Panel V Summary
Defining Unique Science Issues in Biosafety Risk Assessment

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Five main issues were raised during the talks which will likely influence how we will conduct risk assessments in the future.

1. For the *B.t.* toxin transgenics we have a situation similar to that for traditional breeding of disease-resistant crop varieties, in that the loss of insect control through the development of resistance in insect populations will result in the loss of plant varieties or useful cultivars. However, unlike traditional disease-resistant crops, this breakdown should be followed by the immediate withdrawal of all the varieties from cultivation until the resistance is lost.

   We note that the objective is to achieve effective monitoring for resistance in insect populations and it is expected that the *B.t.* toxin transgenics will be used only under conditions of effective integrated pest management systems. While these are very sensible objectives, it is doubtful whether they can operate effectively, especially when the constructs are used in crops for which farm-preserved seeds are employed and in the developing region. Also there is no incentive for farmers to report minor problems if they lose desirable cultivars.

2. For Baculovirus insecticides, it is essential that the costs of production and rate of kill are equivalent to those of competitive chemical pesticides. Genetic manipulation of these double-stranded DNA viruses is well developed and offers exciting opportunities for the construction of improved strains.

   An inherent property of these viruses of particular advantage for the release of genetically modified derivatives is that the wild type is an occluded virus in which many individual virions are encapsidated in a protein matrix. Removal of the gene for this protein results in the production of virus with a very low survival in the environment and concomitantly very low infectivity. Both are properties which significantly affect risk assessments and hence should facilitate the development of derivatives carrying genes that enhance the rate of kill. A large amount of work of this type has been performed and significant advances in the rate of kill have been obtained through the use of insect-specific toxins derived from scorpions.

   The low infectivity and very short shelf-life of the non-occluded viruses are serious problems for commercial development. Both have been overcome by recent work at the Boyce Thompson Institute in which virus is harvested from insects before they

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are killed, yielding virions that are protected by the host-derived membrane and are not damaged by proteases produced when the insects die. We assume that this, and other technical developments in the formulations of virus for use in crops, will lead to the development of a new generation of transgenic baculoviruses for field testing.

3. While our confidence in the future for genetically modified baculoviruses is greatly enhanced, we are less confident about how research presented in Panel V on recombinant plant viruses will affect risk assessment. The work from Tepfer's Laboratory has shown clearly that artificially constructed recombinants can be either less, or more, virulent than either parent. As yet, we have no evidence that the more virulent viruses occur naturally or have attributes that would lead to their selection and persistence in the environment. It is perhaps worth commenting that both plant and animal viruses are still actively evolving and that human intervention in nature is almost certainly responsible for speeding up the rate of their evolution. For example, measles can only survive when human populations are sufficiently large and could not have existed before large populations could be sustained through agricultural development in Mesopotamia. Also we are well aware of the importance of natural recombination within populations of influenza viruses that lead to occasional world pandemics of diseases. We might assume that the extremely large areas of monocultures of modern crops will be equally conducive to the development of evolution in plant viruses.

As well as providing the potential for recombination, transgenic virus-resistant plants also will influence the potential for recombination in the field by greatly reducing the amount of replication of viral nucleic acid arising from natural infections, and hence should reduce significantly opportunities for natural recombination events.

4. It is particularly valuable for regulators to know what kind of research is being carried out that will soon lead to the production of organisms which may need to be assessed for novel risks. In this respect it was important to hear how rapidly the mapping of the rice genome is progressing and that the information gained is also highly applicable to other cereals. The observation that perhaps 1/4 of the cDNAs tested had sequences that code for products already known from other studies was of particuiar interest. If indeed this implies that l/4 of the genes in rice have known functions, it is not unreasonable to assume that within the next 10 years we may move to a situation in which only 1/4 of the genes have functions that are not understood, although this assumption is based on the expectation that research on basic biochemistry and physiology will proceed as rapidly as molecular biology, which is perhaps unlikely. From the point of view of risk assessments, the more we know about gene functions and relationships between species, the fewer are areas of uncertainty. Also, we must assume that the combination of excellent gene mapping

and extensive clone banks of genes from cereals will indicate that there will be rapid advances in the production of transgenic cereals utilizing genes form within the *Gramineae*, rather than from totally unrelated species, as at present.

5. Perhaps the greatest challenge for the development of new crops is to be able to utilize fully those areas of the world in which plant productivity is restricted by stresses arising from salinity, unavailability of water and high temperature. Improvements in the ability to withstand water stress could have an enormous impact in enhancing food production in those countries which are particularly under threat from population growth and limitation on food production. Therefore, any development in finding genes, and regulatory sequences for such genes, that could be used to produce stress-tolerant plants is to be welcomed. Whether or not any of the genes found to date will be useful for the breeding of stress-tolerant crops remains to be seen, but is in itself irrelevant because the great benefit of such work is that it will surely soon lead to the production of transgenic plants that can be tested in the field.

From the regulatory point of view, transgenic stress-tolerant plants are going to be very difficult to handle. Almost by definition stress-tolerant crops will have attributes that should enable them to colonize niches that are presently poorly occupied by existing adapted species. Present concepts that we should not allow the release of organisms which are expected to be invasive as a result of gene cloning will have to be reconsidered because hungry people will need to be fed, despite possible environmental damage.