codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON PESTICIDE RESIDUES
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FEASIBILITY OF ESTABLISHING MRLS FOR GENETICALLY MODIFIED CROPS AND METABOLITE RESIDUES

Background

1. At the 31st Session of the CCPR several delegations expressed reservations regarding establishing MRLs for a metabolite residue resulting from the treatment of a genetically modified crop.

2. At its May 2000 32nd session the Codex Committee on Pesticide Residues (CCPR) considered a paper (CX/PR 00/8) examining the feasibility of establishing maximum residue limits (MRLs) for genetically modified crops and metabolite residues. The paper focussed on the most common type of modification herbicide tolerance and approaches the subject by considering two basic scenarios: the first where the same metabolic pathway is followed but there is a quantitative change in the residue composition and the second where a different metabolic pathway is followed. The document briefly described different scenarios and links them to recent examples considered by the JMPR.

3. In its deliberations the Committee focussed on matters related to residue definitions for control purposes. There was general agreement that separate MRLs *should not* be elaborated for GMO and conventional crops. It was clear that no one approach is applicable to all situations and that at present, a case-by-case approach is needed in which careful consideration is given to the advantages and disadvantages of the proposed approaches for individual active ingredients. In cases where the existing residue definition would be no longer applicable, the Committee encouraged industry to assist the Committee in providing general guidance on residue chemistry data and analytical methodology useful for the development of residue definitions compatible to traditional and resistant varieties.

4. The Committee decided to seek information from governments on how they are approaching the issue of setting MRLs for GMO crops (including residue definition and enforcement considerations), and on the types of pesticides and crops most likely to be subject to modification (CL 2000/27 - PR, Part A, 08/2000). Responses to CL 2000/27-PR, Part 3A

"Feasibility of establishing mrls forgenetically modified crops and for metabolite residues[1] were received from the U.S. and Mexico.

SUMMARIZATION AND DISCUSSION OF COMMENTS RECEIVED FROM GOVERNMENTS

Approach to Tolerant Crops

Standards and Guidelines

5. Mexico: "Los LMRs para cultivos modificados geneticamente, se aplican los mismos limites establecidos para los cultivos convencionales; cuando no existen estos LMRs, se solicitan estudios de "residue chemistry' con base a la Buenas Practicas Agricolas nacionales (BPA)."

> *The MRLs established for genetically modified crops apply similarly to conventional crops; when MRLs do not exist, studies are requested "residue chemistry" that are based on the National Good Agricultural Practices (GAP).*

6. U.S.: The U.S. has approached the issue of tolerant crops with the same standards and guidelines used for traditional crops. The United States Environmental Protection Agency (EPA) regulates the herbicides used on herbicide-tolerant plants, whereas the United States Department of Agriculture (USDA) and the United States Food and Drug Administration (FDA) regulate the plants themselves and the food crops, respectively. The EPA indicates that it is also responsible for regulating pesticides produced by genetically modified plants, but noted that is outside the scope of CL 2000/27-PR, Part 3A.

7. Canada: Canada, utilizes the same data standards and study guidelines as those used for traditional crops. The Pest Management Regulatory Agency (PMRA) regulates the herbicides used on herbicide-tolerant crops and establishes the MRLs for enforcement by the Canadian Food Inspection Agency (CFIA). The CFIA regulates genetically modified crops.

Metabolism

8. The US and Canada has similar approaches to herbicides or any other pesticide intended for use on a crop genetically modified for tolerance or selected through traditional breeding for tolerance;

9. US: For a herbicide (or other pesticide) intended for use on a crop genetically modified for tolerance to that herbicide (or other pesticide), the registrant/owner of the pesticide must provide an in-depth metabolism study of the herbicide (or other pesticide) qualitative and quantitative profile on the tolerant crop.

10. Canada: For new pesticide, a complete data package is required for registration for use on either tolerant or traditional crops. For a herbicide (or other pesticide) already registered on a traditional crop, if the metabolites seen in the tolerant crop differ from those seen in normal crop, a contemporary in-depth metabolism study and residue data are required,

11. The U.S. also indicated that in cases where several tolerant crops are produced by the same mechanism, metabolism data from one tolerant crop may be translated on a case-to-case

[1] In collaboration with Australia, United States of America, Global Crop Protection Federation.

basis to cover another tolerant crop. Canada has a similar approach, and as in the U.S. this is considered on a case-by-case basis.

Residue(s) of Concern

12. The process for definition of the residue (s) of concern is similar in both the U.S. and Canada

13. For a new active on a tolerant crop, the nature of the residues and the magnitudes of the components of the residues are determined. The residue of concern for dietary exposure considerations is defined as those components (parent compound and/or metabolites/degradants) for which there is a significant toxicological concern. The residue of concern for enforcement purposes is defined as the parent and/or possibly one or more metabolites, depending on the relative magnitude of the residue components, the toxicological concerns for the components, and the capabilities of proposed enforcement analytical methods.

14. For an already registered herbicide (or other pesticide) where a residue definition previously existed for the traditional crop, the tentative/proposed residue for enforcement purposes for the tolerant crop is compared to the existing residue definition and if required the residue definitions are harmonized.

15. Thus the process results in a residue of concern that applies to both tolerant and normal crops.

Residue Field Trials

16. U.S.: A full complement of field trials in the principal growing regions is required with the tolerant crop variety to ascertain the magnitude of the residue under GAP conditions. For example, for the recently developed GA21 variety of glyphosate-tolerant corn, 22 field trials were conducted in 1997 in 14 states. These included the mandatory residue decline studies. In this case, the existing tolerances were confirmed by the new studies, except for corn forage, where an increase in tolerance from 1 to 3 ppm was needed. Again, the metabolism/residue requirements for tolerant and normal crops are the same.

17. Canada: A full set of field trials are required in the major growing zones with the tolerant crop to allow the magnitude of the residue to be determined at GAP, which in Canada is determined from efficacy trials. Like the US, Canada requires residue decline trials, bracketing the proposed pre-harvest intervals.

MRL Definition

18. The US and Canada has a similar approach to defining the MRL for crops.

19. Both the US and Canada do not promulgate different tolerances (MRLs) for tolerant and traditional varieties of a given crop or processed commodity of that crop. Both the tolerance and its residue definition must accommodate the qualitative and quantitative characteristics of both the traditional and tolerant crop. The U.S. provide provided a pragmatic rationale in support of this approach "tolerant and normal crops are often mixed in commercial practice and are not easily distinguished". From an enforcement perspective this is an important provision.

20. If it is determined to be necessary, the residue definition of the specific normal crop will be altered to conform to the requirements of the tolerant crop,. For example, a new metabolite

found in significant amounts only in the tolerant variety may be need to be added to the definition previously established for the normal crop. Consequently a single residue definition and a single tolerance (MRL) will be published for the use of a pesticide on a given crop.

21. The U.S. provided examples where the residue definition was not identical for crops for which no tolerant versions have been developed and crops for which tolerant versions have been developed e.g. .bromoxynil tolerance (i.e. 3,5-dibromo-4-hydroxybenzonitrile) for a crop having both tolerant and traditional varieties is different from that of a crop for which only traditional varieties exist.

22. The Canadian residue definition for the same examples are shown for comparison

Pesticide	Commodity	US		Canada	
		Normal	Tolerant	Normal	Tolerant
Bromoxynil	Cotton	Bromoxynil	Bromoxynil + 3,5-dibromo-hydroxybenzoic acid (DBHA)[1]		
Glufosinate	Canola	Glufosinate + 3-methylphosphinico propionic acid[2]	Glufosinate + N-acetyl glufosinate + 3-methylphosphinico propionic acid[2]	Glufosinate + 3-methylphosphinico propionic acid[2]	Glufosinate + N-acetyl glufosinate + 3-methylphosphinico propionic acid[2]
Glyphosate	US: Canola, Corn, Soybean, Sugar Beet Canada: Soybeans, Barley and Oats, Peas, Wheat, Lentils, Corn, Beans	Glyphosate	Glyphosate	Glyphosate	Glyphosate + aminomethyl phosphonic acid (AMPA)[3]

[1] DBHA not included in residue definition of normal crops.`
[2] N-acetyl glufosinate not included in residue definition of normal crop but would be determined by the the analytical method
[3] AMPA is not included in residue definition of normal crops.

23. Because DBHA is considered to be toxicologically significant, the U.S. residue for enforcement is redefined as parent plus DBHA for use on cotton. The U.S. residue definition and tolerance value were set for cotton, not transgenic cotton, and the residue definition was not altered for other crops.

24. Glufosinate-ammonium is metabolized by transgenic plants into a N-acetyl glufosinate (2-acetamido-4-methylphosphinico butanoic acid), which is not herbicidally active. This metabolite is found only in transgenic plants. Again, the definition applies to both traditional and tolerant versions of the relevant crops, not to just the modified crop varieties.

25. Glyphosate exemplifies a herbicide where the nature of the residues are qualitatively the same in both tolerant and normal crops. However, the metabolite aminomethylphosphonoic acid (AMPA) is a much greater percentage of the total residue in certain genetically modified crops. The residue definition for enforcement in the US is parent only for normal and tolerant crops. In Canada the residue definition is parent parent plus AMPA.

Herbicides or other pesticides and crops most likely to be subject to modification

26. Mexico: “En Mexico no se han desarrollado cultivos tolerantes a herbicadas, generalmente se experimentan organismos modificados geneticamente (OGMs) que han sido desarrollados en Estados Unidos de America y Canada, a la vez que se analiza si estos son aplicables a las condiciones de nuesta pais..”

> *In Mexico herbicide tolerant cultivars have not been developed, usually for genetically modified organisms (GMO) that have been developed in the U.S. and Canada, it is determined whether these are applicable for the conditions of our country.*

27. U.S.: Regarding the CCPR request for information about "herbicides or other pesticides most likely to be subject to modification", speculation about future developments is extremely uncertain. EPA has been informed that development work is underway to introduce glyphosate tolerant varieties of alfalfa, lettuce, wheat, and rice and glufosinate tolerant varieties of rice (see table). Therefore, it appears likely that modification of crops to introduce genes providing tolerance to existing non-selective herbicides is likely to be a continuing practice, since it provides a new opportunity for in-crop weed control. However, whether the herbicide tolerance might be achieved through enzymes that chemically modify the herbicide residue or through modification of the herbicide's biochemical target site is unknown but relevant to the question at hand. We can speculate that intentional introduction of genes and enzymes to chemically modify the residues of fungicides or insecticides seems much less likely, since these residues are not generally toxic to the crop and do not therefore impact agronomic utility.

28. Canada: Unlike the EPA, PMRA does not regulate the tolerant varieties of crops, this is the responsibility of CFIA. We have no specific information on potential introduction of new tolerant varieties. Canada agrees, with the US, that the intentional introduction of genes to alter the metabolism of pesticides other than herbicides appears to have a low probability.

29. The number of contributions received were small, consequently this document perspective reflects the experiences of only 3 countries. With this caveat in mind, it is noteworthy that the approach described here uses the same science-based decision framework applied to normal crops.