Various authors. Journal of Allergy and Clinical Immunology. October (2001) Vol. 108 #4. p 654.

The report is taken from a letter which draws attention to the recently published WHO method of assessment of the allergenic potential of GM crops.

The aim is to identify the likelihood that a GMO would create a new risk of exposure to allergens.

The method is based on comparison of the inserted gene or genes with genes which are known to be the source of allergens and, upon animal models.

Given that gene homology tests are only as good as existing knowledge of the relevant gene sequences, it is the animal tests that are most likely to identify new risks. However, the quality of animal tests must reach acceptable standards, it is relatively easy to obtain false negative results with apparent statistical significance, without being particularly thorough. Animal tests should only be performed once the gene homology tests prove negative. Databases of allergen specific genes are growing rapidly.

Compliance with WHO assessment methodology would provide support to an argument proposing that Duty of Care had been met.

The reported framework of assessment is reproduced below, full details are available from the WHO web site: www.who.int/fsf/gmfood/

In general, the difficulties of applying traditional toxicological testing and risk assessment procedures to whole foods, has meant that an alternative approach is now used for the safety assessment of genetically modified foods. This approach is based on the concept of *substantial equivalenc*e.

This approach acknowledges that the goal of the assessment is not establishing absolute safety but to consider whether the genetically modified food is as safe as its traditional counterpart, where such a counterpart exists.

In the situation where the genetically modified food differs from the traditional counterpart by the presence of one or a few new genes and their products, it may be possible to isolate and study these in a manner analogous to conventional toxicity testing of food additives. However it is essential to ensure that the material tested is biochemically and functionally equivalent to that produced in the genetically modified food.

It should be noted that all foods contain DNA, which is ingested in significant quantities. In humans, dietary intakes of RNA and DNA vary widely but are typically in the range from 0.1 to 1.0 g per day. Concerns over the presence of novel DNA in a genetically modified food consumed in the human diet must take into consideration that this DNA would represent less than 1/250,000 of the total amount of DNA consumed. In view of this and the digestibility of dietary DNA, the probability of transfer of genes from genetically modified plants to mammalian cells is extremely low. It is nevertheless necessary to examine this possibility and the consequences of such transfer if it were to occur.

The transfer of plant DNA into microbial or mammalian cells under normal circumstances of dietary exposure would require all of the following events to occur:

- the relevant gene(s) in the plant DNA would have to be released, probably as linear fragments;
- the gene(s) would have to survive nucleases in the plant and in the gastrointestinal tract;
- the gene(s) would have to compete for uptake with dietary DNA;
- the recipient bacteria or mammalian cells would have to be competent for transformation and the gene(s) would have to survive their restriction enzymes;
- the gene(s) would have to be inserted into the host DNA by rare repair or recombination events.

Unlikely!

The framework for the assessment of risk of exposure to allergens is based on the following logic:

- Source of the transferred genetic material: Particular caution must be exercised if the source of this material contains known allergens.
- Sequence homology: The amino acid sequence of many allergens is readily available.
- Immunoreactivity of the newly introduced protein: If the novel protein is derived from a known allergenic source or if it has sequence homology with a known allergen, then the reactivity of this novel protein with IgE from the blood serum of appropriate allergic individuals is determined.
- Effect of pH and/or digestion: Most allergens are resistant to gastric acidity and to digestive proteases.
- Heat or processing stability: Labile allergens in foods that are eaten cooked or undergo

other processing before consumption are of less concern.

Footnotes to Figure (see following page)

a) The figure was adapted from decision-tree approach developed by International Food Biotechnology Council and Allergy and Immunology of the International Life Sciences Institute.

b) The combination of tests involving allergic human subjects or blood serum from such subjects would provide a high level of confidence that no major allergens were transferred. The only remaining uncertainty would be the likelihood of a minor allergen affecting a small percentage of the population allergenic to the source material.

c) Any positive results obtained in tests involving allergenic human subjects or blood serum from such subjects would provide a high level of confidence that the novel protein was a potential allergen. Foods containing such novel proteins would need to be labeled to protect allergic consumers.

d) A novel protein with either, no sequence similarity to known allergens or derived from a less commonly allergenic source with no evidence of binding to IgE from the blood serum of a few allergic individuals (<5), but that is stable to digestion and processing should be considered a possible allergen. Further evaluation would be necessary to address this uncertainty. The nature of the tests would be determined on a case-by-case basis.

e) (e) A novel protein with no sequence similarity to known allergens and that was not stable to digestion and processing would have no evidence of allergenicity. Similarly, a novel protein expressed by a gene obtained from a less commonly allergenic source and demonstrated to have no binding with IgE from the blood serum of a small number of allergic individuals (>5 but <14) provides no evidence of allergenicity. Stability testing may be included in these cases. However, the level of confidence based on only two decision criteria is modest. The WHO Consultation suggested that other criteria should also be considered such as the level of expression of the novel protein.

Assessment of the Allergenic Potential of Foods Derived From Genetically Modified Crop Plants