in the field, but this has not yet led to field failures.

04.04. Evolutionary theory predicts that the evolution of resistance will proceed as directional selection, at least up to the point resistance becomes common. This means that resistance in the field cannot be prevented, it can only be delayed.

Comments by Argentina

We agree. From the above statement by the Expert, it follows that, since a fundamental evolutionary phenomenon is unavoidable with any selective pressure, it cannot be called to support the rejection of approval of Bt crops.

04.05. There is a scientific consensus that resistance to Bt maize is inevitable, even though it still has not been detected in the field. This is based on the preceding empirical and theoretical evidence.

04.06. Generally speaking, of all of the potential environmental risks of transgenic Bt crops, it can be said that resistance in the target pests is a real, tangible risk, while risks associated with gene flow and risks to non-target organisms are mostly only potential risks.

Comments by Argentina

We fully agree.

04.07. There are several risk management options for Bt maize, but they are all concerned with reducing the selective advantage of resistant alleles in populations of the target species.

04.08. The most widely used resistance management strategy for Bt maize (and all Bt crops) has been the high-dose/ refuge strategy. This has been used by the US Environmental Protection Agency (US-EPA). For Bt maize, it is generally accepted that a 20% refuge is needed for the high-dose/ refuge strategy to be effective.

04.09. Low-dose Bt events will require a greater refuge. There is no scientific consensus as to how big a refuge is needed. One approach, used by the US-EPA is to require a 20% refuge during the initial period of use, when market penetration remains low. This may provide enough time for the scientific evidence to accumulate so that an appropriate refuge size can be determined. A different approach was used by Australia, where a very large refuge was required initially, which was gradually reduced over time to a 70% refuge.

04.10. Additional resistance management strategies may become possible to develop after resistance in the target pest is identified and characterized.

04.11. The efficacy of the high-dose/refuge strategy cannot be assessed empirically in the field. Indeed, it would probably be unethical to conduct such a field experiment because it would be necessary to have a positive control treatment where resistance was encouraged. Resistant insects in such a control treatment could escape, leading to field failures that undermine the efficacy of the high-dose/ refuge strategy.

04.12. Some greenhouse experiments have confirmed the efficacy of the high-dose/refuge strategy.

04.13. Theory has predicted that the high-dose/ refuge strategy will be efficacious when resistance allele frequency <0.001, resistance is recessive, and there is sufficient adult movement between the refuge and Bt fields to ensure matings between resistant and susceptible phenotypes.

04.13. These assumptions have been confirmed scientifically for European corn borer (*Ostrinia nubilalis*) in the northern US corn belt. These assumptions are likely for European corn borer in the southern US and in western Europe. They have not been confirmed for southwestern corn borer (*Diatraea grandiosella*) in the southern US, for European corn borer in eastern Europe, or for Mediterranean corn borer (*Sesamia nonagrioides*) in southern Europe. Hence, it can be concluded that in some circumstances it is possible to predict that the high-dose/ refuge strategy should be efficacious. It is possible that the absence of detection of field resistance to Bt maize in the US is partially attributed to the efficacy of the high-dose/ refuge strategy.

Comments by Argentina

We agree. We observe, however, that the need of a practicable (and in fact set in place) management strategy to delay resistance, should not be construed as an impediment for approval.

Question 6

6. On the basis of the information before the Panel, is there any scientific evidence to suggest that herbicide tolerant crops (whether biotech or developed through mutagenesis) are more persistent in the agricultural environment or more persistent in the non-agricultural environment than their conventional counterparts? If so, do herbicide tolerant crops qualify as a potential "pest" as the term is used in the International Plant Convention's (IPPC) International Standard for Phytosanitary Measures (ISPM) 11 (EC-130)?

(a) What is the potential for the establishment and spread of herbicide tolerant plants arising from handling, spillage during transport of the plant/plant parts, or any other means outside of cultivation in the absence of application of the herbicide? How is any potential for establishment and spread affected by environmental conditions, the presences of wild or conventional relatives of the herbicide tolerant plants in an area, or other factors?

(b) What is the potential for the establishment and spread of herbicide tolerant plants in the presence of herbicide application (in fields, urban, domestic or other environments)? How is any potential affected by the existence of feral related plant species; infertile wild relatives; seed survival in relevant pedoclimatic conditions; the reproduction biology of the species; or other factors?

(c) Is this potential different for biotech crops tolerant to two wide-spectrum herbicides? Please explain.

(d) If significant risks of establishment and spread have been identified, what risk management options exist to mitigate any resulting risks and what is their efficacy?

(e) What types of post-market monitoring and data collection activities could be envisaged on the basis of the monitoring and review principles described in ISPM 11?

06.01. I will provide a theoretical response to the main question and address only part (e) of the subparts of this question. I will use the seven kingdom taxonomy here and throughout in discussing organisms.

06.02. Persistence of herbicide tolerant crops (whether biotech or developed through mutagenesis) will be determined by the relative fitness of the crop with the trait and the degree of release of the trait. The only way that a GMHT would be more persistent than a non-GMHT crop would be if it had a higher relative fitness and/or it was released at a higher rate. Both factors would have to be assessed on a case-specific basis. For GMHT maize, cotton, soybean and beet, the question is moot because there are no comparably good non-GMHT varieties. For GMHT oilseed rape, evidence from Canada suggests that the GMHT varieties are used more commonly than the non-GMHT varieties, thus there is some scientific evidence to suggest that GMHT oilseed rape may be more persistent in the agricultural or non-agricultural environment than their conventional HT oilseed rape.

Comments by Argentina

It is not clear to us the meaning attached to the expression "degree of release of the trait".

06.03. A similar argument holds for persistence of herbicide tolerant crops (whether biotech or developed through mutagenesis) compared to their conventional counterparts. When examining release rate, however, the relevant release rate for the conventional counterpart is that of a single variety.

06.04. Annex 2 of ISPM 11 specifies "Phytosanitary risks from LMOs may result from certain traits introduced into the organism, such as those that increase the potential for establishment and spread, or from inserted gene sequences that do not alter the pest characteristics of the organism by that might act independently of the organism or have unintended consequences." Thus phytosanitary effects of the transgene outside of the original organism of introduction are covered by ISPM 11.

06.05. Annex 2 elaborates on this further in the next clause, which states "In cases of phytosanitary risks related to gene flow, the LMO is acting more as a potential vector or pathway for introduction of a genetic construct of phytosanitary concern rather

than as a pest in and of itself. Therefore the term "pest" should be understood to include the potential of an LMO to act as a vector or pathway for introduction of a gene presenting a potential phytosanitary risk." Phytosanitary risks associated with gene flow and persistence are covered by ISPM 11.

06.06. Moreover, Annex 3 "Determining the potential for a living modified organism to be a pest", specifies that "potential phytosanitary risks for LMOs may include: a. Changes in adaptive characteristics which may increase the potential for introduction or spread, … b. Adverse effects of gene flow or gene transfer. This indicates that the potential for introduction and spread are a part of phytosanitary risk, as well as adverse effects of gene flow.

06.07. From the perspective of gene flow and persistence, GMHT crops may qualify as a potential pest according to ISPM 11, as long as they can be shown to be released at a higher rate and/or have a selective advantage compared to a conventional counterpart.

06.08. Of course it is possible for a GMHT crop to qualify as a potential pest according to ISPM 11 if persistence is expected to be the same as a conventional counterpart. This would occur if it potentially resulted directly or indirectly in some adverse effect that was different from the conventional counterpart. For example, if contamination of conventional crop germplasm (related to the "coexistence" issue) were considered an injury to the conventional plant, then there would be a reason to believe that all GMHT crops can be considered potential pests under ISPM 11. All other potential pest risks would probably have to be considered on a case by case basis.

Comments by Argentina

We observe the conditionals in the above paragraph: "… if persistence is expected to be the same …", "… if it potentially resulted directly or indirectly in some adverse affect …", "… if contamination … . were considered an injury … then there would a reason to believe …", "… potential pests risks". The above have a speculative nature, not leading to a clear statement. The whole paragraph deals with speculations.

06.09. ISPM 11 is ambiguous whether all possible effects of GMHT crops can be considered phytosanitary risks. The definition of "pest" is given on page 6 of ISPM 11 as "Any species, strain or biotype of plant, animal or pathogenic agent injurious to plants or plant products [FAO, 1990; revised FAO, 1995; IPPC, 1997]" The concept of "injurious to plants includes environmental risks, as indicated in supplementary text *S1*.

06.10. Annex 2, which covers the scope of IPPC for LMOs states "PRA may constitute only a portion of the overall risk analysis for import and release of a LMO. For example, countries may require the assessment of risks to human or animal health, or to the environment, beyond that covered by the IPPC." This is a clear acknowledgement that there are some environmental risks that are not covered by the IPPC.

06.11. Annex 1 addresses the scope of the IPPC in regard to environmental risk. This text is reproduced here.

"The full range of pests covered by the IPPC extends beyond pests directly affecting cultivated plants. The coverage of the IPPC definition of plant pests includes weeds and other species that have indirect effects on plants, and the Convention applies to the protection of wild flora. The scope of the IPPC also extends to organisms which are pests because they:

– *directly affect uncultivated/unmanaged plants*

Introduction of these pests may have few commercial consequences, and therefore they have been less likely to be evaluated, regulated and/or placed under official control. An example of this type of pest is Dutch elm disease (*Ophiostoma novo-ulmi*).

– *indirectly affect plants*

In addition to pests that directly affect host plants, there are those, like most weeds/invasive plants, which affect plants primarily by other processes such as competition (e.g. for cultivated plants: Canada thistle (*Cirsium arvense*) [weed of agricultural crops], or for uncultivated/unmanaged plants: Purple loosestrife (*Lythrum salicaria*) [competitor in natural and semi-natural habitats]).

– *indirectly affect plants through effects on other organisms*

Some pests may primarily affect other organisms, but thereby cause deleterious effects on plant species, or plant health in habitats or ecosystems. Examples include parasites of beneficial organisms, such as biological control agents.

To protect the environment and biological diversity without creating disguised barriers to trade, environmental risks and risks to biological diversity should be analyzed in a PRA."

06.12. In considering indirect effects, Annex 1 addresses "indirect effects on plants" and "indirect effects on plant through effects on other organisms." Indirect effects are not defined, but the two examples provided are two of the five fundamental two-species interactions in ecological science, consumption (parasite-host or predator-prey or herbivore-plant), competition, mutualism, amensalism, and commensalism. Thus, indirect effects occur via any combination or pathway of these to-species interactions. This is the standard interpretation of the concept of indirect interactions which give rise to indirect effects in the field of ecology. As the IPPC is science-based, I assume that standard scientific usage is appropriate for interpreting key terms taken from science.

06.13. Under this interpretation (and other interpretations as well), the effects of the herbicides applied to the GMHT crops is not covered under Annex 1 and can not be considered a phytosanitary risk. Herbicide use cannot be considered a direct or indirect effect of the GMHT crop, because humans apply the herbicides. It is inaccurate to say that this is an indirect effect of the GMHT crop through effects on other organisms. The GMHT crop does not affect humans to apply herbicides. Causality works the other way. Humans affect the distribution of the GMHT crops and at the same time affect herbicide use. Thus, the effects of herbicide use on GMHT crops is not covered under Annex 1.

06.14. Section 2.3 of ISPM 11 covers "Assessment of potential economic consequences" and also covers environmental risk. Under 2.3.1.2, indirect pest effects are considered. This is a list of potential endpoints to consider given that it is an indirect effect. Thus, section 2.3 does not provide an interpretation to cover the effects of herbicides applied to GMHT crops as a phytosanitary risk.

06.15. It would be disingenuous to suggest that herbicide effects should be considered as if they were independent of the use of a GMHT crop. While it may be true that the environmental effects of herbicides are regulated under independent regulatory structures, this does not change the fact that they are used part and parcel with GMHT crops because that is their intended use. Thus GMHT crops almost always will be accompanied by the use of the specific herbicide.

06.16. The only ecologically consistent position would be to identify humans as the potential pest. This, however, is absurd under ISPM 11.

06.17 Thus I conclude that GMHT crops can qualify as a potential "pest" as the term is used in the International Plant Convention's (IPPC) International Standard for Phytosanitary Measures (ISPM) 11 (EC-130). However, not all of the risks associated with GMHT crops can be considered phytosanitary risks.

Comments by Argentina

We contend that GMHT crops do not qualify as a potential "pest", as the Expert suggest by the use of quotation marks. Only a forced interpretation would allow this qualification.

The key concept is that the LMO nature of a plant or plant product is not inherently related to (and/or considered a priori to be) a pest and/or a phytosanitary risk as such. However, IPPC documents (as well as their wording), regarding phytosanitary risks can be used as a guidance in the elaboration of documents regarding LMO.

Also note: The use of the acronym PRA implies that LMO are considered like pests, which is not right (with the guidance exception mentioned above). LMOs are intended to be agricultural crops which have been reviewed for safety for flora, animal, human health and environmental safety by sound, scientifically based biosafety (the term used in the above is risk) analysis. Although we would not correct the PRA expressions here, which should be just RA, it must be considered with this strong restriction.

(e) Post-market monitoring and data collection

06.18. Section 3.6.1 of ISPM 11 describes the monitoring and review of phytosanitary measures. This concentrates on the principle of "modification", and is repeated here.

> **3.6.1 Monitoring and review of phytosanitary measures**
>
> The principle of "modification" states: "As conditions change, and as new facts become available, phytosanitary measures shall be modified promptly, either by inclusion of prohibitions, restrictions or requirements necessary for their success, or by removal of those

> found to be unnecessary" (ISPM N° 1: *Principles of plant quarantine as related to international trade*).
>
> Thus, the implementation of particular phytosanitary measures should not be considered to be permanent. After application, the success of the measures in achieving their aim should be determined by monitoring during use. This is often achieved by inspection of the commodity on arrival, noting any interceptions or any entries of the pest to the PRA area. The information supporting the pest risk analysis should be periodically reviewed to ensure that any new information that becomes available does not invalidate the decision taken.

06.19. This suggests that an important part of the risk management measures applied to GMHT crops should include a process to review the necessity of the management measures. Given that many ecological effects are scale-dependent, manifesting more readily at larger spatial and temporal scales, some management measures could be linked to the spatial extent of use of the GMHT crop. If the spatial extent of use is not great enough, then certain management measures could be considered unnecessary. Alternatively, if the GMHT trait persists in a given locality for long enough, additional management measures could become necessary.

06.20. In a similar fashion, after certain time and area thresholds have been exceeded, it would be reasonable to review management measures to determine if the measures need to be dropped, retained or strengthened. Such thresholds should be agreed upon in advance.

06.21. Finally, for precautionary management measures, there should be certain time and area thresholds specified which would trigger a review to determine if sufficient information had accumulated to merit a reduction in the level of precaution. Presumably the precautionary management measures would provide data from which it would be possible to assess their necessity.

Question 7

7. On the basis of the information before the Panel, is there any scientific evidence to support the hypothesis that repeated use of a given biotech herbicide tolerant crop has adverse effects on flora and fauna, including soil micro- and macro-fauna? If so, how does this compare with any similar risks of adverse effects from the repeated use of a non-biotech herbicide tolerant crop (i.e, one developed through mutagenesis)?

07.01. I will restrict this answer to the following genetically modified herbicide tolerant (GMHT) crops: oilseed rape, fodder beet, cotton, maize, soybean, and sugar beet. I will use the seven kingdom taxonomy in discussing organisms.

Adverse Effects of GMHT Crops

07.02. There is abundant evidence that repeated use of a given biotech herbicide tolerant crop would likely result in the evolution of resistance in weeds to the herbicide. While it can be debated if this adverse effect results from repeated use of the GMHT crop or from the repeated use of the herbicide of which the GMHT crop is

tolerant, in practice the two are so tightly correlated, and the GMHT crop is expected to have the herbicide applied to it. Hence a risk assessment should consider both as correlated causal factors. In the language before the panel, weed resistance is a risk resulting from the associated changes in agricultural practices.

Comments by Argentina

We agree in that distinction is not made between biotech and non-biotech HT crops, as it is properly pointed out that "changes in agricultural practices" are in the focus of this question.

07.03. Adverse effects on non-target flora and fauna could arise directly from transgene products, directly from the herbicide compounds, or indirectly through the effects of the transgenic crop or the herbicide on the environment. Although the authors of the Farm-Scale Evaluation (FSE) Trials of GMHT crops in the UK concluded that all adverse non-target effects arise indirectly from the effects of the herbicide on the environment, this highly credible argument is not proved conclusively. In any event, the FSE Trials demonstrate that some, but not all, GMHT crops can have adverse effects on non-target organisms. I believe that it is likely that additional adverse effects on non-target organisms may be reported in the future.

Comments by Argentina

The above challenges the FSE trials, which other Expert calls (in a confusing way, in our view) in support of non-target effects. See the comments below, by J.L. London in "Biosafety trials darken Outlook for transgenic crops in Europe", Nature, 425:751, 2003); some excerpts (bold and underlines are ours):

"Britain's Farm Scale Evaluations, Publisher on 16 October, show that two genetically modified crops – spring oilseed rape and beet – are likely to have harmful impacts on farmland biodiversity. Researchers say the levels of weeds, seeds and insects in fields of transgenic crops were lower than those in plots of conventional varieties, and that this could have a knock-on effect on the birds and small animals that feed off these populations.

Although the problems are caused by the herbicide-spraying regime associated with the crops, rather than the crops themselves, the results are likely to make it politically impossible for the British government to license transgenic crops in the immediate future, many observers say. … The trials, which took place between 2000 and 2002 and are published as eight papers in the *Philosophical Transactions of the Royal Society B*, compared conventional and transgenic varieties across 200 plots.

Positive results for a third crop — maize (corn) — have been called into doubt, as the weed-killer used on most of the conventional plants is to be phased out. But the other results have not been directly challenged by most supporters of the technology. The data show that the number of seeds on the ground in the plots of transgenic oilseed rape and beet was one-third to one-sixth lower than in the conventional plots.Levels of some insects and weeds were also lower. "We could see a long-term decline in weeds that feed birds," says Les Firbank, a land-use specialist at Lancaster University, who led the trials. **Firbank and the other authors stress <u>that it is the herbicide-spraying regime, not the genetic modification, that is the</u>**

root of the problem. Herbicide-resistant crops are engineered to resist broad-spectrum weed-killers that remove almost all weeds from a field. (*)

During the farm-scale evaluations, **farmers sprayed the crops once or twice with a broad-spectrum herbicide.** This reduces the labour required for conventional weed management, which involves repeatedly applying less powerful weed-killers. But **the more powerful herbicide used with the transgenic crops also removes more weeds**, as well as the seeds they produce. Representatives of the agriculture industry point out that this leaves open the possibility that another herbicide-spraying regime might have lessened the impact on biodiversity while still reducing farmers' labour. …"… given the intense public opposition to transgenic agriculture, the chances of commercializing herbicide-resistant crops in the short term are slim (see *Nature* **425**, 656–657; 2003)…. No decision will be made until a panel of scientific advisers has considered the results for the government. But environment minister Elliot Morley has already said that no commercial planting will take place in 2004. In the meantime, **work on better spraying regimes continues.**"

(End of quote)

*** Note of this reviewer: The removal of all the weeds from a field is one characteristic of modern agriculture.**

Regarding this FSE trials, we observe the following:

1. They are qualified as "highly credible" but not conclusive.

2. Moreover, the statement:

"In any event, the FSE Trials demonstrate that some, but not all, GMHT crops can have adverse effects on non-target organisms. I believe that it is likely that additional adverse effects on non-target organisms may be reported in the future",

is an anticipated judgement reflecting the Expert beliefs about future research, but no the basis for that is given.

3. Also, the Expert states that

"Adverse effects on non-target flora and fauna could arise *indirectly* through the effects of the transgenic crop or the herbicide on the environment". Here, an *indirect* effect is mentioned. This statement contrasts with the authors of the FSE trials opinion, stressing "that it is the herbicide-spraying regime, not the genetic modification, that is the root of the problem."

07.04. Gene flow from a GMHT crop to a weedy relative can create weeds that are more difficult to control with herbicides. This occurred for GMHT oilseed rape in Canada. GMHT maize, cotton and soybean have not yet been grown legally in locations where there are weedy relatives and none occur in Europe, the US, Canada or Argentina, so this risk is not possible in these countries. Beets have wild relatives

in Europe, and weedy beets have developed as a consequence of gene flow in the past.

07.05. Gene flow from a GMHT crop to another crop cultivar can contaminate seed supplies (part of the "coexistence" issue) or reduce genetic diversity in the crop. Contamination is a serious concern, although it can be debated if this adverse effect is on the flora (the crop) or the growers of the crop. It is clear that the harm is to the growers of the crop. Genetic diversity of cotton, maize and soybean is not known to be great in Europe, so this is unlikely to be a concern. It may be possible that there are significant sources of genetic diversity in oilseed rape and beets in Europe.

Comments by Argentina

1. The same as the term "coexistence" is between quotation marks, the term "contamination" should be treated equally, as the proper wording is "adventitious presence".

2. About genetic diversity of cotton, maize and soybean, it is stated in the above that is "not known to be great in Europe, so this is unlikely to be a concern". An equivalent, but subtle different way of saying the same, would be that "genetic diversity…is known not to be great in Europe, so …". In this latter way, a definite idea is expressed, instead of an open question (… is not known …).

07.06. To my knowledge there are no reports of adverse effects on soil micro- or macro-flora or fauna separate from those in the UK-FSE trials. Nor are there any reports of adverse effects on soil dwelling bacteria, algae, or protozoa. However, to my knowledge there have not been any studies of any of these possible effects. The Panel should not infer that the absence of information implies an absence of effect.

Comments by Argentina

We disagree with the last sentence, addressed at making the Panel to think of or to expect that, effects will (or may) occur. Strictly speaking, the absence of information implies that an effect, if any, have not been studied. Following the same line of reasoning as the suggestive way used in the commented response, it can be equally said that "the absence of information does not imply the presence of effect". To this wording, we can add that "there are no reports" of the presence of effects. We strongly believe that language should not be addressed at suggesting perceptions, but should objectively dealing with actual facts.

07.07. To my knowledge, all reports have not found adverse effects on flora or fauna from antibiotic resistance genes or gene products. Extensive studies on *nptII* did not find any adverse effects, and found that any undetected adverse effects would likely be several orders of magnitude smaller than naturally occurring phenomena.

Comments by Argentina

We agree.

Comparison with non-GM HT Crops

07.08. There are several ways in which GMHT and non-GMHT crops may differ that are significant to risk to flora and fauna.

07.09. GMHT traits are typically hemizygous, which means that there is only one copy of the locus in the plant. Normal plant genes occur in two copies, that are either different (heterozygous) or the same (homozygous). Gene flow to wild relatives or other crop varieties will result in hemizygous offspring for GMHT traits, which are likely to exhibit dominant expression. For non-GMHT traits, hybrid offspring are most likely to be heterozygous and may exhibit varying degrees of dominance. This means that whatever the selective advantage of the trait in the original HT plant, it is likely to be similar for GMHT hybrids, but possibly less for non-GMHT hybrids. Because selective advantage is one of key determinants of spread of genes, this would suggest that GMHT traits could be more likely to spread than equivalent non-GMHT traits.

Comments by Argentina

Sexual compatibility is not mentioned above. This is often (but not always) a significant barrier against gene flow via pollen. The last sentence above is speculative, and, to date, no scientific findings would support it.

07.10. The promoters on most GMHT transgenes keep the transgene turned on and expressing at all times. The non-GMHT transgenes are regulated by plant promoters, which may or may not keep the gene turned on all the time. This may enable the herbicide to be used for a longer period of time on the GMHT crop than the non-GMHT crop. If so, greater degrees of weed reduction may be possible in GMHT than non-GMHT crops, which would result in greater non-target effects and higher selection for weed resistance in more species of weeds.

Comments by Argentina

The constitutive nature of most promoters used in GMHT crops, allows for a reduction, rather than for an increase in the use of herbicides, as a whole. Also, non-target effects have not been proved, and selection for weed resistance would be similar in biotech and non-biotech crops. "More species of weeds", in the context above, suggests that the GMHT may have acquired the ability to jump species barriers, which is not considering the need for sexual compatibility for hybridization to take place.

07.11. Most of the GMHT crops tolerate glufosinate and glyphosate, while most of the non-GMHT crops tolerate imidazolinone and sulfonylurea herbicides. It is possible that there are important differences in these herbicides that result in different risks to flora and fauna. I am unaware of studies that address this possibility. In addition, the options for managing resistant weeds are likely to differ among the different herbicides.

Comments by Argentina

"Most of the GMHT crops tolerate glufosinate and glyphosate" is not an accurate statement. Instead, it should be said that most of the events in GMHT crops are addressed at expressing tolerance to either glufosinate or glyphosate. Although the suggested double tolerance is technically feasible, there are not been developed, to our knowledge.

The Panel should also take into account the alleged unawareness of studies that address the possibility of the suggested (not supported) differences between GMHT and non-GMHT crops.

07.12. Scale of use has a significant effect on risk. Some GMHT crops have gained significant spatial scales of use that dwarf those of non-GMHT crops. For example, RoundUp Ready® soybean now occupies >60 of the US soybean area (>20 million hectares), while no non-GMHT trait has come close. With greater scale, small effects can reinforce each other and become more apparent. This would be especially true for non-target effects, such as those found in the FSE trials.

Comments by Argentina

The same "scale of use" argument can be construed to state the opposite, that is, that being gained significant spatial scales of use, effects were still not found. A word of caution: the effects of the extended use of a GMHT crop has been found to be not different to the similar extended use of any non-GMHT crop, under the same scale and agro-ecological conditions. However, this is an effect of agricultural practice and does not depend on the GM nature of the HT crop, as found in the FSE trials mentioned by the Expert.

07.13. If contamination is an adverse effect on flora, then GMHT crops have this risk while non-GMHT crops do not. This is based on the definition of harm, which is premised on distinguishing between GM and non-GM traits.

Comments by Argentina

We find here an intentional use of the word "contamination", which has a pejorative connotation and can possibly predispose laypersons to think that GMHT crops are inevitably a dangerous source of hazard. Moreover, it is hard to find a definite statement in the above. It is not clear to which kind of "contamination" the Expert is referring to, as there are, at least, the following possibilities: a) gene flow via pollen; b) adventitious presence (seeds, grain). We believe that it is proper to use the appropriate wording as indicated as a) or b). Therefore, we object the wording used by the Expert.

Also, The word "If" at the start of the above point, casts doubts about all that is said afterwards. We believe that this wording, in the context of the Expert's opinion above, is not to be considered as a scientific argument.

Finally, we note that the Expert is relaying in a definition (rather than an actual finding) in support of his statement.

07.14 If all of the factors mentioned in paragraphs 07.09 through 07.13 are equivalent between the GMHT and non-GMHT crop, then there will be no predicted difference in the risks of adverse effects from the repeated use of a GMHT or non-GMHT crop.

Comments by Argentina

See 07.13 on the use of "If", in this case in support of the opposite. We note here the contradictory statement, which is again using the conditional (if) and the final admission that there will be no predicted difference in the risks.

Question 9

9. In what ways does molecular characterization inform the risk assessment for any particular biotech product? Can a risk assessment be carried out in the absence of a comprehensive molecular characterization of each transformation event?

> 09.01. A risk assessment cannot be carried out in the absence of a comprehensive molecular characterization of each transformation event. A risk assessment could not address the risks specific to the transgene of interest without this information. Without the information, there would be no clear basis for knowing when all reasonable scientific risks have been assessed and there would often be an uncertain basis for determining if a specific risk was scientifically justifiable or unjustifiable.

Comments by Argentina

We agree.

Question 24

Monsanto Roundup Ready cotton (RRC1445)
C/ES/97/01 (EC chronology 66)

24. Does the information before the Panel, including the full application (EC-66/At.3-12) and the EC's SCP opinion (EC-66/At.43), provide scientific support for the objections raised by EC member States (EC-66/At.57) concerning the adequacy of the monitoring plan, the antibiotic resistance marker genes, and herbicide residues?

(a) What criteria can be used to judge if the final monitoring plan submitted by Monsanto in January 2003 was complete?

Scientific support for objections

> 24.01. This response addresses only issues related to the adequacy of the monitoring plan, and does not address issues related to antibiotic resistance marker genes and herbicide residues.
>
> 24.02. The lead CA reached the following conclusions (EC-66/At.05, Submission of lead CA to COM, 19 Nov 1997, Overall Assessment).
>
> > 2. From the risk assessment it is concluded that there is no reason to suppose that the harvest and handling of RRC Line 1445 tolerant to glyphosate herbicide, have adverse effects on the environment and human health.
> >
> > 9. The dossier was considered by National Commission on Biosafety. The main aspects considered in the risk assessment were:
> >
> > – Capacity to survive, establish and disseminate.
> >
> > – Potential for gene transfer.

– Products of expression of inserted sequences.

– Phenotypic and genetic stability.

– Pathogenicity to other organisms.

– Potential for adverse effects to humans.

10. The National Commission on Biosafety considers that, for the considered uses, there is no significant difference as far as environmental and human health risks related to other cotton.

16. Finally, as far as potential effects for non-target organisms is concerned, CP4 EPSPS protein is broadly present in nature. Therefore organisms which feed with plants and microorganisms are exposed to this protein. Studies with birds feeded with RRC line 1445 cottonseed meal have been conducted and no significative difference of this feeding was detected. Moreover, EPSPS protein exist in nature and is considered non-toxic to animal species. On the other hand, cotton is a unique crop that mammals and other species which consume vegetation avoid feeding on the plant due to both gossypol in the plant and the morphology of the plant.

24.03. These excerpts show that the risk assessment dated 19 November 1997 by the NCB did not consider indirect effects on non-target organisms, long-term or spatial scale effects on non-target species, effects associated with changes in the cropping system or the evolution of resistance in weeds to glyphosate. The NCB does consider whether there are any significant differences between anticipated risks from RRC 1445 compared to conventional cotton. Although the NCB concludes that there are no significant differences (point 10), they do not provide a scientific argument that this conclusion extends to the potential effects not considered in the risk assessment. Because the NCB considered that the risks they assessed were inconsequential, the NCB did not propose any monitoring plan.

Comments by Argentina

To "consider indirect effects on non-target organisms, long-term or spatial scale effects on non-target species, effects associated with changes in the cropping system or the evolution of resistance in weeds to glyphosate", which the Expert claims, seem addressed at a justification for a "no decision" stand. These considerations refer to effects that have not been found in previous studies, have long-term timeframes for execution of the needed research (e.g., "changes in the cropping system") or are speculative in the sense that:

to any biosafety analysis, new and renewed conditions are feasible to be imposed, in a never-ending process.

By its very nature, biosafety analysis must reach a conclusion based on the state of (all) knowledge available at the time of the analysis. At any rate, new knowledge would indicate if the biosafety analysis should be revised. It is not the matter if the effects are "inconsequential", but if they are significant, or have not been taken into account because of a non exhaustive consideration of the available data. To suggest that the above effects should be examined for a

decision to be reached, will only produce the result that, once the new requested data is presented, new knowledge will be required, and so on.

In fact, if a decision body will be determined to an indefinite suspension, one strategy will be to delay approval. Since accumulation of new knowledge is a constant process, when the time for a decision comes, new questions may arise that will require the elaboration of new data, which will in turn delay approval. The lack of data argument could so work as an indefinite suspension strategy.

24.04. The SCP provided the following Opinion (EC-66/At.43, 14 July 1998. Opinion of the Scientific Committee on Plants).

> 6.3.3. Safety to non-target organisms: Exposure of non-target species to seeds can be considered very low, due to the morphology of the boll. Feeding studies with birds (seeds) and mammals (both proteins) indicate very low toxicity of the proteins which also occur ubiquitously in the environment in plants and microorganisms. Field studies on agronomic performance showed equivalent susceptibility of line RRC 1445 and non-modified varieties to diseases and insect pests.
>
> 6.3.4. Resistance and tolerance issues: Any selective advantage of cotton line RRC 1445 is restricted to cases where no herbicide other than glyphosate is used on early stages of cotton. Under normal application rates, the introduced glyphosate-tolerance is effective up to the 4-leaf stage only. Other herbicide, cultivation of rotational crops or winter conditions will kill both modified and non-modified plants. Volunteers should be dealt with by standard agricultural practice except that glyphosate should not be used.

24.05. These excerpts show that the did not consider indirect effects on non-target organisms, long-term or spatial scale effects on non-target species, effects associated with changes in the cropping system or the evolution of resistance in weeds to glyphosate. Because the SCP considered that the risks they assessed were inconsequential, the SCP did not propose any monitoring plan.

Comments by Argentina

See comments under 24.03.

24.06. Sweden commented as follows (EC-66/At.57, 26 April 1999. Consultation of the Committee by Written Procedure).

> Sweden has, in different EU contexts and in earlier statements, put forward the view that herbicide tolerant crops should not be placed on the market until the long-term effects of herbicide tolerant crops on the environment have been better analysed. Common principles for evaluation and monitoring of the risks connected to the cultivation of herbicide tolerant crops should be established.

24.07. Sweden suggests that long-term effects should be studied prior to marketing and that principles for monitoring risks related to the cultivation of herbicide tolerant crops should be established. Sweden is saying that effects associated with changes in the cropping system should be considered both in the assessment and monitoring of risk. The scientific literature at that time indicated that long-term effects frequently elude detection when assessed on short time scales, so one of the only reasonable ways to address these kinds of effects is via monitoring. It does not seem appropriate to require long-term experiments for risk assessment because that could delay the process by a decade, so monitoring is a possible alternative.

Comments by Argentina

It is not clear from the above if long term monitoring is suggested as an alternative of biosafety analysis.

24.08. The United Kingdom commented as follows (EC-66/At.57, 26 April 1999. Consultation of the Committee by Written Procedure).

> We would also like to draw to the attention of other Member states where GM cotton might be widely grown, that this cotton line may have a negative impact on biodiversity arising from changes in the way the herbicide tolerant crop is managed.

24.09. The United Kingdom is drawing attention to spatial scale effects and effects associated with changes in the cropping system. The scientific literature at that time indicated that large-scale effects frequently elude detection when assessed at smaller spatial scales. One of the reasonable ways to address these kinds of effects is via monitoring.

24.10. The information in the full application (EC-66/At.3-12) and the EC's SCP opinion (EC-66/At.43) do not provide scientific support for the objections raised by EC member States (EC-66/At.57) concerning the adequacy of the monitoring plan. This is because the scientific information in the full application and the EC-SCP opinion do not address the scientific basis for the objections raised by the EC member states concerning the adequacy of the monitoring plan.

Comments by Argentina

See above comments under the points referring to objections raised by EC member States.

24.11. The objections of the member States (EC-66/At.57) concerning the adequacy of the monitoring plan raise new scientific issues that were not assessed in the full application (EC-66/At.3-12) or the EC's SCP opinion (EC-66/At.43). There is no monitoring plan proposed in either the full application (EC-66/At.3-12) or the EC's SCP opinion (EC-66/At.43), so the EC member States' objections can only be interpreted that a monitoring plan may be or is necessary.

Comments by Argentina

As stated before, monitoring is included in the safety analysis, as the nature of the GM and the state of knowledge at the time will lead to specific monitoring strategies. This is so for any new product or technology.

On the other hand, we would point out a lack of consistency: had monitoring been applied to conventional crops under current agricultural practices, they would have most probably qualify for delayed approval, as the same kind of effects the Expert and the EC member States are raising could similarly be applied to them (e.g., consider the effects of current agricultural practices with conventional crops, on biodiversity, environmental quality derived from the use of agrichemicals, changes in the cropping systems, etc).

> 24.12. **The objections of the member States (EC-66/At.57) concerning the adequacy of the monitoring plan are scientifically justifiable**. The EC member States raise specific scientific issues that can be addressed in a monitoring plan. However, the necessity of a monitoring plan cannot be determined from these objections.

Comments by Argentina

The above statement is not clear: it starts emphasizing that the adequacy of a monitoring plan is justifiable, but ends that the need of a monitoring plan cannot be derived from the objections by the EC member States.

At any rate, the need for a monitoring plan and the way it is to be implemented, is strongly crop-dependent, a feature which has not been raised specifically before by the EC member States. As an example, the case of GM cotton would be one in which monitoring in the field would have little sense, as there are not wild relatives in Europe. Of course, if an approval delay is pursued, it can always be invoked as an excuse that the monitoring of the long term effects of the associated agricultural practice is needed before approval.

> 24.13 It should also be noted that the objections of the member States (EC-66/At.57) concerning the adequacy of the monitoring plan are not all clearly stated as monitoring issues, and the objections do not provide clear guidance to an applicant for how to fully respond.

Comments by Argentina

See comments under the preceding point.

> 24.14. Excerpt from EC-66/At.64. Letter from Spanish CA to Monsanto requesting additional information regarding the monitoring plan, 1 January 2003.
>
> > Plan de seguimiento
> >
> > Se deberán concreter y desarrollar aquellos aspectos susceptibles de ser sometidos a una vigilancia general, indicando las posibles actuaciones en cada caso.

> En este sentido, el Plan de seguimiento deberá contemplar, en su caso, el uso del herbicida Glifosato y sus potenciales efectos a largo plazo (incidencia de malas hierbas, resistencias, etc), así como cualquier otro efecto relacionado con cambios en las prácticas agrícolas convencionales.

24.15. I believe the Spanish CA is requesting that the monitoring plan address potential effects of large spatial scale (for example, weed incidence, resistance) and in relation to changes in agricultural practice. These echo the comment of the UK (EC-66/At.57) and some of the comment of Sweden (EC-66/At.57).

Comments by Argentina

The comments under the preceding points are also applicable here. Note that the monitoring recommendation is not clear (general surveillance, possible measures, any other effect) and the only specific mention is made on the agricultural practices, not on the GM nature of the crop.

24.16. The UK Farm Scale Evaluations (FSE) of GMHT crops published in 2003 indicate that one anticipated effect of GMHT crops is an alteration in weed populations and communities compared to conventional production. The precise alteration probably depends on the herbicides used on the GMHT crop and the conventional crop. Nearly all other adverse effects on non-target species would likely follow from these changes in weed populations and communities. Changes to weed populations and communities have not been reported in GMHT cotton on a scale similar to the UK-FSE trials. These studies follow on a concern published in 2000 that GMHT crops could adversely affect skylarks in the UK. Although none of these studies existed at the time of the decisions by the NCB or the SCP, they partially validate some of the hypothetical concerns expressed by the various countries, especially related to spatial and temporal scale.

Comments by Argentina

See comments under 07.03 on the FSE trials. We also observe the conditional (unproven) quality of the following excerpts from the above paragraph:

1. "… alteration *probably* depends on the herbicides used…". The authors of the work quoted did not have any doubt about that.

2. "Changes in weed populations and communities have not been reported in GMHT cotton …".

3. Existing studies "… *partially validate* some of the *hypothetical concerns*…".

24.17. Considerable theory and evidence indicates that another anticipated effect of GMHT crops is the development of resistance to glyphosate in some weed populations. Resistance to glyphosate in a species of morning glory, which is a weed found in GMHT cotton in southeastern US, has been recently reported. However concerns about resistance have been widely recognized for some time before 1998.

Comments by Argentina

As the Expert has stated before, development of resistance in a inescapable evolutionary phenomenon and should be expected to occur with any selective pressure applied in the field.

This will apply to any crop, biotech or non-biotech, agricultural practice and agrichemicals which are used.

24.18. Potential long-term effects of GMHT cotton have not yet been identified and verified scientifically.

Comments by Argentina

The argument of the "long-term effects" is recurrent in the language of the objectors of GM crops. As it has been stated before, it is fundamental aim of the biosafety analysis to predict these effects. Had the long-term effects on the biodiversity and the environment quality derived from conventional modern agriculture been predicted, the latter would not been granted approval by any regulatory body. Also, we agree with what the Expert points out under 24.18.

24.19. The Member States submitted questions to the notifier on 22 February 1999. The notifier submitted materials to the SCP on 6 July 1998. The SCP returned an Opinion on 14 July 1998. The notifier submitted additional information that was circulated on 20 November 1998. After this follow 3 decisions to postpone the decision-making process. Depending on which dates are used, the Member States used either 94 or 231 days to respond to the most recent submission by the notifier. The shorter time frame is reasonable, especially as it spans the winter holiday season when most offices are closed for long periods of time. The longer period of time seems excessive to formulate and provide the responses to the notifier.

Criteria to judge monitoring plan

24.20. **The specific purpose of monitoring should be clearly stated.** This purpose should be linked to the management of some risk. This linkage ties monitoring to risk management, and delimits the monitoring endpoint. Although Annex VII.A of Directive 2001/18/EC provides a statement about the objective of a monitoring plan, this statement is not specific enough as the purpose of any particular monitoring plan. The plan should be more closely linked to actual potential risks, as indicated in Annex VII.C.1-2 of Directive 2001/18/EC.

24.21. For example, there are several possible purposes for monitoring herbicide resistance in weeds, including:

- Purpose R1. Document/Measure the occurrence of herbicide-resistant weeds. This would provide information prior to any control failures that could be used to alter the use of the herbicide or herbicide-tolerant crop to delay or avoid higher levels of resistance in the weed. Because this occurs before any control failures, it would provide time to develop a reasoned response to the threat. This would be particularly advantageous to prolong the useful life of the herbicide in question, especially if it had replaced herbicides that caused greater damage to the environment.

- Purpose R2. Document/Measure the occurrence of a weed problem that cannot be controlled by the herbicide. This could provide information of localized control failures that could be used to alter the use of the herbicide or herbicide-tolerant crop to delay or avoid higher levels of resistance in the weed. Because some control failures will have occurred, it may be necessary to mobilize a rapid response to prolong the useful life of the herbicide.

- Purpose R3. Document/Measure the widespread occurrence of a weed problem that cannot be controlled by the herbicide. This would provide information of widespread occurrence of the risk, and would be an indication that the risk management practices had failed. One crucial use of monitoring is to determine when a predefined point of failure is reached.

Comments by Argentina

We agree with the above explanation by the Expert, as he gives a general view on the subject, not distinguishing between biotech of non-biotech crops.

24.22. Similarly there are several possible purposes for monitoring changes in weed populations and communities, including:

- Purpose W1. In the UK, there has been a concern that GMHT crops would adversely effect the skylark, a desirable species. Skylarks feed on weed seeds, so monitoring of weed populations and communities could be aimed to monitor the abundance of food for skylarks. This approach could be extended for any other non-target species of concern.

- Purpose W2. There is a possibility that "unanticipated" or "unexpected" adverse effects could follow from changes in weed populations and communities. Monitoring these weeds would be a prelude to discovery of unanticipated or unexpected adverse effects.

Comments by Argentina

Here we point out that work published in 2000 is called to support a decision (actually a "non decision") taken well before. As stated before, safety analysis draws from knowledge existing at the time of the decision process. Otherwise, a indefinite postponement may occur.

24.23. In addition, there are several possible purposes served for monitoring for "unexpected" or "unanticipated" effects, including:

- Purpose U1. Document the geographic and temporal pattern of use of the GMHT crop so that there is a database available that would enable retrospective epidemiological-like investigations should an "unanticipated" or "unexpected" effect be observed.

- Purpose U2. Train personnel who normally visit agricultural fields and natural areas near agricultural fields to be aware of the possibility that agriculture generally and GMHT crops specifically may have "unexpected" or "unanticipated" effects. Inform these people of the occurrence of GMHT crops. Training should include information about the potential mechanisms

by which such effects could possibly arise. For example, "unanticipated" effects of weed community shifts should receive attention. This training will provide the many eyes needed to notice possible changes in the environment.

- Purpose U3. Document changes in agricultural practices associated with the use of GMHT crops. There is a possibility that "unanticipated" or "unexpected" adverse effects could follow from changes in agricultural practices. Monitoring these practices could be a prelude to discovery of unanticipated or unexpected adverse effects.

Comments by Argentina

See comments under the preceding point.

24.24. Clear specification of the purpose of monitoring is probably the most critical step in developing a useful monitoring system.

Comments by Argentina

We agree. Most of the references to monitoring which preceded this point lack of this "clear specification".

24.25. **Monitoring must have a sequel.** The act of monitoring should not be an end in itself. The information gathered during the monitoring activities should be used to make a response. This response should be related to the risk, including activities ranging from those to better estimate the risk to those activities to avoid, mitigate or tolerate the risk. Specification of a response is probably the second most critical step in developing a useful monitoring system. Although Annex VII.C.6 of Directive 2001/18/EC states that a response should be considered, it does not require a response.

Comments by Argentina

We agree with the Expert.

24.26. **Action Trigger**. In addition to a sequel, a monitoring system must have a well-defined action trigger. An action trigger is a criterion or set of criteria, which if met (or exceeded) according to the information from monitoring, would require taking the response actions. Without a clear action trigger, it could become quite difficult to determine when monitoring would precipitate a response.

Comments by Argentina

We agree with the Expert.

24.27. Important **logistical issues** include: (1) who will monitor, (2) who is responsible for monitoring, (3) who handles and synthesizes the monitoring information, (4) who verifies the quality of the monitoring, information obtained from monitoring and synthesis of this information, (5) to whom are monitoring results reported and at what frequency, (6) how will the monitoring effort be sustained, (7) how can monitoring be conducted in a cost-effective manner. Most, but not all, of

these logistical issues are recognized in Annex VII.C.3 and 5 of Directive 2001/18/EC.

Comments by Argentina

We agree with the Expert.

24.28. Important **methodological issues** include: (1) what 'endpoint' will be monitored, (2) what frequency will monitoring be conducted, (3) what will be the spatial density (grain) of monitoring, (4) can monitoring be stratified by potential risk. A few of these issues are recognized in Annex VII.C.3 of Directive 2001/18/EC. The endpoint of monitoring is what is actually measured and/or estimated by the people conducting the monitoring. For example, for weed resistance it could be the frequency of resistance genes or resistant phenotypes in the weed population; for non-target effects, it could be total weed biomass, production of weed seeds that are normally consumed by skylarks, and so on. Choice of endpoint can enable or restrict possible responses. The frequency of monitoring will depend on several factors, including the anticipated response. If the response involves a series of processes that would take several years to complete, it might be appropriate to increase monitoring frequency so that the monitoring process does not introduce additional delays in responding to a potential threat. The grain of monitoring will be depend on several factors, including the expected grain of the effect being monitored. For example, if regional weed resistance is the concern, then monitoring can be done at a regional scale. If weed resistance on farms is the concern, then monitoring will probably need to occur at a finer grain. Weed community shifts might be done on several spatial scales. If the adverse consequences are focused on bird species, regional monitoring may be sufficient. If they are focused on less mobile species, then a finer grain will be necessary. Finally, it will be essential that monitoring is stratified so that it occurs at places and times most likely related to possible risks. Monitoring is costly and monitoring resources must be allocated efficiently. For example, monitoring for unanticipated effects could be stratified according to the geographic distribution of the GMHT crop. Monitoring could occur mostly or only at places where the GMHT crop is used considerably, with a threshold intensity of usage determining the distribution of monitoring effort.

Comments by Argentina

We agree with the Expert.

24.29. Monitoring for unanticipated or unexpected effects. The first step in developing a monitoring system for these possible effects is to specify clearly what effects, if any, are anticipated or expected. Without this clear statement, it will not be possible to determine if any observed effect is unanticipated or unexpected. For example, if no adverse effects are anticipated or expected, then it must be granted that any subsequently observed effect must be considered unanticipated or unexpected.

Comments by Argentina

We fully agree with the Expert. Most of the monitoring claims by the EC member States do not comply with the above recommendations by the Expert.

24.30. General critique of proposed monitoring plan (EC-66/At.62). (1) Specific purpose of the proposed monitoring plan is to monitor for unanticipated or unexpected effects. It does not address concerns associated with weed resistance or changes in weed populations and communities, as indicated by the EC officials. The purpose of the monitoring for unanticipated or unexpected effects is not entirely clear. Consequently it is difficult to know how the proposed monitoring will enable the identification of any unanticipated or unexpected effects. (2) The proposed response is to conduct a scientific evaluation of the observed potential unanticipated effect to confirm that it is in fact an unanticipated effect. While it is stated that the response should be proportionate to the risk, it is not clear what procedure and standard will be used to determine a proportionate response. Second is unclear who is responsible for conducting the scientific evaluation and how to ensure that this information will be collected in a timely fashion, who will have access to the information, who determines the adequacy of the design of the evaluation and so on. (3) The triggers for initiating a scientific evaluation are not clear. It would be folly to initiate a scientific evaluation of all possible observations of possible adverse effects. How will these be screened to trigger a scientific evaluation? When does the scientific evaluation provide sufficient evidence to trigger remedial action? These issues are not resolved in the present proposed monitoring plan. (4) The logistical issues are better specified than the other components of the proposed plan. Important weaknesses in the proposal include lack of specification for how the seed supply and distribution network will be linked to the monitoring procedures, that key external networks are not committed to monitoring, procedures to verify the quality of monitoring, information from monitoring and synthesis of this information, short time span and long intervals for reporting, and so on. (5) Methodologically, the proposal has several important weaknesses. No endpoint is specified and it is not clear how people who might be monitoring would recognize an unanticipated effect. In this case these people should be informed that any adverse effect must be considered an unanticipated effect, and should be reported. The frequency and grain of these observations is unclear. There seems to be little stratification of effort by potential risk.

Comments by Argentina

We believe that the proposed monitoring plan, even in the case it deserved the critique by the Expert, would not be a valid reason to delay approval (see also comments under 24.11).

Monsanto Roundup Ready corn (NK603)
C/ES/00/01 (EC chronology 76)

Question 37

Necessity to ensure validity of safety assessment

37. Given the information before the Panel, including the notification (EC-76/At.1-2 and 27), was further information regarding molecular characterisation, nutritional analysis, and environmental impact requested by the lead CA (EC-76/At.6) necessary to ensure that conclusions of the safety assessment were valid?

37.01. I will cover the environmental impact aspects of questions 37 and 38.

Environmental impact of the GMO

Although this is not the direct purpose of this notification, the application covers aspects relating to the imminent request for authorization for cultivation in another Member State. In view of this eventuality, the National Biosafety Committee raises the following questions:

16. **Page 14, Section 3 – Survivability:** The comments on plant survival are incorrect, given that crop repetition is common in many areas and that, in many cases, grain from fallen ears germinates to produce plants in the next season.

17. **Page 16, Section 7 – Potential interactions:** This point must be looked into as broadly and deeply as necessary. The environmental impact of these interactions on target or non-target flora and fauna must be evaluated more thoroughly.

18. **Page 58, Point D.6. – Transferability of genetic material from the genetically modified plant to other organisms:** Although the application refers exclusively to authorization of the grain, detailed knowledge of the dispersal capacity of the pollen under various conditions is necessary and would be of relevance for authorization of cultivation in the State concerned by the application. This information could be decisive when the time comes to draw up a future monitoring plan.

19. **Page 98 – Appendices:** Doses and conditions for application of the herbicide (phenological condition of the plant, dose and date).

37.02. The relevant questions from the lead CA are in EC-76/At.5, 15 February 2001 and are reproduced below.

37.03. It is clear from the opening paragraph of these questions that the lead CA justifies the questions on the basis of an imminent request for authorization for cultivation in another Member State. Thus, I conclude that the lead-CA does not believe that the questions on environmental impact are necessary to ensure that conclusions of the safety assessment were valid.

37.04. I believe that **none of the questions posed under environmental impact are necessary to ensure that conclusions of the safety assessment were valid**.

37.05. Given that the notification is not for cultivation, whether survival is slightly better in continuous maize than in rotated maize ignores the bigger point, which is that maize does not survive very well. While the CA is correct in noting the difference, this difference is not necessary to ensure that conclusions of the safety assessment were valid.

Comments by Argentina

Maize survival is indeed difficult without man's help, as the crop has been extensively bred for production in highly man's managed agroecosystems. It is highly unlikely that grains are to survive and germinate in the ground during transportation.

37.06. While it is true that potential interactions need to be looked into broadly and deeply if the GM crop were to be cultivated, it is not true that such an investigation is necessary for the present notification. It would be better to focus attention on detecting accidental releases and quickly eliminating them.

Comments by Argentina

We agree with the first sentence.

37.07. Although it is true that detailed information on transferability of genetic material from the GM crop to other organisms is needed if the GM crop were to be cultivated, it is not true that detailed information is needed for the present notification. Some information is necessary to consider how gene escape can occur either during processing, storage or transport, but detailed information is not necessary.

Comments by Argentina

We agree.

37.08. As the GM plant is not to be cultivated under the present notification, information on herbicide application is not needed.

Comments by Argentina

We agree.

37.09. From the time that the notification was received (2 January 2001) to the time that the lead CA sent questions for clarification to the notifier (15 February 2001), 44 days had elapsed. This seems to be a rapid turn around time.

Question 38

38. Given the information before the Panel, including the notification and letter from Monsanto providing additional information (EC-76/At.7-9), was additional information necessary regarding molecular composition and environmental impacts associated with accidental germination requested by the lead CA (EC-76/7-9 and 10) necessary to ensure that conclusions of the safety assessment were valid?

38.01. Having received answers from the notifier (5 September 2001), the lead CA requested additional information. On the issue of environmental impacts, the lead CA asked the following question.

- Although cultivation of this maize is not covered by this application for marketing authorisation, details of the

potential environmental impact of any accidental dissemination or germination are needed.

38.02. Based on the SNIF (EC-76/At.2, 4 August 2000) and the responses to the first set of questions from the lead CA (EC-76/At.7-8, 5 September 2001), it is clear that the notifier has not addressed this question. The notifier believes, probably rightly, that the likelihood of accidental dissemination and germination (exposure to the environment) is small. If this is true, the notifier is arguing that when exposure is small, risk is small. Consequently, the notifier may believe that it was not necessary to address this question.

Comments by Argentina

Since cultivation is not contemplated, the only way an environmental impact may be possible is from accidental spills during transport. Therefore, the Expert is right in considering that the risk is small, since germination and appearing later as volunteers plants is very unlikely. Indeed, if no cultivation is contemplated, we are dealing here with grains, not with seeds intended to be planted.

38.03. In either event, the lead CA may reason as follows: if the hazard associated with a rare exposure event is large, then the risk may be large. Hence the **question is necessary to ensure that conclusions of the safety assessment are valid**. However, it would be helpful to the notifier to specify that the lead CA is concerned about large potential environmental impacts. Moreover, it would be even more helpful to the notifier to suggest some possibilities. For example, if contamination of conventional production (related to the "coexistence" issue) is a major concern (and is considered an environmental impact), the notifier would be able to propose how the concern could be managed, thereby facilitating the more rapid completion of the notification process.

Comments by Argentina

See questions below and our comments on the use of the term "contamination", in paragraphs 07.05, 07.13, 69.16 (commenting on point 4), and 103.03.

It is also very unlikely that from an accidental spillage of grains, a plant will emerge in the places travelled through transportation. Also, for this reason (see also the comments under paragraph 38.02), we do not agree with the contention that the risk of spillage and germination of isolated grains is a great hazard and therefore a great risk.

38.04. The time from the responses to the first set of questions from the lead CA (EC-76/At.7-8, 5 September 2001) to the time of the second set of questions from the lead CA (EC-76/At.10, 10 October 2001) was 35 days. This seems to be a rapid turn around time.

Maize Bt-176 (notification C/F/11-03)

Safeguard measure of Austria

Question 69:

*69. Given the information before the Panel, including the evaluations undertaken by France (EC-158/at. 1 to 3); the Scientific Committee for Animal Nutrition in December 1996 (EC-158/At. 4 and 5); the Scientific Committee for Food in December 1996 (US-64) and in March 1997 (US-58); the Scientific Committee for Pesticides in December 1996 (EC-158/At.6) and in May 1997 (US-57); the Scientific Committee for Plants (SCP) in September 2000 (US-66); and the European Commission in its Decision of January 1997 (ARG-37), as well as the information submitted by **Austria** with respect to its safeguard measure (US-52, EC-158/At.11, 12 and 15; EC-144, EC-147), is there any reason to believe that the scientific evidence available to Austria in February 1997 was NOT sufficient to permit it to undertake an appropriate assessment of potential risks to human, plant and animal health, and the environment from the importation and use of Maize Bt-176? If so, what scientific evidence do you believe was insufficient?*

If the evidence was not sufficient in February 1997, was there sufficient evidence available to Austria in August 2003 to permit it to undertake a more objective assessment of potential risks to human, plant and animal health, and the environment from the importation and use of Maize Bt-176 (EC-158/At.30 to 42)? If not, what scientific evidence do you believe was insufficient?

69.01. In my response to this question, I will not address issues related to the antibiotic marker gene and will focus my remarks on environmental risks.

69.02. The initial assessment of Event 176 by France provided in EC-158/At.1-3 (10 January 1995, 1 March 1995, 3 March 1995) does not contain the details of the assessment by the French Biomolecular Engineering Committee (BEC).

69.03. The Opinion of the Scientific Committee on Pesticides (EC-158/At.6SCI, 9 December 1996) on Event 176 did not assess the risk of resistance evolution in the target pests because it considered this risk to be an agricultural risk, not an environmental risk. In either event, the Committee felt that resistance management should be fully considered. The Committee also did not assess non-target effects.

Comments by Argentina

See our comments on non-target effects below, under paragraph 69.06.

69.04. The Opinion of the SCAN (EC-158/At.4, 13 December 1996) did not address any environmental risk, including environmentally mediated indirect effects on animal health. The Opinion of the SCF (US-64, EC-158/At.5, 13 December 1996) did not address any environmental risk, including environmentally mediated indirect effects on human health.

69.05. On 23 January 1997, the EC decided to allow the placing on the market of Event 176 (ARG-37).

69.06. On 13 February 1997, Austria decided to ban the commercialization of Event 176 in Austria (US-52). Austria gave three reasons for this action. 1. A concern that

the risks of the *bla* gene (ampicillin resistance) are greater than that assessed by the SCAN and the SCF (paragraph 69.04). 2. That the Cry1Ab toxin in Event 176 could have risks to non-target organisms, including those in the soil such as collembola. 3. There is an environmental risk that the target insects will evolve resistance to the Cry1Ab toxin, and resistance management measures should be required (they were not required by the EC).

Comments by Argentina

On the reason 1: By 1997 there was sufficient evidence indicating that the risks of the *bla* gene in a GM plant are nebligible (see, e.g., Schlüter, K et al, "Horizontal" Gene Transfer from a Trangenic Potato Line to a Bacterial Pathogen (*Erwinia chrysantemi*) Occurs –if at all- at an Extremely Low Frequency. *Biotechnology*, 13:1094-1098, 1995);

On the reason 2: By the time of the EC decision, there was sufficient evidence supporting that there is a negligible probability for Bt entomotoxins to have toxicity or otherwise being harmful to non-target organisms; that is, the knowledge on the mode of action of the Bt entomotoxins was showing the high specificity of these toxins for insect Orders, based in the binding to specific receptors in the mid-gut of the susceptible insects; therefore, there was sufficient information pointing that the risks for non-target organisms was not a concern so the decision by Austria has no justification;

On reason 3: Development of resistance is an essential phenomenon in evolution, so it is to be expected to occur whenever a selective pressure is applied in the field; by the time of the EC decision, management of this risk was a standard agricultural practice in countries in which Bt events were commercial (the high-dose/refugia strategy).

All in all, we do not see reasons to contradict the decision by the EC, which we considered was correct.

69.07. In the Further Opinion of the Scientific Committee on Pesticides (US-58, 12 May 1997), "The Committee concluded that the reasons and information submitted by the Austrian Authorities did not add new relevant evidence to that already considered by the Committee and that none of its conclusions on the risk to the environment were affected by the Austrian arguments."

69.08. The reasoning in the Further Opinion of the Scientific Committee on Pesticides (US-58, 12 May 1997) is false and did not take into account the scientific information known at the time. The conclusions it reached (paragraph 69.07) do not follow from the evidence available at the time.

Comments by Argentina

This argument is discussed below, when the Expert breaks down the SCP-Austria subject.

69.09. (1) On page 2 the Committee stated that it "recognized the complexity of comparing the exposure of a pest to genetically modified plants, where exposure may be prolonged and maintained, and conventionally applied pesticides, with shorter and repeated exposure. The potential for development of resistance could be either accelerated or retarded."

On the comparison problem mentioned above, when considering development of resistance, it seems that the Expert considers that continuous exposure to a toxin at the level of 0,001 % of total biomass protein (order of magnitude), which is produced by ubiquituous (and harmless) bacteria is considered a potential risk higher than the exposure to a agrichemical proven to be toxic (as most chemical insecticides). Is the Expert indicating that a hypothetical risk of the above kind has a higher value than a proven health and environmental risk? To date, provided Bt plants are properly used (as it should be with any agricultural input), no resistance has been detected that may be considered to be of concern. Moreover, the Expert seems to ignore the impact to the environment of the alternatives (non-biotech) to Bt plants. In the case of Bt maize, for instance, these impacts are negligible and have proved to be even an added benefit, since through an indirect effect on the insects, they prevent the crop to be infested with mycotoxin-producing fungi.

> (a) In its 9 December 1996 Opinion, the Committee nowhere recognized the complexity of comparing the exposure of a pest to genetically modified plants, where exposure may be prolonged and maintained, and conventionally applied pesticides, with shorter and repeated exposure. It must be granted that this is a new consideration for the SCP that was introduced by Austria. (b) While it is true that theoretically the difference in exposure could result in faster or slower resistance evolution, the SCP is not discussing a theoretical case. There was more than adequate data available in 1995 from the notifier's efficacy trials (and efficacy trials on Event 176 conducted by public sector scientists) and a long history of efficacy trials of Bt insecticide sprays on maize to demonstrate without question that Event 176 would exert a selection pressure on corn borers many times stronger (I would estimate ~1000x) than a typical Bt insecticide spray. The conclusion of the Committee either is not case-specific and therefore inappropriate, or it is case-specific and therefore false.

<u>Comments by Argentina</u>

The rather strong sentence at the end of point (b) above, seems to based on the estimation by the Expert of a ~ 1000x increase of the selection pressure (Bt plants vs. Bt sprays), but no appropriate reference is given, in spite of the Expert mentioning that "there was more than adequate data available in 1995 …". Key comparison data in support of the Expert's estimate are not found even in the comprehensive study by the Expert as a co-author, (*Fitt, G.P. et al*, Resistance Risks and Management Associated with Bt Maize in Kenya, in Hilbeck, A. and Andow, D.A., eds., (2004) *Environmental Risk Assessment of Genetically Modified Organisms*. Vol. 1. A Case Study of Bt Maize in Kenya. CAB International, Wallingford, UK, pp. 209-250). Thefore, to say that the conclusion of the Committee is "… inappropriate … or … false" is going too far. Moreover, we can find (*Schnepf, E. et al, Bacillus thuringiensis* and Its Pesticidal Crystal Proteins, Microbiol. Molec. Biol. Rev., (1998) 62:775-806, see pp, 796) the statement below (obioulsly based in research existing before the date of publication):

> **"If transgenic plants can express a *cry* gene at doses high enough to kill even homozygous resistant insects, that crop will become a nonhost. While such an ultra high dose migh be impractical with a sprayable product…it may be possible with toxin-engineered plants, taking into account the currently attainable levels of Cry expression in planta. (A reference is quoted) … For example, a Colorado potato beetle population 100-fold resistant to a Cry3A-containing *B. thuringiensis* spray could not survive on potato plants expressing the same protein (Two references are quoted)" End of quote.**

From the above, we can conclude that: 1) the Committee has reached and appropriate and valid conclusion, and 2) data presented here seem to lead to a conclusion wich is the opposite to the one expressed by the Expert.

> 69.10 (2) On page 2, the Committee stated "Based on available information, soil exposure from the GMO maize plants will be less than the exposure resulting from a single conventional spray application including the run-off from the plants. Only trace amounts of toxin can be detected in the roots of the maize and furthermore, normal agricultural practice would involve removal of the greater part of the plant at harvest. The plant remains are often shredded and transformed into silage for use as animal feed at a later stage." (a) In its 9 December 1996 Opinion, the Committee nowhere made the assessment that based on available information, soil exposure from the GMO maize plants will be less than the exposure resulting from a single conventional spray application including the run-off from the plants. Nowhere did the Committee note that these issues were addressed satisfactorily in the dossier submitted by the notifier. It must be granted that these considerations are new to the Committee and that they were introduced by Austria.

Comments by Argentina

From the wording of the quoted Committee statement, we reach the conclusion that the Committee did have and processed the relevant information on which the conclusion was based. This information combined toxin concentration data in soil and the effects of normal agricultural practices. Is the Expert suggesting that the above kind of data do not satisfactorily address the issue?

> (b) The conclusion that soil exposure from the Event 176 maize plants will be less than the exposure from a single Bt spray application was debatable even in May 1997. The Committee did not appear to take into account that nearly all of the Cry toxin applied in a Bt spray would be inactivated by sunlight in less than week after spraying.

Comments by Argentina

The Committee was not dealing with a Bt spray but with a Bt plant. Therefore, the relevant information was of the kind discussed above.

> The Committee did not appear to consider that most farmers incorporate maize residue into the soil after harvest. This would incorporate several tons of biomass per hectare, putting Cry toxin out of the sun, where it could persist for some time. The Committee seemed to believe that the maize residue would be ensiled. Silage requires green plant material, and most silage maize is cut while still green, long before it would be harvested for grain. Thus it is not clear that very much residue would be removed for silage. Finally risk assessments should not rely on one study for key conclusions (in this case the Palm et al. study, cited as study 4 in the Opinion). The SCP assessment should have acknowledged that scientific information was scarce at that time, and it would have been better had the SCP maintained a more agnostic position with respect to the risk assessment.

Comments by Argentina

On the information available at the time of the SCP assessment, see above. It seem to be odd the recommendation for "a more agnostic position" for the SCP.

(Note of this reviewer: *Agnosticism*: Phylosofical doctrine that declares that every notion of the absolute is not accessible to the human understanding, so Science is reduced to the knowledge of the phenomenologic and relative). As the phenomenologic facts were analized by the SCP, and Science goes well beyond the phenomenologic, we are left with the impression that the Expert is suggesting that the SCP should have admitted that a definitive understanding is not accessible to us humans, and therefore declared the impossibility to take a position. Also, the Expert seems to shift the issue towards a epistemological question, departing from the core, technical issue, by using a meta-language argument.

> Thus, I conclude that the Committee did not consider all available scientific evidence and did not appropriately weigh potentially conflicting information when coming to their conclusion.
>
> 69.11. (3) On page 2-3, the Committee states "The Committee stated in its previous report of 9 December 1996 that resistance management strategies are needed during the years of use of any pesticide, Bt sprays included. The Committee drew attention once again to the need for effective resistance management, including monitoring on agronomic grounds, to prolong the effectiveness of Bt toxin both in conventional sprays and in genetically modified maize. It also felt that the submission of a satisfactory monitoring and resistance management programme should be a requirement for the authorization to use genetically modified maize seeds expressing Bt-toxin. (a) In its 9 December 1996 Opinion, the Committee nowhere made the recommendation that the submission of a satisfactory monitoring and resistance management programme should be a requirement for the authorization to use genetically modified maize seeds expressing Bt-toxin. The acknowledgement that it should be a requirement in this 12 May 1997 Opinion is a major change in the conclusions and recommendations of the Committee. It must be granted that this change was due to Austria's insistence that resistance management measures are required for commercial authorization. (b) The Committee does not address Austria's main point on this issue, which is that resistance risk should be considered an environmental risk. The Committee also seems to be unaware of the position of the US-EPA in 1996, which was that resistance risk is an environmental risk. This is a critical issue because it determined whether resistance risk could be considered under Directive 90/220/EEC. Thus, the Committee did not engage on a critical reason submitted by Austria.

Comments by Argentina

From the above wording by the Expert on the conclusions of the SCP (the Expert quotes the SCP under 69.10 (2)), it seems quite clear that, whatever the claim made by Austria, the issue at focus was environmental. Toxin presence and persistence in soil, effects on agricultural practices, are clearly environmentally-related issues. Which additional environmental issues were ignored by the SCP?

> 69.12. (4) It must be granted that the reasons and information submitted by the Austrian Authorities added new relevant evidence that the Scientific Committee on

Pesticides had not considered in their previous deliberation, and that that a key conclusion was affected by the Austrian arguments. Moreover, the key conclusions by the Committee in this Opinion on non-target risks are overstated and/or false.

Comments by Argentina

On non-target effects, see comments under paragraph 69.06.

69.13. I conclude that the scientific evidence available to Austria in February 1997 was NOT sufficient to permit it to undertake an appropriate assessment of potential risks to plants and the environment from Event 176. The evidence on risks to non-target organisms, including those in the soil such as collembola was insufficient. Austria could have mustered sufficient evidence to argue that there was an environmental risk that the target insects will evolve resistance to the Cry1Ab toxin, and resistance management measures should be required. There was probably insufficient evidence available to determine what measures should be required. This determination by Austria was in direct contradiction to the EC decision. In this case, Austria probably did not then and does not now need to claim that their safeguard measure is a precautionary one.

Comments by Argentina

On non-target effects, see comments under paragraph 69.06. On the other hand, since the Expert comments on what Austria could or could not have done, including the last sentence above on the non-precautionary nature of the safeguard, we observe that it is somewhat contradictory. Austria's safeguard was a precautionary measure, as the Expert himself recognizes "… that the scientific evidence available to Austria in February 1997 was NOT sufficient to permit it to undertake an appropriate assessment of potential risks…". The very essence of a precautionary measure is that complete available knowledge is not available to take a decision. On the other hand, the Expert says that Austria do not need to claim it was a precautionary measure.

69.14. By 2003, the basis for risk assessment of Bt crops had changed because several significant scientific points had come to light. (1) It became widely appreciated that the molecular basis of transformation was more complex than originally thought, and the implications of these findings for risk assessment were articulated. Annex II of Directive 2001/18/EC is one consequence, but additional regulatory changes have occurred since then. Indeed, knowledge in molecular biology continues to accumulate at remarkably fast rates, and I expect that there will be continued change in regulation in the future. (2) Non-target risk assessment shifted from assessing indicators of environmental risk to assessing actual identified potential environmental risks. Presently this is done on an ad hoc basis, as no systematic methodology has gained widespread acceptance.

Comments by Argentina

This is consequence of the case-by-case nature of the risk assessment.

(3) Gene flow risk assessment has shifted from being based primarily on an assessment of the probability of gene flow to being based on an assessment of both the probability of gene flow and the conditional hazard probability. (4) Resistance

risk is considered an environmental risk, and science-based resistance management measures are required.

Comments by Argentina

All points (1) to (4) above show that scientific methods and concepts improve or change with time, *which is to be expected in every field of human activities*. We observe, however: a) it is not reasonable to postpone indefinitely a decision waiting for a methodological improvement or change, because these will always come anyway and will turn to be obsolete with time; b) it is not reasonable to expect that any progress will only result in the detection of more risks, not previously detected, (as the Expert seems to suggest), rather than in a deeper knowledge and understanding leading to an improvement of scientific tools; it can be argued that this improvement could also confirm the safety with regard to decisions previously taken.

Following on the above, we do not see any valid reason to delay approval based on the Expert's view under this point.

On part (1), while the Expert is right, we note that all improvements and new knowledge (sensitivity increase in PCR and Southern methods, microarrays, genomics, proteomics, metabolomics, the latter ones still to be perfected) including those on the complexity of transformation, have not resulted so far in the detection of any undesirable phenomena; change in regulation is justified at any time that new methods are developed that will improve characterization (regulation is a dynamic field, the same as Science); new knowledge about transformation is welcomed, as increases our insight on the underlying phenomena, but it was never found to demand the modification of any previous decision, nor drastic changes in characterization data requirements.

On part (2): Non-target risk assessment based on assessing indicators of environmental risk is still an accepted approach; assessing actual identified potential environmental risks, done on an *ad hoc* basis, continue to lack a systematic methodology, but newly gained knowledge will help to be more specific and to make results more and more meaningful; if by "systematic methodology" the Expert suggests a general, trait-independent methodology, then we would disagree, as the very nature of the event, the crop, the trait and the environmental issued are very specific.

On part (3): Continued progress in gene flow phenomena is also welcomed; several instances have been reported in which this issue was specifically dealt with, leading to new regulation requirements; but, again, other than improper use (geographic location, presence of wild sexually compatible plants populations) no drastic new restrictions appear to be necessary, so delay on this basis would continue to be unjustified.

On part (4): Nobody would deny that resistance risk is an environmental risk, as well as a technology-related one; science-based resistance management measures are in the field from the very inception of GM crops (e.g., insects refugia); all parties recognized the fact that the lifetime of their products (as well as the related biological control products, like Bt sprays) are to be protected.

69.15. Thus, evidentiary standards for what constitutes an objective environmental risk assessment had changed substantially from 1997 to 2003. This is particularly true in Europe and the United States, and particularly true for the Bt crops.

Comments by Argentina

See comments above.

> 69.16. (1) Thus, in 2003, there remains some uncertainty about non-target risks of Event 176, but it could be argued that a risk assessment could be conducted using scientifically justified worst-case assumptions. On the other hand, Austria could reasonably maintain that there is still insufficient information to know which non-target species may be at risk, and therefore it is not possible to conduct an objective risk assessment. The findings in 2003 by Székács and Darvas (EC-158/At.37) – that two protected butterfly species in Hungary, *Inachis io* and *Vanessa atalanta*, might be exposed to Bt corn pollen and suffer higher mortality – certainly suggests that not all of the non-target species at risk to Event 176 have been identified in Europe. (2) As in 1997, Austria could muster sufficient evidence in 2003 to argue that there is an environmental risk that the target insects will evolve resistance to the Cry1Ab toxin in Event 176, and resistance management measures should be required. Moreover, in 2003, Austria should have sufficient evidence to determine what kind of resistance management measures to require. (3) Unlike in 1997, in 2003 Austria could argue that the molecular characterization of Event 176 is insufficient to conduct a risk assessment. (4) In 2004, Austria suggested that an additional gene flow risk that needs assessment is contamination of conventional production. It is possible that the scientific evidence to support risk management measures for this risk is available to conduct an objective risk assessment today.

Comments by Argentina

We observe:

1. On point (1): As the Expert states above, "a risk assessment could be conducted using scientifically justified worst-case assumptions". This is not only a "could be" situation but almost the only way to conduct risk assessments, as the instrincis nature of these is to make the best assumption about future facts based in the relevant current data.

2. On point (1): Obviously, to object to a judgment made in 1998 based on new findings that came to light in 2003-2004, is equivalent to assuming that the Committee did have an anticipated knowledge (but anyway ignored) reports to be known five years later. Is the Expert saying that: a) the Committee did have the ability to predict the future?, and/or, b) the Committee was aware (by a unknown mechanism which was not a regular, scientific publication) of new findings but anyway decided to ignored them? If in the view of the Expert the b) possibility is the right one, he should indicate by which mechanism this knowledge was available ahead of time to the Committee.

3. On point (1): The observation by the Expert that "two protected butterfly species in Hungary, … might be exposed to Bt corn pollen and suffer higher mortality (Székács and Darvas, EC-158/At.37)…", should not come to a surprise, as butterfly are Lepidopteran and these are susceptible to the Bt toxin expressed in the event under consideration. Therefore, the "might" situation should be illustrated by adding the necessary data that will make this "non-target" effect not only an undesirable effect (which we agree it is, if produced in the relevant agroecosystem) but also a real situation (the monarch case illustrates this dilemma: after alarming news, the real case, field situation was found very different from the laboratory

conditions the first research was done, making the latter not relevant as far as the field conditions).

4. On point (2): The statement: "As in 1997, Austria could muster sufficient evidence in 2003 to argue that there is an environmental risk…" is unclear, simply because the 2003 evidence was not available (or ignored?) in 1997 (see 2 above). On the development of resistance, please see comments above, under 69.09 (b).

5. On point (3): The same timing problem is in "Unlike in 1997, in 2003 Austria could argue that the molecular characterization of Event 176 is insufficient to conduct a risk assessment". It can be added that molecular characterization is a fast-evolving scientific field, so that in a given point in time there always be refinements and breakthroughs that will make the previous information more complete, accurate or calling for a new review. The experience with this event, which is not showing any biosafety problem in spite of its expensive use in other countries, may be called to suggest that new molecular characterization data, are, in this case, of the "nice to know" category and not of the "need to know" one.

6. On point (4): "… contamination of conventional production ... It is possible that the scientific evidence to support risk management measures for this risk is available to conduct an objective risk assessment today". The use of the word "contamination" are lessening the (desirable) objective description of the Expert's view, as it brings to mind a pejorative value. We suggest to use "adventitious presence" instead.

7. On point (4): On the part "to conduct an objective risk assessment today", shows the same timing problem indicated above.

Question 70

70. With reference to the definition of a risk assessment in the SPS Agreement (see Background above), to what extent does the scientific evidence and other documentation submitted by Austria evaluate the relevant risks to human, plant or animal health, and the environment from the importation and use of Maize Bt-176?

How does the scientific evidence and other documentation submitted by Austria compare with the relevant international guidelines for risk assessment and analysis identified above?

> 70.01. In my response to this question, I will not address issues related to the antibiotic marker gene and will focus my remarks on environmental risks.
>
> 70.02 With reference to the SPS Agreement, Austria has evaluated relevant risks to plant health. Specifically, Austria has taken into account available scientific evidence (Article 5.2).

Comments by Argentina

The Expert do not makes it clear whether Austria "has taken into account available scientific evidence" at the time the report of the Committee was released. Any scientific evidence released after 1997-8 will have the timing problem commented under paragraph 69.16. On the other hand, we have pointed out that scientific evidence was available at the time (see comments under paragraph 69.16).

70.03. It is not clear, however, that Austria conducted the risk assessment according to the phytosanitary measures which might be applied. Austria did not present their safeguard measure as a possible phytosanitary measure, and did not conduct the risk assessment according to their safeguard measure. Thus it is not clear that Austria conducted the risk assessment consistent with Annex A, paragraph 4.

70.04. Austria did take into account relevant economic factors (Article 5.3), however it did not explicitly compare the relative cost-effectiveness of alternative approaches to limiting risks.

70.05. The "potential pest" concept of ISPM 11 must first be considered. This is a special case of the general argument in my response to question 6, and that argument holds for this case because Austria argues that there is a plant pest risk.

70.06. For those risks within the scope of ISPM 11 the risk assessment process is consistent with ISPM 11. However, the economic assessments called for in ISPM 11 were not conducted.

70.07. It appears that some of the ISPM 11 guidance on risk management has not been followed. However, this is not to imply that the actions of Austria contradict this guidance. My reading of the materials before the Panel is that Austria did not explicitly address this guidance. Specifically I note Section 3.4 (principles), and Section 3.4.6 (on prohibition) were not explicitly addressed.

70.08. In US-52, Austria made it clear that they are applying a different standard for acceptable risk than reflected in the assessments of the SCAN, SCF, Scientific Committee on Pesticides in the EC decision (ARG-37) itself. In so doing, Austria fulfilled ISPM 11, Section 3.1 (level of acceptable risk should be expressed).

70.09. ISPM 11, Section 3.4.6 (prohibition) states "If no satisfactory measure to reduce risk to an acceptable level can be found, the final option may be to prohibit importation of the relevant commodities. This should be viewed as a measure of last resort and should be considered in light of the anticipated efficacy, especially in instances where the incentives for illegal import may be significant." With respect to resistance risk, in 1997 Austria had established the existence of an environmental risk, and required the development of measures to manage this risk to acceptable levels. As the EC was not willing to make such a requirement, Austria had no choice but to intervene with its own safeguard measure. In 1997, however, there was probably insufficient scientific evidence to establish what necessary measures should be taken. Scientifically credible suggestions at that time focused on using refuges (maize that was not Bt maize) ranging from 10-70% of the maize grown by any farmer who chose to grow Bt maize. It is unlikely that Austria could have implemented any of these suggestions in time for the 1997 growing season, so I conclude that Austria had fulfilled ISPM 11, Section 3.4.6, at least for the 1997 growing season.

Comments by Argentina

With regard to the environmental risk involved in resistance, see above comments under paragraph 69.09.

With regard to the Expert's view that ...

> **"In 1997, however, there was probably insufficient scientific evidence to establish what necessary measures should be taken. Scientifically credible suggestions at that time focused on using refuges (maize that was not Bt maize) ranging from 10-70% of the maize grown by any farmer who chose to grow Bt maize. It is unlikely that Austria could have implemented any of these suggestions in time for the 1997 growing season, so I conclude that Austria had fulfilled ISPM 11, Section 3.4.6, at least for the 1997 growing season"**

... we observe that Austria chose to take a precautionary stand ignoring what the Expert qualifies as "Scientifically credible suggestions at that time". Therefore, as "it is unlikely that Austria could have implemented any of these suggestions in time for the 1997 growing season", it is implied that Austria *could* have implemented these suggestions in the following seasons (which the Expert recognizes by saying the measure was correct "at least for the 1997 growing season").

> 70.09. The science, documentation and reasoning of Austria are consistent with Annex III of the Cartagena Protocol on Biosafety to the Convention on Biological Diversity. Specifically, Annex III, Section 8(f) states "Where there is uncertainty regarding the level of risk, it may be addressed by requesting further information on the specific issues of concern or by implementing appropriate risk management strategies and/or monitoring the living modified organism in the receiving environment."

Question 71

71. Does the scientific evidence and other information submitted by Austria support the adoption of a temporary prohibition on the importation and use of Maize Bt-176? In light of any potential risks identified by Austria, what other risk management options were available in February 1997? What other risk management options are now available?

> 71.01. In my response to this question, I will not address issues related to the antibiotic marker gene and will focus my remarks on environmental risks.
>
> 71.02. The adoption of a temporary prohibition can be justified on the basis of the scientific evidence and other information submitted by Austria.

Comments by Argentina

Based on our arguments, we state that the information available to Austria did not justify a temporary prohibition.

> 71.03. Other risk management options could not have been justified in February 1997. However, had Austria worked to develop its own acceptable resistance management measures, perhaps by 1999 other risk management options would have been possible.

Comments by Argentina

See comments under paragraphs 69.16 and 70.02.

71.04. Today several alternative risk management options are available. Risk management strategies include risk avoidance, risk mitigation, and risk tolerance. Tolerance strategies are probably inappropriate. One alternate risk avoidance strategy would be to implement country-specific resistance management measures, to limit planting to a restricted region, and to conduct intensive non-target experiments. This would allow progressive determination of non-target effects.

Comments by Argentina

See comments under paragraphs 69.16 and 70.02.

Maize Bt-176 (notification C/F/11-03)

Safeguard measure of Germany

Question 72

*72. Given the information before the Panel, including the evaluations undertaken by France (EC-158/at. 1 to 3); the Scientific Committee for Animal Nutrition in December 1996 (EC-158/At. 4 and 5); the Scientific Committee for Food in December 1996 (US-64) and in March 1997 (US-58); the Scientific Committee for Pesticides in December 1996 (EC-158/At.6) and in May 1997 (US-57); the SCP in September 2000 (US-66); and the European Commission in its Decision of January 1997 (ARG-37); as well as the information submitted by **Germany** with respect to its safeguard measure (US-65, EC-158/At.18-29, EC-144), is there any reason to believe that the scientific evidence available to Germany in March 2000 was NOT sufficient to permit it to undertake an appropriate assessment of potential risks to human, plant and animal health, and the environment from the importation and use of Maize Bt-176? If so, what scientific evidence do you believe was insufficient?*

If the evidence was not sufficient in March 2000, was there sufficient evidence available to Germany in August 2003 to permit it to undertake a more objective assessment of potential risks to human, plant and animal health, and the environment from the importation and use of Maize Bt-176? If not, what scientific evidence do you believe was insufficient?

72.01. In my response to this question, I will not address issues related to the antibiotic marker gene and will focus my remarks on environmental risks.

Comments by Argentina

The Expert begins by more or less repeating what he said in respect of the Austrian safeguard. Only in paragraph 72.11 does he begin speaking of the German safeguard.

72.02. The initial assessment of Event 176 by France provided in EC-158/At.1-3 (10 January 1995, 1 March 1995, 3 March 1995) does not contain the details of the assessment by the French Biomolecular Engineering Committee (BEC).

72.03. The Opinion of the Scientific Committee on Pesticides (EC-158/At.6_SCI, 9 December 1996) on Event 176 did not assess the risk of resistance evolution in the target pests because it considered this risk to be an agricultural risk, not an environmental risk. In either event, the Committee felt that resistance management should be fully considered. The Committee also did not assess non-target effects.

Comments by Argentina

Comments under paragraphs 69.09 (b), 69.06, 69.16, and 70.02 are pertinent here.

72.04. The Opinion of the SCAN (EC-158/At.4, 13 December 1996) did not address any environmental risk, including environmentally mediated indirect effects on animal health. The Opinion of the SCF (US-64, EC-158/At.5, 13 December 1996) did not address any environmental risk, including environmentally mediated indirect effects on human health.

Comments by Argentina

Comments under paragraphs 69.06, 69.09(b) through 69.11, and 69.13 are pertinent here.

72.05. On 23 January 1997, the EC decided to allow the placing on the market of Event 176 (ARG-37).

72.06. Luxembourg (US-63, 7 February 1997) and Austria (US-52, 13 February 1997) decided to ban the commercialization of Event 176 for reasons covered in questions 69 and 75.

72.07. The reasoning in the Further Opinion of the Scientific Committee on Pesticides (US-58, 12 May 1997) is false and did not take into account the scientific information known at the time. This is fully discussed in my response to question 69, paragraphs 69.07-69.12, and will not be repeated here.

Comments by Argentina

See comments under paragraphs 69.09 through 69.16.

72.08. In my response to question 69 and question 75, I have concluded that the scientific evidence available to Luxembourg and Austria in February 1997 was NOT sufficient to permit them to undertake an appropriate assessment of potential risks to plants and the environment from Event 176.

Comments by Argentina

See comments under paragraphs 69.06, 69.09, 69.10 and 70.02, which we elaborate on the information available by the relevant dates above.

72.09. The Regulatory Committee under Directive 90/220/EC met three times to consider Draft Commission Decisions to require that the temporary prohibitions by Luxembourg and Austria be repealed. The first two meetings (EC-158/At.13, 10 November 1997 and EC-158/At.16, 22 January 1998) resulted in decisions to delay making a decision. The final meeting (EC-158/At/17, 29 April 1998) resulted in no decision (neither to repeal nor not to repeal).

72.10. On 11 November 1997, an Expert Working Group on Bt resistance management was launched. However, I cannot find any of the proceedings of this Working Group in the materials before the Panel.

Comments by Argentina

The Expert could have used the kind of information commented under paragraph 69.09 (b) above.

72.11. On 31 March 2000 (US-65), Germany decided to prohibit the unrestricted commercial use of Event 176 in Germany. Germany considered the scientific information for risk assessment to be inadequate in the following areas: effects on non-target organisms, development of resistance, countermeasures against development of resistance, effects of Bt toxin in the soil, horizontal or vertical gene transfer of antibiotic resistance gene, harm to humans from antibiotic resistance gene.

Comments by Argentina

On the above subjects, please see comments under the following paragraphs:

on non-target effects: paragraphs 69.06, 69.13, and 69.16 (1)
on resistance development: paragraph 69.09 (b),
on Bt toxin in soil: paragraphs 69.09 (1), 69.10, 69.11, 69.16 (overall comment)
on horizontal gene transfer: paragraph 69.16 (1)

72.12. On 9 November 2000 (US-66), the SCP provided an Opinion on the German decision. The SCP concluded that the scientific information provided by the German Competent Authority does not alter the original risk assessments on Event 176. The Opinion of the SCP is one possible scientific opinion that can be reached from the information available at the time, but the SCP should have acknowledged that the new information also allows several other scientifically valid opinions that were not justifiable in 1996.

Comments by Argentina

The first sentence above is correct. The second sentence leads to an epistemological question: that any scientific opinion based in the information available at one given time T-1, should acknowledge that new information gained at a later time T-2, (being T-2 > T1) will allow for other (supposedly different) scientifically valid opinions that were not justifiable at time T-1. Of course, this is absolutely true but inconsistent with the logical reasoning applied to the facts we are discussing here, when the irreversibility of the time arrow is considered.

See also, our comments under paragraph 69.16, numbered (2), (3) and (4) by the Expert, corresponding to ours numbered 4), 5) and 7), respectively.

72.13. On page 3-4 of this Opinion, the SCP deliberates on non-target risks, focusing on three organisms, green lacewing, monarch butterfly and black swallowtail. For the lacewing and monarch, the SCP considered the experiments difficult to interpret and extrapolate to the field. It did not interpret the swallowtail case. Rather than provide a point by point discussion of the SCP Opinion, I will list a series of valid scientific perspectives and interpretations on the lacewing and monarch studies that illustrate some of the diversity of valid scientific opinion that is not reflected in the SCP Opinion. (1) According the tiered non-target risk assessment protocols (which are consistent with ISPM 11 and Annex III of the Biosafety Protocol and widely used in the US and Europe), the purpose of laboratory experiments is to expose the organisms

to concentrations higher than would be considered typical for the field. By doing so, one reduces the probability of false negative effects. Experimental positives then should undergo additional evaluation. (2) Both lacewings and monarchs were exposed to concentrations of Cry1Ab toxin that would be expected to be higher than typical for the field. Swallowtails were not exposed to high concentrations. (3) Both lacewings and monarchs were adversely affected by Cry1Ab toxin in these laboratory experiments. (4) Additional assessment should have been conducted on lacewings and monarchs to determine the relevance to the field. (5) Cry1Ab is supposed to be a toxin specific to moths and butterflies, but lacewings are not closely related to moths and butterflies. Hence the toxicity spectrum of Cry1Ab toxin is broader than previously expected. (6) Several years later, it has been suggested that Event 176 would have caused significant risk to monarchs had it become a popularly used variety.

Comments by Argentina

The Expert announces that he is not offering a point by point discussion but "a series of valid scientific perspectives and interpretations on the lacewing and monarch studies…". Here, we offer a point by point discussion on the German position. See please, comments under paragraph 72.11.

On the monarch example, a conclusive body of published research is currently available, which can not be ignored by the Expert, indicating that the toxicity is negligible under field conditions.

72.13. On page 4 of the Opinion, the SCP deliberates on resistance risk and management, considering two organisms, European corn borer and Mediterranean corn borer. The SCP advised on the establishment of non-Bt refuges adjacent to modified crops but pointed out that, in view of the slow introduction into Europe, crops would be surrounded by natural refuges for some time to come. Rather than provide a point by point discussion of the SCP Opinion, I will list a series of valid scientific perspectives and interpretations that illustrate the prevailing scientific opinion on resistance risk and management in 2000 that is not reflected in the SCP Opinion. (1) The rate of market penetration after initial introduction of Bt maize in the US was the fastest of any crop variety or crop protection technology in the history of US agriculture. Prior to introduction, many predicted that market penetration would be slow. They were wrong. (2) Resistance evolves locally. Thus refuges must be available wherever Bt-maize is locally used. Thus, refuges need to be required from the beginning. (3) Resistance management is the responsibility of each farmer who uses Bt maize. Thus, each farmer should be required to implement refuges. Thus, refuges need to be required from the beginning.

Comments by Argentina

See our comments under paragraph 72.11 for a point by point discussion the Expert is not offering.

72.15. On page 4 of the Opinion, the SCP deliberates on toxin release to soil on-target risks, focusing on degradation processes. The SCP suggests that because protein turnover occurs routinely in soils and degradation of Bt toxin would be expected to degrade at rates similar to other proteins or DNA in the soil, there is no evidience that Bt-toxins will persist in soils and have adverse effects. Rather than

provide a point by point discussion of the SCP Opinion, I will list a series of valid scientific perspectives and interpretations that illustrate some of the diversity of valid scientific opinion that is not reflected in the SCP Opinion. (1) The actual rates and degradation processes for large proteins in soils is poorly understood. (2) Bt toxin loading in maize fields during and after harvest can be substantial. Thus, scale effects are possible. (3) Presently it is known that Bt toxin in the soil can have an adverse effect on earthworms. Whether this translates into an actual risk is not yet known.

Comments by Argentina

On points (1): Altough basically we agree with the Expert, we disagree in that his statement invalidates the SCP Opinion. We can allow ourselves to make a series of valid scientific "perspectives and interpretations" on the issue (as the Expert does), and say: since one of the technical problems found in the isolation of proteins from plant tissues is the quick release of proteases, we can expect that protein degradation following plant tissue injury (as in agricultural practice) will result in rapid degradation of plant proteins.

On point (2): We disagree. In the same spirit as before, we can offer our perspective and interpretation and say that, since Bt toxin concentration in plant biomass is extremely low (see comments under paragraph 69.09 (1)), when total protein content in soils is considered, we would come to very low figures for the Bt toxin.

On point (3): the Expert do not advance a specific literature reference, but refers to it as "Presently it is known that …". We object that such an argument be construed to invalidate SCP Opinion. This observation also have the recurrent time arrow problem referred to in previos paragraphs 69.16 and 72.12.

72.16. A close reading (paragraphs 72.13-72.15) of the SCP Opinion (US-66, 9 November 2000) suggests that it has not considered all scientific perspectives (and in some cases ignored prevailing scientific opinion). Thus, the SCP Opinion does not invalidate the scientific opinion of Germany.

Comments by Argentina

On the above, please see comments under paragraphs 69.06, 69.09, 69.10 and 69.13.

72.17. I conclude that the scientific evidence available to Germany in March 2000 was NOT sufficient to permit it to undertake an appropriate assessment of potential risks to plants and the environment from Event 176. The evidence on risks to non-target organisms, including those in the soil could be considered insufficient. Germany could have mustered sufficient evidence to argue that there was an environmental risk that the target insects will evolve resistance to the Cry1Ab toxin, and resistance management measures should be required. There may have been sufficient evidence available to determine what measures should be required, but there probably was insufficient evidence to determine how to implement these measures effectively. This determination by Germany was in direct contradiction to the EC decision. In this case, Germany probably does not need to claim that their safeguard measure is a precautionary one.

Comments by Argentina

The Expert reproduces here, almost exactly, what he has said in paragraph 69.13 for Austria. The same comments we did there apply here. In addition, we note again the somewhat dubious comments by the Expert ("could have", "may have sufficient evidence", "but there probably was insufficient evidence"). And, of course, there is also the time arrow problem commented before (please see paragraphs 69.16 and 72.12).

> 72.18. By 2003, the basis for risk assessment of Bt crops had changed because several significant scientific points had come to light. (1) It became widely appreciated that the molecular basis of transformation was more complex than originally thought, and the implications of these findings for risk assessment were articulated. Annex II of Directive 2001/18/EC is one consequence, but additional regulatory changes have occurred since then. Indeed, knowledge in molecular biology continues to accumulate at remarkably fast rates, and I expect that there will be continued change in regulation in the future. (2) Non-target risk assessment shifted from assessing indicators of environmental risk to assessing actual identified potential environmental risks. Presently this is done on an ad hoc basis, as no systematic methodology has gained widespread acceptance. (3) Gene flow risk assessment has shifted from being based primarily on an assessment of the probability of gene flow to being based on an assessment of both the probability of gene flow and the conditional hazard probability. (4) Resistance risk is considered an environmental risk, and science-based resistance management measures are required.

Comments by Argentina

In this point, the Expert copies himself (please see paragraph 69.14). The same comments apply here.

> 72.19. Thus, evidentiary standards for what constitutes an objective environmental risk assessment had changed substantially from 1997 to 2003. This is particularly true in Europe and the United States, and particularly true for the Bt crops.

Comments by Argentina

Same as paragraph 69.15.

> 72.20. (1) Thus, in 2003, there remains some uncertainty about non-target risks of Event 176, but it could be argued that a risk assessment could be conducted using scientifically justified worst-case assumptions. On the other hand, Germany could reasonably maintain that there is still insufficient information to know which non-target species may be at risk, and therefore it is not possible to conduct an objective risk assessment. The findings in 2003 by Székács and Darvas (EC-158/At.37) – that two protected butterfly species in Hungary, *Inachis io* and *Vanessa atalanta*, might be exposed to Bt corn pollen and suffer higher mortality – certainly suggests that not all of the non-target species at risk to Event 176 have been identified in Europe. (2) As in 1997, Germany could muster sufficient evidence in 2003 to argue that there is an environmental risk that the target insects will evolve resistance to the Cry1Ab toxin in Event 176, and resistance management measures should be required. Moreover, in 2003, Germany should have sufficient evidence to determine what kind of resistance management measures to require. (3) Unlike in 1997, in 2003 Germany could argue

that the molecular characterization of Event 176 is insufficient to conduct a risk assessment. (4) It is also possible for Germany to suggest that an additional gene flow risk that needs assessment is contamination of conventional production. It is possible that the scientific evidence to support risk management measures for this risk is presently available.

Comments by Argentina

In this point, the Expert copies himself almost exactly (please see paragraph 69.16). The same comments apply here.

Question 73

73. With reference to the definition of a risk assessment in the SPS Agreement (see Background above), to what extent does the scientific evidence and other documentation submitted by Germany evaluate the relevant risks to human, plant or animal health, and the environment from the importation and use of Maize Bt-176?

How does the scientific evidence and other documentation submitted by Germany compare with the relevant international guidelines for risk assessment and analysis identified above?

73.01. In my response to this question, I will not address issues related to the antibiotic marker gene and will focus my remarks on environmental risks.

73.02 With reference to the SPS Agreement, Germany has evaluated relevant risks to plant health. Specifically, Germany has taken into account available scientific evidence (Article 5.2).

Comments by Argentina

Please see our comments to paragraph 70.02.

73.03. It is not clear, however, that Germany conducted the risk assessment according to the phytosanitary measures which might be applied. Germany did not present their safeguard measure as a possible phytosanitary measure, and did not conduct the risk assessment according to their safeguard measure. Thus it is not clear that Germany conducted the risk assessment consistent with Annex A, paragraph 4.

73.04. Germany did not take into account relevant economic factors (Article 5.3).

73.05. The "potential pest" concept of ISPM 11 must first be considered. This is a special case of the general argument in my response to question 6, and that argument holds for this case because Germany argues that there is a plant pest risk.

73.06. For those risks within the scope of ISPM 11 the risk assessment process is consistent with ISPM 11. However, the economic assessments called for in ISPM 11 were not conducted.

73.07. It appears that some of the ISPM 11 guidance on risk management has not been followed. However, this is not to imply that the actions of Germany contradict this guidance. My reading of the materials before the Panel is that Germany did not

explicitly address this guidance. Specifically I note Section 3.4 (principles), and Section 3.4.6 (on prohibition) were not explicitly addressed.

73.08. In US-65, Germany made it clear in some points that they are applying a different standard for acceptable risk than reflected in the assessments of the SCAN, SCF, Scientific Committee on Pesticides in the EC decision (ARG-37) itself. In so doing, Germany fulfilled ISPM 11, Section 3.1 (level of acceptable risk should be expressed).

73.09. ISPM 11, Section 3.4.6 (prohibition) states "If no satisfactory measure to reduce risk to an acceptable level can be found, the final option may be to prohibit importation of the relevant commodities. This should be viewed as a measure of last resort and should be considered in light of the anticipated efficacy, especially in instances where the incentives for illegal import may be significant." With respect to resistance risk, in 1997 Austria had established the existence of an environmental risk, and required the development of measures to manage this risk to acceptable levels. Germany concurred in 2000. As the EC was not willing to make such a requirement, Germany had no choice but to intervene with its own safeguard measure. In 2000, however, there was probably sufficient scientific evidence to establish what necessary measures should be taken. Scientifically credible suggestions at that time focused on using refuges (maize that was not Bt maize) ranging from 20-30% of the maize grown by any farmer who chose to grow Bt maize. It is unlikely that Germany could have implemented any of these suggestions in time for the 2000 growing season, so I conclude that Germany had fulfilled ISPM 11, Section 3.4.6, at least for the 2000 growing season.

73.09. The science, documentation and reasoning of Germany are consistent with Annex III of the Cartagena Protocol on Biosafety to the Convention on Biological Diversity. Specifically, Annex III, Section 8(f) states "Where there is uncertainty regarding the level of risk, it may be addressed by requesting further information on the specific issues of concern or by implementing appropriate risk management strategies and/or monitoring the living modified organism in the receiving environment."

Question 74

74. Does the scientific evidence and other information submitted by Germany support the adoption of a temporary prohibition on the importation and use of Maize Bt-176? In light of any potential risks identified by Germany, what other risk management options were available in March 2000? What other risk management options are now available?

74.01. In my response to this question, I will not address issues related to the antibiotic marker gene and will focus my remarks on environmental risks.

74.02. The adoption of a temporary prohibition (with <500ha for research purposes) can be justified on the basis of the scientific evidence and other information submitted by Germany.

Comments by Argentina

Although different from paragraph 70.02, the same comments apply here as under paragraph 70.02, with the difference that here the Expert is saying that the measure adopted by Germany can be justified on the basis of the submitted scientific evidence and other information.

> 74.03. Other risk management options could not have been justified in March 2000. However, had Germany worked to develop its own acceptable resistance management measures, perhaps by 2002 other risk management options would have been possible.

Comments by Argentina

Please see our comments to paragraph 70.02.

> 74.04. Today several alternative risk management options may be available. Risk management strategies include risk avoidance, risk mitigation, and risk tolerance. Tolerance strategies are probably inappropriate. One alternate risk avoidance strategy would be to implement country-specific resistance management measures, to limit planting to a restricted region, and to conduct intensive non-target experiments. This would allow progressive determination of non-target effects.

Comments by Argentina

Please see our comments to paragraph 71.04.

Maize Bt-176 (notification C/F/11-03)

Safeguard measure of Luxembourg

Question 75

*75. Given the information before the Panel, including the evaluations undertaken by France (EC-158/at. 1 to 3); the Scientific Committee for Animal Nutrition in December 1996 (EC-158/At.4 and 5); the Scientific Committee for Food in December 1996 (US-64) and in March 1997 (US-58); the Scientific Committee for Pesticides in December 1996 (EC-158/At.6) and in May 1997 (US-57); the SCP in September 2000 (US-66); and the European Commission in its Decision of January 1997 (ARG-37), as well as the information submitted by **Luxembourg** with respect to its safeguard measure (US-63, EC-158/At.9, EC-144), is there any reason to believe that the scientific evidence available to Luxembourg in February 1997 was NOT sufficient to permit it to undertake an appropriate assessment of potential risks to human, plant and animal health, and the environment from the importation and use of Maize Bt-176? If so, what scientific evidence do you believe was insufficient?*

If the evidence was not sufficient in February 1997, was there sufficient evidence available to Luxembourg in August 2003 to permit it to undertake a more objective assessment of potential risks to human, plant and animal health, and the environment from the importation and use of Maize Bt-176? If not, what scientific evidence do you believe was insufficient?

> 75.01. In my response to this question, I will not address issues related to the antibiotic marker gene and will focus my remarks on environmental risks, specifically the resistance monitoring program.

75.02. The initial assessment of Event 176 by France provided in EC-158/At.1-3 (10 January 1995, 1 March 1995, 3 March 1995) does not contain the details of the assessment by the French Biomolecular Engineering Committee (BEC).

75.03. The Opinion of the Scientific Committee on Pesticides (EC-158/At.6SCI, 9 December 1996) on Event 176 did not assess the risk of resistance evolution in the target pests because it considered this risk to be an agricultural risk, not an environmental risk. In either event, the Committee felt that resistance management should be fully considered.

Comments by Argentina

Please see our comments to paragraph 69.03.

75.04. The Opinion of the SCAN (EC-158/At.4, 13 December 1996) did not address any environmental risk, including environmentally mediated indirect effects on animal health. The Opinion of the SCF (US-64, EC-158/At.5, 13 December 1996) did not address any environmental risk, including environmentally mediated indirect effects on human health.

Comments by Argentina

Please see our comments to paragraph 72.04.

75.05. On 23 January 1997, the EC decided to allow the placing on the market of Event 176 (ARG-37).

75.06. On 7 February 1997, Luxembourg decided to ban the commercialization of Event 176 in Luxembourg (US-63). Luxembourg gave two reasons for this action. 1. A concern that the risks of the *bla* gene (ampicillin resistance) have not been properly evaluated by the SCAN and the SCF (paragraph 75.04). 3. That a monitoring program must be implemented to monitor the development of resistance in the target pest to Cry1Ab toxin in Event 176.

Comments by Argentina

See pertinent parts in comments under paragraph 72.11. We note that either the reasons were three (one is missing in the explanation), or only two (the numbering in the explanation was wrong).

75.07. The Further Opinion of the Scientific Committee on Pesticides (US-58, 12 May 1997) is a major shift in the position of the Committee on Event 176.

Comments by Argentina

Please see our comments to paragraph 69.14.

75.08. On page 2-3 of US-58, the Committee states "The Committee stated in its previous report of the 9 December 1996 that resistance management strategies are needed during the years of use of any pesticide, Bt sprays included. The Committee drew attention once again to the need for effective resistance management, including

monitoring on agronomic grounds, to prolong the effectiveness of Bt toxin both in conventional sprays and in genetically modified maize. It also felt that the submission of a satisfactory monitoring and resistance management programme should be a requirement for the authorization to use genetically modified maize seeds expressing Bt-toxin. (a) In its 9 December 1996 Opinion, the Committee nowhere made the recommendation that the submission of a satisfactory monitoring and resistance management programme should be a requirement for the authorization to use genetically modified maize seeds expressing Bt-toxin. The acknowledgement that it should be a requirement in this 12 May 1997 Opinion is a major change in the conclusions and recommendations of the Committee. (b) The Committee does not address a significant issue implicit in Luxembourg's statement, which is that resistance risk should be considered an environmental risk. The Committee also seems to be unaware of the position of the US-EPA in 1996, which is that resistance risk is an environmental risk. This is a critical issue because it determined whether resistance risk could be considered under Directive 90/220/EEC.

Comments by Argentina

Please see our comments to paragraphs 69.13 (point (a)), and 69.11(point (b)).

75.09. I conclude that the scientific evidence available to Luxembourg in February 1997 was NOT sufficient to permit it to undertake an appropriate assessment of potential risks to plants and the environment from Event 176. Luxembourg could have mustered sufficient evidence to argue that there was an environmental risk that the target insects will evolve resistance to the Cry1Ab toxin, resistance management measures should be required and resistance monitoring is a critical measure. There was probably insufficient evidence available to determine what kind of monitoring should be required. This determination by Luxembourg was in direct contradiction to the EC decision. In this case, Luxembourg probably does not need to claim that their safeguard measure is a precautionary one.

Comments by Argentina

Please see our comments to paragraph 69.13.

75.10. By 2003, the basis for risk assessment of Bt crops had changed because several significant scientific points had come to light. (1) It became widely appreciated that the molecular basis of transformation was more complex than originally thought, and the implications of these findings for risk assessment were articulated. Annex II of Directive 2001/18/EC is one consequence, but additional regulatory changes have occurred since then. Indeed, knowledge in molecular biology continues to accumulate at remarkably fast rates, and I expect that there will be continued change in regulation in the future. (2) Non-target risk assessment shifted from assessing indicators of environmental risk to assessing actual identified potential environmental risks. Presently this is done on an ad hoc basis, as no systematic methodology has gained widespread acceptance. (3) Gene flow risk assessment has shifted from being based primarily on an assessment of the probability of gene flow to being based on an assessment of both the probability of gene flow and the conditional hazard probability. (4) Resistance risk is considered an environmental risk, and science-based resistance management measures are required.

Comments by Argentina

Please see our comments to paragraph 69.14.

75.11. Thus, evidentiary standards for what constitutes an objective environmental risk assessment had changed substantially from 1997 to 2003. This is particularly true in Europe and the United States, and particularly true for the Bt crops.

Comments by Argentina

Please see our comments to paragraph 69.15.

75.12. (1) As in 1997, Luxembourg could muster sufficient evidence in 2003 to argue that there is an environmental risk that the target insects will evolve resistance to the Cry1Ab toxin in Event 176, resistance management measures should be required, and resistance monitoring should be required. Moreover, in 2003, Luxembourg probably had sufficient evidence to determine what kind of resistance management and monitoring measures to require. (2) Unlike in 1997, in 2003 Luxembourg could argue that the molecular characterization of Event 176 is insufficient to conduct a risk assessment. (3) Also in 2003, Luxembourg could argue that an additional gene flow risk that needs assessment is contamination of conventional production. It is possible that the scientific evidence to support risk management measures for this risk were available to conduct an objective risk assessment at that time.

Comments by Argentina

Please see our comments to paragraph 69.16.

Question 76

76. With reference to the definition of a risk assessment in the SPS Agreement (see Background above), to what extent does the scientific evidence and other documentation submitted by Luxembourg evaluate the relevant risks to human, plant or animal health, and the environment from the importation and use of Maize Bt-176?

(a) How does the scientific evidence and other documentation submitted by Luxembourg compare with the relevant international guidelines for risk assessment and analysis identified above?

76.01. In my response to this question, I will not address issues related to the antibiotic marker gene and will focus my remarks on environmental risks, specifically the resistance monitoring program.

76.02. With reference to the SPS Agreement, Luxembourg has evaluated relevant risks to plant health. However, it is not clear that Luxembourg has taken into account available scientific evidence (Article 5.2). This is not to say that Luxembourg has not taken into account available scientific evidence.

Comments by Argentina

See pertinent parts of our comments under paragraph 72.11.

76.03. It is not clear that Luxembourg conducted the risk assessment according to the phytosanitary measures which might be applied. Luxembourg did not present their safeguard measure as a possible phytosanitary measure. Luxembourg did not conduct the risk assessment according to their safeguard measure. Thus it is not clear that Luxembourg conducted the risk assessment consistent with Annex A, paragraph 4.

76.04. It is not clear that Luxembourg took into account relevant economic factors (Article 5.3). This is not to say that Luxembourg has not taken into account relevant economic factors.

76.05. The "potential pest" concept of ISPM 11 must first be considered. This is a special case of the general argument in my response to question 6, and that argument holds for this case because Luxembourg argues that there is a plant pest risk.

76.06. For those risks within the scope of ISPM 11 the risk assessment process may be consistent with ISPM 11. However, the economic assessments called for in ISPM 11 were not conducted.

76.07. It appears that much of the ISPM 11 guidance on risk management has not been followed. However, this is not to imply that the actions of Luxembourg contradict this guidance. My reading of the materials before the Panel is that Luxembourg did not explicitly address this guidance. Specifically I note Section 3, *S1* (measures should be designed in proportion to the risk), Section 3.1 (level of acceptable risk should be expressed), Section 3.4 (principles), and Section 3.4.6 (on prohibition) were not explicitly addressed.

76.08. The reasoning of Luxembourg is consistent with Annex III of the Cartagena Protocol on Biosafety to the Convention on Biological Diversity.

Comments by Argentina

Please see our comments to paragraphs 69.06, 69.09, 69.10, and 70.02.

Question 77

77. Does the scientific evidence and other information submitted by Luxembourg support the adoption of a temporary prohibition on the importation and use of Maize Bt-176? In light of any potential risks identified by Luxembourg, what other risk management options were available in February 1997? What other risk management options are now available?

77.01. In my response to this question, I will not address issues related to the antibiotic marker gene and will focus my remarks on environmental risks, specifically the resistance monitoring program.

71.02. The adoption of a temporary prohibition can be justified on the basis of the scientific evidence and other information available to Luxembourg. As there are no materials before the Panel containing scientific evidence submitted by Luxembourg,

> it is not possible to make a determination of the justification for the temporary prohibition based only on submissions from Luxembourg.

Comments by Argentina

Please see our comments to paragraphs 69.06, 69.09, 69.10 and 70.02.

Also, it is useful to point out that the statement by the Expert seems contradictory: "… can be justified on the basis of scientific evidence … available…" (first sentence) vs. "… it is not possible to make a determination of the justification for the temporary prohibition based only on submissions from Luxembourg" (second sentence).

> 71.03. Other risk management options probably could not have been justified in February 1997. However, Luxembourg could have proposed its own acceptable resistance monitoring measures, which perhaps by 1999 would have been possible to implement.

Comments by Argentina

Please see our comments to paragraph 71.03.

> 71.04. Today several alternative risk management options are available for monitoring for resistance. Although there is still no scientific consensus around the best monitoring method, the cost-efficiency trade-offs are known, and considerable experience has accumulated so that several can be feasibly implemented.

Comments by Argentina

Please see our comments to paragraph 71.04.

Maize MON 810 (notification C/F/95/12-02)

Safeguard measure of Austria

Question 78

*78. Given the information before the Panel, including the evaluations undertaken by France (EC-159/At.1 and 2); and the Scientific Committee on Plants in February 1998 (CDA-82), September 1999 (US-55), and September 2000 (CDA-86), and the European Commission in its Decision of April 1998 (CDA-81), as well as the information submitted by **Austria** with respect to its safeguard measure (US-54, EC-159/At.4, EC-144, EC-147, EC-148), is there any reason to believe that the scientific evidence available to Austria in June 1999 was NOT sufficient to permit it to undertake an appropriate assessment of potential risks to human, plant and animal health, and the environment from Maize MON 810? If so, what scientific evidence do you believe was insufficient?*

If the evidence was not sufficient in June 1999, was there sufficient evidence available to Austria in August 2003 to permit it to undertake a more objective assessment of potential risks to human, plant and animal health, and the environment from Maize MON 810 (EC-158/At.30-42)? If not, what scientific evidence do you believe was insufficient?

78.01. My response to this question is the same as my response to question 72, except in the following way. It is apparent from the Commission Decision (CDA-81, 22 April 1998) that resistance management and monitoring measures have been proposed by the notifier. However, I could not find in the materials before the Panel a full description of these resistance management and monitoring measures.

Comments by Argentina

In comments under paragraphs 69.06, 69.09, 69.10 and 70.02, we show that these materials were in the public domain before 1999.

78.02. The Opinion of the SCP (CDA-82, 10 February 1998) does not provide a full description of the proposed resistance management and monitoring measures.

78.03. Austria decided to prohibit the unregulated commercial use of Mon810 (EC-159/At.4, 10 June 1999). In its explanation for this action, Austria does not provide a full description of the proposed resistance management and monitoring measures.

78.04. The further Opinion of the SCP (US-55, 24 September 1999) does not provide a full description of the proposed resistance management and monitoring measures.

78.05. Rather than repeat the arguments in my response to question 72, I summarize as follows. I conclude that the scientific evidence available to Austria in June 1999 was NOT sufficient to permit it to undertake an appropriate assessment of potential risks to plants and the environment from Event 176. The evidence on risks to non-target organisms, including those in the soil could be considered insufficient. I cannot provide a scientific judgment about the sufficiency of the scientific evidence on resistance management and monitoring, because a full description of these measures is not available in the materials before the Panel.

Comments by Argentina

On the information available at the relevant time above see comments under paragraphs 69.06, 69.09, 69.10, and 70.02.

78.06. (1) In 2003, there remained some uncertainty about non-target risks of Mon810, but it could be argued that a risk assessment could be conducted using scientifically justified worst-case assumptions. On the other hand, Austria could reasonably maintain that there is still insufficient information to know which non-target species may be at risk, and therefore it is not possible to conduct an objective risk assessment. The findings in 2003 by Székács and Darvas (EC-158/At.37) – that two protected butterfly species in Hungary, *Inachis io* and *Vanessa atalanta*, might be exposed to Bt corn pollen and suffer higher mortality – certainly suggests that not all of the non-target species at risk to Mon810 have been identified in Europe. However, the toxicity of Mon810 pollen had been determined not to be high, so it is also possible that a worst case risk assessment would have found insignificant risk even for these unknown species exposed to pollen. (2) Unlike in 1999, in 2003 Austria could argue that the molecular characterization of Event 176 is insufficient to conduct a risk assessment. (3) In 2004, Austria suggested that an additional gene flow risk that needs assessment is contamination of conventional production. It is possible that the scientific evidence to support risk management measures is available today.

Comments by Argentina

Please see our comments to paragraphs 69.14 and 69.16.

Question 80

80. Does the scientific evidence and other information submitted by Austria support the adoption of a temporary prohibition on Maize MON 810? In light of any potential risks identified by Austria, what other risk management options were available in June 1999? What other risk management options are now available?

80.01. In my response to this question, I will not address issues related to the antibiotic marker gene and will focus my remarks on environmental risks.

80.02. The adoption of a temporary prohibition can be justified on the basis of the scientific evidence and other information submitted by Austria.

Comments by Argentina

Please see our comments to paragraphs 69.06, 69.09, 69.10, and 70.02.

80.03. Other risk management options may have been justified in June 1999. Because the full resistance management and monitoring measures were not before the Panel, the scientific basis for a concrete discussion of this is not possible.

Comments by Argentina

Please see our comments to paragraphs 69.06, 69.09, 69.10, and 70.02.

80.04. Today several alternative risk management options may be available. Risk management strategies include risk avoidance, risk mitigation, and risk tolerance. Tolerance strategies are probably inappropriate. Because the full resistance management and monitoring measures were not before the Panel, the scientific basis for a concrete discussion of this is not possible.

Comments by Argentina

Please see our comments to paragraphs 69.06, 69.09, 69.10, and 70.02.

Maize T25 (notification C/F/95/12-07)

Safeguard measure of Austria

Question 84

84. Given the information before the Panel, including the evaluations undertaken by France (EC-160/At.1 and 2); the SCP in September 2000 (CDA-75) and September 2001 (CDA-86 and CDA-77), and the European Commission in its Decision of April 1998 (CDA-74), as well as the information submitted by Austria with respect to its safeguard measure (EC-160/At.3 and 5, CDA-76, EC-144, EC-153), is there any reason to believe that the scientific evidence available to Austria in April 2000 was NOT sufficient to permit it to undertake an appropriate assessment of potential risks to human,

plant and animal health, and the environment from Maize T25? If so, what scientific evidence do you believe was insufficient?

(f) If the evidence was not sufficient in April 2000, was there sufficient evidence available to Austria in August 2003 to permit it to undertake a more objective assessment of potential risks to human, plant and animal health, and the environment from Maize T25 (EC-158/At.30-42)? If not, what scientific evidence do you believe was insufficient?

84.01. The reasons for Austria's safeguard measure are provided by Austria (CDA-76, EC-160/At.3, 20 April 2000). While the exact statement (unofficial translation) is reproduced below, there are 6 reasons stated. (1) The environmental risks of T25 have not been sufficiently evaluated under realistic conditions. (2) There is no post-commercialization monitoring program. (3) Although harm from pollen transfer to conventional maize production fields is likely absent, the potential for this risk should be monitored. (4) There is no provision for the protection of ecologically sensitive regions. (5) There is a need for regionally differentiated "good farming practice" guidelines to minimize the danger of resistance. (6) There is a need to assess long-term and secondary ecological effects.

> The maize line T25 had not been examined under realistic conditions of the use of this herbicide and of correspondent agricultural practice. Neither the notification seeking approval of the placing on the market of T25 nor the decision of the European Commission are foreseeing a monitoring programme.
>
> Furthermore special measures monitoring the possible – mostly regarded as safe – spread of pollen to fields in the surroundings cultivated with conventional maize are missing.
>
> The lack of a monitoring programme regarding long-term effects of genetically modified plants or herbicides can be criticized especially because of the fact that the approval conditions are not foreseeing a protection of sensitive areas (Hoppichler J., Expert Innenbefragung zur Bewertung und Evaluation, "GVO-freier ökologisch sensibler Gebiete", Study on behalf of the Austrian Federal Chancellery, Vienna, 1999).
>
> Furthermore regional ecological aspects are not differentiated: the use of herbicide resistant plants in areas of unavoidable applications of herbicides seems to be useful, if the good agricultural practice minimizes the danger of a resistance development.
>
> Under other ecological – respectively agricultural – conditions the use of herbicide resistant plants such as maize should only take place after further investigations of eventual long-term – also secondary – ecological effects.

84.02. Regarding these reasons, (1) is possible grounds for the safeguard measure. (2) is a risk management measure and must be justified by reference to a risk. Austria does not reference any particular risk, so this cannot be grounds for the safeguard

measure. (3) is a possible grounds for the safeguard measure. (4) is a risk management measure and must be justified by reference to a risk. Austria does not reference any particular risk, so this cannot be grounds for the safeguard measure. (5) Austria provides no argument that region-specific guidelines are necessary even when the risk of resistance is regionally differentiated. Regarding the risk of resistance, Austria has not differentiated between the risk associated with volunteers and the risk associated with the evolution of resistance in weeds. There is no scientific ground for resistance risk associated with maize volunteers in Europe. Thus the only possible ground for the safeguard measure is the risk of resistance evolution in weeds. (6) presents a class of risks that are possible grounds for the safeguard measure. Thus, I will concentrate on the following four reasons – (1) The environmental risks of T25 have not been sufficiently evaluated under realistic conditions; (3) Although harm from pollen transfer to conventional maize production fields is likely absent, the potential for this risk should be monitored; the specified part of (5), viz., resistance risk in weeds, and (6) There is a need to assess long-term and secondary ecological effects – as possible grounds for the safeguard measure.

84.03. Regarding (6), long-term effects are certainly possible, but it is difficult to assess long-term effects in pre-commercial risk assessments. In other words, risks that do manifest on long-term time scales are difficult to predict, and unknown long-term effects must be managed after the fact. Thus, the lack of long-term assessments of unknown effects cannot be considered a reason for the safeguard measure. As no long-term effects have been identified beyond resistance risk, this part of (6) cannot be used to justify the safeguard measure. The remaining part of (6), secondary ecological effects, is a specific case of reason (1) and will be treated together with (1).

Comments by Argentina

We agree. In particular, the phrase: "the lack of long-term assessments of unknown effects cannot be considered a reason for the safeguard measure" is absolutely correct. The only way of dealing with long-term effects is relying in the predictive nature of a risk assessment which, of course, must consider all the scientific evidence available at the time.

84.04. Regarding (3), Austria has acknowledged that the possible harm is likely absent, but does not specify concretely the possible harm. It is obvious that Austria cannot be thinking about contamination of conventional production (related to the "coexistence" issue) at this time. If it had considered this, it would not acknowledge that the possible harm is likely absent. As the amended SCP Opinion (CDA-77, 20 July 2001) also does not specific a possible harm, it is difficult to see how this reason can justify the safeguard measure.

Comments by Argentina

We agree. The Expert correctly points out the conditions which Austria did not comply with regard to supporting the reasons for the safeguard measure.

84.05. Regarding (1), the amended SCP Opinion (CDA-77, 20 July 2001) does not provide an assessment of environmental risks beyond gene flow risks. These would include non-target and other biodiversity risks. However, Austria does not provide any scientific evidence that such risks may exist for T25 maize. A risk assessment

cannot be considered insufficient if all concrete possible risks are addressed. In this respect (1) cannot be used to justify the safeguard measure.

Comments by Argentina

Same comments as under paragraph 84.04.

84.06. This leaves only resistance risk in weeds as the only possible grounds for the safeguard measure. The amended SCP Opinion (CDA-77, 20 July 2001) does not provide an assessment of this environmental risk. Even though Austria did not provided any scientific evidence that this risk exists for T25 maize, resistance risks are widely recognized, and the consistent use of glufosinate with T25 maize would result in a resistance risk. Thus, there was insufficient scientific evidence available to the SCP and Austria to assess weed resistance risk and appropriate risk management measures.

Comments by Argentina

The development or tolerance in weeds is an inescapable phenomenon: Any selective pressure applied on the field will lead to the development of tolerance. It is an evolutionary principle that could not be ignored by Austria.

84.07. Managing resistance risk in maize should be easier than managing resistance risk in oilseed rape, so I would expect that adequate information for a risk assessment could have been made available by 2003, had the parties made concerted efforts to bring it together.

Comments by Argentina

We agree. See the results of the FSE trials in the UK.

84.08. However, as I have stated repeatedly, the evidentiary standards for what constitutes an objective environmental risk assessment had changed substantially from 1997 to 2003. While this has been particularly true for the Bt crops, there has also be a shift for GMHT crops. (1) It became widely appreciated that the molecular basis of transformation was more complex than originally thought, and the implications of these findings for risk assessment were articulated. Annex II of Directive 2001/18/EC is one consequence, but additional regulatory changes have occurred since then. Indeed, knowledge in molecular biology continues to accumulate at remarkably fast rates, and I expect that there will be continued change in regulation in the future. (2) The UK-FSE trials have indicated that there are possible risks to biodiversity associated with herbicide use on GMHT crops. However, for GMHT maize, no adverse effects were found. (3) Contamination of conventional production (related to the "coexisitence" issue) is a new issue that could be new grounds for the safeguard measure. It is possible, however, that the scientific evidence to support risk management measures for this risk to conventional maize were available in 2003. Thus, in 2003, Austria could also argue that T25 was inadequately characterized.

Comments by Argentina

See comments under paragraph 69.14.

Question 86

86. Does the scientific evidence and other information submitted by Austria support the adoption of a temporary prohibition on Maize T25? In light of any potential risks identified by Austria, what other risk management options were available in April 2000? What other risk management options are now available?

86.01. The adoption of a temporary prohibition was probably not justified on the basis of the scientific evidence and other information submitted by Austria. Austria needed to clarify the rationale and provide substantial scientific evidence. A temporary prohibition probably could have been justified at the time because the appropriate scientific information did exist.

Comments by Argentina

We agree that there was no justification for a prohibition.

86.02. Several other risk management options could also have been justified in April 2000. Risk management strategies include risk avoidance, risk mitigation, and risk tolerance. In 2000 mitigation and tolerance strategies were probably inappropriate. Here I consider only the resistance risk. One risk avoidance strategy would have been to allow limited planting in a restricted region. This would allow observing how T25 would be used and enable assessment of the selective pressure on weeds. Another approach would have been to limit use on any particular field to once every 4-5 years. This would reduce selection pressure for a long time, allowing alternative management measures to be developed.

Comments by Argentina

We recall that there was no justification for such a measure.

86.03. Today the same measures are available.

Question 97

97. On the basis of the information before the Panel, is there new scientific evidence since 1998 that would suggest that the potential risks to human, plant or animal health, or to the environment, from any of the specific biotech products subject to this dispute (including products subject to the member State safeguard measures), are different in nature or magnitude as compared to the scientific understanding of the risks associated with such biotech products prior to 1998, taking into account:

- *the intended use of each product (direct human or animal consumption, further processing for consumption, planting or any other specified use);*
- *any potential risks that may arise from the combination or successive use of biotech products.*

Does the information before the Panel support the view that the potential risks from the products in this dispute should be assessed differently than the risks from biotech products approved prior to 1998?

Changes since 1998

97.01. The main changes that have occurred since 1998 are related to risk assessment methodologies and the evidence needed in a risk assessment. There are some differences between the transgenic crops evaluated and approved before 1998 by the EC and those evaluated later, but these differences are not as great as the changes in risk assessment methodologies and evidence needed. These changes came about from increased scientific knowledge about transgenic crops. This has affected risk assessment for transgenic crops intended for planting in the environment. Scientific investigation of risks of combination biotech products has lagged behind.

97.02. As I indicated in previous answers, the basis for risk assessment of transgenic crops had changed because several significant scientific points had come to light. (1) It became widely appreciated that the molecular basis of transformation was more complex than originally thought, and the implications of these findings for risk assessment were articulated. (2) Non-target risk assessment shifted from assessing indicators of environmental risk to assessing actual identified potential environmental risks. Presently this is done on an ad hoc basis, as no systematic methodology has gained widespread acceptance. (3) Gene flow risk assessment has shifted from being based primarily on an assessment of the probability of gene flow to being based on an assessment of both the probability of gene flow and the conditional hazard probability. (4) Resistance risk is considered an environmental risk, and science-based resistance management measures are required.

Comments by Argentina

See comments under paragraph 69.14.

97.03. Thus, risk assessment methodologies and evidentiary standards for what constitutes an objective environmental risk assessment had changed substantially from 1998 to 2005. This is particularly true in Europe and the United States, and particularly true for the Bt crops.

Comments by Argentina

See comments under paragraph 69.14.

97.04. Below, I will sketch some of the changes in non-target risk assessment and resistance risk assessment and management.

Non-target risk assessment

97.05. Through 1997, most studies on non-target and biodiversity risks of transgenic plants showed no effect of the transgenic plant (Fitt *et al.* 1994; Sims 1995; Dogan *et al.* 1996; Orr & Landis 1997; Pilcher *et al.* 1997; Yu *et al.* 1997; EPA 2001; Monsanto Company 2002a, b). The methodological approach used in nearly all of the studies was an indicator species approach similar to the ecotoxicological

assessments of pesticides where indicator species are used to extrapolate to risks in the actual environment. Only one laboratory study showed a lower survival of the springtail *Folsomia candida* (Willem) when fed with high concentrations of Bt corn leaf protein (EPA 2001), but the significance of this result is not clear. These indicator species are not usually closely associated with the transgenic plant tested or the area where the plants are grown. Based on these studies, many scientists believed that non-targets were not significantly at risk.

Comments by Argentina

We note that there is only one study, whose significance is not clear, indicating that a particular non-target organism was affected by the GM plant trait. We believe that the indicator species tests are an acceptable guidance, but agree on the value of commercial-scale field studies. Again, with the sole exception of the monarch butterfly, which is still under debate (and seems not to support the hypothesis of a significant non-target effect; see above, comments on the monarch butterfly experiments made by this reviewer), no significant full-scale non-target effects have been reported. While we still agree with the Expert in that studies on non-target effects should continue, we do not find this to be a justification for delaying approval, neither in 1998 nor today.

97.06. In 1998, studies by Hilbeck et al (1998a,b) invigorated consideration of non-target risks by reporting an unexpected adverse effect of Bt corn on the predatory green lacewing *Chrysoperla carnea* Stephens. They fed *C. carnea* larvae with Cry1Ab Bt corn-fed prey or a diet containing purified Cry1Ab toxin, and found higher immature mortality compared to controls. These results were surprising because the Cry1Ab toxin is believed to be Lepidopteran-specific, while *C. carnea* belongs to the Neuroptera, an order that is more closely related to the Coleoptera than to the mecopteroid orders including the Lepidoptera. These results have been confirmed by additional studies (Hilbeck *et al.* 1999; Dutton *et al.* 2002; Dutton *et al*. 2003), although the mechanism is still uncertain. These studies suggested that Cry toxins may be less specific than previously believed.

Comments by Argentina

While we would expect the exact mechanism for the above findings to come to light, we note that the reported results have been obtained under laboratory conditions, which in general were criticized by the Expert. Moreover, when the 1999 paper by theses authors is examined, we find (Hilbeck et al; Entom. Exper. Appl. 1999, 91:305-316; excerpts):

"… In agreement with the previous studies, total development time of C. carnea was not consistently, significantly affected by the Bt-treatments except at the highest Cry1Ab toxin concentration. However, both highest mortality and delayed development of immature C. carnea raised on Cry1Ab toxin 100 _g g_1 diet – fed prey may have been confounded with an increased intoxication of S. littoralis larvae that was observed at that concentration. At all other B. thuringiensis protein concentrations S. littoralis was not lethally affected. Comparative analyisis of the results of this study with those of the two previous studies revealed that in addition to prey/herbivore by B. thuringiensis interactions, also prey/herbivore by plant interactions exist that contribute to the observed toxicity of B. thuringiensis – fed S. littoralis larvae for C. carnea. These

> **findings demonstrate that tritrophic level studies are necessary to assess the long-term compatibility of insecticidal plants with important natural enemies…"**

We observe that the above findings, while very interesting, do not qualify for a approval delay of Bt crops.

> 97.07. In the years following 1998, publications on non-target risks began to shift from indicator species to the actual (or tangible) potential risks on species that naturally occur in areas where transgenic plants are meant to be cultivated. In early 1999, Losey *et al.* (1999) suggested that monarch larvae (*Danaus plexippus* L.) suffered higher mortality when feeding on their primary host plant, the common milkweed *Asclepias syriaca* L., dusted with transgenic Cry1Ab Bt pollen. This initial observation was later confirmed by Jesse & Obrycki (2000) and coupled with the realization that ~50% of the monarch breeding habitat is located in the Corn Belt (Wassenaar & Hobson 1998), this triggered concerns that large-scale cultivation of Bt corn would harm the monarch population. Monarch butterflies attract wide interest in the US for multiple reasons, such as their beauty, iconic significance to the public, and spectacular migration over several thousand miles. Stimulated by these results, a group of researchers conducted a series of studies to estimate the actual risk of Bt corn to monarch butterflies (Hellmich *et al.* 2001; Oberhauser *et al.* 2001; Pleasants *et al.* 2001; Sears *et al*. 2001; Stanley-Horn *et al.* 2001; Zangerl *et al*. 2001). Sears *et al.* (2001) concluded that the risk to monarch populations was insignificant, and in an excellent review, Oberhauser & Rivers (2003) summarized the events and findings associated with these studies. Recent studies (Anderson *et al.* 2004; Jesse & Obrycki 2004; Dively *et al.* 2004), however, have revealed a higher toxicity of Bt pollen and anthers than found in previous studies. Although Dively *et al.* (2004) suggested that the risk to monarchs remains insignificant, a close analysis of the issues may allow other interpretations of risk to monarchs.

Comments by Argentina

1. On the paper by Anderson et al, we reproduce here the abstract: (italics and underlined are ours. In capital letters, we indicated the relevant findings which contradict the Expert contention that Bt toxin is a significant risk for monarca butterfly):

> **Previous studies suggest that exposure to corn, *Zea mays* L., anthers expressing *Bacillus thuringiensis* (Bt)-derived protein may have adverse effects on the larvae of monarch butterfly, *Danaus plexippus* (L.). To examine the potential effects of Bt anthers on monarch butterflies, studies were designed to test toxicity *in the laboratory*; examine anther distribution in space and time; compare distributions of anthers, pollen, and larval feeding; and *measure effects of long-term exposure in the field*. In the laboratory, monarch butterfly larvae fed on whole corn anthers, but anther feeding was sporadic. Larvae exposed TO *0.3 ANTHER/CM^2* fed and weighed less after 4 d compared with larvae exposed to non-Bt anthers. Adverse effects increased with increasing anther density. Monarch butterfly larvae exposed to *0.9 ANTHER/CM^2* had reduced feeding, weight, and survival and increased developmental time compared with larvae exposed to non-Bt anthers. Later instars were more tolerant of Bt toxin. For all studies, *laboratory testing probably magnified effects because larvae were confined to petri dishes. Field studies showed toxic anther densities are uncommon on milkweed (Asclepias) leaves in and near cornfields during anthesis. Mean anther***

densities on milkweed leaves in cornfields during peak anthesis were between 0.06 AND 0.1 ANTHER/CM^2 (3–5 ANTHERS PER LEAF). When exposure to a density OF FIVE ANTHERS PER LEAF WAS TESTED IN FIELD-CAGE STUDIES, no effects on growth, development, or survival were detected. Based on probability of exposure to toxic densities, BT ANTHERS ALONE ARE NOT LIKELY TO POSE A SIGNIFICANT RISK TO MONARCH BUTTERFLIES IN IOWA.

2. On the paper by Dively et al, we reproduce here some excerpts: (italics and underlined are ours. In capital letters, we indicated the relevant findings which contradict the Expert contention that Bt toxin is a significant risk for monarca butterfly):

> **"The potential non-target risks to monarch butterfly, *danaus plexippus* l., of transgenic corn transformed with a gene from the bacterium *Bacillus thuringiensis* (Bt) have been the focus of much scientifc research and debate after a laboratory study by Losey et al. (1999) revealed toxicity to monarch butterfly larvae consuming Bt corn pollen deposited on milkweed plants (*Asclepias* spp.). *SUBSEQUENT STUDIES INDICATED THAT THE ACUTE EFFECT OF BT CORN POLLEN EXPRESSING LEPIDOPTERAN-ACTIVE CRY PROTEIN ON MONARCH BUTTERFLY POPULATIONS WAS NEGLIGIBLE (SEARS ET AL.2001). LARVAL EXPOSURE TO POLLEN ON A POPULATION-WIDE BASIS IS LOW, GIVEN THE PROPORTION OF LARVAE IN CORNFIELDS DURING POLLEN SHED, THE PROPORTION OF FIELDS PLANTED IN BT CORN, AND THE LEVELS OF POLLEN WITHIN AND AROUND CORNFIELDS THAT EXCEED THE TOXICITY THRESHOLD (OBERHAUSER ET AL. 2001, PLEASANTS ET AL.2001).CONSERVATIVELY, THE PROPORTION OF THE MONARCH BUTTERFLY POPULATION EXPONED TO BT CORN POLLEN WAS ESTIMATED TO BE 0.8% (SEARS ET AL.2001).LABORATORY BIOASSAYS ALSO SHOWED THAT ACUTE TOXIC AND SUBLETHAL EFFECTS OF POLLEN FROM THE MOST WIDELY PLANTED BT CORN HYBRIDS (EVENTS MON810 AND BT11) ARE UNLIKELY, EVEN AT PEAK LEVELS OF POLLEN SHED (HELLMICH ET AL.2001).THE ONLY TRANSGENIC CORN POLLEN THAT CONSISTENTLY AFFECTED MONARCH BUTTERFLY LARVAE WAS FROM THE CRY1AB EVENT 176 HYBRIDS, WHICH HAVE BEEN PHASED OUT OF COMMERCIAL USE IN THE UNITED STATES. FURTHERMORE, FIELD STUDIES PERFORMED IN IOWA, MARYLAND, NEW YORK, AND ONTARIO, CANADA, REPORTED THAT GROWTH TO ADULTHOOD OR SURVIVAL OF MONARCH BUTTERFLY LARVAE WAS UNAFFECTED AFTER EXPOSURES FOR 4-5 D TO MILKWEED LEAVES WITH NATURAL DEPOSITS OF CRY1AB EXPRESSING (EVENTS BT11 AND MON810) CORN POLLEN (STANLEY-HORN ET AL.2001).THESE RESULTS INDICATED NEGLIGIBLE EFFECTS OF BT POLLEN TO MONARCH BUTTERFLY LARVAE FROM SHORT-DURATION EXPOSURES IN FIELD SETTINGS. ALL SCIENTIFIC INFORMATION ON ACUTE TOXICITY AND EXPOSURE SUPPORTS THE CONCLUSION THAT BT CORN POSES A LIMITED RISK TO MONARCH BUTTERFLY POPULATIONS (SEARS ET AL.2001).WHAT RISK EXISTS IS CAUSED BY THE LIMITED EXPOSURE OF MONARCH BUTTERFLY POPULATIONS TO BT POLLEN IN NATURE .NEVERTHELESS, THE STUDIES TO DATE EXAMINED ACUTE AND SUBLETHAL EFFECTS AFTER 4-5 D OF EXPOSURE OF DEVELOPING LARVAE TO BT POLLEN.***

IN CORNFIELDS, LARVAE HATCHING AT THE ONSET OF ANTHESIS MAY BE EXPONED TO BIOLOGICALLY ACTIVE CRY1AB PROTEIN FOR PERIODS OF 12 D OR MORE (RUSSELL AND HALLAUER 1980).THIS WORST-CASE SCENARIO COULD POTENTIALLY IMPACT THE 0.8% OF THE MONARCH BUTTERFLY POPULATION EXPOSED TO BT …

Long-term exposure of monarch butterfly larvae throughout their development to Bt corn pollen is detrimental to only a fraction of the breeding population because *THE RISK OF EXPOSURE IS LOW*. When this impact is considered over the entire range of the Corn Belt, *THE ECOLOGICAL OUTCOME IS VERY SMALL.* Moreover, *BT CORN ADOPTION IS ASSOCIATED WITH LOWER INSECTICIDE USE AGAINST TARGET LEPIDOPTERA (PILCHER ET AL.2002), AND MOST INSECTICIDES ARE ACUTELY TOXIC TO LARVAE OCCURRING IN CORN OR IN OTHER CROPS THAT PROVIDE HABITAT FOR MONARCH BUTTERFLY POPULATIONS*. In field bioassays, larvae died within hours after feeding on milkweeds exposed to a single application of a pyrethroid insecticide (Stanley-Horn et al.2001)…..

… IT IS LIKELY THAT BT CORN WILL NOT AFFECT THE SUSTAINABILITY OF MONARCH BUTTERFLY POPULATIONS IN NORTH AMERICA…."

(Note of this reviewer) The above shows that Bt corn could be considered a protection to monarca butterfly, as its use would decrease the use of chemical insecticides, which are acutely toxic to larvae.

3. On the paper by *Jesse and Obrycki (2004),* we reproduce here some excerpts from the abstract:

"We present THE FIRST EVIDENCE that transgenic Bacillus thuringiensis (Bt) corn pollen naturally deposited on Asclepias syriaca; common milkweed, in a corn field causes significant mortality of Danaus plexippus L. (Lepidoptera: Danaidae) larvae. Larvae feeding for 48 h on A. syriaca plants naturally dusted with pollen from Bt corn plants suffered significantly higher rates of mortality at 48 h (20±3%) compared to larvae feeding on leaves with no pollen (3±3%), or feeding on leaves with non-Bt pollen (0%). Mortality at 120 h of D. plexippus larvae exposed to 135 pollen grains/cm2 of transgenic pollen for 48 h ranged from 37 to 70%. … We conclude that the ecological effects of transgenic insecticidal crops NEED TO BE EVALUATED MORE FULLY before they are planted over extensive areas."

We agree that the results shown here are the first evidence of an effect, but they should be validated by further research, as the authors recognized.

97.08. This shift to considering tangible risks may have helped identify potential adverse effects to the Federally endangered Karner blue butterfly (*Lycaeides melissa samuelis* Nabokov, Lepidoptera, Lyceanidae). Instead of focusing only on commercial corn fields, dispersal of pollen and the production of corn in wildlife refuges could expose this endangered species to Bt pollen. The 2000 Scientific Advisory Panel (SAP) of the US Environmental Protection Agency (EPA) acknowledged the possibility that this species may come in contact with Bt pollen

(see also Andow *et al*. 1995), and the EPA (2001) required additional assessment of the risks to Karner Blue butterfly.

Comments by Argentina

These studies were preliminary, or published later than 1998. Therefore, they do not qualify ad a justification for delaying approval.

97.09. During 1999, research oriented toward assessing the tangible potential risks associated with soils was published. Saxena *et al*. (1999) found that Cry1Ab is released into the soil via corn root exudates, where it can persist for at least 350 days (Saxena *et al*. 2002). These results suggested that Bt corn could possibly affect rhizosphere and soil communities. Later, Zwahlen *et al*. (2003a) reported that the Cry1Ab toxin in Bt corn litter persisted for at least 8 months. Together these studies showed that long-term exposure of soil organisms to Bt toxins was possible and that the risks of Bt crops on soil ecosystem functioning should be assessed. Zwahlen *et al.* (2003b) also showed that mortality and weight development of adult and juvenile earthworms, *Lumbricus terrestris* L., were not significantly different when fed Bt or non-Bt corn residues, with the exception that after 200 days, adult Bt corn-fed earthworms had a significant weight loss compared to the non-Bt corn-fed ones.

Comments by Argentina

See comments under paragraph 97.08.

97.10. Non-target risks associated with herbicide-tolerant crops were hardly studied until 2000, when Watkinson *et al.* (2000) suggested that these crops might adversely effect skylark populations in the UK. A large-scale field evaluation of herbicide-tolerant crops in the UK was established to investigate possible actual effects on non-target species, and results were published in 2003. For the most part, ecological effects propagated from whatever changes in the weed community that resulted from the change in herbicide use. The non-target effects of herbicide tolerant crops have not been studied intensively elsewhere.

Comments by Argentina

See comments under paragraph 97.08.

97.11. In 2004, Andow & Hilbeck (2004) presented the outline of a new risk assessment model for non-target effects of transgenic crops. Implicitly they are proposing to systematize the actual/ tangible risk assessment process that has been building since 1999. An important innovation is to select locally occurring non-target species that are most likely to be exposed to a transgenic crop and likely to make significant contributions to the ecological functioning of the local ecosystem.

Comments by Argentina

Knowledge obtained at such later dates, could not possibly justify delay for approval.

97.12. Non-target and biodiversity risk assessments of transgenic plants continue to be improved. While indicator species continue to be used in many risk assessments,

there is a trend towards assessing actual/ tangible risks involving species that naturally occur in areas where transgenic crops will be planted. In the future it will continue to be important to assess not only the effects of the transgenic plant itself but also the effects associated with changes in agricultural practices. In addition, although they may be difficult to develop and verify, effective methods for biodiversity assessment have not yet been developed.

Comments by Argentina

See comments under the paragraphs above.

Resistance risk assessment and management

97.13. The evolution of pest resistance to pest control measures has been known for nearly 100 years, but it became a significant problem after World War II, when modern, intensive agricultural technologies proliferated, resulting in strong uniform selection over large areas. About 536 species of arthropods, 60 genera of plant pathogenic fungi, and 174 weed species have evolved resistance to pesticides (Eckert 1988; WeedScience.org 2003; Whalon *et al.* 2004), and resistance to Bt toxins has been documented in >17 insect species (Tabashnik 1994, Huang *et al.* 1999). Interestingly, virologists remain unconvinced that resistance will evolve to transgenic virus resistant crops (Tepfer 2002), however, despite some disagreement (reviewed in Tabashnik 1994), entomologists and weed scientists agree that resistance evolution is a real risk for which some management is desirable (NRC 1986).

97.14. At the beginning of the 1990s, it had proven difficult to implement effective resistance management for most pesticides. Indeed, there was pessimism that a high-dose/ refuge resistance management system could ever be implemented for insecticide resistance management because a high dose could not be reliably maintained (Roush 1989; Tabashnik 1989). With the advent of transgenic Bt crops, hopes were renewed (Gould 1994; Roush 1994), but it was not clear that a high-dose/ refuge strategy would delay resistance enough with a reasonably sized refuge (Comins 1977).

97.15. In a series of simple simulations based on Comins (1977) early work, Alstad & Andow (1995) showed that the high-dose/ refuge strategy could delay resistance in European corn borer to Bt corn for more than 30 years with a 50% non-Bt corn refuge. Subsequent research suggested that smaller refuges would also substantially delay resistance, proving that effective resistance management was possible theoretically (Gould 1998; Shelton *et al.* 2000).

Comments by Argentina

In the above statement, the Expert shows that resistance management is possible. Although some of the above papers were published later, this concept was already prevailing in 1998, and therefore could not be construed to support delay for approval.

97.16. The focus shifted to practicalities. Could an effective resistance management strategy be implemented? In the US, this question was answered through a series of decisions made by the EPA. In early 1995, the EPA registered Bt potato, and although resistance risk was recognized, no resistance management was required. By

the end of that year, EPA issued conditional registrations and required the development of resistance management for all subsequent Bt crops (Matten *et al.* 1996). Conditional registrations were used to motivate the development and implementation of a scientifically justified resistance management strategy.

Comments by Argentina

See comments under paragraph 97.15.

97.17. The key issues in 1995 were how large a refuge was needed, did the refuge need to be spatially structured relative to the Bt fields, and could the refuge be managed to limit pest losses? Aspects of some of these questions remain unresolved today. In Australia, Bt cotton did not provide a high-dose against the key pest, cotton bollworm *Helicoverpa armigera* (Hübner), and growers and researchers agreed to require 70% refuges to make the likelihood of resistance remote (Fitt 1997). In the US, Bt cotton provided a high-dose against the key pest, cotton budworm *Heliothis virescens* (F.), but not against another important pest, *Helicoverpa zea* (Boddie), however, refuge requirements were set at 4% unsprayed or 20% sprayed refuge outside of the Bt field with minimal requirements of spatial structure. In 2001, spatial structure requirements were added for Bt cotton along with other modifications. These initial requirements and changes represent a compromise among various interests, although science played a significant role.

Comments by Argentina

See comments under paragraph 97.15.

97.18. Resistance management requirements for Bt corn developed with strong scientific input. Early in 1997, the USDA regional research committee NC-205 reviewed model results and information on the ecology of European corn borer and suggested to registrants and the EPA that a 20-25% refuge was needed near all Bt corn fields (Anon. 1998). Research results supporting this recommendation were published in the ensuing years (Onstad & Gould 1998; Hunt *et al.* 2001; Bourguet *et al.* 2003). One of the key results was a bioeconomic model suggesting that a 20% refuge would be nearly optimal for growers who consider the trade-off between the immediate costs of the refuge and delayed costs of resistance failures (Hurley *et al.* 2001). Canada required a 20% refuge within 0.5 miles (~800 meters) of Bt corn in 1998, and during 1999 a consensus was reached in the US and the EPA required a 20% refuge within 0.5 miles of Bt corn for the 2000 growing season and thereafter.

Comments by Argentina

See comments under paragraph 97.15.

97.19. Several scientific issues remain unresolved. Understanding the mechanisms of resistance is necessary to tailor resistance management to the particular system, but these are just beginning to be revealed for Bt crops (Gahan *et al.* 2001). The details of adult movement may play a key role in the evolution of resistance (Caprio 2001; Ives & Andow 2002). Limited dispersal of adults from natal fields (Comins 1977), pre- versus post-mating adult movement, and male versus female movement (Ives & Andow 2002) may have significant effects on models of resistance evolution, and

estimating these movement rates in the field is challenging. Farming practices, such as crop rotation (Peck & Ellner 1997), management of the refuge (Onstad *et al.* 2002; Ives & Andow 2002), and rational approaches to pest management, may affect the rates of resistance evolution. Significantly, a consensus for managing low-dose events has yet to emerge, and scientific analysis of this problem is incomplete. For example, Australia implemented 70% refuges for one low-dose event, while the US has used 20% refuges for both high- and low-dose events.

Comments by Argentina

See comments under paragraph 97.15.

97.20. Monitoring for the occurrence and frequency of resistance and methods to improve compliance to resistance management requirements among growers are areas of current research. The key monitoring problem is how to estimate resistance when it is rare and recessive. One promising approach is the F_2 screen (Andow & Alstad 1998; Andow & Ives 2002; Stodola & Andow 2004). It is a genic screen and works by inbreeding isofemale lines so that recessive phenotypes are expressed in the F_2 generation, when they can be screened. If mated females are collected from natural populations, each carries four haplotypes (two of her own and two of her mate's) and only 250 female lines need to be screened instead of 10^6 field-collected individuals. The F_2 screen has been used for several species (Bentur *et al.* 2000, Bourguet *et al.* 2003; Génissel *et al.* 2003). Other genetic and phenotypic methods have been used on some cotton pests (Gould *et al.* 1997; Tabashnik *et al.* 2000), but usually phenotypic screens will have lower sensitivity and higher cost than genic screens (Andow & Ives 2002). Improving compliance will require a combination of bioeconomic modeling, surveys of grower behavior and motivations, and development of effective educational materials.

Comments by Argentina

See comments under paragraph 97.15.

97.21. Our understanding of resistance risk and management continues to evolve. Presently, none of the Bt crops now used has suffered a resistance failure despite widespread use. While this may be due to good fortune, in some cases, such as Bt cotton in Australia, resistance management must have been crucial to avoiding failure, and in other cases, such as Bt cotton in Arizona, US, other factors must also be important (Tabashnik *et al.* 2003). Interestingly, relatively little research has focused on weed resistance to herbicides used with the herbicide tolerant crops. This problem has been treated as a theoretical herbicide resistance problem (Gressell *et al.* 1996), but with recent reports of weed resistance (WeedScience.org 2003), this may change.

Comments by Argentina

See comments under paragraph 97.15. We note that the Expert states that … "Presently, none of the Bt crops now used has suffered a resistance failure despite widespread use…" This statement proves that, although basically correct on the need to improve methodology and further research, the Expert grants that no significant harm was done to biodiversity, by using

concepts and knowledge already existing in 1998, and therefore no justification for delaying approval would have scientific grounds.

Question 99 – Monitoring

99. For those biotech products at issue in this dispute for which no significantly different nature or level of risk has been identified, does the information before the Panel provide a scientific or technical rationale for monitoring the occurrence of potential adverse effects, or of unintentional effects, arising from the consumption or use of these products compared to those products of biotechnology approved by the European Communities prior to October 1998?

99.01. There are some biotech products at issue in this dispute for which one committee or another has determined that were no significant risks. I have taken issue with some of these determinations in my previous responses. For all of the products at issue in this dispute, there are some member countries that disagree with the assessment of the relevant SCP (for example) that there are no significant identified risks. This disagreement is sometimes related to different standards of acceptable risk being applied by the disagreeing parties.

Comments by Argentina

The Expert has pointed out, in the relevant comments on the Member States claims, that most of them were unclear and do not have had justification at the time of the suspending approvals.

99.02. This disagreement provides the only rationale for monitoring potential adverse effects. If all parties agreed that there were no significant identified risks, there would no need to consider monitoring for potential adverse effects.

99.03. Unanticipated effects could arise from a transgene by any of the following mechanisms: new ORFs, insertional mutagenesis, post-transcriptional or post-translational processing, other pleiotropy or epistasis, and gene-by-environment interaction. New ORFs and insertional mutagenesis can be addressed through molecular characterization of all transgene loci. Post-transcriptional or post-translational processing can be addressed to the most part by molecular and biochemical analysis. Other pleiotropy or epistasis and gene-by-environment interaction cannot be addressed without extensive planting in the field.

Comments by Argentina

All the above requirements were addressed in 1998, according with the state of the art at that date.

99.04. All of these possible sources unanticipated effects are equally likely to occur for plant biotech products before 1998 and plant biotech products after 1998. It is possible that more recent events (after 2001) are less likely to have such unanticipated effects than those prior to 1998. The main difference between them is that new ORFs, insertional mutagenesis and post-transcriptional and post-translational processing was not looked for very much before 1998, while after 2001, the methods and standards have become increasingly targeted to assess these possibilities. This provides a rationale for monitoring.

Comments by Argentina

The Expert is correct, but although methodologies were improved since 1998, none of the GM crops revised under the more recent techniques and concepts were shown to lead to a decision such as the one taken in 1998. Moreover, the new methods and regulatory requirements even reinforced the robustness of the early decisions.

Question 100 - Agricultural management practices

100. For those biotech products at issue in this dispute for which an approval has been sought for environmental release (notifications submitted under Directives 90/220 or 2001/18), and for which no significantly different nature or level of risk has been identified, does the information before the Panel provide a scientific or technical rationale for requiring specific agricultural management practices that differ from those for products of biotechnology approved by the European Communities prior to October 1998?

100.01. A parallel argument to my response to question 99 holds for this question.

Comments by Argentina

See our comments under question 99.

Question 101 – Mitigation

101. Does the information before the Panel support the argument that any potential risks from any of the biotech products at issue in this dispute should be mitigated in a manner different than the products of biotechnology approved by the European Communities prior to October 1998? If so, what means of risk mitigation might be envisaged?

101.01. None of the products approved by the EC prior to October 1998 have been mitigated in any manner by the EC because no mitigable risks have been reported and verified. Should any of the biotech products cause a verifiable risk, this would be sufficient argument for mitigating them differently.

Comments by Argentina

Note that the Expert is indirectly indicating that no delay would have been justified in 1998 based in mitigable risks.

101.02. However, as indicated in my response to question 97, there are new risk methodologies and assessment standards being applied to biotech products today than prior to 1998. Thus, it is possible that risks will be identified for new products that were not even considered in the older products. Under such conditions, differences could be justified.

Comments by Argentina

See comments under question 97. See also, comments under paragraph 69.14.

Question 102

102. Does the information before the Panel support the view that the biotech products at issue in this dispute (including products subject to the member State safeguard measures) give rise to the same types of potential risks to human, plant or animal health or to the environment as novel non-biotech products, such as plant products produced by selective breeding, cross-breeding and induced mutagenesis? If so, for any biotech product at issue in this dispute are there significant differences, from a scientific perspective, in the nature or magnitude of any potential risks from these products compared to comparable novel non-biotech products taking into account:

- *the specific genetic modification introduced and the resulting product;*
- *the intended use of each product (direct human or animal consumption, further processing for consumption, planting or other use);*
- *any potential risks that may arise from the combination or successive use of biotech products or comparable novel non-biotech products.*

Please explain with reference to specific products at issue in this dispute.

Comparable non-biotech products from plant breeding

102.01. Regarding the differences between conventional breeding and so-called "molecular breeding," none of the parties fully represent the comparison accurately. Breeding involves two important processes: (1) finding and introducing usable genetic variation into the breeding population and (2) improving and selecting desired varieties from the breeding population. The methods used will depend on the crop, with major differences for clonal species, such as potato and banana versus sexual species, such as oilseed rape, maize and soybean. Among the sexual species, there are major differences in breeding methods between outcrossing species, such as maize and oilseed rape, and inbreeding species, such as soybean, and wheat.

102.02. Transgenesis is a process to introduce genetic variation into the breeding population. Transgenesis is not a process for finding genetic variation or for selecting and improving varieties. Thus, there is no such thing as molecular breeding. Transgenesis is merely a part of the breeding process.

Comments by Argentina

Here the Expert makes several statements that merit incidental comment.

(a) "Transgenesis is a process to introduce genetic variation into the breeding population". We would prefer: "Transgenesis is a process to introduce a precise genetic construct into the breeding population".

(b) "Thus, there is no such thing as molecular breeding". Since the Expert points out repeatedly about new methodologies, he must recognize that molecular assited selection is a very useful way to use molecular biology in conventional breeding.

102.03. It would seem important then to determine a comparable conventional counterpart to transgenesis for introducing genetic variation into the breeding population. A comparable conventional process would be one typically used in breeding programs rather than one rarely used. If possible a comparable conventional process would introduce genetic variation during a similar or analogous step in the breeding process. The breeding process can eliminate considerable genetic variation, so variation introduced very early in the breeding process, will be screened and selected multiple times by multiple breeding programs prior to use, while variation introduced much later in the process will receive fewer screenings and possibly no additional selection.

102.04. Several other methods exist to introduce genetic variation into the breeding population. These include wide crossing, crossing or using unadapted material, mutagenesis, and recombining diverse adapted material. Wide crossing involves crosses with different species. Unadapted material are plants of the same species (or subspecies) that have not previously been used in breeding programs. Adapted materials are those that have already been used to produce modern conventional varieties. There is a range of "adaptedness" even within these materials, with some breeding programs relying primarily on the most recently used popular varieties and other programs reaching further back in time for older varieties as the source of genetic variation.

Comments by Argentina

We would add diversity obtained through somaclonal variation, as a way to introduce genetic variation into the breeding population.

102.05. Crossing methods are difficult to use routinely for clonal and inbreeding species. For example, in potato, genetic variation is conventionally introduced by growing plants to flowering and crossing material, or via deliberate or spontaneous mutation during cell culture. The crossing methods take a longer time to produce usable varieties. For example some characters have not been incorporated in usable varieties despite over 30 years of work. Cell culture is essential for producing new potato seed stock, so it is a routine way to introduce genetic variation and transgenesis introduces genetic variation in cell culture. Thus for transgenic potatoes, the most relevant conventional comparison is deliberate or spontaneous mutation in cell culture.

Comments by Argentina

We do not see the comparison the Expert is proposing. Spontaneous mutation in cell culture is a "spontaneous" process, not under control by the breeder. Further selection is under the breeder's control. Also, we must clarify some confusion and distinguish between the genetic variation introduced through genetic engineering vs. the one introduced via spontaneous mutation and selection: in g.e. methods, the selection in focused at the deliberately introduced character, while in conventional breeding it is addressed at the desired character, already existing or generated through mutation.

On the other hand, cell culture is not a natural process, and spontaneous mutations are not the same as those induced trough mutagenesis, which is made by the breeder. In conventional breeding, further selection of the desired individuals, is close to be under the breeder's control.

102.06. For inbreeding species, such as soybean and dry bean, variation can be introduced by hand pollinations (usually involving adapted material), or by using new collections because inbreeding lines will breed true to type. In some cases it is possible to create situations where the inbreeding plant will outcross at higher rates. In this way, it is possible to introduce variation using crossing methods. However, because the crossing methods typically are difficult, most programs do not use them very much. All programs rely on evaluating collections (sometimes an old collection in a new environment) for new, usable genetic material. For these species, transgenesis is a new and powerful method for introducing genetic variation directly into the adapted modern varieties, thereby avoiding the expense of crossing and the arbitrariness of collections. Thus, it is not clear that there is a comparable conventional method.

Comments by Argentina

See paragraph 102.5 and our comments.

102.07. For outcrossing species, such as maize and oilseed rape, there are many means to introduce genetic variation. For modern maize breeding, however, wide crosses and crossing with unadapted materials are not used in the vast majority of breeding programs in the world. Many public sector programs devote some resources to these, but they are viewed as long term breeding efforts that may produce improved populations over decadal periods. These improved populations may or may not be picked up by other breeding programs for introduction into their unimproved breeding populations. By far the most common method for introducing new genetic variation into a maize population for breeding is recombination of adapted material. However, dwarfing even this method is "backcrossing," which is a method for introducing a specific genetic trait into an adapted inbred line. Both conventional and transgenic traits are introduced into adapted inbred lines via backcrossing. However, for maize, recombination of adapted material is probably the most relevant conventional comparison to transgenesis.

Types of risks

102.08. As found by all scientific panels addressing this issue, there are no differences in the types or kinds of risks posed by biotech crops compared with their non-biotech counterparts. The kinds of risks include toxicity to humans and animals, allergenicity, nutrition, potential for producing disease, gene flow risks, non-target and biodiversity risks, and resistance risks.

Comments by Argentina

We fully agree. We would add that non-biotech crops have never been regulated so stringently as biotech crops.

Nature or magnitude of risks

102.09. Within these kinds of risk, there are new risks of biotech plants.

102.10. The EC is correct in pointing out that both biolistic and *Agrobacterium*-mediated transformation typically results in multiple transgene loci, typically with complex structure. Unlike bacterial transformation, where what is intended to be inserted typically is inserted just as intended, this is not typical using the present plant transformation methods. One of the main concerns arising from this are new open reading frames (ORFs). An ORF is a DNA sequence that could theoretically produce a protein. A new ORF could theoretically produce a new protein, which could cause or influence a new risk.

Comments by Argentina

ORFs are no a concern but a regulatory issue, i.e., an information requirement. Complete characterization of inserted sequences (PCR, Southern), will allow the detection and characterization of restriction fragments containing ORF spanning into flanking plant DNA sequences. Bioinformatics methods are then used to assess the potential risk of toxicity or allergenicity of the putative proteins resulting from the transcription and translation of these hypothetic ORFs. Northern blots will detect new transcripts. In the future, microarrays will provide also very accurate and comprehensive information. Although most of these improvements and concepts were not widely in place by 1998, when later applied to old (as well as to new) GM crops, they have shown that no risks existed that may have gone undetected by 1998. Therefore, although advanced, new methods in this area can not be called to justify a suspension of approvals. Moreover, progresses in that area have confirmed the robustness of the approaches in place by 1998.

102.11. The EC and the US is correct to identify insertional mutagenesis as another outcome of transgenesis that is new to breeding, and could cause or influence a new risk.

Comments by Argentina

Insertional mutagenesis (if leading to a viable individual), is likely to show a phenotypic effect, and thereby the generated transformants will be discarded in the selection steps. When it does not, then stability of the inserts (lack of mobility phenomena), sequencing towards the plant genome and other techniques (e.g.,, microarrays, genomics, transcriptomics) will provide the necessary information. The alleged risks fall therefore within the scope of regulatory requirements and would not constitute real risks, as the developer has means to detect them and will never be submitted for approval.

102.12. Canada is incorrect to claim that transgenesis allows more precise control than selective breeding. First both transgenic and conventional varieties undergo some level of selective breeding, so the comparison is inappropriate. More importantly, transgenesis allows control over the intended result (and in this sense, there is no dispute that transgenesis allows more precise control), but the actual result is often different.

102.13. The US, Canada and Argentina are correct to say that translocations and other genomic disruptions can occur in conventional breeding. However, these genomic disruptions are normally rare in conventional breeding. Moreover, their frequency of occurrence is much higher when genetic variation is introduced using wide crossing than the more typically used recombination of adapted materials.

Comments by Argentina

We can look at this question the other way. Translocations and other genetic disruptions in conventional breeding may lead, for instance, to the movement of transcription factors or other DNA binding and regulatory proteins to other regions in the genomes. This would lead to a major change in phenotype. In fact, yield, a common objective in conventional breeding, has been shown to be a multigenic trait, involving regulation of, e.g., circadian rithm, hormone synthesis, abiotic stress resistance factors, pathogen resistance, plant architecture, flowering time and other relevant multigenic traits. This would not result in increased risks (which anyway are not regulated) or in different, new risks, as 100 years of "modern" breeding have shown. Recent microarray experiments (to be confirmed) indicate that a larger number of genes are turned on by conventional breeding than by g.e. transformation.

102.14. Thus, the magnitude of ORFs and insertional mutagenesis introduced by transgenesis is higher than that introduced by recombination of adapted materials. It also may be higher than deliberate or spontaneous mutation in cell culture, although this is less certain.

Comments by Argentina

See comments under the previous paragraphs.

102.15. There is considerable research being conducted to understand and control the transgene insertion process, and it is likely that over the next decade technical improvements will alter these concerns.

102.16. Some of the ORFs and extraneous transgene loci can be eliminated by independent assortment for outbreeding plants, such as maize. This is less possible for inbreeding plants and clonal plants.

102.17. Nearly all risks associated with novel toxins (e.g., all Bt crops) introduced into crop plants are new risks. While there are comparable risk assessment models for assessing these risks (toxins in plants), and the risks of the particular toxins may have been investigated outside the plant, the fact that the plant is used as the delivery vector for the toxin and the precise expression patterns in the plant mean that new species are exposed in new ways. These are new risks.

Comments by Argentina

Again, this is a regulatory issue. For a developer to go ahead with a transformant, the equivalence between the expressed protein in the crop to the one isolated outside the plant should be inequivocally demonstrated. The methods to prove that were well known by 1998.

102.18. Other risks of a new nature have been identified in some of my responses to the other questions.

Comments by Argentina

See above the relevant comments.

102.19. The intended use of the product does not affect the nature of the risk, but it does affect the rusk quantitatively. This is an effect of scale. For example, risks associated with releases for processing are smaller than the same risks for the same product for planting and other use. It is not clear how much smaller, but in some cases (biodiversity risks of GMHT crops), it could be nil for processing uses while it at the same time is was substantial for cultivation uses.

Comments by Argentina

The Expert uses here a confusing wording. It is not clear the distinction between risks in processing vs. risks for planting. Usually, a crop is planted for direct use or for further processing. Moreover, we suggest that to use the expression "release for processing" in relation to biodiversity risks, may be nonsense when talking on the industrial setting in which the called "release" is made.

102.20. Risks may change quantitatively from the combination of transgenes, because it will not be possible to maintain seed supplies of all possible combinations of traits. Suppose a crop, such as cotton, was available mainly with both a GMHT gene and at Bt gene. Suppose the insect pest is a sporadic one on cotton, but a major one on maize. Farmers would have less incentive to use the Bt gene, but may have a strong desire to use the GMHT gene. This would lead to an over use of the Bt gene in cotton, increasing resistance risk both in cotton and maize.

Comments by Argentina

We disagree. Is totally speculative, close to a future-predicting statement, to say that the HT and IR traits will be always in the same variety in the future. Developers usually go the other way, and develop a wider array of different products to gain access to different markets or clients.

Question 103

103. Does the information before the Panel support the view that any of the biotech products at issue in this dispute poses a substantially greater risk as regards the direct or indirect consequences of unintentional "contamination" of other plant varieties than a comparable novel non-biotech products, such as one of the 2300 different crop varieties that have been developed using induced mutagenesis?[1] *If so, what means of risk mitigation might be envisaged?*

Risk and "contamination"

103.01. This will depend on the scale of release and the nature of the adverse effect.

Comments by Argentina

We agree.

103.01. Risk is a combination of exposure and an adverse effect. Exposure will be determined by the properties of the crop plant and the quantity of each planted (scale

[1] FAO/IAEA (Food and Agriculture Organization of the United Nations/International Atomic Energy Agency). 2001. *FAO/IAEA Mutant Varieties Database*. Available online at http://www-infocris.iaea.org/MVD/.

of release). There is little evidence to suggest that *ceteris parabis*, gene flow will be greater from a transgenic variety than a conventional one.

103.03. The definition of an adverse effect entails specification of who or what will be affected and how is this effect considered adverse. Thus an organic farmer may find contamination adverse because it removes his or her product from the organic food stream. This could be considered adverse because of economic loss and lose of quality of life or livelihood.

Comments by Argentina

We object "contamination". It should be "adventitious presence". On the other hand, it is for organic farmer to keep his product GM-free as it commands a higher price. Also, some organic farmers are shifting their position and start to believe that GM crops are not incompatible with organic farming practices and rules.

103.04. There has been little discussion and less agreement over the nature of the adverse effects of contamination. For example, there can be economic and livelihood harms associated with the perception of adverse effects. It is not clear to me that there is agreement that these kinds of perceived risks should be considered.

103.05. For the example in paragraph 103.03, the risk associated with biotech crops is substantially greater than the risk associated with any of the conventionally produced varieties. However, this is largely due to the definition of the harm.

Comments by Argentina

See comments under paragraph 103.3.

103.06. Although there is little data to support this hypothesis, I would suggest that the probability of cross-contamination rises slowly with spatial scale for very small scale production, but once it reaches a large-size threshold, the probability rises much faster. In general, "contamination" will be a spread process for which there is no advantage of the transgene in the invaded/ contaminated habitat, but there is an advantage in the habitat of origin. In these cases, spread scales with the length of the boundary between the two habitats (not the area of either) and linearly with the square of time. However, at very small spatial scales, it is likely that managers will be able to take greater care in limiting accidents, resulting in lower contamination rates.

Comments by Argentina

Here the Expert is talking on "gene flow", which he calls "contamination". Also, we can find other confusing statements by the Expert.

When talking on the "spread process" his comments are speculative. It does not distinguish between "habitats" and "agroeosystems", which is a relevant issue. The spread the Expert calls "contamination" will depend on several factors, which all must be present for the so called "spread process" (which the Expert subtly associates with invasiveness) to occur: where the seed or grain falls, which is trait of the GM crop, the frequency of the spillage and its quantity, the selective advantage of the hybrid, the existence of the relevant selection pressure in the new

habitat and finally the risk which will result from the above facts occurring simultaneously. Frequently, the answer to this kind of questions has been answered by recognized authorities with the "so what?" question. We propose this kind of exercise to be made also by the Expert.

Also, when considering the above risks, the Expert is actually referring to the efficiency of the transportation system, rather to the GM crop properties, as the first event, that is spillage, is the necessary pre-requisite for the other successive phenomena to take place. In other words, we are talking here on "management" but not of the crop but of the transportation system.

Moreover, research is in progress to introduce "gene restriction" constructs (t-GURTs), which will not allow the introduced trait to introgress into the hybrid. Although unpopular in their variety version (v-GURTs), trait-removing GURTs show interesting possibilities to avoid gene flow.

Question 105

Rationale for monitoring

105. For those biotech products at issue in this dispute for which no significantly different nature or level of risk has been identified, is there a scientific or technical rationale for monitoring the occurrence of potential adverse effects, or of unintentional effects, arising from the consumption or use of these products compared to novel non-biotech products, such as plant products produced by selective breeding, cross-breeding and induced mutagenesis? If so, would such monitoring relate to the specific genes or traits introduced into a biotech product, and how would this compare with the monitoring of induced changes in novel non-biotech products?

105.01 There are some biotech products at issue in this dispute for which one committee or another has determined that were no significant risks. I have taken issue with some of these determinations in my previous responses. For all of the products at issue in this dispute, there are some member countries that disagree with the assessment of the relevant SCP (for example) that there are no significant identified risks. This disagreement is sometimes related to different standards of acceptable risk being applied by the disagreeing parties.

Comments by Argentina

Please see our comments to paragraph 99.01.

105.02. This disagreement provides the only rationale for monitoring potential adverse effects. If all parties agreed that there were no significant identified risks, there would no need to consider monitoring for potential adverse effects.

105.03. Unanticipated effects could arise from a transgene by any of the following mechanisms: new ORFs, insertional mutagenesis, post-transcriptional or post-translational processing, other pleiotropy or epistasis, and gene-by-environment interaction. New ORFs and insertional mutagenesis can be addressed through molecular characterization of all transgene loci. Post-transcriptional or post-translational processing can be addressed to the most part by molecular and biochemical analysis. Other pleiotropy or epistasis and gene-by-environment interaction cannot be addressed without extensive planting in the field.

Comments by Argentina

Please see our comments to paragraph 99.03.

105.04. Under present technologies, transgenes can generate new ORFs and insertional mutagenesis. Post-transcriptional and post-translational processing may relate to the structure of the transgene and the nature of the gene product. Products novel to the plant probably require closer assessment. A gene product native to the recipient plant may be less subject to processing, except if it is expressed in new tissues. Novel products probably require closer assessment than native products for other pleiotropy or epistasis and gene-by-environment interaction.

105.05. Monitoring can be used to look for unanticipated effects.

105.06. A less thorough molecular and biochemical characterization of the transgene locus and transgene products provides increased potential for unanticipated effects.

105.07. Monitoring may be partially substitutable for molecular and biochemical characterization.

105.08. Monitoring may also substitute for identifying all possible effects, by covering various categories of unanticipated effects. If a thorough molecular analysis is conducted, it would seem important to ensure that monitoring for the remaining unanticipated effects is not too expensive.

Comparison with non-biotech varieties

105.09. For monitoring related to a specific potential adverse effect, this would have to relate to the specific genes/ traits in the transgenic crop. For monitoring for unanticipated effects, a more general approach is needed.

105.10. First, I should make clear that some conventional non-transgenic plants have risks, some of which may justify monitoring (and management).

Comments by Argentina

We fully agree. This is the case in HT crops bred from spontaneous mutants with this trait.

105.11. For potential adverse effects, the reasoning I have used here implies that the potential adverse effect is not a potential adverse effect from a conventional non-transgenic plant. Otherwise there would be no disagreement as I have posited in paragraph 105.01.

105.12. For unanticipated effects, there is a quantitative difference in some of the concerns related to the process of transgenesis (paragraph 102.13), and differences related to the novelty of the transgene product (paragraph 105.04). Native biotech products may or may not be different from conventional breeding for unanticipated effects stemming from other pleiotropy or epistasis and gene-by-environment interaction.

Rationale for management

106. For those biotech products at issue in this dispute for which an approval has been sought for environmental release (notifications submitted under Directives 90/220 or 2001/18), and for which no significantly different nature or level of risk has been identified, does the information before the Panel provide any scientific or technical rationale for requiring specific agricultural management practices that differ from those for novel non-biotech products, such as plant products produced by selective breeding, cross-breeding and induced mutagenesis?

106.01. There are some biotech products at issue in this dispute for which one committee or another has determined that were no significant risks. I have taken issue with some of these determinations in my previous responses. For all of the products at issue in this dispute, there are some member countries that disagree with the assessment of the relevant SCP (for example) that there are no significant identified risks. This disagreement is sometimes related to different standards of acceptable risk being applied by the disagreeing parties.

Comments by Argentina

Please see our comments to paragraph 99.01.

106.02. This disagreement provides the only rationale for risk management. If all parties agreed that there were no significant identified risks, there would no need to consider monitoring for potential adverse effects. If only some of the parties recognized the risk, then some kind of conditional risk management could be justified. For example, one condition for the management measures could be the country of use.

COMMENTS ON REPLIES TO QUESTIONS BY DR. SQUIRE

Measures affecting the approval and marketing of biotech products

Notes on ecological and environmental standards

1. These notes are intended to summarise my views on some general issues pertaining to the questions set by the panel. The notes touch on –

   - the general weakness of current criteria and standards, particular in relation to ecological topics, by which products of the type under review might be judged,
   - the importance of context and scale when assessing new global products for specific markets,
   - some recent and current research in geneflow and ecological impacts.

Criteria and standards

Information required to prove that a biotech product is safe

2. No product can be assessed as being absolutely safe. There seems to be general agreement on that. However, there is no general agreement on what should be considered as acceptably safe. As information is first gathered on a product, the likelihood that the product is safe or not may increase quite steeply, but gradually each further piece of information comes to contributes less and less to the likelihood that the product is safe. (The knowledge/safety curve assumes the form of 'diminishing returns'). Among the present arguments, however, there seems no agreement as to when there is enough information to satisfy all reasonable parties that a product is safe. This is largely because there is no benchmark or set of standards by which ecological safety can be judged.

Comments by Argentina

There seems to be a confusion here, in the way the issue is presented. We believe it would be more understandable to talk in this particular case on the "likelihood of being safe (LBS) vs. knowledge (K)" curve. The acceptable safety standard (ST) would be a line parallel to the K axis so a product will be considered safe if the curve surpasses that ST line going upwards (of course, the ST should be considerably lower than the "irreversible damage" line). Whenever new knowledge is introduced, the LBS curve may depart further from the ST in either direction (e.g., Bt maize has been shown to be safer that regular maize, with regard to mycotoxin contamination, the LBS curve will move upwards; *trans*-fatty acids have shown to behave as saturated, and therefore have similar risks as the latter, the LBS curve will move downwards).

Considering the last sentences ("Among the present arguments, ..."), and taking this argument to the extreme, as new knowledge is incorporated all the time, it seems that it will never be enough information that will possibly set the ST line at a given value; the practical consequence of this situation, is that the ST line will move either up or down and no information will satisfy all reasonable parties, as the standards themselves will move.

3. There is an important set of exceptions to the 'diminishing returns' shape of a knowledge/safety curve. If the body of knowledge reveals a new property of the biotech product, or if the external 'environment' – the context – changes, then the knowledge/safety curve could well steepen again because much additional knowledge is then required to ascertain that the product is safe in relation to the new property or context. In some instances, new properties might emerge only after a product is grown over a period of time or over a wide area of land. Several of the arguments and uncertainties in the dispute over geneflow and contamination are of this type: current knowledge seems insufficient to model and predict the extent of a potential problem.

Comments by Argentina

In the context of the above, there seems that the K axis no longer refers to "knowledge" (source: the scientific literature) but to "additional knowledge required to ascertain safety" (source: the regulatory requirements); within this interpretation, the Expert seems to refer to "long term effects"; see below on that subject; we believe that this reasoning leads to a justification of the

suspension of approvals: it will never be enough knowledge to satisfy the regulatory requirements for information, as the release of new information is a never ending process.

International Standards and Guidelines

> 4. The standards and guidelines referred to in the panel's questions are (to this reviewer) important steps towards an agreed set of standards. They differ in their stringency and required detail. Recommendations are relatively well defined and stringent in the *WTO Sanitary and Phytosanitary Measures*, in *ISPM 11*, and in the *Guideline for the Conduct of Food Safety Assessment of foods derived from recombinant-DNA plants.* The latter in particular requires great detail in characterising and describing the genetic material, plant metabolites and other constituents. Many of the 'requests for further information' by the EC or its member states are consistent with (i.e. not beyond) the level of detail indicated in that publication.

Comments by Argentina

We agree with the expert that the SPS Agreement is an acceptable source for standards.

> 5. Less detailed and prescriptive are the 'Proposed draft annex on the assessment of possible allergenicity.....' and the Annex III of the Cartagena protocol on biosafety to the Convention on Biological Diversity'. Both offer less well defined guidelines, largely because the issues (allergenicity, impact on ecosystems) are complex and, as indicated at paragraphs 2 and 7, there are no or few obvious quantitative criteria on which to base assessments. This weakness of criteria makes risk assessment very difficult in relation to these topics.

Comments by Argentina

We agree with the expert that the other quoted documents are less detailed and prescriptive than the SPS Agreement.

> 6. As many others have said, non-biotech crop plants are not subjected to anything like the same degree of testing as biotech plants. If they had been, the ecological standards might now be in place.

Comments by Argentina

The fact that non-biotech crop plants have not been subjected to anything like the same degree of testing as biotech plants, as accepted by the Expert, also implies that, since the non-biotech have been considered safe (as far as ecological standards), they should constitute an acceptable comparator to review biotech crops. Otherwise, this reasoning leads to a dead-end situation: 1) non-biotech were not subjected to testing, but generally recognized as having acceptable safety; 2) if biotech can not be compared with the suitable non-biotech crops, then…; 3) there is no way to test the biotech because there are no "standards" (the concept of "standards" implies the comparison with a specified product or set of quantitative values they should comply with), therefore…; 4) there is no way for biotech products to be tested or reviewed. This reasoning contradicts the experience over the years and in many countries, indicating that the tests set in place in these countries (as well as the regulatory requirements that go with them) were valid

indicators of safety, as no harmful incident has been reported, other that those which would have had occurred with non-biotech crops under similar conditions. In the context of the above, there seems that the K axis no longer refers to "knowledge" (source: the scientific literature) but to "additional knowledge required to ascertain safety" (source: the regulatory requirements); within this interpretation, the Expert seems to refer to "long term effects"; see below on that subject.

Criteria and comparators for ecological effects

> Many of the arguments around the ecological benefits or harm of biotech crops are carried on without reference to objective criteria. *Annex III of the Cartagena Protocol on Biosafety to the Convention of Biological Diversity* indicates only the general type of information that might be considered. Even when discussing specific products in relation to specific ecosystems, neither the biotech companies nor the responding EC bodies refer to objective criteria when stating that a product is safe or not. For instance, an assessing body might require more information on long-term ecological safety without stating what type of information is necessary to ascertain safety.

Comments by Argentina

Again appears the argument that there are no objective criteria in international reference documents. The example of the long-term ecological safety also leads to a dead-end situation as proposed above. How long is "long term?". Besides this, should it be understood that an appropriate risk analysis has no predictive value? Among other objectives, the risk analysis methods and criteria are not "present value" data (i.e., decaying in validity with time) for decision making. If not were for their predicting feature, they would be worthless. However, one must recognize that, for the risk analysis to have this predictive value, it has to consider comprehensively all the variables involved as well as *all the knowledge available at the time*.

> 7. The problems referred to in paragraph 7 arise because we lack a set of properties –physical, chemical, biological, social and economic – which define that a production system is resilient and 'healthy'. As a stop-gap, ecological studies have compared GM products with non-GM isogenic lines when making initial comparisons on a small scale, and then with another agronomic practice when making comparisons on a field scale. Even when a comparator is used (e.g. current practice), it is not yet clear that the comparator is an appropriate standard, one that will sustain crop production. Neither side in the argument over any product has indicated, even in general terms, what a suitable set of ecological standards might be.

Comments by Argentina

The expert is criticizing both sides in the argument, pointing the "lack of standards" issue.

Scale and context in assessing biodiversity and ecological impact

> 8. The arguments in paragraphs 7 and 8 are complicated further because ecological criteria will be influenced by the context – the combination of weather, soil, landscape, the agronomy and economics - of which the flora and fauna are an essential part. The companies seem to have been unaware

of, or not appreciated, the context in which biodiversity exists when presenting many of the cases in support of their products. Biodiversity is important primarily because it keeps an ecosystem intact and functioning and makes it resilient to external perturbations. The diversity-function relation - i.e. that diversity in microorganisms, plants and animals is required to maintain essential functions such as decomposition, nutrient transformations, soil formation, detoxification, regulating pests, etc. - has been largely ignored in arguments over the safety of biotech crops (and non-biotech crops).

Comments by Argentina

This consideration, which is essentially true, must be applied also to agriculture as a whole as practiced today. Therefore it applies also to non-biotech crops. However, biodiversity conservation data are an essential part in the regulatory process in our country, and has been so to the extent that we require data in general and specifically, whenever it was reasonable to expect impacts, e.g., phenotype-environment interactions, non-target effects. All approved GM crops must comply with these requirements.

9. It is necessary therefore that the biodiversity in the cropped field is taken into account as much as the biodiversity of the semi-natural habitats surrounding agriculture. Moreover –

- what is considered the valuable biodiversity in one part of the world might be very different from what is considered valuable in another part, and

- a product that is considered to have negligible impact on total biodiversity in one part of the world might have a large effect in another (and vice versa).

There are some large differences between Europe and North America in these respects. In many parts of Europe, valuable biodiversity is considered not just that of natural and semi-natural areas (mountains, extensive forests), but must include the flora and fauna within arable fields, both for the reasons in paragraph 9 above (i.e. the diversity-function relation) and because biodiversity in the form of farmland plants, insects and birds is perceived by people as being valuable.

Comments by Argentina

Again, the Expert emphasizes the fact that, in his view, there are no standards.

10. *Emergent properties at the landscape scale*. Moreover, it is scientifically unreasonable to assume that an effect (positive or negative), or the absence of effect, of a biotech product when measured at the scale of the single plant or small field plot will be the same when measured at the scale of the field, farm or landscape. Up-scaling of biological effect to the landscape was a major topic of research in the 1990s and still is. Questions include -

- Will cross-pollination frequencies at a field or feral population rise substantially as the proportional area of a donor type increases in the landscape?

- Will volunteer and feral populations become more competitive and longer persisting as they evolve through selection and the incorporation of new traits?

- To what extent will variation in local physical conditions and occasional human error seriously reduce the efficacy of mitigation protocols?

11. One of the main difficulties in predicting the effect of any type of innovation is still the uncertainty over up-scaling. What will happen as more and more of the land area is affected by the innovation? Again, progress is limited by the absence of hard criteria that define resilient or sustainable states at the scales in question.

New research since 1998 on relevant <u>ecological</u> topics

12. In part to address issues in paragraphs 8 to 12, a large body of research has been commissioned on ecological impacts and geneflow in Europe. Much of the previous research on GM plants in the early and mid-1990s compared genetic lines with and without a GM trait, either in containment, or in small areas of field. However, it was increasingly accepted during the 1990s that this was insufficient to provide knowledge of the spread, persistence and ecological effects of biotech crops at scales of the field and landscape. An important watershed was the symposium held in 1999 - *Geneflow in agriculture: relevance for transgenic crops* - which brought together researchers from Europe and North America to compare latest studies on geneflow and persistence of GM and non-GM crops in the environment. This symposium drew attention to the fact that geneflow at the landscape-scale had spatial and temporal features that were not evident at smaller scales of study

Geneflow in Agriculture: relevance for transgenic crops. (1999) Proceedings of a Symposium held at the University of Keele, 12-14 April 1999. Chaired by PJW Lutman. British Crop Protection Council, Farnham, UK.

13. Both the EC and several EC countries have commissioned multi-partner studies on geneflow and GM impacts. Results are reported for some studies; others are in progress or partly completed. They include the following projects.

- SIGMEA - Sustainable Introduction of GM crops into European Agriculture (http://sigmea.dyndns.org/) a EC-funded project which began in 2004 and has the main aims of (a) collating European information on the spread, persistence and ecological effect of the main crop species under review here and (b) developing models and decision support tools for the introduction of GM crops and their coexistence with other forms of cropping. SIGMEA has contributions from 45 partner organisations, and will be conducted over three years. Progress to date indicates that a very large part of the scientific knowledge on this topic is not yet in the public domain, because it is either recently completed and not published or is still in progress.

- ECOGEN – Soil ecological and economic evaluation of genetically modified crops (http://ecogen.dk), an EC-funded project in progress, examining the effect of Bt maize and other biotech crops on soil communities and processes at field sites in Denmark and France.

- The Farm Scale Evaluations of GMHT crops compared GMHT and conventional crop management on arable plants and invertebrates at more than 250 sites in the UK. The first findings for spring-sown crops were published in 2003 and the effects of winter oilseed rape on biodiversity will be in 2004. Studies on gene movement and persistence of the GMHT trait are in progress.

The Farm Scale Evaluations of spring-sown genetically modified crops. 2003. Philosophical Transactions of the Royal Society, Biological Sciences, 358, Theme Issue.

Comments by Argentina

We believe these studies do not apply and quoting them here is taking them out of context. Also, it seems that the quote, if carefully analyzed, does not put a blame the GM crops, but, on the contrary, indicate the weakness of the arguments against them.

See the comments below, by J.L. London in "Biosafety trials darken Outlook for transgenic crops in Europe" (Nature, 425:751, 2003); some excerpts (bold and underlines are ours):

"Britain's Farm Scale Evaluations, Publisher on 16 October, show that two genetically modified crops – spring oilseed rape and beet – are likely to have harmful impacts on farmland biodiversity. Researchers say the levels of weeds, seeds and insects in fields of transgenic crops were lower than those in plots of conventional varieties, and that this could have a knock-on effect on the birds and small animals that feed off these populations.

Although the problems are caused by the herbicide-spraying regime associated with the crops, rather than the crops themselves, the results are likely to make it politically impossible for the British government to license transgenic crops in the immediate future, many observers say. … The trials, which took place between 2000 and 2002 and are published as eight papers in the *Philosophical Transactions of the Royal Society B*, compared conventional and transgenic varieties across 200 plots.

Positive results for a third crop — maize (corn) — have been called into doubt, as the weed-killer used on most of the conventional plants is to be phased out. But the other results have not been directly challenged by most supporters of the technology. The data show that the number of seeds on the ground in the plots of transgenic oilseed rape and beet was one-third to one-sixth lower than in the conventional plots. Levels of some insects and weeds were also lower. "We could see a long-term decline in weeds that feed birds," says Les Firbank, a land-use specialist at Lancaster University, who led the trials. **Firbank and the other authors stress that it is the herbicide-spraying regime, not the genetic modification, that is the root of the problem. Herbicide-resistant crops are engineered to resist broad-spectrum weed-killers that remove almost all weeds from a field. (*)**

During the farm-scale evaluations, **farmers sprayed the crops once or twice with a broad-spectrum herbicide**. This reduces the labour required for conventional weed management, which involves repeatedly applying less powerful weed-killers. But **the more powerful herbicide used with the transgenic crops also removes more weeds**, as well as the seeds they produce. Representatives of the agriculture industry point out that this leaves open the possibility that another herbicide-spraying regime might have lessened the impact on biodiversity while still reducing farmers' labour. …"… given the intense public opposition to transgenic agriculture, the chances of commercializing herbicide-resistant crops in the short term are slim (see *Nature* **425,** 656–657; 2003)…. No decision will be made until a panel of scientific advisers has considered the results for the government. But environment minister Elliot Morley has already said that no commercial planting will take place in 2004. In the meantime, **work on better spraying regimes continues**."

(End of quote)

*** Note of this reviewer: The removal of all the weeds from a field is one characteristic of modern agriculture.**

- Botanical and rotational implications of genetically modified herbicide tolerance in winter oilseed rape and sugar beet (BRIGHT project). Several years of study at 5 sites in the UK comparing the management of various herbicide tolerant varieties.

Final report at www.hgca.com and look under *Crop research*.

- GMO Guidelines Project, under the auspices of the International Organisation for Biological Control (IOBC), funded by the Swiss Development Cooperation; the aim is to develop international biosafety testing guidelines for transgenic plants, with emphasis on ecological communities and processes in developing countries, but in principle applicable to Europe.

Hillbeck A. and Andow DA (Eds) 2004. Environmental risk assessment of genetically modified organisms. Volume 1. A case study of Bt maize in Kenya. Eds. CAB International, Wallingford, UK. Further case studies are in progress.

- Additionally, there are many other country-specific studies, notably in Germany, France, Denmark and the UK that are still in progress.

14. In summary, the understanding of environmental and ecological risk and benefit has lagged behind the understanding of most other forms of risk. There is no set of agreed criteria for defining 'ideal' arable ecosystems and this has restricted logical and rational argument on ecological impacts in most of the cases under review. Research is in progress in a range of European contexts to provide the scientific information which could be used to define the necessary criteria.

Comments by Argentina

The expert's remarks are addressed at demonstrating that new knowledge is just appearing now (or is just in progress), so one could interpret that it is advisable to suspend approvals indefinitely, waiting for any new data which could justify these suspensions. The question here is whether the Technical Commission did or did not have all the available knowledge needed for decision making.

> **Annex to Notes. Persistence and movement of genes among crops, weeds and wild relatives**
>
> The summary in Table 1 is offered as background to several of the panel's questions that refer to persistence and spread of GM plants. Several of the crops under review have the potential to shed seed and leave descendents. The following definitions are used. Volunteer(s): plants that originate from seed or vegetative material shed or left by a crop and that inhabit fields, usually emerging as a weed within a crop. Feral: plants that originate from seed or vegetative material shed or left by a crop and that exist outside fields, in waysides and the margins of agriculture. (Some authors use the term feral for plants descended from a crop whether they are found inside or outside fields.) The table shows that transmission among crops, feral/volunteer plants and wild relatives is highly species-specific. Persistence and spread are generally greatest for oilseed rape, low for beet providing the crop is prevented from flowering, very low for maize except between flowering maize crops and negligible for cotton as presently grown in EC countries.
>
> A relevant factor in all arguments over biotech oilseed rape is that the perception of oilseed rape as a weed pest in Europe has increased as more findings from research became available from the mid-1990s and through the early 2000s. Notable facts include –
>
> - It persists over 5 to 10 years at relatively high density in the soil (e.g. around 100 seeds per square metre).
> - It is very widespread in the arable seedbank, commonly among the top 10 species within fields and occurs frequently as a wayside plant.
> - Its re-seeds in subsequent crops of oilseed rape.
> - Pollen-transfer causing low-frequency cross-pollination occurs over several kilometres: insect vectors are important in moving pollen.
>
> For the sake of balance, oilseed rape should also be seen as a valuable and flexible 'break crop' in cereal rotations; it needs lower agrochemical inputs than many other crops and supports a high level of in-field biodiversity.

Table 1. The ability of the crops to disperse genetic material through feral or volunteer progeny, pollen movement and outcrossing to form hybrids in Europe. Author's summary.

	Beet	Maize	Oilseed rape	Cotton
Feral / volunteer weeds persistence in field persistence outside field	 medium medium	 zero[1] low	 high medium	 zero zero
Pollen transfer crop to crop	 low[2]	 high	 high	 low
crop to feral /volunteer	low[2]	zero	high	zero
crop to wild relative	low[2]	zero	low	zero
Crossing frequency (on arrival of pollen at flowering plants)				
crop to crop	high	high	high	low
crop to feral	high	zero[1]	high	-
crop to wild relative	high (local)	zero	low	-

[1] In most of Europe; potential for some survival in the south.
[2] Provided few or no crop plants allowed to flower.

Comments by Argentina

See comments on Table 1.

The presence of a GM construct should not markedly affect the qualities in Table 1 nor the status of oilseed rape and other crops as a weed. However, if the GM construct is accompanied by genes that make the plant more or less male-fertile than other sexually compatible plants, then the GM trait might be spread differentially. Oilseed rape can again be used as an example since it varies commonly in male fertility (i.e. the proportion of plants that produce pollen): in some crop varieties all (or nearly all) the plants are male fertile, but other varieties plants can be mixtures of male-fertile (20%) and male sterile (80%) individuals. Also, volunteers (including GM volunteers) produced from seed shed by some types of GMHT crop plant can be variously male fertile or male sterile. Generally, crops and plants that have more male sterility get more cross-pollination from other fields or plants than those that are fully fertile. It is important to know when assessing the risk of spread and persistence whether the variety and its offspring are fully, partly or not male fertile.

Replies to Questions

3. *Effect of Bt maize on non-target organisms*

Bt crops are grown widely in some regions of the world. They are used to target crop-specific pests, with a consequent, intended benefit that less chemical insecticide is used. They have a potential disadvantage, in that they might harm other organisms in the ecosystem. Among these are the predators and parasitoids that feed on the pests, and organisms not normally reached by chemical insecticides. Important examples of

the latter are soil fauna that might be exposed to the toxin if it occurs in or moves out of roots, and detritus feeders and other decomposers that encounter the toxin in dead or dying plant matter. There are therefore arguable advantages and disadvantages in the use of the product. The emerging results from North America show that pesticides have been reduced, but not in all instances – context is important. Much less information on non-target organisms has come from existing Bt maize-growing areas.

Potential for ecosystem effects. Assessments of potential ecological harm or benefit in areas such as Europe have so far relied largely on findings from research in the laboratory or in contained systems in which the Bt plant and organisms tested have no, or restricted, contact with the outside world. Three of the exhibits referred to in Q.3 (EC-150, -151 and -152) are among this body of research. The potential for ecological effects is indicated by these and other studies, and some of them have shown that the toxin might well affect soil organisms. Exhibit EC-149 is a review of laboratory and field data up to 1999, and concludes that, because of the small area and short duration of the experiments, only limited inferences can be made about large scale or long term ecological effects. Since then, there have been few field-scale experiments on Bt crops in Europe comparable to those in the present ECOGEN project, from which results should be available in 2005.

Comments by Argentina

"Potential for ecological effects", "the toxin might well affect soil microorganisms", "limited inferences", and finally the reference to studies from "which results should be available in 2005", as listed, are all statements more close to opinions than to a report of scientific facts. What scientific facts have already established at all, molecular, anatomical and physiological levels, is that Bt entomotoxins are highly specific to insect Orders. Also, because of their mechanism of action (which starts by binding to specific receptors in susceptible insects' mid-gut), Bt entomotoxins are very unlikely to have harmful effects on other organisms. This lack of harmful effects has been widely reported in available scientific literature. Also, it will help to point out that Bt entomotoxins, as well as the bacteria producing them, are in the fields for over 60 years now, in the form of sprayable, not purified insecticide formulations. The bacteria producing the toxins, on the other hand, are present in soils all over the world.

Scaling, timescales and dilution. The published studies do not demonstrate one way or the other what would happen if Bt maize were grown widely in Europe. There is no general consensus among scientists of what would happen when a Bt crop is introduced into any new region. It is argued by some that there could be a range of unforeseen, negative effects.

Comments by Argentina

Expressions like "do not demonstrate one way or the other", "There is no general consensus", "It is argued … there could be a range of unforeseen, negative effects", are opinions rather than information based on available hard data.

In support of this view, the authors of Exhibit EC-149 write:

Although such regulatory trials provide valuable initial toxicity information, basing ecological assessments solely on bi-trophic feeding trials that provide the insecticidal protein in a highly processed form directly to the non-target organism is not

sufficient. Ecologically important interactions between plants and herbivores and natural enemies/non-target organisms …. may be missed.

Comments by Argentina

The above is another example of statements of the "information is not sufficient" kind, which is followed by a statement on "important" data missing, often expressed by this Expert. Mention should also be made, to be fair, on the *lack of data supporting that negative effects are actually observed,* which he is not considering, in spite of all reports available in existing literature. Moreover, the expression "highly processed" used when referring to the insecticidal protein, could be interpreted in many ways (some of them deceptive). "Highly processed" could mean: 1) different from the relevant protein as expressed in the plant; 2) produced by genetic engineered microorganisms; 3) obtained by processing the plant tissue; 4) obtained by expressing the active protein sequence; 5) obtained by converting *in vitro* the pro-toxin into the active toxin; 6) using only the active, truncated protein. This ambiguity is not relevant with regards to the statement quoted by the Expert, but it reveals lack of precision and descriptive value.

The implication here is that exposure to the Bt plant over wider spatial zones, and season after season, might cause negative ecological effects that are not observed in short-term feeding trials in the laboratory or small-plot trials in the field.

Comments by Argentina

See above.

Conversely, it is argued that 'feeding' trials might create such artificial conditions, removing choice of food, etc. that they greatly overestimate effects that would occur in an ecosystem. An example of such a 'dilution' of effect is that of the monarch butterfly in North America, for which damaging effects of Bt maize pollen, found in the laboratory, were subsequently shown unlikely to occur in the ecosystem. There were several reasons for this: much of the insect's food plant occurred outside Bt maize fields, the seasonal timing of the insect and the release of pollen only partly overlapped and the actual exposure of the insect to the toxin was lower in maize fields than in the laboratory. A lay article *Butterflies and Bt corn: allowing science to guide decisions*, published by several US universities and the USDA provides a summary of the study; scientific papers are assembled in the journal *Proc. Natl. Acad. Sci.* USA, vol. 98, 2001. The results of many other feeding experiments would similarly be 'diluted' (this reviewer believes) when examined in the context of the ecosystem.

Comments by Argentina

We fully agree with the above paragraph by the Expert.

The general absence of ecological standards and comparators. As discussed in the introductory notes, and in relation to herbicide-tolerance (Q.6), a context and comparator are vital to any assessment, and as in the case of herbicide-tolerance, they have rarely been taken fully into account when assessing Bt crops. Assessments purporting to show harm, for instance, should compare the effects of the Bt crop with an existing practice or standard, such as current pesticide management, or options

using application of Bt preparations (for which there appears little ecological information). As for assessment of GMHT crops, there is no definition or set of criteria for an acceptable, resilient and sustainable ecosystem. It should be feasible for scientists to define such criteria, which would be generic but with location-specific elements. A recent case study of Bt maize in Kenya shows what can be done quickly by combining global and location-specific knowledge (Hilbeck A & Andow DA, eds. 2004. Environmental risk assessment of genetically modified organisms. Vol 1, A case study of Bt maize in Kenya. CABI Publishing).

Comments by Argentina

Again, the Expert calls on the lack of both, comparators and criteria for establishing acceptable ecological safety information. Again, he ignores the body of evidence and practical information available. Also he is suggesting that "ecosystem" is the place in which agriculture is practiced, rather than the more precise concept of "agro-ecosystem", that is, a highly perturbed, man-managed ecosystem. Also, the Expert refers to the lack of "comparators", but do not mention "indicators", whose reliability is often a strong indication of potential for harmful effects.

Mitigation. It much more easy to confine maize within cropped fields than it is oilseed rape or beet, for example, so the ecological risks are mainly to do with the in-field food web and with any wide ranging organisms that visit the field (i.e. there are no risks in much of Europe through ferals and volunteers). To plan a mitigation strategy needs understanding of the existing state of the food web. In the UK Farm Scale Evaluations (see *Notes*), which used >60 fields of GMHT, not Bt, maize, the maize fields supported a small set of organisms compared to the organisms in oilseed rape and beet. This was so because the persistent herbicides then used on maize severely reduced the arable plants available for the insects to eat.

Comments by Argentina

Clearly, as the Expert points out, the negative effect was due to the persistent herbicides used, reducing the arable plants for insects to eat, and not to the biotech nature of the crop.

Moreover, only a few species in the above-ground food web were found on the maize itself. If maize is adopted over wide areas of a country where it had not been grown, that itself would affect biodiversity whether or not it was Bt maize.

Comments by Argentina

We fully agree with this consideration by the Expert, who, in this way, is indicating that agricultural practices turn an "ecosystem" (biodiversity saved) into an "agro-ecosystem" (biodiversity only partially conserved), no matter which, biotech or non-biotech crop is adopted.

Any additional effect of Bt should be seen in relation to the effect caused by the introduction of maize as a crop species. However, if Bt maize was found to harm the in-field biodiversity, it should be feasible to reverse the effect by growing different crops in a rotation. Perhaps the main uncertainty is the effect of Bt maize on the soil food web. As indicated, the ECOGEN project should inform on this. Effects in the soil would be harder to monitor because it is very difficult to assess soil biodiversity, particularly among bacteria and fungi. Nevertheless, any adverse effects should be mitigatable through a rotation.

Comments by Argentina

On the expression "if Bt maize was found to harm the in-field biodiversity it should be feasible to reverse the effect by growing different crops in a rotation", we observe the following: a) is a conditional statement; b) whatever crop is sowed which cause adverse effects on resources (minerals depletion, changes in soil texture and structure, pathogens concentration, viability of weeds, among others), it is a regular agronomic practice to rotate crops to alleviate the problems; i.e., it is the same for biotech or non-biotech crops.

Q.3 addresses a complex topic. the following is offered in summary.

- The evidence is insufficient to confirm whether widespread cultivation of Bt crops in Europe would affect non-target organisms.

- The weight of evidence from contained experiments and small-plot field experiments generally favours the view that little immediate toxic effect of Bt maize on the food web will occur in the field; but the evidence admits the possibility of chronic effects following long-term exposure to Bt maize.

- The question could only be answered by long-term study of the effects of Bt maize and a comparator on the complex interactions among non-target organisms; it would be difficult to see how that would be done without intensely monitored, field-scale experimental plantings in Europe.

- Criteria for resilient food webs would need to be proposed and agreed as a standard for any new research: without such criteria, progress is impossible.

Comments by Argentina

The comments on the topics referred to in the above summary, are addressed in each case. Again, the impossibility of progress comes as an argument. Extrapolated, this argument would make the progress of Science impossible.

4. *Emergence of Bt resistance under field conditions*

The emergence of resistance by pest insects to pesticides differs widely from context to context depending on factors such as the exposure to and strength of the toxin, the movement of insect populations from areas where the pesticide is not applied, and the genetics and mating system of the insect. Resistance to Bt crops has occurred and is influenced by the 'dose' of toxin delivered to the pest and the genetic nature of the pest, among other factors. Because of long-standing scientific interest in pest resistance generally, knowledge has been imported from that body of work to construct models for the evolution and mitigation of Bt resistance. The processes involved in Bt resistance and its management are generally appreciated by scientists, and mitigation strategies that have a strong scientific basis have been considered. By the late 1990s, mathematical models of the population dynamics of resistant and susceptible biotypes were being used to estimate the number of years for which the GM trait would remain effective in the face of genetic adaptation by the pest. The point is that sound scientific knowledge has been applied to this problem for several years.

A strategy for mitigation needs protocols for both pre-emptive management, testing for resistance and managing it if found. The strategies might involve providing refuges in or near the crop where resistant individuals do not have an advantage over resistant ones, periodically controlling the pest by other means and growing different 'types' of Bt maize, or Bt and non-Bt maize, either together or in sequence. Mitigation will be much easier to implement where the existing ethos is sympathetic to integrated pest management based on genetic and ecological principles. A useful, recent summary of the topic, much of it in layman's terms, directed at Bt maize in Kenya but based on generic arguments, is given by:

> Fitt GP et al., (2004). Resistance risks and management associated with Bt maize in Kenya. In Hilbeck A & Andow DA, eds. 2004. Environmental risk assessment of genetically modified organisms. Vol 1, A case study of Bt maize in Kenya. CABI Publishing.

5. *Toxicity to animals of Bt maize compared to conventional maize*

(This response does not address the part of this question relating to humans. Toxicity was considered as part of the Response to Q.3 and some of the argument here is repeated.) Assessing a product's toxicity to ecological processes is usually more complicated than assessing the toxicity of, for example, a feedstuff for a domestic or farm animal. The domestic or farm animal may have the food under test as its sole or main diet in reality, whereas non-target organisms generally have a wider choice of food throughout the habitat. Also, the expression of a toxin in a plant and its effect on animals eating the plant are influenced by local growing conditions, the weather, the behaviour or the local animals, etc., all of which differ between sites. Therefore making inferences about toxicity to animals in one part of the world (e.g. a maize field in a European country) from information in a constrained experiment, or field experience in another part of the world, should be done with great caution. The contention that nothing adverse has occurred when growing Bt maize in, say, North America, should not be taken as definitive evidence by itself that nothing will occur in Europe, where the organisms and their interactions are different.

Feeding experiments in which organisms are exposed to live or dead Bt plant matter, and have no other choice of food, should be viewed as providing information only on the possibility that the Bt plant might be toxic to the animals in the field. Many of the studies in contained experimental systems are of this type. Some do and others do not indicate harm occurred, but none should by themselves be taken to indicate that harm will necessarily occur in the field. (Several major crop species would fail toxicity tests of this type.) Many of the plot-scale experiments examined in EC-149 were criticised by the authors of that review for a range of reasons, <u>but taken as a whole, experiments at the scale of small field plots and one season's exposure indicate no acute toxicity to animals other than the pest.</u>

<u>Comments by Argentina</u>

It would be convenient to remember also what is already known about the mode of action of the Bt entomotoxins: their require specific receptors in the susceptible insects, and these receptors are not found in other animals. It would also be useful, that the Expert quote the experiments "that (do) indicate harm occurred". Also, see the underlined (by this reviewer) text.

Evidence, either way, of harm to animals of growing Bt crops in the field in Europe is therefore inconclusive at present. The question could be approached by a range of experimental studies over longer periods, but the results would need to be compared against the effects of other crop species on the animals, and against independent criteria defining a normal or healthy state for the animals in question (as for Q.3).

Comments by Argentina

The Experts calls on the "inconclusiveness" of the evidence, pointing out the relevance of local studies, with which we agree with the following exception: the value of evidence in other, non European areas is not considered. We agree that local effects could be different in some respects (e.g., animals choice of feed), but the entomotoxin would be the same, and therefore will provide a strong indication on toxicity to animals. These data are not considered as valuable. Also, the Experts calls for studies over longer periods; we already pointed out that risk analysis value is its predictive ability.

6. *Persistence of HT plants in the environment*

The background to this question is that several of the crops have become widespread feral plants or weeds (see Notes, Annex). Oilseed rape has been grown in Europe for centuries, but has become a weed in many parts of Europe following a great increase in its cropped area since the 1970s. It is now a regular and persistent member of the arable and wayside seedbank (buried viable seeds). Oilseed rape is not considered a problem on waysides and is ousted by perennial vegetation such as grass. Within fields, it is treated as part of the broadleaf weed flora. It also contributes to yield of the next oilseed rape crop, but has generally not been considered a problem in this respect, since the quality of oil has generally been similar in the volunteers and crop plants. Similarly weed beet, arising from seeding crop beet, is common in beet-growing areas and brings similar but lesser problems.

Are HT plants a potential pest? Oilseed rape and beet are both crops and pests, as are many other crop plants (pests as defined in ISPM-11, page 6). The volunteers or ferals arising from HT crops would be no greater pests than those arising from non-HT crops, unless the specific herbicide was used to favour them as pests, or their presence in the field or in the yield itself had greater significance than the presence of non-HT. Since agriculture began, crops and weeds of the same species have existed side by side and exchanges genes – but this does not mean that volunteer/feral weeds are not pests.

More serious problems to do with their persistence as pests will arise if labelling or marketing 'rules' specified that a non-biotech crop had to be of a high degree of purity, i.e. to contain less than, say, 0.9% of GM in the yield.

6a. In the absence of use of the specific herbicide, HT plants would have the same potential as non-HT, as indicated in 6 above. Species would differ as in Table 1. Establishment and spread depends on local conditions in ways that are not clear. For example, feral wayside populations of oilseed rape differ greatly in number in areas studied in France and the UK. Also, wild, weedy relatives differ in their presence and number in different parts of Europe, as do hybridisation rates between crops and between crops and wild relatives. But the essential point is that - in the absence of

the specific herbicide to which the plants are tolerant – plants having HT and non-HT traits should act similarly.

6b. Suppose that HT plants were growing in mixed vegetation with non-HT plants of the same and other species, then applying the herbicide would favour the HT plants, lead to greater seed set on HT plants and their increase in the seedbank. This would happen wherever the plants were growing and whether the HT trait was in volunteer/feral plants of had been transferred to wild relatives. Whether such differences occurred in practice would then depend on the how widely the specific herbicides were used (which itself would vary between countries and crops).

6c. In the absence of the specific herbicide, the potential for establishment and spread should be similar for biotech plants tolerant to the wide-spectrum herbicides glufosinate ammonium and glyphosate. The genes conferring tolerance to either should not enable the plants to be better at, say, persisting in the soil. Relative persistence between the two GMHT types would differ if one or both of the herbicides was used. As indicated, this will be highly specific to the agronomy of a farm or region. For instance, in the UK, glyphosate has risen in the last few years to be the second (or maybe first) most widely applied herbicide in arable fields, while glufosinate ammonium is used little in fields or waysides. If GMHT glyphosate tolerant plants were present in fields, then they would be advantaged at this specific time and area, where glufosinate ammonium tolerant plants would not.

6d. Risk management options should be similar to those recommended for non-biotech varieties (oilseed rape and beet), but would need to be more stringently applied if cropping was to ensure the proportion of GM in non-GM remained below a threshold. Establishment can be reduced by –

- Reducing or preventing seed loss to the soil, e.g. by harvesting oilseed rape before too many pods split (not always possible), uprooting flowering beet plants.

- Not cultivating soil after harvest, leaving seeds to germinate on soil and then killing them by cultivation or herbicide spray.

- As part of normal broadleaf weed control, ensure they do not flower and seed in later crops of other species.

Spread can be reduced by –

- Clearing seed from combine harvesters and other machinery between crops.

- Transporting seed from field to market in sealed containers or vehicles.

- Cutting or spraying roadsides that support large populations of feral oilseed rape, but these practices will impinge on the semi-natural flora.

- Using a pollen barrier to reduce field-to-field geneflow (oilseed rape and maize), such as a strip of flowering crop 50 to 100 m wide between the donor and recipient crops and which is not harvested as part of the recipient crop.

The main difficulty in preventing establishment and spread is with oilseed rape, specifically in that it will enter the soil and become dormant even if soil is not cultivated after harvest, it will flower and seed, usually unseen, in a later crop of oilseed rape and it is impractical to remove all seed from farm machinery. Lesser problems occur with weed beet.

6e. *Post-market monitoring*

ISPM 11 does not give great detail on monitoring. The type of monitoring in this instance would differ depending on purpose: for example, monitoring the effect of a HT cropping on biodiversity or ecosystem functioning would require a different set of measurements from monitoring the presence or abundance of a HT trait. What is clear from existing data and work in progress is that monitoring of this type is far from simple and needs much time and effort, especially if the aim to measure low frequencies (e.g. 1%, 0.1%) or small effects (e.g. 1.5-fold effects on populations or ecological processes). Recently introduced populations are highly aggregated or clumped and this increases the number of samples and area over which samples have to be taken. At present, there are no reliable and accepted monitoring schemes for the presence or impact of biotech-derived plants: research is in progress to develop such schemes (see *Notes, paragraph 14*), but it is not even certain that it would be feasible or practicable to monitor low frequency occurrences or ecological effects routinely in the field.

Comments by Argentina

Again the Expert calls attention about research in progress or just published. On this issue, see above. Although the data presented refers to oilseed rape, it is often referred to as "biotech-derived plants" in general. This generalization does not consider the "case by case" criteria, which is at the very foundation of the risk analysis. The purpose of this text seems to stress again that there are not enough data for decision making. In the following paragraphs, it is difficult to distinguish to which specific HT crop the Expert is referring to.

7. *Adverse effects on flora and fauna*

The difficulties of argument in this topic revolve around what is classed as an adverse effect (*Notes, paragraphs 7-10*). There are no objective criteria for what is an ideal state and what therefore might be judged an adverse effect against that state. At best, HT cropping has been compared against an existing cropping system. Certainly in Europe, the important and relevant flora and fauna should include those within the managed areas of fields.

The Farm Scale Evaluations (FSE) in the UK (*Notes, paragraph 14*) detected small, but important shifts caused by using GMHT rather than the conventional management, and illustrate issues of context. The difference in weed management rather than the GM or conventional crop plants per se was the effective agent. The direction of effect differed depending on the severity of the conventional management. In maize, where conventional management uses persistent, highly toxic herbicides, GMHT increased the flora and fauna; in spring oilseed rape and beet, where current practice was less effective against arable plants, it had the opposite effect, reducing the flora and fauna. The crucial point about the FSE – and one that has been missed or misrepresented by many international commentators – is that the

effects on the arable flora or weeds (though small by international standards) were important in the context of the UK's arable scene in the early 21st century. The flora and fauna of arable fields were important in the national biodiversity as perceived by many people; these flora and fauna had already been severely depleted by intense agriculture, so further depletion was unnecessary and unacceptable.

Comments by Argentina

The underlined (by us) phrase above speaks for itself.

In principle, there should be no difference between the effects of GMHT cropping and non-biotech HT cropping, though this has not been compared on a suitable scale. The BRIGHT project (*Notes, paragraph 14*) made some comparisons of GMHT and non-GM HT crops.

A general knowledge of the macro- and micro-fauna in the soil suggests they will be much less sensitive to GMHT cropping than will the above-ground flora and fauna. The FSE and some other work included macrofauna caught on the soil surface, but no large-scale studies of herbicide tolerance have included soil micro-and macro-fauna. (ECOGEN will provide information on soil communities at three field sites for Bt maize.) All evidence from small-scale work in field plots and containers points to the herbicides glyphosate or glufosinate ammonium being much less directly toxic to soil fauna than other agrochemicals and the GMHT plants themselves having no effect on soil organisms different from that of non-GM plants.

Comments by Argentina

This underlined (by us) phrase above speaks for itself.

9. *Molecular characterisation informing risk assessment*

The *Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA plants* indicate full characterisation of the genetic change should be provided. Such information may be essential for assessing some aspects of the product but is not always necessary when considering spread or persistence of the biotech product or its effect on the ecosystem.

Spread and persistence. In many of the studies in Europe (ongoing and not yet published), the purposes of the study can be achieved by detection based on an outward or phenotypic trait (i.e. whether a plant dies if sprayed with a specific herbicide), a protein test (e.g. an antibody based test for the protein produced by the genes conferring tolerance to glyphosate or glufosinate ammonium) or a DNA test for the gene (e.g. the bar gene). None of these tests is absolutely accurate since they are affected by the condition of the plant tissue. If sampling of plant material is done in real agricultural fields, it is impossible to ensure the plant tissue is in the right condition – often it is not. Consequently, false-positives and false-negatives occur. Moreover, if the GM trait is thought to be at low frequency, e.g. 0.5% or lower, and the individuals possessing it are unevenly distributed or clumped in the field, then very large numbers of individuals have to be sampled to estimate presence or % frequency with a high degree of certainty.

Ecological impact. For some aspects of comparing GM and non-GM plants, detailed knowledge of the molecular construct is not necessary. For instance, if comparing the ecological effects of GMHT or Bt plants, the studies could be done equally well without detailed molecular knowledge of the construct.

More information would be necessary if research was following the volunteers or pollen-vectored genes originating from the GM crop: at least, knowledge of the genetic factors determining the proportions of male sterility and male fertility would be important, but even then the detailed molecular knowledge of the construct would not be essential. However, if many GM varieties had been grown in an agricultural area, and if it were important to ascertain the origin of an individual plant or population, then more detailed molecular characterisation would be required.

More generally it can be argued, given the scientific and public interest in GM issues, that it is reasonable for an assessing body to request full characterisation (according to standards in the *Guideline for the conduct…)* of a GM construct (a) to enable its officers to confirm whether impurities existed in the original seed if they were found or suspected (e.g. the presence in the breeding line of GM traits such as antibiotic resistance) and (b) to trace the persistence or spread of the GM trait if this was necessary in later years.

While much of the text above under Responses 9 is generally appreciated by workers in the field, many of the scientific findings pertaining to the spread and persistence of GM traits in Europe are not yet in the public domain (*Notes, paragraph 14).*

ISSUE 1

Bayer oilseed rape Falcon (GS40/90)

11. If long term events or emergent properties are envisaged as a result of introducing a GM plant and practice (and this seems to be the case for oilseed rape in Europe), then it is legitimate to expect a rigorous post-event monitoring protocol to be integral to a pre-release risk assessment. Risk management options for this GMHT product are similar to the generic ones included in *Responses 6d-e*. When they are applied, the practices appear to work in keeping weedy oilseed rape to manageable levels, but the general level and type of management have not prevented it from becoming established throughout Europe as a weed.

13. In that oilseed rape as a volunteer or feral plant is a pest as defined in ISPM 11, e.g. a weed competing with a crop for resources, and having other potential influences, the Bayer oilseed rape (Falcon GS40/90) has the potential to be a pest, since it would leave volunteer and feral descendents. Whether it would be more or less a pest than other forms of oilseed rape depends on whether it would be sprayed as a volunteer or feral with the herbicide glufosinate ammonium (see *Responses 6b-c*). That would be context-specific, e.g. whether farmers in the region or country used this specific herbicide widely or repeatedly in fields.

Bayer hybrid oilseed rape (MS8/RF3)

14. The basic answer is similar to that given for Q.13. A few statements need comment, however. The EC SCP (EC-63/At.54, section 6.3.1) gave the opinion that

"rape is a poor competitor" and "not regarded as an environmentally-hazardous colonising species", and while the latter is still probably acceptable in semi-natural habitats, the continued widespread persistence of oilseed rape in and around arable fields, both from original seed and from re-seeding, points to its competitive ability being greater than "poor" but similar to many second-order weeds (i.e. weeds that are less important than the most aggressive few species but are still important). The proposed post-marketing monitoring plans (EC-63 At.060) are generally consistent with the principles in ISPM 11, but do not give specific detail on, say, how a field is to be sampled to estimate % GM presence among volunteers with a stated degree of certainty (see *Responses 6e and 9*).

19. The updated environmental risk assessment is comprehensive on topics for which data are available. The further information on ecological effects requested by the lead CA was clearly not available, and could only be in existence if there had been either large scale experimental measurements on the habitats typical of where the crop would be grown commercially or specially commissioned experiments on trial crops, as in the UK's Farm Scale Evaluations. Since cropping with this variety and its herbicide has potentially new effects on the arable flora (i.e. different from those of other oilseed rape varieties with other herbicides), which may be severely depleted in any case, it is legitimate to ask what such effects might be. However, the general matter of the need for a comparator is relevant here (*Notes, paragraphs 7-10*). Surely it is incumbent on both sides in the argument to proffer their standard or comparator against which the new technology should be judged.

20. The question is whether the words "impracticable, hardly workable and hard to control" used by the Belgian Biosafety Advisory Council are justified on the basis of the report by its Group of Experts. The Group of Experts does not use this wording as such but makes cautionary remarks that the guidelines are not sufficient as they stand and should be extended and that there could be practical problems in successfully implementing them. Examples include –

- "each farmer growing *B. napus*, *B. rapa* and *B. juncea*, in the neighbourhood of the transgenic oilseed rape field is aware of the agricultural guidelines": this requires that non-GM farmers need to make themselves aware of GM issues, and that all farmers will be cooperative neighbours.

- "every operator should be informed on the appropriate management measures to be taken in the case of accidental seed spillage …etc.": this in reality is probably unworkable, since many spillage events will go unnoticed, and there are such a large number of feral populations arising from such events.

- "seed should be swept or shovelled into sealed containers" and "(spillage sites) should be recorded and monitored in subsequent years": these are likely to be impracticable in commercial agricultural areas; the measures would place an intolerable burden on whoever was considered responsible if that could be decided (the grower, the transported, the buyer, the roads authority?).

Several other of the Group of Experts' recommendations are workable, but the above three examples would appear to justify the Belgian Safety Advisory Council's choice of words.

Monsanto *Roundup ready cotton (RRC 1445)*

24. The EC's SCP opinion is generally positive about the application, whereas the EC member states raise several objections. The issue of antibiotic resistance was considered in the SCP's opinion (EC-66/At.53) and found not to pose risk, but there is now widespread perception that antibiotic resistance should not be introduced through GMHT products.

Comments by Argentina

Horizontal gene transfer (from GM crop to bacteria) is a very unlikely phenomenon, and this has been demonstrated and published in scientific journals. (see, e.g., Schlüter, K. et al, "Horizontal" Gene Transfer from a Transgenic Potato Line to a Bacterial Pathogen (*Erwinia chrysanthemi)*, Occurs -if at all- at Extremely Low Frequency; *Biotechnology*, 13: 1094-1098, 1995)

The basis of objection by some member states is that general effects of HT cropping on farmland habitats are uncertain, and this applies whatever the species or the land area it occupies. However, the context for this biotech product in cotton is very different from the context of those products which are varieties of oilseed rape. Cotton occupies a very small area in Europe and does not present potential problems of the type associated with oilseed rape or even maize or beet (Table 1).

This notwithstanding, and as in other instances, unless criteria can be given, from both the proposer and objector as to what is a desirable or acceptable comparator, then progress with the discussion is impossible, as it became in this instance.

Comments by Argentina

We observe the following: a) … cotton is very different from … oilseed rape; b) Cotton occupies a very small area in Europe and, c) … does not present potential problems of the type associated with other crops. The fact that a crop (in this case, cotton) does not present potential problems of the type associated with other crops, should led to a statement on the safety of the first crop (whatever this statement should be in the opinion of the Expert). We do not find this, and are only left with the impression that cotton is different, but with no reference to its safety or to how the relevant safety difference would justify a suspension of approval.

Additionally, we want to refer to the "no acceptable standards" argument, which was discussed above. It goes beyond, suggesting that, being this the case, progress with the discussion is impossible. We do not believe that the question here is an "abstract" one, and consider that discussion is possible and amenable to a final judgement.

(a) There appeared to be no monitoring *plan* in the original proposal, and in the 2003 document, the relevant section indicated that little specific monitoring was necessary because of the low risk. Monitoring the effects on habitat would be feasible but suitable criteria on which to base monitoring have not been proposed or agreed by either side.

Monsanto *Roundup Ready Corn (NK603)*

37-39. The weakness of suitable criteria is again at issue here (*Notes, paragraphs 2, 7, 8*). Documentation from the company is least on environmental matters, partly because of changed context (what might be an acceptable impact in one part of the world is considered unacceptable in another), while the counter-arguments take no step towards indicating what standards might be applied. On the more specific question of whether GMHT maize persists (accidental germination), it is justified to query the original statement since emergence has been recorded in some southern European areas**.**

Comments by Argentina

It is not clear whether the weakness of criteria are from the proposal or from the reviewers. The approval process requires environment tests in several different environments (worldwide and local), which to date have shown to render very strong data. About the persistence issue, we can say that GM crops are not different from non-GM in this respect, and therefore it should not be mentioned as an argument in the context of this document.

41. Pioneer/Dupont *High oleic soybean*

(difficulty in viewing some of the relevant files)

Pioneer LibertyLink and Bt (T25 x MON810) corn (stack)

57. Similar difficulties are evident in the exchanges to those in 37-39 and elsewhere! Even so, the requests by the Netherlands are arguably consistent with the type of information indicated in the *Codex Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA plants*.

ISSUE 2

Opinion on the value of the Guidelines and Protocols in providing criteria against which to assess biotech crops was given earlier (*Notes, paragraphs 4, 5, 7*). It was suggested that the types of information and criteria given for molecular characterisation and food safety were stronger and more definite than those given for environmental and ecological factors.

Safeguard measure of France: Oilseed rape MS1 x RF1.

59. The view expressed by France was that insufficient information was available to provide clear conclusions on several aspects of cross-pollination and persistence of GMHT oilseed rape. The EC Scientific Committee on Plants had considered that the risks arising from outcrossing to volunteer, feral and wild relatives were definite, but small because any progeny could be controlled later in the rotation. France appeared to take a stronger line, indicating the risks were larger or more uncertain. The EC SPC and the information submitted by France therefore agreed on the nature of this potential problem, but differed on its importance or extent. In November 1998 and July 2001, there was knowledge about the mechanisms involved in cross-pollination and persistence, but one of France's main arguments was based on the up-scaling effect - the uncertainty of what might occur if GMHT crops were grown widely in the

country (*Notes, paragraphs 11, 12*). There was insufficient knowledge at that time to be able to predict accurately, for a country such as France, what the rates of spread and cross pollination would be (GM to non-GM) if a large part of the rapeseed areas were GM.

(a) The documentation is also correct when it tates that relevant new experimental information was being placed before the public (see example references below). The new information was providing greater knowledge of cross-pollination in oilseed rape, particularly over distances of several kilometres. This new information would not have provided qualitatively different knowledge (it was already known that oilseed rape could cross-pollinate at distance) but would provide better quantitative estimates of the pollination frequencies and the subsequent survival of GM hybrids among volunteer populations. Even by the end of 2003, there was still uncertainty as to what the field-to-field cross pollination might be if GMHT crops came to be grown in many fields throughout a landscape in Europe. Data in Europe was confined to knowledge of crossing from a relatively small source (one or a few fields of donor oilseed rape) to a large potential sink (many fields on recipient oilseed rape). Work is still in progress, not least as one of the main aims of the SIGMEA project (*Notes, paragraph 14*), to estimate spread and cross-pollination on a regional scale in Europe.

Rieger MA, Lamond M, Preston C, Powles SB, Roush R. 2002. Pollen-mediated movement of herbicide resistance between commercial canola fields. Science 296, 2386-2388.

Ramsay G, Thompson CE, Squire GR. 2003. Quantifying landscape-scale geneflow in oilseed rape. Final report on Project RG 0216, 48 pp. Defra: London.

60. As indicated earlier, the requirements in the international guidelines are quite stringent. It could be argued that France's position was compatible with the tone of the SPS Agreement, Annex A, paragraph 4 (including economic as well as biological consequences) and compatible also with ISPM-11 Annex 3 on 'Determining the potential for a LMO to be a pest'.

61. The risk management options were and are similar to those indicated generally for oilseed rape at *Responses 6d and 101*. The risk of spread and cross-pollination can be reduced by such measures but not eliminated.

62. *Topas 19/2 and the Farm scale evaluations (FSE).*

The FSE compared the effects of GMHT and conventional weed management. Its results should have no bearing on the risk associated with the importation of seeds for processing. Even if these seeds were spilled and became part of the wayside feral population or volunteer population in a field, they would have no effect unless the management of the field changed away from current management in a way comparable to the differences between GMHT and conventional cropping in the FSE.

ISSUE 3

96. *Significant change in understanding of biotech products etc. since 1998?*

From this reviewer's perspective, most of the underlying molecular and biochemical knowledge of the subject has not changed substantially during this period.

Comments by Argentina

This answer contradicts some of the above mentioned by the expert. See the "long term effects" problem in decision making. We agree with this new view of the reviewer.

There is still uncertainty over unintended side-effects occurring in biotech products, and the continued stability of phenotype in biotech plants or continued expression of their genes outwith the crop itself (i.e. in volunteers and feral plants).

Comments by Argentina

It can be said that in almost 10 years of planting GM crops around the world, no scientific evidence has been published in a peer-review journal that will provide evidence of unintended side-effects (*), lack of stability of phenotype or detectable expression of their sequences introduced through genetic engineering in other organisms outside the crop itself, in the absence of sexual compatibility, all these phenomena in a way different from than with the no-GM species.

(*) Note of this reviewer: the expression "side-effects" is reminiscent of pharmaceutical drugs. In the case of these, they are known and deemed to be tolerated when the benefits outweigh them. Due to this connotation, the above expression should be replaced by "unintended effects" which reflects better the phenomena under analysis and is coherent with the wording used in this area. We believe the language used should not be equivocal or suggesting associations with matters not pertinent to the arguments.

97. *Is there new scientific evidence since 1998?*

The argument presented in *Notes 11-12* is that knowledge of the ecological impacts of biotech products and their spread and concentration in the agricultural environment has changed, particularly in that emergent properties at the scales of the field and landscape are now much better appreciated even if they are still far from fully understood. Examples of where knowledge has increased substantively are –

Comments by Argentina

Quoted Notes are not included in this document. Should they refer to the studies quoted above (see Nature …), please see our comments.

- Spread and persistence of some crops plants, notably oilseed rape.
- The important role of insects as carriers of pollen over the landscape. *
- The importance of the weed flora to in-field biodiversity and food webs. *

*** Referring to the last two points: both are no exclusively biotech-crop-dependent but more so from agricultural practice.**

100. *Are different agricultural practices needed for pre- and post-1998 products?*

Following the points made in answer to Q.97, the innate biological qualities and behaviour of a product may not have changed, but it is quite possible that the context in which that product would operate has changed, in two ways. (A) The physical or agronomic environment is different. The agronomy of these crops changes rapidly: examples of factors that have changed markedly in Europe in recent times are the proportion of autumn-sown crops, the area covered by oilseed rape, and the type and effectiveness of pesticides used. An example, given already, of the change in pesticides is the rise in use of glyphosate as an arable herbicide in some countries in the past few years. (B) The understanding of the GM product's role in the ecosystem has changed. It was also reported previously that some major effects of intensification on arable ecosystems have become well established scientifically only in the last few years. The way arable plants and their food webs are considered is now different from the way they were generally considered in the early 1990s. The question is sometimes referenced back to before the early 1990s: why was the large scale change to autumn-sown cropping in some parts of Europe not scrutinised with the same rigour as the potential change to GM cropping? The answer is that it was thought not to be important, while it is now known to have been very important for farmland food webs.

Comments by Argentina

On the questions here we believe: (A) we agree; (B) GM crops are approved only if their role in the agro-ecosystem is the same as the comparator non-GM crop, except for the newly introduced characteristic. Negative unintended effects, to the extent that they are significant for the farmland food webs are carefully assessed and, if any, not tolerated in the approval process. Also, when it is referred to "ecosystems" it seems to be referring to all crops, biotech and non-biotech. We argue that this distinction should be clearly made in the document. It is even asked why some agricultural practice in Europe has not been scrutinised with the same rigour as…GM cropping. The use of these arguments, when applied to GM crops only, seems not well based.

101. *Change in mitigation of potential risk.*

The answers follow from the responses above to questions 97 and 100. While products might have very similar qualities, mitigation might differ as a result of new information informing risk or a new perception of the importance of a particular risk.

Comments by Argentina

Perception of risk is not the same as real risk. Failure in recognizing this fact, will make the advance of Science difficult, as any new technology implies risks, and therefore the distinction is relevant.

Among ecological topics, the perceived mitigation to reduce the 'severity' of a risk to biodiversity and ecosystem functioning has changed because of a greater appreciation that arable systems have been affected by intense agriculture.

Comments by Argentina

The Expert refers to intense agriculture, which has been widely recognized as negative to biodiversity, no matter which type of crop, biotech or non-biotech, is used. This should not imply that a different approach is to be considered to agriculture as a whole.

> Mitigation is unlikely to remain constant. For example, some current mitigation measures which leave margins round the cropped area of land are insufficient when it is appreciated that biodiversity in the cropped areas is necessary to main ecological function there.
>
> That risk has not remained the same over time is an inevitable consequence of scientific information on arable systems being collected at increasingly larger scales since the mid-1990s. Early research using GMOs in small parcels of land could not possibly have generated the knowledge that pollen from large fields of oilseed rape is moved widely in the landscape.

Comments by Argentina

As in many occasions before, the Expert refers to oilseed rape as an example of GM crops. However, this crop has characteristics of its own, non biotech-dependent, and therefore we do not consider appropriate to refer to it when a generalization is made We respectfully recall that any generalization would oppose to the "case-by-case" criteria, which we believe should apply to these products.

> Moreover, the present guidelines about pollen barriers, e.g. a strip of flowering crop between the GM field and non-GM recipient field, may have to change if the proportion of GM fields in the landscape increased to, say, 50%.

Comments by Argentina

As with any new technology, precautions should be exercised in its use. Unintended gene flow via pollen, is an inescapable phenomenon if sexually compatible plants are at appropriate distances. This is also true with non-biotech crops. Consequently, biotech crops do not deserve such a different treatment.

> 103. *Is contamination risk greater than for non-GM varieties*
>
> A certain level of impurity – through one crop type growing within or giving pollen to another type – seems to have been generally accepted for many years. Such impurity varies greatly with crop type: it is common in oilseed rape, and less common in beet and maize, for example. Where the nature of the yield is different, e.g. for high erucic oilseed rape (HEAR), impurities are kept to acceptably low values by using registered growers who are familiar with the crop and with the requirements for separation, and many of whom farm in a restricted part of the country. There are clear criteria for the acceptable presence of HEAR in non-HEAR oil. Outside specialist varieties such as HEAR, impurities have largely gone unobserved, and in many instances where non-GM oilseed rape volunteers emerge in a non-GM oilseed rape crop, the percentage impurity is unknown and is ignored. The potential of a crop variety to convey an impurity is not the same for all varieties but differs depending on factors such as the proportion of seeds that enter dormancy, the persistence of seeds

in the soil and the relative pollen 'strength' of potential donor and recipient fields (for example caused by different proportions of male sterile plants). These factors may or may not differ between GM and non-GM varieties but should not differ because one is GM and the other not. They would differ in any case. Given present knowledge of the life cycle and reproductive behaviour of the crops, there is no reason to suppose that biotech crops confer different degrees of impurity compared with crops produced from, say, induced mutagenesis.

106. *Rationale for different management practices*

Provided no significant level or type of risk has been detected, then no particular change in practice above the highest recommended existing practice to ensure a high purity, should be needed. As in Q.103, however, if thresholds are imposed for whatever reason, e.g. 0.9%, specifically for GM varieties in non-GM varieties, then there will need to be different agricultural practices for those GM varieties that leave volunteers or spread genes by pollen to neighbouring, sexually compatible crops. These practices are well appreciated – reducing volunteers to a minimum by appropriate soil cultivation after harvest, preventing volunteers from flowering in subsequent crops, leaving several years before growing the same type of crops again so that volunteer seed decays by natural means, leaving a separation strip between crops which is not harvested and beyond which geneflow is reduced to very low values, and not planting crops having reduced self-pollen in the vicinity.

Under a system of coexistence in which a threshold (GM in non-GM) was imposed, the agricultural practice might well have to change in a crop such as oilseed rape to ensure that threshold would be met. Longer intervals than normal between oilseed rape crops, some regional segregation of GM and non-GM crop types and the dropping of varietal associations (80% male sterile, 20% own pollen) from general use would probably be necessary. Given present knowledge, these changes would be in consequence of an imposed threshold of GM in non-GM product, not of any inherent food-risk in the GM product itself.

Comments by Argentina

Again, the discussion pertains more to oilseed rape than to GM crops as a category. It should be separated clearly when the arguments do refer specifically to oilseed rape and when they do to all GM crops. We recall the importance of the "case-by-case" criteria.

(Table 1, referring to point 14 – under the title "Criteria and standards")

Table 1. The ability of the crops to disperse genetic material through feral or volunteer progeny, pollen movement and outcrossing to form hybrids in Europe. Author's summary.

	Beet	Maize	Oilseed rape	Cotton
Feral / volunteer weeds persistence in field persistence outside field	 medium medium	 zero[1] low	 high medium	 zero zero
Pollen transfer crop to crop	 low[2]	 high	 high	 low
crop to feral /volunteer	low[2]	zero	high	zero
crop to wild relative	low[2]	zero	low	zero
Crossing frequency (on arrival of pollen at flowering plants)				
crop to crop	high	high	high	low
crop to feral	high	zero[1]	high	-
crop to wild relative	high (local)	zero	low	-

Comments by Argentina

No footnotes are explained in the document received. They only refer to maize. We observe, however, with regard exclusively to maize:

1. **Maize persistence outside agro-ecosystems have been proved to have very low frequency, as domesticated maize hardly survive without man's help. Domestication has increased advantages on food and agronomical traits (by conventional breeding) at the expense of independent (feral) growth.**

2. **Volunteer weeds? Is the Expert referring to the weed characteristics of domesticated maize? Is the Expert indicating that weeds (volunteer?) other than maize can grow (al low frequency) outside the specific agro-ecosystem dedicated to maize production?**

   If the observation in square 2, first data row, we must read, among other statements, that ability for "volunteer weeds persistence outside field" is low. It is now clear to this reviewer if the Expert is referring to maize as "the crop" or to weeds in maize fields.

3. **Pollen transfer ability from crop to crop is indeed high. However, pollen viability is very low and dependent from weather conditions. This will only affect the quality of the F2 progeny. This consideration also applies to crop to crop "Crossing frequency (on arrival of pollen at flowering plants)"**