# REPORT OF

# THE JOINT FAO/WHO MEETING ON PESTICIDE RESIDUES (JMPR)

# WORKSHARING PILOT PROJECT ON

# TRIFLOXYSTROBIN

## Residues

**WORLD HEALTH ORGANIZATION**

**And**

**FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS**

**Rome, December 2004**

# Report of the JMPR Work Sharing Pilot Project

# Part 1- Residues

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# LIST OF ABBREVIATIONS

| | |
|---|---|
| APVMA | Australian Pesticides and Veterinary Medicines Authority |
| CCPR | Codex Committee on Pesticide Residues |
| EPA | United States Environmental Protection Agency |
| EU | European Union |
| FAO | Food and Agriculture Organisation |
| JMPR | Joint Meeting on Pesticide Residues (FAO/WHO) |
| MRL | Maximum Residue Limit |
| OECD | Organisation for Economic Co-operation and Development |
| PMRA | Pesticide Management Regulatory Agency (Canada) |
| RSG | Registration Steering Group (OECD) |
| WGP | Working Party on Pesticides (OECD) |

# SUMMARY

The FAO/WHO/OECD pilot project on work sharing was carried out to test the use of national and international evaluations of pesticide residues and toxicology by the JMPR. The 2003 CCPR selected trifloxystrobin as the first compound for the work sharing pilot project because it had been evaluated in Australia, Canada, the USA and the EU and was scheduled for evaluation by the JMPR in 2004. The project is supported by the OECD, FAO, WHO, JMPR and national and regional authorities.

The objective of the work sharing project is to use national and regional evaluations to facilitate and expedite reviews, while maintaining independence and incorporating global perspectives. Work sharing is intended to increase efficiency, resulting in a reduction of the workload.

The purpose of the pilot project is to investigate the feasibility of using the evaluations for new pesticides prepared by national or regional authorities for JMPR evaluations.

Trifloxystrobin residue data had already been assessed in Australia, Canada, USA and EU and the detailed assessment documents were provided to the JMPR evaluator, who also received full data submissions from the company, as is the normal practice.

For the residue review, the generic studies include: pesticide identity, physical and chemical properties, metabolism, environmental fate in soil and water-sediment systems, analytical methods, freezer storage stability tests, fate of residues in processing and in farm animal feeding. For these subjects, national or regional summaries of the data with their assessments were taken into account. Supervised residue trials, which constitute the major part of a residue evaluation, were not included in this pilot project.

The requirements for the work sharing project including the availability of the experts involved in the national/international reviews for consultation and the availability of complete study reports from the applicant/sponsor were fullfilled in February 2004.

The following methodological approach was made:

- As a first step, an independent JMPR evaluation and an appraisal based on the full data submission of the applicant were prepared by the FAO evaluator. The use of national/regional evaluations was limited to the comparison of findings and conclusions.

- In the second step, the national or regional monographs/reviews were compared with each other and with the JMPR evaluation with respect to for the data submitted/evaluated and concerning their results.

The trifloxystrobin assessment documents submitted by Australia and the EU were prepared in a monograph format. In the monograph format, excerpts of the dossier prepared by the applicant may be used and copied (e.g. tables, metabolism schemes, some text paragraphs) in preparation of the monograph. The monograph does not discuss the applicant's proposals and recommendations. Independent, complete and final evaluations of a compound are conducted without direct reference to registration purposes.

The trifloxystrobin assessment documents submitted by Canada and USA were presented in a review format. In the review approach, the scientific results are first summarised and then the applicant's dossier is subjected to a critical review. This includes discussions of the applicant's proposals and recommendations regarding registration procedures of the special plant protection products.

Because of the differences in the studies submitted for trifloxystrobin at the national or regional level, it was not practical to use a national or regional monograph as a "master". Also, the sets of studies in the dossier provided to JMPR did not always match those assessed at the national and regional levels. (The set of studies provided to the four national and regional authorities and JMPR was identical only for farm animal metabolism).

The trifloxystrobin example showed that currently there are similarities but also differences among procedures and approaches for residue evaluations used by the national and regional agencies. These result in some divergence in conclusions, such as those for residue definitions and processing factors. It should also be noted that JMPR considers the world-wide use of pesticides when recommending MRLs for food commodities in international trade and therefore its approach is not exactly the same as national and regional approaches, which operate within registration systems.

### *Comparison of scientific results*

Physical and chemical properties

- Very limited information on physical and chemical properties was received by Australia and the USA.
- Canada and the EU evaluated nearly the same studies which were submitted to the JMPR.
- The studies provided by the applicant to the JMPR cover all information on physical and chemical properties relevant according to the requirements by JMPR only for the active ingredient. It is noted that further studies relevant to the requirements by Canada and the EU were not submitted to the JMPR.

Farm animal metabolism

- The participants of the work sharing project received the same studies. All studies were included into the specific evaluations. The results of each specific evaluation – resulting in the residue definition - are in general identical. The residue of concern for animal commodities both for enforcement and risk assessment was defined as the parent and the acetic acid metabolite (CGA 321113).
- Canada and the USA recommended to include also the taurine conjugate of CGA 321113 (L7a) in the residue definition for risk assessment.
- Australia, the EU and the JMPR decided, howerver, not to include the metabolite L7a into the residue definition.

Plant metabolism

- The participants of the work sharing project did not receive the same studies caused by the differences in the dates of evaluation with regard to the times of finishing the studies. Studies on apples, cucumber and several wheat studies (apples CMR-12/97, apples CMR-13/97, cucumbers CMR-22/97, cucumbers CMR-23/97, wheat CMR-15/97, wheat CMR-18/97, wheat CMR-25/97) were evaluated by all participants. The peanut study ABR-97084 and the sugar beet studies 99MK09 and 99MK10 were not evaluated by Australia, Canada and the EU but by the USA and the JMPR. The wheat study CMR-04/97 was evaluated by Australia, the EU and the JMPR, but not by Canada and the USA. The 2002 wheat studies MR-027/02 and MR-028/02 were only evaluated by the JMPR.
- The results of the evaluation - the residue definition - are identical for the evaluations carried out by Australia, Canada and the USA. The residue of concern for plant commodities both for enforcement and risk assessment was defined as the parent and the acetic acid metabolite (CGA 321113).
- The EU concluded not to include CGA 321113 into the residue definition for plants both for enforcement and risk assessment for the reason that "*it is not of toxicological concern at the levels present in crops as a result of trifloxystrobin being applied at rates comparable with those of proposed GAPs*" (in the EU).

- The JMPR agreed with the EU that the residue definition for enforcement purposes for plant commodities should be trifloxystrobin *per se* but, like Australia, Canada and the USA, the JMPR included the metabolite CGA 321113 into the residue definition for risk assessment.

Nature of residues in processing
- The national/regional agencies did not receive the hydrolysis study 00MO02 which was submitted to the JMPR only.
- The absence of the study was not addressed by Australia, Canada and the USA as deficiency. The EU addressed this open point in their evaluation as follows *"... the nature of the residues following processing is considered to have been adequately addressed."*
- Based on the hydrolysis study 00MO02, the JMPR stated that acid metabolite CGA 321113 is relevant for the residue definition for dietary intake.

Environmental fate in soil and water-sediment systems
- No information on the environmental fate (hydrolysis etc.) was received by the Canadian PMRA and the US EPA.
- Australia and the EU evaluated two hydrolysis studies.
- The hydrolysis studies and a residue degradation study in water-sediment systems were evaluated by the JMPR. The JMPR stated that trifloxystrobin and its main metabolite CGA 321113 are rapidly degraded in paddy rice fields.

Crop rotation
- No information on rotational crops was received by the Australian Agency. The Canadian PMRA and the US EPA evaluated two US studies and the EU two studies carried out in Europe. All four studies available were evaluated by the JMPR.
- Generally, the metabolic pathway of trifloxystrobin in rotational crops was qualitatively similar to the pathway observed in apples, wheat and cucumbers with the exception of trifluoroacetic acid (TFA) that was detected in rotational crops but not in target crops. The rotational crop studies suggest that trifloxystrobin itself and the acid metabolite CGA 321113 will very rarely be occuring as residues in rotational crops and at levels <0.01 mg/kg.

Analytical methods
- The participants of the work sharing project did not receive the same studies.
- It was decided by all participants that the analytical methods for the determination of trifloxystrobin in plant materials are acceptable.
- In the case of methods for animal products, full details of the analytical methods used to determine trifloxystrobin residues in animal tissues, milk and eggs were not submitted by the applicant to the Australian APVMA. Therefore, the Australian evaluation is incomplete.
- The Canadian PMRA decided that the enforcement method AG-659A is unacceptable for the analysis of residues in animal matrices.
- The EU, the USA and the JMPR decided that the analytical methods for enforcement and risk assessment of residues of trifloxystrobin and the acid metabolite CGA 321113 in animal matrices are acceptable.
- Information on the extraction efficiency of residue analytical methods (radiolabeled) was reported by Canada, the USA and JMPR but not by Australia and the EU.

Stability of pesticide residues in stored analytical samples
- The evaluations by Australia and the EU are incomplete because the final studies were not submitted.
- Canada, the USA and the JMPR came to the conclusion that residues of trifloxystrobin and CGA 321113 are stable under freezer storage conditions for 1 - 2 years depending from the study period.

Residue definition

- The residue definitions for enforcement and risk assessment of animal products by all participants are identical with the minor difference that the USA and Canada additionally included the taurine conjugate of CGA 321113 into the risk assessment for liver.
- The residue definitions for enforcement of plant commodities recommended by Australia, Canada and the USA are identical but different from those recommended by the EU and the JMPR which are also identical.
- The residue definitions for risk assessment of plant commodities by Australia, Canada, the USA and the JMPR are identical. The EU did, however, not include the acid CGA 3211113 into the residue definition.
- A statement for the fat solubility was only made by the JMPR.

Processing

- The processing factors derived by the participants of the work sharing project were summarized in a table (see point 4.11.6). The calculation of the factors is based on residues expressed according to the respective residue definition. Therefore, the Australian-, US- and JMPR-factors can only partially be compared with the factors derived by the EU.
- Canada reported the maximum processing factors instead of mean values. Furthermore the calculation was made for both trifloxystrobin and CGA 321113 separately instead of the sum. These values cannot be used for a comparison with the factors calculated by other participants.
- For the reasons mentioned above, the possibilities for a comparison of the processing factors are limited. However, in some cases when data are available such as for orange juice, oil, dried pulp; apple juice, sauce, dried fruit, wet pomace; grape juice, must, wine, wet pomace; dried prunes, tomato paste; sugar beet dried pulp, molasses; rice polished grains, bran, hulls and final wheat bran, and when considering the limitations, the processing factors are nearly in the same order.

Farm animal feeding

- All participants of the work sharing project received the cattle feeding study. The poultry feeding study was submitted to Canada, the USA and the JMPR but not to Australia and the EU.
- The results of the evaluation - the recommendation of MRLs for animal products - are not identical. MRLs were recommended by Australia, the USA and the JMPR but not by Canada and EU.

Conclusion:

- A direct transfer of an participant's evaluation by the JMPR was not possible.
- With the exception of the subject farm animal metabolism, the database for the evaluations by the participants was not identical.
- The criteria and principles of the assessment were not identical for the participants.
- This results in different residue definitions, different processing factors etc.
- Currently, a comprehensive acceptance by the JMPR of national or regional conclusions and recommendations is not practical for the residue-supporting topics because of the differences in the database, criteria and principles of the assessment.

# RECOMMENDATIONS

*The JMPR came to the following recommendations:*

- Further development of the project, with changes based on the experiences with trifloxystrobin, is needed before work sharing can be routinely implemented with its anticipated benefits. Currently, based on experience with trifloxystrobin, a comprehensive acceptance by the JMPR of national or regional conclusions and recommendations is not practical for the residue-supporting topics included in this pilot project.

- Work sharing should focus on the mutual use of summaries of data validated at the national, regional and international levels. This would offer a possibility of exchange of a valid database which would be timesaving and would potentially reduce the workload. This could include all areas of the residue evaluation, including supervised residue trials data.

- For further progress in international work sharing it is proposed that national and regional evaluations should separate the summary of the submitted data from the conclusions. This would facilitate the mutual exchange of data summaries.

- A use of specific assessment results, such as the definition of residue, could potentially be done on a case by case basis.

- The evaluation process, including standardization of formats, should be harmonized at the international level.

- JMPR evaluators should use national and regional evaluations as support for the independent JMPR review.

- A further pilot work sharing project should be followed in a more flexible procedure. Procedures should be revised when there is more progress in the harmonisation of formates and evaluation procedures (harmonisation of guidance documents).

- The current workload of the JMPR precludes additional time spent by FAO Panel Members on this project if it is at the expense of normal residue evaluation commitments, which are regarded by Panel Members as the priority.

# REPORT OF THE JMPR WORK SHARING PILOT PROJECT

## Part 1- Residues

## 1 INTRODUCTION

The revised FAO/WHO pilot project proposal on work sharing for the JMPR was presented by FAO to the OECD-Working Group on Pesticides (WPG) in June 2003 following the recommendations of the OECD Registration Steering Group (RSG) meeting in March 2003 and of the small management group of the pilot project on work sharing which met also in June 2003.

The pilot project proposal was revised to facilitate the use of national and international evaluations of pesticide residues and toxicology by the JMPR. The work sharing process will be used for new compounds only during this pilot phase.

The 2003 CCPR selected trifloxystrobin as the first compound for the work sharing pilot project as this had been evaluated in Australia, Canada, the USA and the EU and is scheduled for evaluation by the 2004 JMPR.

The 2003 JMPR acknowledged that national assessments are already being extensively used; the work sharing pilot project is intended to promote, facilitate and formalize this practice.

A formal letter was sent to Australia, Canada, the USA and the EU requesting the governments' permission to have access to national evaluations of trifloxystrobin, as well as requesting the availability of the reviewers in case of questions needing clarification.

For the residue review, the generic studies include: identity; physical and chemical properties, metabolism, environmental fate in soil and water sediments, residue analysis and stability of pesticide residues in stored analytical samples, analytical methods, storage stability tests under cold storage, residue definition, fate of residues in processing and farm animal feeding.

Requirements for the work sharing project include the availability of the experts involved in the national/international reviews for consultation and availability of complete study reports from the sponsor.

## 2 OBJECTIVE

The objective of the work sharing project is to use national/regional evaluations to facilitate and expedite reviews, while maintaining independence and incorporating global perspectives.

# 3 PROCEDURE

## 3.1 National evaluations and other documents submitted by participants

| Participant | Contact person | Submission date | Documents |
|---|---|---|---|
| **AUSTRALIA**<br>Australian Pesticides & Veterinary Medicines Authorithy (APVMA) | Raj Buhla | 12/12/03 | - Reference list<br>- Environmental assessment report, page 1 – 81<br>- Residues evaluation report, page 1 - 79 |
| **EUROPEAN UNION (EU)**<br>European Commission (EC) | Lois Rossi | 12/12/03 | Council Directive 91/414/EEC:<br>Trifloxystrobin, Volume 3, Report and Proposed decision of the United Kingdom made to the European Commission under Article 8(1) of 91/414/EEC. Summary, Scientific Evaluation and Assessment, April 2000. 11343c/ECCO/BBA/00.<br>Volume 3<br>- B.2 Physical and chemical properties, pages 10 - 33<br>- B.5 Methods of analysis, pages 59 – 79<br>- B.6 Toxicology and metabolism, pages 80 – 103<br>- B.7 Residue data, pages 205 - 367 |
| **CANADA**<br>Pesticide Management Regulatory Agency (PMRA ARLA) | Lynn Lee | 19/2/04 | - Product Chemistry Data Requirements (DP-Bar Code 2000-3147)<br>- Nature of the Residue in Animals-Laying Hens; OPPTS 860.1300 (February 8, 2001)<br>- Nature of the Residue in Animals-Lactating Goats; OPPTS 860.1300 (February 19, 2001)<br>- Nature of the Residue in Plants-[apples; Golden Delicious]; OPPTS 860.1300 (March 25, 2001)<br>- Nature of the Residue in Plants-[cucumbers; Hausgurke, cucumis sativus L.]; OPPTS 860.1300 (March 25, 2001)<br>- Nature of the Residue in Plants-[spring wheat; LONA]; OPPTS 860.1300 (March 25, 2001)<br>- Residue Analytical Method; OPPTS 860.1340 and 860.1360 (April 30, 2001)<br>- Storage Stability Data-Grapes, Cucumbers, Potato, Wheat, Apples, Peanuts and all Processed Commodities, Beef Muscle, Beef Liver, Milk and Eggs; OPPTS 860.1380 (April 25, 2001)<br>- Confined Accumulation in Rotational Crops-[Wheat, Spinach, Turnip] (2001)<br>- Field Accumulation in Rotational Crops-Leaf lettuce, turnips and wheat] (2000)<br>- Processed Food/Feed-[Tomatoes, grapes, apples, potatoes, sugar beets and wheat]; OPPTS 860.1520 (June 1, 2001)<br>- Ruminant Feeding Study-Dairy cattle - OPPTS 860.1480 (May 28, 2001)<br>- Poultry Feeding Study; OPPTS 860.1480 (May 31, 2001) |

| Participant | Contact person | Submission date | Documents |
|---|---|---|---|
| **USA**<br>United States Environmental Protection Agency (US EPA) | Stephen Funk | 12/12/03 | - Memorandum of July 13, 1999. Trifloxystrobin. Results of HED Metabolism Assessment Review Committee Meeting held 6/15/99. DP Barcode D257835<br>- Memorandum of July 22, 1999. PP#8F04955. Request for Uses and Tolerances forTrifloxystrobin (proposed ISO common name) on Curcurbit Vegetables, Grapes, Peanuts, and Pome Fruit and a Tolerance for Imported Bananas. DP Barcode: 257888, 254208<br>- Memorandum of April 6, 2000. PP#9F5070. Trifloxystrobin on Almond, Fruiting Vegetables, Hops, Sugar Beet, Potato, and Wheat. Review of Analytical Methods and Residue Data. DP Barcode: D254221, D254213, D254217, D254218<br>- Memorandum of May 8, 2000. PP#9F5070. Human Health Risk Assessment for Trifloxystrobin on Almonds, Hops, Fruiting Vegetables, Potatoes, Sugar Beets, and Wheat. DP Barcode: D263040<br>- Memorandum of January 17, 2002. PP#0F06121. PC Code 129112. CAS#141517-21-7. Trifloxystrobin on Barley, Citrus, Corn (Field and Pop), Pecan, Pistachio, Rice, and Stone Fruit. Review of Analytical Methods and Residue Data. EPA Reg#s: 3125-559, 3125-562. DP Barcode: D267787, D272054 |
| **JMPR**<br>**FAO Panel** | Ursula Banasiak | 30/9/04 | - JMPR Draft Evaluation 2004, Trifloxystrobin<br>- JMPR Draft Report 2004, Trifloxystrobin |
| **APPLICANT**<br>**BAYER CropScience** | Eva Klamroth | 12/12/03<br><br><br>15/2/04 | - Index of the material to be submitted to JMPR 2004<br>- Comments by Bayer AG on the draft EU monograph<br><br>- Full data submission for JMPR evaluation, see reference list trifloxystrobin |

## 3.2 Methodological approach

*Approach proposed by the FAO JMPR secretariat*

A guidance on work sharing to the FAO evaluator (9/12/03) by the FAO JMPR secretariat proposes the following approach:

- The Australian evaluation should be used as the master, since the dossier is closest to the JMPR format.
- Existing differences between the evaluations have to be listed, and the evaluator should perform an independent evaluation based on the original data. Even in cases where existing evaluations are in agreement, the evaluator should use personal judgement whether more in depth review would be required.
- In case there are new data not intergrated in any of the existing evaluations they need to be evaluated and integrated in the monograph.
- Overall a JMPR monograph according to the FAO guidelines on pesticide residues is established based on the existing evaluations as far as possible (and justified).
- A critique of the formate of all dosssiers should be provided, as well as problem areas identified, and suggestions for improvements listed for discussion at the meeting.

- A final evaluation report, evaluating the work experience in this pilot project using the different existing evaluations should be written. Aspects to consider are e.g. ease or difficulty in extracting/using tables and summaries. Estimates of time and cost savings should be made, as well as suggestions for improved work sharing.

*Actual approach*

In general, the FAO evaluator tried to follow the proposed procedure in most of the points. A national monograph/review prepared by the participants of the project could not be used as "master" because of extensive differences in the database.

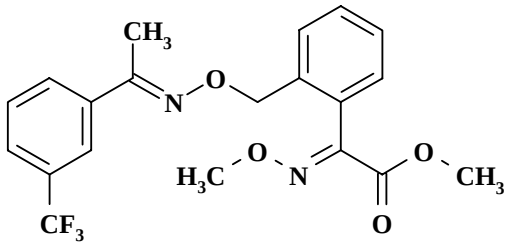
As a first step, an independent JMPR evaluation and an appraisal based on the full data submission of the applicant were prepared by the FAO evaluator. The use of national evaluations was limited to the comparison of findings and conclusions.

In the second step, the national/regional monographs/reviews were compared in the subjects defined with each other and with the JMPR evaluation with respect to the data submitted/evaluated and concerning their respective results (*quoted in italics in the text*). Comments are made by the FAO evaluator. The results were summarized for each subject. An annex in table format to compare the studies submitted was prepared. It shows an overview on the differences and confirmations of the databases of the monographs/reviews compared.

# 4 EVALUATION

## 4.1 Identity

| | |
|---|---|
| Common name: | Trifloxystrobin |
| Chemical name: | |
| IUPAC: | Methyl(E)-methoxyimino-{(E)-α-[1-(α,α,α,-trifluoro-m-tolyl)-ethylideneaminooxy]-o-tolyl}acetate |
| CA (index): | Benzeneacetic acid, α-(methoxyimino)-2-[[[(E)-[1-[3-(trifluoromethyl)phenyl]ethylidene]amino]oxy] methyl]-, methyl ester, (αE)- |
| Manufacturer's code number: | CGA 279202 |
| CAS number: | 141517-21-7 |
| CIPAC number: | 617 |
| Molecular formula: | $C_{20}H_{19}F_3N_2O_4$ |
| Structural formula: | |




Molecular mass: 408.4 g/mol

Comments

The identity facts are identical by all participants of the project.

## 4.2 Physical and chemical properties

### 4.2.1 Australia

Studies on physical and chemical properties were submitted by the applicant to the Australian APVMA, but an evaluation was not received.

Studies submitted by the applicant

- Angly, H. 1997. Report on explosive properties. Test No. 97.4006EXP. Institute of Safety and Security, Basel, Switzerland. 02.06.97.
- Angly, H. 1997. Report on oxidizing properties. Test No. 97.4006OXP. Institute of Safety and Security, Basel, Switzerland. 02.06.97.
- Angly, H. 1997. Report on flammability of solids. Test No. 97.4006FLS. Institute of Safety and Security, Basel, Switzerland. 02.06.97.
- Angly, H. 1997. Report on self-heating properties of solids. Test No. 97.4006.BCC. Institute of Safety and Security, Basel, Switzerland. 02.06.97.
- Kundel, P. 1997. Report on physico-chemical properties. A-9360B. Study Report 50210. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 16.06.97.
- Kundel, P. 1997. Report on physico-chemical properties. A-9360B. Study Report 50208. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 15.05.97.
- Kundel, P. 1997. Report on product stability. A-9360B. Study Report 50215. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 22.12.97.
- Stultz, J. 1997. Report on chemical stability. A-9360B. Study Report 50215. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 25.04.97.

Studies submitted to other participants and not reviewed by Australia

- Burkhard, N. 1997. Henry's law constant - CGA 279202. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: MO-01-003756. Unpublished.
- Das, R. 1996. Report on boiling point / boiling range. Ciba-Geigy Muenchwilen AG, Muenchwilen, Switzerland. Rep. No. 46881, 12.12.1996
- Das, R. 1996. Report on melting point / melting range - CGA 279202. Ciba-Geigy Limited, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46880, Edition Number: MO-01-003724. Unpublished.
- Das, R. 1996. Report on general physico-chemical properties, pure a.i. (aspect, colour, odour) - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46887, Edition Number: MO-01-003759. Unpublished.
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- Fueldner, H. 1997. Report on density of solids - CGA 279202. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: PP-96/63P.DES, Edition Number: MO-01-003749. Unpublished.

- Kitschmann, P. 1996. Hydrolysis of (U)-14C-phenyl-glyoxylate-labeled CGA 279202 under laboratory conditions. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 94PK01, Edition Number: MO-01-001565. Unpublished.
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- Ryser, M. 1997. Report on surface tension of aqueous solutions. Novartis Services AG, Basel, Switzerland. Rep. No. PP-97/23T.SUR, 25.08.1997
- Stamm, E. 1997. Atmospheric oxidation of CGA 279202 by hydroxyl radicals rate estimation. Novartis Crop Protection AG, Basel, Switzerland. Rep. No. 95A96112SM, 06.01.1997
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- Stulz, J. 1997. Report on solubility in organic solvents - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 53276, Edition Number: MO-01-003784. Unpublished.
- Stulz, J. 1997. Report on dissociation constant in water - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46883, Edition Number: MO-01-003808. Unpublished.
- Stulz, J. 1997. Report on octanol / water partition coefficient - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46884, Edition Number: MO-01-003797. Unpublished.
- Stulz, J. 1997. CGA 279202 - Purification report. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Statement, 10.09.1997
- Stulz, J. 1997. Report on spectra. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Rep. No. 54028, 26.08.1997
- Ulbrich, R. 1997. Hydrolysis of (trifluormethyl-phenyl-(U)-14C)-labeled CGA 279202 under laboratory conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 94UL04, Edition Number: MO-01-001568. Unpublished.
- Widmer, H. 1996. Vapour pressure of CGA 279202. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 96WI29, Edition Number: MO-01-003754. Unpublished.

Result

The studies mentioned above under "studies submitted by the applicant" are reported in the Australian reference list. But, an evaluation of these studies is not included in the *Residues Evaluation Report* (File No. P53871) or the *Environmental Assessment Report*. The only information on physical and chemical properties is a short summary in the *Environmental Assessment Report* on page 4 without any reference and is quoted below.

| | |
|---|---|
| *Odour:* | *odourless* |
| *Colour:* | *white* |
| *Physical state:* | *Fine powder* |
| *Melting point:* | *70.9°C* |
| *Density at 20°C:* | *1.36 g/cm$^3$* |
| *Vapour Pressure:* | *3.4 x 10-6 Pa at 25°C (extrapolated)* |

*Solubility in water:* *610 µg/L at 25°C*
*$LogP_{oct\text{-}water}$:* *4.3*
*Henry's Law Constant:* *2.3 X $10^{-3}$ Pa $m^3$/mol (EA calculates 2.8 X $10^{-3}$ Pa $m^3$/mol)*

Comments

Some critical studies were not submitted or not evaluated by the Australian.APVMA. Therefore, the Australian evaluation sent to the FAO evaluator is incomplete.

### 4.2.2 Canada

Studies submitted by the applicant and reviewed by Canada

- Stulz, J. 1997. Report on water solubility - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46885, Edition Number: MO-01-003778. Unpublished.
- Stulz, J. 1997. Report on solubility in organic solvents - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 53276, Edition Number: MO-01-003784. Unpublished.
- Stulz, J. 1997. Report on dissociation constant in water - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46883, Edition Number: MO-01-003808. Unpublished.
- Stulz, J. 1997. Report on octanol / water partition coefficient - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46884, Edition Number: MO-01-003797. Unpublished.
- Widmer, H. 1996. Vapour pressure of CGA 279202. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 96WI29, Edition Number: MO-01-003754. Unpublished.

Studies submitted to other participants and not reviewed by Canada

- Angly, H. 1997. Report on screening test for thermal stability and stability in air. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.TSA, 26.08.1997
- Angly, H. 1997. Report on flammability of solids. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.FLS, 26.08.1997
- Angly, H. 1997. Report on relative self-ignition temperature for solids. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.AFS, 26.08.1997
- Angly, H. 1997. Report on explosive properties. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.EXP, 26.08.1997
- Angly, H. 1997. Report on oxidizing properties of solids. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.OXP, 26.08.1997
- Burkhard, N. 1997. Henry's law constant - CGA 279202. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: MO-01-003756. Unpublished.
- Das, R. 1996. Report on boiling point / boiling range. Ciba-Geigy Muenchwilen AG, Muenchwilen, Switzerland. Rep. No. 46881, 12.12.1996
- Das, R. 1996. Report on melting point / melting range - CGA 279202. Ciba-Geigy Limited, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46880, Edition Number: MO-01-003724. Unpublished.
- Das, R. 1996. Report on general physico-chemical properties, pure a.i. (aspect, colour, odour) - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46887, Edition Number: MO-01-003759. Unpublished.

- Das, R. 1997. Report on general physico-chemical properties, technical grade a.i. (aspect, colour, odour) - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 53274, Edition Number: MO-01-003765. Unpublished.
- Fueldner, H. 1997. Report on density of solids - CGA 279202. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: PP-96/63P.DES, Edition Number: MO-01-003749. Unpublished.
- Kitschmann, P. 1996. Hydrolysis of (U)-14C-phenyl-glyoxylate-labeled CGA 279202 under laboratory conditions. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 94PK01, Edition Number: MO-01-001565. Unpublished.
- Kitschmann, P. 1997. Aqueous photolysis of [trifluormethyl-phenyl-(U)-14C]-CGA 279202 under laboratory conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 94PK02, Edition Number: MO-01-001584. Unpublished.
- Kundel, P. 1997. Report on physico-chemical properties. A-9360B. Study Report 50210. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 16.06.97.
- Kundel, P. 1997. Report on physico-chemical properties. A-9360B. Study Report 50208. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 15.05.97.
- Kundel, P. 1997. Report on product stability. A-9360B. Study Report 50215. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 22.12.97.
- Phaff, R. 1997. Rate and quantum yield of the direct Phototransformation of CGA 279202 under laboratory conditions in water. Novartis Crop Protection AG, Basel, Switzerland. Rep. No. 96RP03, 09.06.1997
- Ryser, M. 1997. Report on surface tension of aqueous solutions. Novartis Services AG, Basel, Switzerland. Rep. No. PP-97/23T.SUR, 25.08.1997
- Stamm, E. 1997. Atmospheric oxidation of CGA 279202 by hydroxyl radicals rate estimation. Novartis Crop Protection AG, Basel, Switzerland. Rep. No. 95A96112SM, 06.01.1997
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- Stultz, J. 1997. Report on chemical stability. A-9360B. Study Report 50215. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 25.04.97.
- Stulz, J. 1997. CGA 279202 - Purification report. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Statement, 10.09.1997
- Stulz, J. 1997. Report on spectra. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Rep. No. 54028, 26.08.1997
- Ulbrich, R. 1997. Hydrolysis of (trifluormethyl-phenyl-(U)-14C)-labeled CGA 279202 under laboratory conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 94UL04, Edition Number: MO-01-001568. Unpublished.

Result

The evaluation was made by the PMRA ARLA in 2000. A *Review "Product Chemistry Data Requirements"* (DP-Bar Code 2000-3147) by the reviewer Ron Scharfe gives in table 2 on pages 3 – 4 detailed information on physical and chemical properties. The conclusion presented in the report on page 2 is quoted below.

> *The Part 2 Chemistry Data are complete for trifloxystrobin.*

Comments

The review prepared by the Canadian PMRA was presented in a table format including author's name and report number. A list of references was not submitted. Canada evaluated 5 (report no. 96W129, 46883, 46884, 46885, 53276) of the 13 studies submitted to the JMPR. Eight further studies (report no. 355-96,

46882, 53275, 53278, 53279, 54028, 56883, ASR-292) were evaluated but no reference was given. It is concluded that some critical studies were not submitted to Canada or were not evaluated by Canada.

### 4.2.3 EU

Studies submitted by the applicant and reviewed by the EU

- Angly, H. 1997. Report on screening test for thermal stability and stability in air. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.TSA, 26.08.1997
- Angly, H. 1997. Report on flammability of solids. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.FLS, 26.08.1997
- Angly, H. 1997. Report on relative self-ignition temperature for solids. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.AFS, 26.08.1997
- Angly, H. 1997. Report on explosive properties. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.EXP, 26.08.1997
- Angly, H. 1997. Report on oxidizing properties of solids. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.OXP, 26.08.1997
- Burkhard, N. 1997. Henry's law constant - CGA 279202. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: MO-01-003756. Unpublished.
- Das, R. 1996. Report on boiling point / boiling range. Ciba-Geigy Muenchwilen AG, Muenchwilen, Switzerland. Rep. No. 46881, 12.12.1996
- Das, R. 1996. Report on melting point / melting range - CGA 279202. Ciba-Geigy Limited, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46880, Edition Number: MO-01-003724. Unpublished.
- Das, R. 1996. Report on general physico-chemical properties, pure a.i. (aspect, colour, odour) - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46887, Edition Number: MO-01-003759. Unpublished.
- Das, R. 1997. Report on general physico-chemical properties, technical grade a.i. (aspect, colour, odour) - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 53274, Edition Number: MO-01-003765. Unpublished.
- Fueldner, H. 1997. Report on density of solids - CGA 279202. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: PP-96/63P.DES, Edition Number: MO-01-003749. Unpublished.
- Kitschmann, P. 1996. Hydrolysis of (U)-14C-phenyl-glyoxylate-labeled CGA 279202 under laboratory conditions. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 94PK01, Edition Number: MO-01-001565. Unpublished.
- Kitschmann, P. 1997. Aqueous photolysis of [trifluormethyl-phenyl-(U)-14C]-CGA 279202 under laboratory conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 94PK02, Edition Number: MO-01-001584. Unpublished.
- Phaff, R. 1997. Rate and quantum yield of the direct Phototransformation of CGA 279202 under laboratory conditions in water. Novartis Crop Protection AG, Basel, Switzerland. Rep. No. 96RP03, 09.06.1997
- Ryser, M. 1997. Report on surface tension of aqueous solutions. Novartis Services AG, Basel, Switzerland. Rep. No. PP-97/23T.SUR, 25.08.1997
- Stamm, E. 1997. Atmospheric oxidation of CGA 279202 by hydroxyl radicals rate estimation. Novartis Crop Protection AG, Basel, Switzerland. Rep. No. 95A96112SM, 06.01.1997
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- Stulz, J. 1997. Report on water solubility - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46885, Edition Number: MO-01-003778. Unpublished.
- Stulz, J. 1997. CGA 279202 - Purification report. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Statement, 10.09.1997
- Stulz, J. 1997. Report on spectra. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Rep. No. 54028, 26.08.1997
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- Stulz, J. 1997. Report on dissociation constant in water - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46883, Edition Number: MO-01-003808. Unpublished.
- Stulz, J. 1997. Report on octanol / water partition coefficient - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46884, Edition Number: MO-01-003797. Unpublished..
- Widmer, H. 1996. Vapour pressure of CGA 279202. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 96WI29, Edition Number: MO-01-003754. Unpublished.

Studies submitted to other participants and not reviewed by the EU

- Kundel, P. 1997. Report on physico-chemical properties. A-9360B. Study Report 50210. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 16.06.97.
- Kundel, P. 1997. Report on physico-chemical properties. A-9360B. Study Report 50208. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 15.05.97.
- Kundel, P. 1997. Report on product stability. A-9360B. Study Report 50215. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 22.12.97.
- Ulbrich, R. 1997. Hydrolysis of (trifluormethyl-phenyl-(U)-14C)-labeled CGA 279202 under laboratory conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 94UL04, Edition Number: MO-01-001568. Unpublished.

Result

The evaluation was made by the United Kingdom as EU Rapporteur Member State in April 2000. A *Draft Assessment Report* was prepared (11343c/ECCO/BBA/00). Complete information on physical and chemical properties for the active substance and the plant protection products “Twist” and “Flint” is presented in detail on pages 10 – 22 under point B.2. A summary discussion is presented on page 23 and is quoted for the active ingredient below.

> *Trifloxystrobin (pure) is a white powder which melts at 73 °C and decomposes above 285 °C. It is not very volatile (vapour pressure 3 x $10^{-6}$). It does not dissociate and is only slightly water-soluble (0.6 mg/l). Solubility in organic solvents increases with increasing solvent polarity. The log octanol-water partition coefficient is 4.5, suggesting bioaccumulation may occur. Trifloxystrobin is hydrolytically stable at environmental pHs, however photochemical degradation was shown to occur. The technical active substance was not considered to be explosive or flammable.*

Comments

The review prepared by the EU was complete and presented in a table format. A list of references was submitted. The EU evaluated 12 of the 13 studies submitted to JMPR. Furthermore, 12 additional studies

were evaluated and complete reported. All critical studies were submitted by the applicant and evaluated by the EU.

### 4.2.4 USA

Studies submitted by the applicant and evaluated by the USA
none

Studies submitted to other participants and not reviewed by the USA

- Angly, H. 1997. Report on screening test for thermal stability and stability in air. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.TSA, 26.08.1997
- Angly, H. 1997. Report on flammability of solids. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.FLS, 26.08.1997
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- Angly, H. 1997. Report on explosive properties. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.EXP, 26.08.1997
- Angly, H. 1997. Report on oxidizing properties of solids. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.OXP, 26.08.1997
- Burkhard, N. 1997. Henry's law constant - CGA 279202. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: MO-01-003756. Unpublished.
- Das, R. 1996. Report on boiling point / boiling range. Ciba-Geigy Muenchwilen AG, Muenchwilen, Switzerland. Rep. No. 46881, 12.12.1996
- Das, R. 1996. Report on melting point / melting range - CGA 279202. Ciba-Geigy Limited, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46880, Edition Number: MO-01-003724. Unpublished.
- Das, R. 1996. Report on general physico-chemical properties, pure a.i. (aspect, colour, odour) - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46887, Edition Number: MO-01-003759. Unpublished.
- Das, R. 1997. Report on general physico-chemical properties, technical grade a.i. (aspect, colour, odour) - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 53274, Edition Number: MO-01-003765. Unpublished.
- Fueldner, H. 1997. Report on density of solids - CGA 279202. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: PP-96/63P.DES, Edition Number: MO-01-003749. Unpublished.
- Kitschmann, P. 1996. Hydrolysis of (U)-14C-phenyl-glyoxylate-labeled CGA 279202 under laboratory conditions. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 94PK01, Edition Number: MO-01-001565. Unpublished.
- Kitschmann, P. 1997. Aqueous photolysis of [trifluormethyl-phenyl-(U)-14C]-CGA 279202 under laboratory conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 94PK02, Edition Number: MO-01-001584. Unpublished.
- Kundel, P. 1997. Report on physico-chemical properties. A-9360B. Study Report 50210. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 16.06.97.
- Kundel, P. 1997. Report on physico-chemical properties. A-9360B. Study Report 50208. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 15.05.97.
- Kundel, P. 1997. Report on product stability. A-9360B. Study Report 50215. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 22.12.97.

- Phaff, R. 1997. Rate and quantum yield of the direct Phototransformation of CGA 279202 under laboratory conditions in water. Novartis Crop Protection AG, Basel, Switzerland. Rep. No. 96RP03, 09.06.1997
- Ryser, M. 1997. Report on surface tension of aqueous solutions. Novartis Services AG, Basel, Switzerland. Rep. No. PP-97/23T.SUR, 25.08.1997
- Stamm, E. 1997. Atmospheric oxidation of CGA 279202 by hydroxyl radicals rate estimation. Novartis Crop Protection AG, Basel, Switzerland. Rep. No. 95A96112SM, 06.01.1997
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- Stulz, J. 1997. Report on dissociation constant in water - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46883, Edition Number: MO-01-003808. Unpublished.
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- Widmer, H. 1996. Vapour pressure of CGA 279202. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 96WI29, Edition Number: MO-01-003754. Unpublished.

Result

No information on the subject physical and chemical properties was received by the US EPA.

Comments

none

### 4.2.5 JMPR

Studies submitted by the applicant and evaluated by the JMPR

- Burkhard, N. 1997. Henry's law constant - CGA 279202. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: MO-01-003756. Unpublished.
- Das, R. 1996. Report on melting point / melting range - CGA 279202. Ciba-Geigy Limited, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46880, Edition Number: MO-01-003724. Unpublished.

- Das, R. 1996. Report on general physico-chemical properties, pure a.i. (aspect, colour, odour) - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46887, Edition Number: MO-01-003759. Unpublished.
- Das, R. 1997. Report on general physico-chemical properties, technical grade a.i. (aspect, colour, odour) - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 53274, Edition Number: MO-01-003765. Unpublished.
- Fueldner, H. 1997. Report on density of solids - CGA 279202. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: PP-96/63P.DES, Edition Number: MO-01-003749. Unpublished.
- Kitschmann, P. 1996. Hydrolysis of (U)-14C-phenyl-glyoxylate-labeled CGA 279202 under laboratory conditions. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 94PK01, Edition Number: MO-01-001565. Unpublished.
- Kitschmann, P. 1997. Aqueous photolysis of [trifluormethyl-phenyl-(U)-14C]-CGA 279202 under laboratory conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 94PK02, Edition Number: MO-01-001584. Unpublished.
- Stulz, J. 1997. Report on water solubility - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46885, Edition Number: MO-01-003778. Unpublished.
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- Stulz, J. 1997. Report on dissociation constant in water - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46883, Edition Number: MO-01-003808. Unpublished.
- Stulz, J. 1997. Report on octanol / water partition coefficient - CGA 279202. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Bayer CropScience AG, Report No.: 46884, Edition Number: MO-01-003797. Unpublished.
- Ulbrich, R. 1997. Hydrolysis of (trifluormethyl-phenyl-(U)-14C)-labeled CGA 279202 under laboratory conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 94UL04, Edition Number: MO-01-001568. Unpublished.
- Widmer, H. 1996. Vapour pressure of CGA 279202. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 96WI29, Edition Number: MO-01-003754. Unpublished.

Studies submitted to other participants and not reviewed by JMPR

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- Angly, H. 1997. Report on flammability of solids. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.FLS, 26.08.1997
- Angly, H. 1997. Report on relative self-ignition temperature for solids. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.AFS, 26.08.1997
- Angly, H. 1997. Report on explosive properties. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.EXP, 26.08.1997
- Angly, H. 1997. Report on oxidizing properties of solids. Institute of Safety and Security, Basel, Switzerland. Rep. No. 97.4029.OXP, 26.08.1997
- Das, R. 1996. Report on boiling point / boiling range. Ciba-Geigy Muenchwilen AG, Muenchwilen, Switzerland. Rep. No. 46881, 12.12.1996
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- Kundel, P. 1997. Report on physico-chemical properties. A-9360B. Study Report 50208. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 15.05.97.

- Kundel, P. 1997. Report on product stability. A-9360B. Study Report 50215. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 22.12.97.
- Phaff, R. 1997. Rate and quantum yield of the direct Phototransformation of CGA 279202 under laboratory conditions in water. Novartis Crop Protection AG, Basel, Switzerland. Rep. No. 96RP03, 09.06.1997
- Ryser, M. 1997. Report on surface tension of aqueous solutions. Novartis Services AG, Basel, Switzerland. Rep. No. PP-97/23T.SUR, 25.08.1997
- Stamm, E. 1997. Atmospheric oxidation of CGA 279202 by hydroxyl radicals rate estimation. Novartis Crop Protection AG, Basel, Switzerland. Rep. No. 95A96112SM, 06.01.1997
- Stulz, J. 1996. Solubility in organic solvents. Ciba-Geigy Muenchwilen AG, Muenchwilen, Switzerland. Statement, 11.12.1996
- Stultz, J. 1997. Report on chemical stability. A-9360B. Study Report 50215. Novartis Crop Protection Munchwillen AG, Munchwillen, Switzerland. 25.04.97.
- Stulz, J. 1997. CGA 279202 - Purification report. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Statement, 10.09.1997
- Stulz, J. 1997. Report on spectra. Novartis Crop Protection Muenchwilen AG, Muenchwilen, Switzerland. Rep. No. 54028, 26.08.1997

Result

The evaluation was made by the FAO Panel of the JMPR in 2004. A detailed *Evaluation* including the physical and chemical properties of the active ingredient was prepared. The report prepared by the EU as well as by applicant's dossier were used. An appraisal including the conclusion is quoted below.

> *Trifloxystrobin is a white powder which melts at 73 °C. It is not very volatile (vapour pressure 3 x $10^{-6}$ Pa). It does not dissociate and is only slightly water-soluble (0.6 mg/l). Solubility in organic solvents increases with increasing solvent polarity. The log $P_{OW}$ is 4.5, suggesting bioaccumulation may occur. Trifloxystrobin is hydrolytically stable at environmental pHs, however photochemical degradation was shown to occur. The technical active substance was not considered to be explosive or flammable.*

Comments

The studies provided by applicant to the JMPR cover the information on physical and chemical properties relevant according to the requirements by JMPR (only for the active ingredient).

### 4.2.6 Results – physical and chemical properties

Very limited information on physical and chemical properties was received by Australia and the USA. Canada and the EU evaluated nearly the same studies which were submitted to the JMPR. The studies provided by the applicant to the JMPR cover all information on physical and chemical properties relevant according to the requirements by JMPR only for the active ingredient. It is noted that further studies relevant to the requirements by Canada and the EU were not submitted to the JMPR.

## 4.3 Farm animal metabolism

### 4.3.1 Australia

Studies submitted by the applicant and evaluated by Australia

- Ruembeli, R. 1997. The Metabolism of [trifluormethyl-phenyl-(U)-14C} CGA 279292 after Multiple Oral Administration to Lactating Goats. Novartis Crop Protection AG, Basel, Switzerland. Report No.09/97, 27.08.1997, Novartis File No. 279292/270.
- Ruembeli,R. 1997. The Metabolism of [Glyoxyl-phenyl-(U)-14 C] CGA 279202 after Multiple Oral Administration to Lactating Goats. Novartis Crop Protection, AG, Basel, Switzerland. Report No. 14/97, 09.12.1997. Novartis File No. 279202/504.
- Ruembeli, R. 1997.The Metabolism of {Trifluormethyl-phenyl-(U)-14C] CGA 279202 after Multiple Oral Administration to Laying Hens. Norvartis Crop Protection, AG, Basel, Switzerland. Report No. 10/97. 08.12.1997. Novartis file No. 279202/503.
- Ruembeli, R. 1998. The Metabolism of (Glyoxyl-phenyl-(U)-C14) CGA 279202 after Multiple Oral Administration to Laying Hens: Lab Project Number: PR 22/97 :198-98 :CRA 96/017.

Studies submitted to other participants and not reviewed by Australia

none

Result

The evaluation was made by APVMA in 2000. A monograph entitled *Residues Evaluation Report* (File No. P53871) was prepared. Information on the test conditions, analytical methods, total radioactive residues, characterisation/identification of metabolites and storage stability of residues were presented in detail on pages 11 – 17 under point 4.2 and 4.3. A summary discussion is presented on page 5 and quoted below.

> *The metabolism of trifloxystrobin was investigated in rats, goats and poultry, and the metabolic pathways were found to be comparable in all three species.*
> *In the goat, <0.1 % of the total dose was eliminated via milk. The highest tissue residues were found in the liver (0.41 to 0.54 % of total dose), bile (0.08 to 0.17 %) and kidney (0.03 to 0.04 %). Lower residues were found in fat, muscle and blood. In hens, 0.1 to 0.2 % of the applied dose was found in eggs. Residues were found in lean meat (0.11 to 0.22 % of total dose), peritoneal fat (0.07 to 0.21 %), skin and attached fat (0.14 to 0.39 %), kidney (0.11 to 0.25 %) and liver (0.28 to 0.68 %).*
> *Characterisation of the radioactive tissue residues revealed that parent trifloxystrobin was the principal component of the radioactivity in muscle, fat and skin, and egg yolk of laying hens. In contrast, the carboxylic acid derivative of trifloxystrobin (CGA 321113) was the major residue component in egg white and chicken liver. Analysis of the tissue residue composition of lactating goats revealed the presence of three main metabolite fractions – the parent compound and CGA 321113 (similar to poultry), along with amino acid conjugates (taurine and glycine) of CGA 321113. Amino acid conjugates of CGA 321113 were the principal residue component in goat liver and kidney. CGA 321113 was the main radioactive residue in muscle, and parent trifloxystrobin was the principal component in milk and fat.*
>
> <u>*Residue definition animal products:*</u> *Trifloxystrobin and CGA 321113, expressed as trifloxystrobin*

Comments

The studies sent by the applicant were critical reviewed. The results were presented in a report in monograph format including new created tables (not a copy of applicant's dossier). The Australian report was partly used by the 2004 JMPR for preparing the evaluation in this subject.

### 4.3.2 Canada

Studies submitted by the applicant and evaluated by Canada

- Ruembeli, R. 1997. The Metabolism of [trifluormethyl-phenyl-(U)-14C} CGA 279292 after Multiple Oral Administration to Lactating Goats. Novartis Crop Protection AG, Basel, Switzerland. Report No.09/97, 27.08.1997, Novartis File No. 279292/270.
- Ruembeli,R. 1997. The Metabolism of [Glyoxyl-phenyl-(U)-14 C] CGA 279202 after Multiple Oral Administration to Lactating Goats. Novartis Crop Protection, AG, Basel, Switzerland. Report No. 14/97, 09.12.1997. Novartis File No. 279202/504.
- Ruembeli, R. 1997.The Metabolism of {Trifluormethyl-phenyl-(U)-14C] CGA 279202 after Multiple Oral Administration to Laying Hens. Norvartis Crop Protection, AG, Basel, Switzerland. Report No. 10/97. 08.12.1997. Novartis file No. 279202/503.
- Ruembeli, R. 1998. The Metabolism of (Glyoxyl-phenyl-(U)-C14) CGA 279202 after Multiple Oral Administration to Laying Hens: Lab Project Number: PR 22/97 :198-98 :CRA 96/017.

Studies submitted to other participants and not reviewed by Canada

none

Result

The evaluation was made by the PMRA ARLA in 2001. A *Review* prepared each for goats (February 19, 2001) and laying hens (February 8, 2001) by the PMRA reviewer Monica Thomas gives detailed information on the points *materials and methods, total radioactive residues, results (extraction and hydrolysis of residues, characterisation/identification of residues, storage stability), final summary, conclusions, definition of the residue of concern, study deficiencies.* The conclusions presented in the respective report on pages 1 - 2 are quoted below.

> *Goats*
> *The metabolism of [trifluoromethyl- Phenyl-(U)-14 C]trifloxystrobin and [glyoxyl-Phenyl-(U)-14 C] trifloxystrobin in goats dosed intraruminally at an average rate of 100 mg/kg feed/day for four consecutive days demonstrated that there was minimal transfer and bioconcentration of the parent compound and the metabolites in milk, muscle, fat, liver and kidneys. Of the total dose applied, an average of 0.07% , 18% and 40% was released in the milk, urine and faeces, respectively, for both labels. Tissue residues accounted for an average of ca. 0.66% of the administered dose. When including the radioactivity in blood, bile, GI tract*
> *and cage wash, 84% of the administered dose was recovered. The parent compound was the predominant residue in milk, fat and GP-labelled faeces while CGA 321113 was the predominant metabolite identified in muscle, kidney, urine, GP-labelled liver and , TFMP-labelled faeces. The taurine conjugate of CGA- 321113 (metabolite L7a) was the predominant metabolite in TFMP-labelled liver. Based on the structures identified, the metabolism of trifloxystrobin appears to have proceeded predominantly via hydrolysis, demethylation, hydroxylation followed by conjugation with taurine, glycine and glucuronic acid. Comparing the metabolites identified, the metabolism of trifloxystrobin in goats appeared to proceed via the same major metabolic pathways as elucidated in the hen and rat, therefore, a swine metabolism study was not required. The analytical method used in the metabolism study briefly involved extraction with acetonitrile:water, liquid-liquid partitioning with hexane followed by cleanup on a RP-18 cartridge column prior to*

*analysis using HPLC and/or 2d-TLC. Microwave assisted extraction was used for the additional release of nonextractable residues in liver. Overall, the analytical method appeared capable of determining the identity of the residue of concern (ROC).*
*Based on the lactating goat metabolism study, the ROC for enforcement and risk assessment purposes was defined as the parent, trifloxystrobin, and the acid metabolite (CGA 321113). However, the liver contribution of metabolite L7a (taurine conjugate of the acid metabolite CGA 321113) will also be included for risk assessment purposes, assuming the same toxicology effect as the parent trifloxystrobin.*
*No study deficiencies were identified.*

*Hens*
*The metabolism of [trifluoromethyl-phenyl-(U)-14 C] trifloxystrobin and [glyoxyl-phenyl-(U)-14 C]trifloxystrobin in hens dosed orally at an average rate of 100 ppm (equivalent to ~2000x the maximum anticipated dietary burden) in the feed for four consecutive days demonstrated that there was minimal transfer and bioconcentration of the parent compound and the metabolites in eggs, liver, fat and attached skin and lean meat. Of the total dose applied, an average of 0.14% and 79% was released in the eggs and excreta, respectively, for both labels.Tissue residues accounted for an average of ca. 1.2% of the administered dose. When including the radioactivity in blood, bile, GI tract and cage wash, 87% of the administered dose was recovered.The parent compound was the predominant residue in fat and skin, lean meat and excreta while CGA 357276 and 1U were the predominant metabolites in egg whites, 2F in egg yolks and L13b in liver. Based on the structures identified, the metabolism of trifloxystrobin appears to have proceeded predominantly via hydrolysis, demethylation, hydroxylation, oxidation and decarboxylation reactions. Comparing the metabolites identified, the metabolism of trifloxystrobin in hens appeared to proceed via the same major metabolic pathways as elucidated in the goat and rat, therefore, a swine metabolism study was not required. The analytical method used in the metabolism study briefly involved extraction with acetonitrile:water, liquid-liquid partitioning with hexane followed by cleanup on a RP-18 cartridge column prior to analysis using HPLC and/or 2d-TLC. Microwave assisted extraction was used for the additional release of nonextractable residues in egg yolks and liver. Overall, the analytical method appeared capable of determining the identity of the residue of concern (ROC).*
*Based on the laying hen metabolism study, the ROC for enforcement and risk assessment purposes was defined as the parent, trifloxystrobin, and the acetic acid metabolite (CGA 321113), since, in the absence of data, it was assumed that the toxicity of the acid metabolite was equivalent to that of the parent compound.*
*No deficiencies were identified.*

<u>*Residue definition animal products for enforcement and risk assessment:*</u> *Trifloxystrobin and CGA 321113, expressed as trifloxystrobin. However, the liver contribution of metabolite L7a (taurine conjugate of CGA 321113) will also be included for risk assessment purposes.*

<u>Comments</u>

The studies sent by the applicant were critical reviewed. The results were presented in a review format including new created tables. It was clearly stated that the metabolite CGA 321113 and its taurine conjugate should be included into the residue definition because of the absence of toxicological data for these compounds.

### 4.3.3 EU

Studies submitted by the applicant and evaluated by the EU

- Ruembeli, R. 1997. The Metabolism of [trifluormethyl-phenyl-(U)-14C} CGA 279292 after Multiple Oral Administration to Lactating Goats. Novartis Crop Protection AG, Basel, Switzerland. Report No.09/97, 27.08.1997, Novartis File No. 279292/270.
- Ruembeli,R. 1997. The Metabolism of [Glyoxyl-phenyl-(U)-14 C] CGA 279202 after Multiple Oral Administration to Lactating Goats. Novartis Crop Protection, AG, Basel, Switzerland. Report No. 14/97, 09.12.1997. Novartis File No. 279202/504.
- Ruembeli, R. 1997.The Metabolism of {Trifluormethyl-phenyl-(U)-14C] CGA 279202 after Multiple Oral Administration to Laying Hens. Norvartis Crop Protection, AG, Basel, Switzerland. Report No. 10/97. 08.12.1997. Novartis file No. 279202/503.
- Ruembeli, R. 1998. The Metabolism of (Glyoxyl-phenyl-(U)-C14) CGA 279202 after Multiple Oral Administration to Laying Hens: Lab Project Number: PR 22/97 :198-98 :CRA 96/017.

Studies submitted to other participants and not reviewed by the EU

none

Result

The evaluation was made by the United Kingdom as EU Rapporteur Member State in April 2000. A monograph entitled *Draft Assessment Report* was prepared (11343c/ECCO/BBA/00). Information on the test conditions, analytical methods, total radioactive residues and characterisation and identification of metabolites and storage stability of residues were presented in detail on pages 258 - 289 under point B.7.2. A summary discussion is presented on page 289 and quoted below.

> *Goats were given daily doses of [14C-TP] Trifloxystrobin at 103.8 mg/kg diet (40N) and [14C-GP] Trifloxystrobin at 100.4 mg/kg diet (39N) for four days. Goats were sacrificed 6 hours after the last dose. Up to 18.9% of the dose was excreted in the urine and 44.5% in faeces. Highest residue levels in milk were 0.121 and 0.153 mg/kg and a plateau was reached after 48 hours. CGA 27902 was the dominant residue.*
> *After sacrifice the highest amount of residue was found in liver and kidney (up to 4.8 and 2.3 mg/kg respectively). Highest residues in muscle and fat were 0.08 and 0.35 mg/kg respectively. Trifloxystrobin and/or CGA 321113 were dominant in muscle, fat, kidney and liver. The taurine and glycine conjugates of CGA 321113 (L7a (CGA 321113 taurine conjugate) and L7b (CGA 321113 glycine conjugate)) were also major metabolites in liver. Other identified metabolites did not individually exceed 5% TRR. Identified metabolites comprised up to 93.5% TRR (milk), 84.5% (muscle), 93% (fat), 90% (kidney) and 60% (liver). There was some evidence of cleavage of the molecule between to two phenyl rings with the formation of metabolites 11U and 12U (CGA 354870). The goat metabolites were all identified in the rat metabolism studies.*
>
> *Hens were given daily doses of [14C-TP] Trifloxystrobin at 100.7 mg/kg diet (1060N) and [14C-GP] Trifloxystrobin at 98.9 mg/kg diet (1041N) for four days and were sacrificed 6 hours following the last dose. Up to 78.8% of the of the dose was excreted. A plateau was not reached in egg yolk. Residue levels appeared to be increasing rapidly at the end of the study. After sacrifice the highest residues were found in kidney, liver, peritoneal fat and fat + skin (up to 12.6, 8.6, 2.7 and 1.8 mg/kg respectively). Highest residues in egg white, egg yolk and muscle were 0.21, 3.01 and 0.35 mg/kg respectively.*
> *Parent compound predominated in muscle and fat + skin, accounting for up to 27.8 and 55.3% TRR respectively. Major metabolites were CGA 321113, 1U and 6U (egg white), 2F (NOA*

*405637) (fat + skin, muscle), 12U (CGA 354870) (muscle) and L13b & L14 (liver). Other identified metabolites did not individually exceed 8% TRR.. Unextracted residues were up to 79% and 35% TRR in liver and egg yolk respectively, however residues in poultry products are highly unlikely to be determinable at N rate exposure.*
*The hen metabolites were all identified in the rat metabolism studies, except for the following:*
*Met EW1b, Met L13b, Met EW11, Met L24, EGR10a-c, EGR8, EGR1, EX5.*
*These metabolites are not considered to be of toxicological concern at the levels found.*

*Based on the metabolism data submitted for goats and hens, residues in products of animal origin should be defined as the sum of parent + CGA 321113 (acid). Metabolism was more extensive in some tissues, however metabolites were not considered to be of toxicological concern at the levels present. Residues in poultry products as a result of predicted N Rate exposure are highly unlikely to be determinable. CGA 321113 was found in the rat and is considered of no greater toxicological concern than the parent molecule.*

*Residue definition animal products: Trifloxystrobin and CGA 321113, expressed as trifloxystrobin*

Comments

The studies sent by the applicant were critical reviewed. The report (in monograph format) is very detailed. Tables of applicant's dossier were copied after checking for correctness. The EU report was partly used by JMPR for evaluation of this subject.

### 4.3.4 USA

Studies submitted by the applicant and evaluated by the USA

- Ruembeli, R. 1997. The Metabolism of [trifluormethyl-phenyl-(U)-14C} CGA 279292 after Multiple Oral Administration to Lactating Goats. Novartis Crop Protection AG, Basel, Switzerland. Report No.09/97, 27.08.1997, Novartis File No. 279292/270.
- Ruembeli,R. 1997. The Metabolism of [Glyoxyl-phenyl-(U)-14 C] CGA 279202 after Multiple Oral Administration to Lactating Goats. Novartis Crop Protection, AG, Basel, Switzerland. Report No. 14/97, 09.12.1997. Novartis File No. 279202/504.
- Ruembeli, R. 1997.The Metabolism of {Trifluormethyl-phenyl-(U)-14C] CGA 279202 after Multiple Oral Administration to Laying Hens. Norvartis Crop Protection, AG, Basel, Switzerland. Report No. 10/97. 08.12.1997. Novartis file No. 279202/503.
- Ruembeli, R. 1998. The Metabolism of (Glyoxyl-phenyl-(U)-C14) CGA 279202 after Multiple Oral Administration to Laying Hens: Lab Project Number: PR 22/97 :198-98 :CRA 96/017.

Studies submitted to other participants and not reviewed by the USA
none

Result

The evaluation was made by the US EPA in 1999. A *Memorandum (PP#8F04955, 7/22/99 review, DP Barcodes D257888 and D254208)* including the metabolism of trifloxystrobin in ruminants and poultry was prepared by the reviewer Fred Ives. Information on the test conditions, analytical methods, total radioactive residues, characterisation/identification of metabolites and storage stability of residues were presented in detail on pages 98- 134 under points 18.- 20. Summary discussions were presented for goat metabolism on page 113 and for poultry metabolism on page 134. Both are quoted below.

*Goats*

*The qualitative nature of the residue in ruminants is adequately understood. Following oral administration of [TFMP-14C]trifloxystrobin or [GP-14C]trifloxystrobin to goats at -100 ppm (-23x the maximum theoretical dietary burden) in the diet for 4 days, total radioactive residues were 0.015-0.153 ppm in milk, 2.626-5.249 ppm in liver, 1.746-2.939 ppm in kidney, 0.044-0.095 ppm in muscle, and 0.148-0.525 ppm in fat.*

*Approximately 62-82% TRR were characterized/identified in milk and tissues. Trifloxystrobin was identified in all matrices. It was a major residue in milk, muscle, and fat (16.8-71.8% TRR, 0.010-0.242 ppm) but a minor metabolite in liver and kidney (1.5-2.1% TRR, 0.029-0.102 ppm). CGA-321113 was a major metabolite in muscle, liver, and kidney (10.1-64.4% TRR, 0.029-1.502 ppm) but a minor metabolite in milk and fat (2.9-9.3% TRR, 0.002-0.033 ppm). MET L7a was identified in all matrices, except fat, at 0.2-20.3% TRR (<0.001-0.980 ppm). Additional metabolites identified at levels <10% TRR were: CGA-166988 and MET* 1U, MET 2U, MET 6U, MET 11U, MET 12U, MET 2F, MET 3F, MET 1G, and MET L7b.

*Hens*

*The qualitative nature of the residue in poultry is adequately understood. Following oral administration of [TFMP-14C]trifloxystrobin or [GP-14C]trifloxystrobin to hens at -100 ppm (-8,000x the maximum theoretical dietary burden) in the diet for 4 days, total radioactive residues were <0.0003-0.563 ppm in egg white, <0.0006-3.607 ppm in egg yolk, 3.849-8.576 ppm in liver, 0.126-0.347 ppm in muscle, 0.841-2.746 ppm in peritoneal fat, and 0.656-1.783 ppm in skin with attached fat.*

*Approximately 30-86% TRR were characterized/identified in eggs and tissues. Trifloxystrobin was identified in all matrices except egg white. It was a major metabolite in egg yolk (TFMP label only), muscle, and fat (4.1-53.0% TRR, 0.007-0.785 ppm) but a minor metabolite in egg yolk (GP label only) and liver (0.2-1.1% TRR, 0.002-0.067 ppm). CGA-321113 was a major metabolite in egg white (10.3-19.5% TRR, 0.008-0.024 ppm) but a minor metabolite in other matrices (0.3-4.6% TRR, 0.003-0.290 ppm). MET 1U was identified in egg white only at 4.1-1.7% TRR (0.005-0.017 ppm); the presence of CGA-357276 in TFMP-label egg white at 28.9% TRR (0.036 ppm) was believed to be a result of degradation of MET 1U or a conjugate of MET 1U during sample workup. MET 2F was identified in all matrices except egg white, at 1.3-14.3% TRR (0.009-0.308 ppm). MET L13b was identified in all matrices, at 0.5-11.2% TRR (0.002-0.707 ppm). Additional metabolites identified at levels <10% TRR were: CGA 166988, CGA-357276, NOA-417076, MET 2U, MET 3U, MET 4U, MET 5U, MET 6U, MET 12U, MET 3F, MET 1G, MET EW1b, MET EW11, and MET L24. The major metabolites in egg yolk, comprising 4.4-35.2% TRR, could not be identified.*

*Because residues of trifloxystrobin would be expected to be <0.01 ppm at a 10x feeding level, the Agency concludes that the there is no reasonable expectation of finite residues of trifloxystrobin in poultry commodities resulting from the proposed uses.*

*Animal metabolism conclusions:*

*The HED MARC determined June 15, 1999 that the qualitative nature of the residue in animals is adequately understood based on acceptable studies conducted on goats and laying hens. The Committee determined that the total toxic residues for animals, both for regulatory and risk assessment purposes, is trifloxystrobin and the free form of its acid metabolite CGA321113. Additionally, the liver contribution for metabolite L7a (taurine conjugate of trifloxystrobin) is to be included for risk assessment purposes, assuming equal toxicity as trifloxystrobin. Although the petitioner has not proposed tolerances for animal commodities, based on the ruminant feeding study reviewed herein, tolerances are required for residues of concern in milk; and the meat, fat and meat byproducts of cattle, goats, hogs, horses and sheep.*

*Residue definition animal products for enforcement and risk assessment: Trifloxystrobin and CGA 321113, expressed as trifloxystrobin. However, the liver contribution of metabolite L7a (taurine conjugate of CGA 321113) will also be included for risk assessment purposes*

Comments

The studies sent by the applicant were critical reviewed. The results were presented in a report in review format including new created tables. Although the petitioner has not proposed tolerances for animal commodities, it was clearly stated that, because MRLs are required for animal commodities, a residue definition for animal products is needed. The reviewer recommends to include the metabolite CGA 321113 and its taurine conjugate into the residue definition.

### 4.3.5 JMPR

Studies submitted by the applicant and evaluated by the JMPR

- Ruembeli, R. 1997. The Metabolism of [trifluormethyl-phenyl-(U)-14C} CGA 279292 after Multiple Oral Administration to Lactating Goats. Novartis Crop Protection AG, Basel, Switzerland. Report No.09/97, 27.08.1997, Novartis File No. 279292/270.
- Ruembeli,R. 1997. The Metabolism of [Glyoxyl-phenyl-(U)-14 C] CGA 279202 after Multiple Oral Administration to Lactating Goats. Novartis Crop Protection, AG, Basel, Switzerland. Report No. 14/97, 09.12.1997. Novartis File No. 279202/504.
- Ruembeli, R. 1997.The Metabolism of {Trifluormethyl-phenyl-(U)-14C] CGA 279202 after Multiple Oral Administration to Laying Hens. Norvartis Crop Protection, AG, Basel, Switzerland. Report No. 10/97. 08.12.1997. Novartis file No. 279202/503.
- Ruembeli, R. 1998. The Metabolism of (Glyoxyl-phenyl-(U)-C14) CGA 279202 after Multiple Oral Administration to Laying Hens: Lab Project Number: PR 22/97 :198-98 :CRA 96/017.

Studies submitted to other participants and not reviewed by JMPR
none

Result

The evaluation was made by the FAO Panel of the JMPR in 2004. A detailed *Evaluation* including the metabolism of trifloxystrobin in ruminants and poultry was prepared. Information on the test conditions, analytical methods, total radioactive residues, characterisation/identification of metabolites and storage stability of residues were presented in detail under point animal metabolism. The reports prepared by Australia, Canada, EU and the USA as well as the applicant's dossier were used. An appraisal including the conclusions is presented for farm animal metabolism and is quoted below.

*Lactating goats were given daily doses of [glyoxyl-phenyl-U-$^{14}$C]-trifloxystrobin and [trifluoromethyl-phenyl-U-$^{14}$C]-trifloxystrobin at the equivalent of 100 ppm in the diet for four days and slaughtered 6 hours after the last dose. Up to 20% of the applied dose was excreted in the urine and 45% in faeces. 0.05–0.08% of the total dose was eliminated via milk which corresponds to about 0.1 mg/kg trifloxystrobin equivalents and a plateau was reached after 48 hours.*

*Major tissue residues were found in liver, bile and kidney accounting for 0.28-0.57%, 0.07-0.24% and 0.026-0.052% of the applied dose respectively. These values correspond to 2.6-5.2, 29-77 and*

*1.7-2.9 mg/kg as trifloxystrobin equivalents. Lower residues were found in fat, muscle and blood. The main components of the residue were the parent compound, its carboxylic acid CGA 321113 (chemical name:(E,E)-Methoxyimino-{2-[1-(3-trifluoromethyl-phenyl)-ethylideneaminooxy-methyl]-phenyl}-acetic acid) and taurine and glycine conjugates of CGA 321113. The amino acid conjugates were the principal residue components in the liver (up to 28% TRR). These metabolites were not considered to be of toxicological concern. CGA 321113 was the main radioactive residue in muscle (up to 57% TRR) and kidney (up to 74% TRR), and trifloxystrobin was the principal component in milk (up to 74% TRR) and fat (up to 82% TRR).*

*Hens were given daily doses of [glyoxyl-phenyl-U-$^{14}$C]-trifloxystrobin or [trifluoromethyl-phenyl-U-$^{14}$C]-trifloxystrobin at the equivalent of 100 ppm in the diet for four days and killed 6 hours after the last dose. Up to 0.16% and 87% of the applied dose were eliminated in the eggs and excreta respectively. A plateau was not reached in egg yolk. Residue levels appeared to be increasing rapidly at the end of the study.*

*Eggs contained 0.1 to 0.2% of the applied dose. The maximum concentration in egg white was 0.56 mg/kg and in egg yolk 2.3 mg/kg as trifloxystrobin equivalents.*

*Lean meat contained 0.11-0.22% of the dose (0.13-0.35 mg/kg trifloxystrobin equivalents), skin and attached fat 0.14-0.39% (0.8-1.8 mg/kg trifloxystrobin equivalents), peritoneal fat, 0.07-0.21% (1.9-2.7 mg/kg trifloxystrobin equivalents), kidney 0.11-0.25% (6-13 mg/kg trifloxystrobin equivalents), and liver 0.28-0.68% (3.8-8.6 mg/kg trifloxystrobin equivalents). Total recovered radioactivity (including intestinal and gizzard radioactivity) was between 78 and 91%.*

*Characterisation of the radioactive tissue residues revealed that parent trifloxystrobin was a major residue in muscle (up to 28% of TRR), fat and skin (up to 55% of TRR), and egg yolk (up to 9% of TRR) of laying hens. The carboxylic acid derivative of trifloxystrobin (CGA 321113) was the major residue in egg white (up to 26% of TRR) and liver (up to 5.1% of TRR).*

*Residue definition animal products for enforcement and risk assessment: Trifloxystrobin and CGA 321113, expressed as trifloxystrobin.*

Comments

The studies sent by the applicant were critical reviewed. It was stated that the liver metabolite L7a (taurine conjugate of CGA 321113) was not considered to be of toxicological concern and was not included into the residue definition for risk assessment purposes.

### 4.3.6 Results - farm animal metabolism

The participants of the work sharing project received the same studies. All studies were included into the specific evaluations.

The results of each specific evaluation – resulting in the residue definition - are in general identical. The residue of concern for animal commodities both for enforcement and risk assessment was defined as the parent and the acetic acid metabolite (CGA 321113).

Canada and the USA recommended to include also the taurine conjugate of CGA 321113 (L7a) in the residue definition for risk assessment. Australia, the EU and the JMPR decided, howerver, not to include the metabolite L7a into the residue definition.

## 4.4 Plant metabolism

### 4.4.1 Australia

Studies submitted by the applicant and evaluated by Australia

- Gross, D. 1997. Distribution and degradation of CGA 279202 in field grown spring wheat after treatment with (CF3-phenyl-(U)-) CGA 279202 labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR15/97, Edition Number: MO-01-015761. Unpublished.
- Gross, D. 1997. Metabolism of [CF3-phenyl-(U)-14C]CGA 279202 in field grown spring wheat. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR18/97, Edition Number: MO-01-001658. Unpublished.
- Kiffe, M. 1997. Metabolism of CGA 279202 in greenhouse grown apple trees after application of [trifluoromethyl-phenyl-(U)-14C]labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR12/97, Edition Number: MO-01-010615. Unpublished.
- Kiffe, M. 1997. Metabolism of CGA 279202 in greenhouse grown apple trees after application of [glyoxyl-phenyl-(U)-14C] labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR13/97, Edition Number: MO-01-001686. Unpublished.
- Stingelin, J. 1997. Behaviour and metabolism of CGA 279202 in field grown spring wheat after treatment with [Glyoxyl-Phenyl-(U)-14C] labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR04/97, Edition Number: MO-01-012305. Unpublished.
- Stingelin, J. 1997. Metabolism of [glyoxyl-phenyl-(U)-14C] CGA 279202 in field grown spring wheat. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR25/97, Edition Number: MO-01-001675. Unpublished.
- Stingelin, J. 1997. Behaviour and metabolism of CGA 279202 in greenhouse grown cucumbers after treatment with [CF3-phenyl-(U)-14C]labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR23/97, Edition Number: MO-01-001692. Unpublished.
- Stingelin, J. 1997. Behaviour and metabolism of CGA 279202 in greenhouse grown cucumbers after treatment with [glyoxyl-phenyl-(U)-14C]labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR22/97, Edition Number: MO-01-001695. Unpublished.

Studies submitted to other participants and not reviewed by Australia

- Kiffe, M. 2000. Behaviour and metabolism of [glyoxyl-phenyl-(U)-14C] CGA 279202 in field grown sugar beets. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 99MK10, Edition Number: MO-01-015673. Unpublished.
- Kiffe, M. 2000. Behaviour and metabolism of [trifluoromethyl-phenyl-(U)-14C] CGA 279202 in field grown sugar beets. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 99MK09, Edition Number: MO-01-015671. Unpublished.
- Reiner, H. and Bongartz, R. 2002. Metabolism of [trifluoromethyl-phenyl-UL-14C]trifloxystrobin in spring wheat. Bayer AG, Bayer CropScience, Monheim, Germany. Bayer CropScience AG, Report No.: MR-027/02, Edition Number: MO-02-009343. Unpublished.

- Reiner, H. and Bongartz, R. 2002. Metabolism of [glyoxyl-phenyl-UL-14C]trifloxystrobin in spring wheat. Bayer AG, Bayer CropScience, Monheim, Germany. Bayer CropScience AG, Report No.: MR-028/02, Edition Number: MO-02-009727. Unpublished.
- Rezaaiyan, R. 1997. Uptake and metabolism of CGA-279202 in field grown peanuts after spray treatment with phenyl (A)-14C-CGA-279202 and phenyl (B)-14C-CGA-279202. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97084, Edition Number: MO-01-016005. Unpublished.

Result:

The evaluation was made by the APVMA in 2000. A monograph entitled *Residues Evaluation Report* (File No. P53871) was prepared. Information on the test conditions, analytical methods, total radioactive residues, characterisation/identification of metabolites and storage stability of residues were presented in detail on pages 17 and 18 (apples), 19 (cucumber), 20 – 24 (wheat) under point 4.4. A summary discussion is presented on pages 4 - 5 and quoted below.

> *Metabolism studies have been conducted in apples, cucumbers and wheat using two 14C-radiolabelled compounds, [glyoxylphenyl-U-14C]-trifloxystrobin and [trifluoromethylphenyl-U-14C]-trifloxystrobin.*
> *Data from apple metabolism studies indicated that trifloxystrobin penetration into fruit tissues was relatively low. Approximately 82 to 87% of the applied radioactivity was located on the surface of the apple (14 DAT) and only about 18% of the radioactivity was present in the fruit.*
> *Studies with wheat showed that trifloxystrobin penetration in wheat plants was quite rapid, with TRR reaching ~ 15% within the first 24 hours, ~ 30% within 3 days, and ~ 44% in 14 days. Characterisation of the surface radioactivity in wheat revealed that trifloxystrobin is relatively stable to photodegradation, with the parent compound comprising up to 80 % of the surface radioactivity after 14 days.*
> *In contrast to the radioactivity found on the crop surface, penetrated radioactivity appears to undergo quite rapid degradation. In wheat, the trifloxystrobin concentration declined exponentially, with an apparent half-life of 12 hours. Characterisation of the metabolite profile in plants is complex due to isomerisation of the parent compound and its metabolites. Up to 35 metabolite fractions were found in wheat, most of which comprised less than 1% of the TRR. The number of metabolite fractions in apples and cucumbers was significantly lower than that found in wheat. It was postulated that this observation may be due to the longer interval between application and harvest in wheat, compared to that of apples and cucumbers; the higher levels of cytochrome P-450 activity in cereal crops compared to non-cereal crops and limited penetration of trifloxystrobin through the waxy surface of apples and cucumbers.*
> *Irrespective of the observed differences in the number of metabolite fractions present in different plant species, the metabolic pathways for each crop are comparable. The primary residue component is the parent compound; trifloxystrobin and its isomers (CGA 331409, CGA 357262 and CGA 357261) comprised ~92 % of the residues in apples (14 DAT), with the remainder of the residues being due to NOA 417076 and its isomers (0.1 to 0.3 %), sugar conjugates of NOA 417076 and its isomers (1.0 to 1.5 %), and unidentified compounds (3.3 to 4.8 %). In cucumbers (leaves and fruit), the residue was comprised of trifloxystrobin (80 to 93 %), isomers of trifloxystrobin (2.3 to 3.8 %), and the demethylated derivative of trifloxystrobin, CGA 321113 (0.9 to 4.2 %).*
> *Based on the studies conducted on wheat, apples and cucumbers, the metabolism of trifloxystrobin occurs primarily via:*
> - *isomerisation to CGA 331409 (EZ-isomer), CGA 357262 (ZZ-isomer) and CGA 357261 (ZE-isomer);*
> - *cleavage of the methyl ester group to form CGA 321113;*

- *hydroxylation of the trifluoromethylphenyl group to form NOA 414412 and NOA 417076;*
- *oxidation of the 2-ethylideneaminooxymethyl group to the corresponding carboxylic acids to form the isomeric metabolites NOA413161 and NOA 413163; and*
- *sugar conjugation of hydroxylated metabolites, to give their water-soluble derivatives.*

*Residue definition plant commodities: Trifloxystrobin and CGA 321113, expressed as trifloxystrobin*

Comments

The studies sent by the applicant were critical reviewed. The results were presented in a report in a monograph format including new created tables (not a copy of applicant's dossier). The Australian report was partly used by the JMPR for preparing the evaluation in this subject.

Australia evaluated 2 studies on apples, 2 on cucumbers and 4 on wheat. Because no intended uses exist in Australia on root crops and oil seeds, the metabolism studies on peanuts and sugar beet were not submitted by the applicant. The new wheat studies MR-027/02 and MR-028/02 by Reiner and Bongartz (2002) were finished later than the Australian evaluation was prepared and could not be submitted.

### 4.4.2 Canada

Studies submitted by the applicant and evaluated by Canada

- Gross, D. 1997. Distribution and degradation of CGA 279202 in field grown spring wheat after treatment with (CF3-phenyl-(U)-) CGA 279202 labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR15/97, Edition Number: MO-01-015761. Unpublished.
- Gross, D. 1997. Metabolism of [CF3-phenyl-(U)-14C]CGA 279202 in field grown spring wheat. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR18/97, Edition Number: MO-01-001658. Unpublished.
- Kiffe, M. 1997. Metabolism of CGA 279202 in greenhouse grown apple trees after application of [trifluoromethyl-phenyl-(U)-14C]labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR12/97, Edition Number: MO-01-010615. Unpublished.
- Kiffe, M. 1997. Metabolism of CGA 279202 in greenhouse grown apple trees after application of [glyoxyl-phenyl-(U)-14C] labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR13/97, Edition Number: MO-01-001686. Unpublished.
- Stingelin, J. 1997. Metabolism of [glyoxyl-phenyl-(U)-14C] CGA 279202 in field grown spring wheat. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR25/97, Edition Number: MO-01-001675. Unpublished.
- Stingelin, J. 1997. Behaviour and metabolism of CGA 279202 in greenhouse grown cucumbers after treatment with [CF3-phenyl-(U)-14C]labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR23/97, Edition Number: MO-01-001692. Unpublished.
- Stingelin, J. 1997. Behaviour and metabolism of CGA 279202 in greenhouse grown cucumbers after treatment with [glyoxyl-phenyl-(U)-14C]labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR22/97, Edition Number: MO-01-001695. Unpublished.

Studies submitted to other participants and not reviewed by Canada

- Kiffe, M. 2000. Behaviour and metabolism of [glyoxyl-phenyl-(U)-14C] CGA 279202 in field grown sugar beets. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 99MK10, Edition Number: MO-01-015673. Unpublished.
- Kiffe, M. 2000. Behaviour and metabolism of [trifluoromethyl-phenyl-(U)-14C] CGA 279202 in field grown sugar beets. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 99MK09, Edition Number: MO-01-015671. Unpublished.
- Reiner, H. and Bongartz, R. 2002. Metabolism of [trifluoromethyl-phenyl-UL-14C]trifloxystrobin in spring wheat. Bayer AG, Bayer CropScience, Monheim, Germany. Bayer CropScience AG, Report No.: MR-027/02, Edition Number: MO-02-009343. Unpublished.
- Reiner, H. and Bongartz, R. 2002. Metabolism of [glyoxyl-phenyl-UL-14C]trifloxystrobin in spring wheat. Bayer AG, Bayer CropScience, Monheim, Germany. Bayer CropScience AG, Report No.: MR-028/02, Edition Number: MO-02-009727. Unpublished.
- Rezaaiyan, R. 1997. Uptake and metabolism of CGA-279202 in field grown peanuts after spray treatment with phenyl (A)-14C-CGA-279202 and phenyl (B)-14C-CGA-279202. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97084, Edition Number: MO-01-016005. Unpublished.
- Stingelin, J. 1997. Behaviour and metabolism of CGA 279202 in field grown spring wheat after treatment with [Glyoxyl-Phenyl-(U)-14C] labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR04/97, Edition Number: MO-01-012305. Unpublished.

Result

The evaluation was made by the PMRA ARLA in 2001. A *Review* prepared each for apples (March 25, 2001), cucumber (March 25, 2001) and wheat (March 25, 2001) by the reviewer Monica Thomas gives detailed information on the points *materials and methods, total radioactive residues, results (extraction and hydrolysis of residues, characterisation/identification of residues, storage stability), final summary, conclusions, definition of the residue of concern and study deficiencies.* The conclusions presented in the respective reports are quoted below.

> *Apples*
>
> *Total radioactive residues (TRRs) in apples and foliage following four spray applications with TFMP-label or GP-label trifloxystrobin, formulated as WG50, resulting in a maximum seasonal application rate of 400 g ai/ha, ranged from 0.8-1.3 ppm and 46.4-72.2 ppm, respectively, indicating that the majority of the residues within the foliage did not translocate to the fruit. The majority of the radioactivity in the apple matrices was extractable with ACN:water. The nonextractable residues remaining after microwave extraction with 1-propanol:water were low. Almost all of the extractable radioactivity was identified. Trifloxystrobin was the predominant residue in the surface rinses, apple peel and flesh (TFMP-label only) and foliage. Although trifloxystrobin was identified in GP-label flesh, the majority of the radioactivity in this matrix remained at the origin in TLC analysis. The penetration study demonstrated that trifloxystrobin is not systemic in nature as the majority of the applied radioactivity was located on the peel, with minimal translocation and bioconcentration into the flesh. The overall metabolic pathway proceeds via cis/trans isomerization of trifloxystrobin, hydrolysis of the methyl ester to form the acid metabolite, CGA 321113, and its isomer and/or cis/trans isomerization of the acid metabolite to form CGA 373466, oxidation of the trifluoromethyl ring in position 4 and hydrolysis of the oxime methyl ether or the acetic acid methyl ester to form NOA 417076 and cis/trans isomers II22a and II22b, with subsequent conjugation as O-glycoside to the metabolite II10a and isomers II8a and II11a and cleavage of the ethylideneaminooxymethyl group of CGA 321113 to form CGA 320299 via a speculated intermediate (GP-label specific).*
>
> *According to the apple metabolism study, the Residue of Concern (ROC) for enforcement and risk assessment purposes was defined as the parent, trifloxystrobin and the acetic acid metabolite*

*(CGA 321113), since, in the absence of adequate data, the metabolite was deemed to be of equivalent toxicity to the parent.*
*No deficiencies were identified.*

*Cucumbers*
*Total radioactive residues (TRRs) in small and large cucumbers and foliage, following three spray applications of 14 C-labelled trifloxystrobin, formulated as WG50, resulting in a maximum seasonal application rate of 940 g ai/ha (equivalent to ~3.35X the US label rate), ranged from 0.59-2.29 ppm, 0.19-0.53 ppm and 16.6-34.7 ppm, respectively. The metabolite distribution indicated that the majority of the residues did not translocate from the foliage to the fruit, rather they are a result of direct application of the fungicide, and that lower residues in the large fruit can be attributed to growth dilution. The majority of the radioactivity in the cucumber matrices was extractable with ACN:water (8:2, v:v). Almost all of the extractable radioactivity was identified, with trifloxystrobin representing the predominant residue in the fruits and foliage. The overall metabolic pathway proceeds via cis/trans isomerization of trifloxystrobin, hydrolysis of the methyl ester to form the acid metabolite, CGA 321113, oxidation of the trifluoromethyl-phenyl ring and hydrolysis of the oxime methyl ether or the acetic acid methyl ester with subsequent conjugation as O-glycoside. The metabolic pathway also involves the oxidation of the methyl group at the ethylideneaminooxymethyl bridge and hydrolysis of the acetic acid methyl ester with subsequent conjugation as the O-glycoside.*
*According to the cucumber metabolism study, the Residue of Concern (ROC) for enforcement and risk assessment purposes, was defined as the parent, trifloxystrobin and the acetic acid metabolite (CGA 321113), since, in the absence of adequate data, the acid metabolite was deemed to be of equivalent toxicity to the parent.*
*No deficiencies were identified.*

*Wheat*
*Total radioactive residues (TRRs) in mature grains, husks and straw following two spray applications with TFMP-label or GP-label trifloxystrobin, formulated as WG50, resulting in a maximum seasonal application rate of 500 g ai/ha (equivalent to ~3X the registered rate on the US Stratego label) and harvested 52 days following the second application, ranged from 0.020-0.099 ppm, 0.142-0.780 ppm and 3.85-5.48 ppm, respectively. When treated with a single application of 500 g ai/ha and harvested 49 days post-treatment, TRRs in TFMP-labelled grains, husks and straw were 0.056 ppm, 1.7 ppm and 7.49 ppm, respectively. The low residue levels in grain are an indication of minimal translocation from the leaf to the grain. The majority of the radioactivity in the immature and mature wheat matrices was extractable with ACN:water. Microwave assisted extraction using 1-propanol:water released an additional percentage of the TRRs. The nonextractable residues remaining after cold and hot extraction were low. Almost all of the extractable radioactivity was either identified or characterized. Trifloxystrobin and its isomers were not identified in TFMP-labelled grain, while in GP-labelled grain, trifloxystrobin and its isomers were present at very low levels. In stalk, husks and straw, trifloxystrobin and its isomers were identified at low levels, demonstrating that the parent compound was extensively metabolized. The penetration study demonstrated that translocation and penetration of trifloxystrobin into the wheat shoots was relatively slow, however, metabolism was rapid and extensive. The overall metabolic pathway proceeds via hydrolysis of the methyl ester to form the acid metabolite (CGA 321113), hydroxylation of TFMP ring to metabolite NOA 414412, oxidation of the aminooxymethyl group on the bridge to form I10 and I12 and subsequently NOA 413161 and NOA 413163, sugar conjugation of metabolites I10, I12 and NOA 414412 and further breakdown of the methoxyimino acetic acid side chain in combination with methyl group oxidation to form phthalide. The registrant concluded that cis/trans isomerization of CGA 279202 to form CGA 357261, CGA 357262 and CGA 331409 was a very minor pathway.*

*Based on the wheat metabolism study, the Residue of Concern for enforcement and risk assessment purposes was defined as the parent, trifloxystrobin, and the acetic acid metabolite (CGA 321113), since in the absence of adequate data, the metabolite was deemed to be of equivalent toxicity to the parent.*
*No deficiencies were identified.*

*<u>Residue definition plant commodities:</u> Trifloxystrobin and CGA 321113, expressed as trifloxystrobin*

<u>Comments</u>

The studies sent by the applicant were critical reviewed. The results were presented in a review format including new created tables (not a copy of applicant's dossier).

Canada evaluated 2 studies on apples, 2 on cucumbers and 3 on wheat. The metabolism studies on peanuts and sugar beet were not submitted by the applicant. The new wheat studies MR-027/02 and MR-028/02 by Reiner and Bongartz (2002) were finished later than the Canadian evaluation prepared and could not be submitted.

### 4.4.3 EU

<u>Studies submitted by the applicant and evaluated by the EU</u>

- Gross, D. 1997. Distribution and degradation of CGA 279202 in field grown spring wheat after treatment with (CF3-phenyl-(U)-) CGA 279202 labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR15/97, Edition Number: MO-01-015761. Unpublished.
- Gross, D. 1997. Metabolism of [CF3-phenyl-(U)-14C]CGA 279202 in field grown spring wheat. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR18/97, Edition Number: MO-01-001658. Unpublished.
- Kiffe, M. 1997. Metabolism of CGA 279202 in greenhouse grown apple trees after application of [trifluoromethyl-phenyl-(U)-14C]labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR12/97, Edition Number: MO-01-010615. Unpublished.
- Kiffe, M. 1997. Metabolism of CGA 279202 in greenhouse grown apple trees after application of [glyoxyl-phenyl-(U)-14C] labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR13/97, Edition Number: MO-01-001686. Unpublished.
- Stingelin, J. 1997. Behaviour and metabolism of CGA 279202 in field grown spring wheat after treatment with [Glyoxyl-Phenyl-(U)-14C] labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR04/97, Edition Number: MO-01-012305. Unpublished.
- Stingelin, J. 1997. Metabolism of [glyoxyl-phenyl-(U)-14C] CGA 279202 in field grown spring wheat. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR25/97, Edition Number: MO-01-001675. Unpublished.
- Stingelin, J. 1997. Behaviour and metabolism of CGA 279202 in greenhouse grown cucumbers after treatment with [CF3-phenyl-(U)-14C]labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR23/97, Edition Number: MO-01-001692. Unpublished.
- Stingelin, J. 1997. Behaviour and metabolism of CGA 279202 in greenhouse grown cucumbers after treatment with [glyoxyl-phenyl-(U)-14C]labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR22/97, Edition Number: MO-01-001695. Unpublished.

Studies submitted to other participants and not reviewed by the EU

- Kiffe, M. 2000. Behaviour and metabolism of [glyoxyl-phenyl-(U)-14C] CGA 279202 in field grown sugar beets. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 99MK10, Edition Number: MO-01-015673. Unpublished.
- Kiffe, M. 2000. Behaviour and metabolism of [trifluoromethyl-phenyl-(U)-14C] CGA 279202 in field grown sugar beets. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 99MK09, Edition Number: MO-01-015671. Unpublished.
- Reiner, H. and Bongartz, R. 2002. Metabolism of [trifluoromethyl-phenyl-UL-14C]trifloxystrobin in spring wheat. Bayer AG, Bayer CropScience, Monheim, Germany. Bayer CropScience AG, Report No.: MR-027/02, Edition Number: MO-02-009343. Unpublished.
- Reiner, H. and Bongartz, R. 2002. Metabolism of [glyoxyl-phenyl-UL-14C]trifloxystrobin in spring wheat. Bayer AG, Bayer CropScience, Monheim, Germany. Bayer CropScience AG, Report No.: MR-028/02, Edition Number: MO-02-009727. Unpublished.
- Rezaaiyan, R. 1997. Uptake and metabolism of CGA-279202 in field grown peanuts after spray treatment with phenyl (A)-14C-CGA-279202 and phenyl (B)-14C-CGA-279202. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97084, Edition Number: MO-01-016005. Unpublished.

Result

The evaluation was made by the United Kingdom as EU Rapporteur Member State in April 2000. A monograph entitled *Draft Assessment Report* was prepared (11343c/ECCO/BBA/00). Information on the test conditions, analytical methods, total radioactive residues, characterisation/identification of metabolites and storage stability of residues were presented in detail on pages 205 - 257 under point B.7.1. A summary discussion is presented on pages 254 – 256 and quoted below.

> *Metabolism of trifloxystrobin was investigated in wheat, apples and cucumber by applying [14C-GP] trifloxystrobin and [14C-GP] trifloxystrobin as a foliar application to wheat at a rate of 250 g a.s./ha (N), to apples at a rate of 100 g a.s/ha (1.3N) and to cucumbers at a rate of 312.5 g a.s/ha (1.7N). At harvest, total 14C mg/kg residues (expressed as parent equivalent) were up to 5.5 (wheat forage), 0.1 (wheat grain), 0.78 (wheat husk), 5.5 (wheat straw), 1.3 (apple) and 1.99 (cucumber, the largest residues were associated with the smallest fruit).*
>
> *In apples and cucumbers, on extraction and characterisation the parent compound predominated, representing up to 76% and 85% of the TRR respectively. Trifloxystrobin isomers (CGA 357261, 357262 & 331409) accounted for up to 10% in apples and 4% in cucumbers. Several other metabolites were identified ( II 22 a-c, I12 & I14 (NOA 414412), their corresponding sugar conjugates II10a, II8 & II11a (isomer of II10a); II11, and the acid metabolite CGA 321113), which individually did not represent more than 4%TRR.*
>
> *In apples and cucumbers, metabolism proceeded along cis/trans isomerisation; hydrolysis of the methyl ester and subsequent hydroxylation of the trifluoromethyl benzene ring; and oxidation of the methyl group on the ethylideneaminooxymethyl bridge with subsequent conjugation of the metabolites formed.*
>
> *In wheat, trifloxystrobin was extensively metabolised. Parent compound only accounted for up to 3.9% TRR (forage), 1.3% (grain) and 2.2% (straw). The remaining three isomers of trifloxystrobin represented a total of up to 1.8%, 1.2% and 2.1% TRR in forage, grain and straw respectively. The following major metabolites were present: I10 & I12 and their respective sugar conjugates II8 & II11 accounted for, in total, up to 23.7% TRR (forage), 9% (grain) & 10.7% (straw); I5 (NOA 413161) & I6 (NOA 413163) accounted for up to 7.4% TRR (forage),10.1% (grain) & 5.6% (straw); I14 (NOA 414412) & its sugar conjugate represented up to 8.1% TRR (forage), 5.3% (grain) and 7.7% (straw).*

*In wheat, up to 47% (grain) and 46% (straw) remained unextracted (including the fractions which were only microwave extractable), although total residues in grain were low (0.1 mg/kg). Incorporation into grain starch accounted for up to 47.9%TRR in grain. Incorporation of radioactivity into natural components in straw was small, pectin (0.2%TRR), cellulose (2.5 %TRR) and lignin (5.5 %TRR).*
*It should be noted that the PHI for cereals is 35 days, however grain and straw were harvested 52 days after the second application. Therefore metabolism may be more extensive than if the crop had been harvested at the recommended PHI and residue levels may be underestimated as they are volatile and easily degraded. Residue trials data show trifloxystrobin residues to be higher in cereal trials conducted in accordance with the GAP compared to metabolism studies in wheat. At a shorter PHI, levels of unextractable residues are expected to be lower. The residues trials conducted at a later timing of application indicate a similar decline profile with higher residues, as expected.*
*Metabolism in wheat proceeded along a similar pathway to that in apples and cucumbers.*

*Based on the metabolism data submitted for wheat, apple and cucumber, residues in primary crops should be defined as parent only. Trifloxystrobin was extensively metabolised in wheat, however, metabolites were not considered to be of toxicological concern. The ratio of trifloxystrobin to its isomers is such that the levels of the isomers are not of concern. Residues in following crops should be defined as parent only as trifluoroacetic acid is not of toxicological concern at the levels present in crops as a result of trifloxystrobin being applied at rates comparable with those of proposed GAPs.*

<u>*Residue definition plant commodities:*</u> *Trifloxystrobin*

<u>Comments</u>

The studies sent by the applicant were critical reviewed. The report is very detailed. Tables of applicant's dossier were copied after checking for correctness. Several parts of the EU monograph were used by the JMPR for evaluation of this subject.

The EU evaluated 2 studies on apples, 2 on cucumbers and 4 on wheat. The metabolism studies on peanuts and sugar beet were not submitted by the applicant. The new wheat studies MR-027/02 and MR-028/02 by Reiner and Bongartz (2002) were finished later than the EU evaluation was prepared and could not be submitted.
The EU concluded not to include CGA 321113 into the residue definition for plants for the reason that "*it is not of toxicological concern at the levels present in crops as a result of trifloxystrobin being applied at rates comparable with those of proposed GAPs*" (in the EU).

### 4.4.4 USA

<u>Studies submitted by the applicant and evaluated by the USA</u>

- Gross, D. 1997. Distribution and degradation of CGA 279202 in field grown spring wheat after treatment with (CF3-phenyl-(U)-) CGA 279202 labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR15/97, Edition Number: MO-01-015761. Unpublished.
- Gross, D. 1997. Metabolism of [CF3-phenyl-(U)-14C]CGA 279202 in field grown spring wheat. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR18/97, Edition Number: MO-01-001658. Unpublished.

- Kiffe, M. 1997. Metabolism of CGA 279202 in greenhouse grown apple trees after application of [trifluoromethyl-phenyl-(U)-14C]labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR12/97, Edition Number: MO-01-010615. Unpublished.
- Kiffe, M. 1997. Metabolism of CGA 279202 in greenhouse grown apple trees after application of [glyoxyl-phenyl-(U)-14C] labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR13/97, Edition Number: MO-01-001686. Unpublished.
- Kiffe, M. 2000. Behaviour and metabolism of [glyoxyl-phenyl-(U)-14C] CGA 279202 in field grown sugar beets. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 99MK10, Edition Number: MO-01-015673. Unpublished.
- Kiffe, M. 2000. Behaviour and metabolism of [trifluoromethyl-phenyl-(U)-14C] CGA 279202 in field grown sugar beets. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 99MK09, Edition Number: MO-01-015671. Unpublished.
- Rezaaiyan, R. 1997. Uptake and metabolism of CGA-279202 in field grown peanuts after spray treatment with phenyl (A)-14C-CGA-279202 and phenyl (B)-14C-CGA-279202. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97084, Edition Number: MO-01-016005. Unpublished.
- Stingelin, J. 1997. Metabolism of [glyoxyl-phenyl-(U)-14C] CGA 279202 in field grown spring wheat. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR25/97, Edition Number: MO-01-001675. Unpublished.
- Stingelin, J. 1997. Behaviour and metabolism of CGA 279202 in greenhouse grown cucumbers after treatment with [CF3-phenyl-(U)-14C]labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR23/97, Edition Number: MO-01-001692. Unpublished.
- Stingelin, J. 1997. Behaviour and metabolism of CGA 279202 in greenhouse grown cucumbers after treatment with [glyoxyl-phenyl-(U)-14C]labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR22/97, Edition Number: MO-01-001695. Unpublished.

Studies submitted to other participants and not reviewed by the USA

- Reiner, H. and Bongartz, R. 2002. Metabolism of [trifluoromethyl-phenyl-UL-14C]trifloxystrobin in spring wheat. Bayer AG, Bayer CropScience, Monheim, Germany. Bayer CropScience AG, Report No.: MR-027/02, Edition Number: MO-02-009343. Unpublished.
- Reiner, H. and Bongartz, R. 2002. Metabolism of [glyoxyl-phenyl-UL-14C]trifloxystrobin in spring wheat. Bayer AG, Bayer CropScience, Monheim, Germany. Bayer CropScience AG, Report No.: MR-028/02, Edition Number: MO-02-009727. Unpublished.
- Stingelin, J. 1997. Behaviour and metabolism of CGA 279202 in field grown spring wheat after treatment with [Glyoxyl-Phenyl-(U)-14C] labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR04/97, Edition Number: MO-01-012305. Unpublished.

Result

The evaluation was made by the US EPA in 1999 and in 2002.

The 1999 *Memorandum (PP#8F04955, 7/22/99 review, DP Barcodes D257888 and D254208)* including the metabolism of trifloxystrobin in apples, cucumbers, peanuts and wheat was prepared by the reviewer Fred Ives. Information on the test conditions, analytical methods, total radioactive residues, characterisation/identification of metabolites and storage stability of residues were presented in detail on pages 21 - 98 under points 13.- 17. Summary discussions are presented for plant metabolism from pages 2 to 6 and are quoted below.

*Apples*

*The qualitative nature of the residue in apples is adequately understood. Total radioactive residues (TRR) were 72.193 and 46.422 ppm in foliage, 0.697 and 0.752 ppm in apple peel, and 0.032 and 0.012 ppm in apple flesh harvested 14 days following the last of four sequential applications each of [14C]trifloxystrobin, uniformly labeled in the glyoxyl-phenyl (GP) and trifluoromethylphenyl (TFMP) ring, respectively, at -0.089 lb ai/A/application (total application rate of -0.356 lb ai/A; -1x the maximum proposed seasonal rate).*

*Approximately 67-95% TRR were characterized/identified in apple foliage, surface rinse, peel and flesh. Trifloxystrobin was identified in all apple matrices, and was the major residue in the surface rinses, and apple peel, flesh (TFMP label only), and foliage (16.9-92.7% TRR, 0.002-54.217 ppm). Although trifloxystrobin was identified in GP-label flesh at 3.9-11.5% TRR (0.001-0.004 ppm), the majority of the radioactivity (35.9%-39.4% TRR) in this matrix remained at the origin in TLC analysis. Trifloxystrobin isomers CGA-331409, CGA-357261, and CGA-357262 were also identified in all matrices at 0.3%- 12.2% TRR (<0.001-2.600 ppm). Metabolite CGA-321113 and its isomer CGA-373466 were also identified at <9.9% TRR (combined) in apple peel, flesh, and foliage from both labels, and metabolite CGA-320299 was identified at <3% TRR in GP-label foliage and flesh. Metabolite NOA-417076 (II22c) was identified in apples, but was not separately quantitated; the petitioner tentatively identified isomer II22a in GP-label peel and flesh (at <6% TRR with related isomers II22b-c ), and in TFMP-label flesh (<9% TRR). Metabolites II11a, II10a, and II8a, characterized as the sugar conjugates of metabolites II22a-c, represented a major portion of the radioactivity in GP-label apple flesh (15.4-24.3% TRR, 0.003-0.008 ppm; combined) and were characterized in all other apple matrices except the ACN:water rinses at up to 14.7% TRR (combined).*

*Cucumbers*

*The qualitative nature of the residue in cucumbers is adequately understood. Total radioactive residues were 24.850 and 16.643 ppm in foliage, 0.300 and 0.193 ppm in large cucumbers, and 2.289 and 0.586 ppm in small cucumbers harvested 7 days following the last of three foliar spray applications each of uniformly ring-labeled [GP-14C]trifloxystrobin and [TFMP-14C]trifloxystrobin, respectively, at -0.280 lb ai/A/application (total application rate of -0.839 lb ai/A; -1x the maximum proposed seasonal rate).*

*Approximately 87-97% TRR were characterized/identified in cucumber foliage, and large and small cucumbers. Trifloxystrobin was identified as the major metabolite in all cucumber matrices (79.1-92.9% TRR, 0.166-29.022 ppm). Trifloxystrobin isomers CGA-331409, CGA-357261 and CGA-357262 and metabolite CGA-321113 were also identified in all matrices at <0.1-3.9% TRR (<0.001-0.719 ppm). Metabolites I12 and NOA-414412 (metabolite I14), which were identified in the spring wheat metabolism study were also identified in cucumber matrices from both labels at #0.6% TRR. Although quantitative results were not provided for NOA-417076 (II22c; identified in the apple metabolism study), metabolite II10a (the sugar conjugate of II22c) was present in cucumber matrices at #1.4% TRR, and another tentatively identified sugar conjugate, metabolite II11 was present at #0.8% TRR in cucumber matrices.*

*Peanuts*

*The qualitative nature of the residue in peanuts is adequately understood. Total radioactive residues were 0.274 and 0.165 ppm in nutmeat, and 26.340 and 27.922 ppm in hay harvested 14 days following the last of four sequential applications each of uniformly ring-labeled [GP-14C]trifloxystrobin and [TFMP-14C]trifloxystrobin at -0.5 lb ai/A (total application rate of 1.8-1.9 lb ai/A; ca. 4x the maximum proposed seasonal rate). TRR were 7.734 and 9.114 ppm in immature vines harvested 14 days following the second of the four applications of GP- and TFMP-labeled [14C]trifloxystrobin, respectively.*

*Approximately 69-95% TRR were characterized/identified in peanut nutmeat, hay, and immature vines. Trifloxystrobin was identified in all matrices; it was the major residue in hay and immature vines (29.3-46.5% TRR, 2.568-12.987 ppm) but a minor metabolite in nutmeat. The petitioner demonstrated that triglycerides were the major residue components in nutmeat from both labels (23.7-29.3% TRR, 0.048-0.065 ppm). The metabolite profiles for hay and immature vines for both labels were similar, with the following metabolites identified at <15% TRR: CGA-331409, CGA-357261, CGA-357262, CGA-373465 (vines only), CGA-373466, CGA-321113 and its malonyl glucose and sugar conjugates, hydroxy-CGA-321113.In nutmeat, isomers of trifloxystrobin, CGA-357261, CGA-373466, and CGA-321113 were all identified at <3% TRR. Phthalic acid, and metabolites A, B, and WFH-IX-86 were identified at <8% TRR in GP-label nutmeat, hay, and/or immature vines, and trifluoroacetic acid, and metabolites A-7a and A-7b were identified at <3% TRR in TFMP-label hay and immature vines. Malonyl glucose conjugates of CGA-328364 and CGA-300624 were identified as minor metabolites in TFMP-labeled hay and/or immature vines.*
*Aqueous soluble residues identified in GP and TFMP-labeled immature vines and hay were different, indicating cleavage of the N-O bond and the formation of the metabolites unique to each label. Metabolites identified in the aqueous extracts consisted of primarily malonyl sugar and/or sugar conjugates.*

*Wheat*
*The qualitative nature of the residue in wheat is adequately understood for purposes of this petition, but additional studies will be required to support possible future uses on cereals. Total radioactive residues were 10.240 and 14.370 ppm in wheat shoots harvested 1 hour after one application and 7.255 and 10.986 ppm in wheat shoots harvested 1 hour after the second of two applications, each of uniformly ring-labeled [GP-14C]trifloxystrobin and [TFMP-14C]trifloxystrobin, respectively, at -0.22 lb ai/A/application (total application rate of 0.44 lb ai/A). TRR were 0.411 and 0.081 ppm in immature wheat heads, 4.650 and 5.473 ppm in immature wheat stalks (forage) harvested 24 days after the second application, and 0.099 and 0.020 ppm in wheat grain, 0.780 and 0.142 ppm in hulls, and 5.482 and 3.851 ppm in straw harvested 52 days following the second applications of GP- and TFMP-labeled [14C]trifloxystrobin, respectively. In a second plot of wheat which received a single foliar application of [TFMP-14C]trifloxystrobin at 0.44 lb ai/A, TRR were 0.056 ppm in grain, 1.700 ppm in hulls, and 7.493 ppm in straw.*
*Approximately 24-76% TRR were characterized/identified in immature and mature wheat matrices. Although trifloxystrobin and its isomers CGA-331409, CGA-357261, and CGA-357262 were identified in all matrices, they were identified at low levels, indicating that residues were extensively metabolized. The metabolite profiles appear to have been similar for forage, hulls, and straw from both labels; however, because different analyses were conducted on selected matrices within each label treatment, a conclusive determination is not possible. The petitioner extrapolated the results of a starch derivatization procedure in TFMP-label grain to conclude that starch accounted for 47.9% TRR in grain at harvest (based on specific activity of the recrystallized osazone derivatives, specific activity of grain, and an average reference factor of 70% starch content for grain).*
*Sugar conjugates of the aglycone metabolites I10, I12, and NOA-414412 were the major metabolites in immature wheat stalk from both labels, representing 2.5-12.0% TRR (0.116-0.657 ppm). In straw, the aglycones themselves were the major metabolites, accounting for 3.6-7.0% TRR (0.139-0.270 ppm) in TFMP-label straw and 3.2-5.4% TRR (0.175-0.296 ppm) in GP-label straw. The acid metabolite CGA-321113 was identified in GP-label stalk (0.2% TRR, 0.009 ppm), hulls (0.6% TRR, 0.005 ppm), and straw (1.8% TRR, 0.099 ppm); and TFMP-label grain (1.1% TRR, <0.001 ppm), hulls (1.1% TRR, 0.002 ppm), and straw (0.8% TRR, 0.031 ppm). The following metabolites were also identified in wheat matrices: isomers NOA-413161 and NOA-*

*413163 (these were the major identified component in GP-label grain at a combined level of 10.1% TRR, 0.010 ppm).*
*Because different analytical procedures were used between the two labels, the petitioner compared the ACN:water extracts of mature hulls and straw from the GP and TFMP labels on TLC System I, and the DCM phases following partitioning at pH 7 of straw on TLC System III; in both cases, the qualitative natures of the extracts were identical. In addition, isolated polar metabolites II8, II10, and II11 (sugar conjugates of I10, I12, and NOA-414412) from various GP- and TFMP-label material sources were subjected to co-chromatography on several TLC systems to confirm they were identical.*
*The petitioner conducted extensive analyses to characterize nonextractable residues in wheat grain and straw which demonstrated that only small amounts of the nonextractable radioactivity were associated with cell wall fractions (pectin, cellulose, lignin). The petitioner concluded that the findings indicated that nonextractable residues consisted largely of metabolites arising from incomplete extraction at room temperature.*

*Plant metabolism conclusions*
*The HED Metabolism Assessment Review Committee (MARC) determined 6/15/99 that the qualitative nature of the residue in plants is adequately understood for fruits, fruiting vegetables, cucurbit vegetables and peanuts, based on acceptable studies conducted on apples, cucumbers, peanuts, and a supplementary study on wheat. The Committee concluded that additional metabolism studies would be needed to support possible future uses on leafy vegetables, cereals or crops other than those in this petition. The Committee further determined that the total toxic residues of concern for plants, both for regulatory and risk assessment purposes, is trifloxystrobin and its free form of acid metabolite CGA321113.*

The 2002 *Memorandum (PP#0F06121, 1/17/02 review, DP Barcodes D267787 and D272054)* including the metabolism of trifloxystrobin in sugar beets was prepared by the reviewer Leung Cheng. Information on the test conditions, analytical methods, total radioactive residues and characterisation/identification of metabolites and storage stability of residues were presented in detail on pages 18 – 44. A summary discussion is presented for plant metabolism from pages 6 to 7 and is quoted below.

*It was stated in an earlier petition (PP#8F4955) that the qualitative nature of the residue in plants is adequately understood for fruits, fruiting vegetables, cucurbit vegetables and peanuts, based on acceptable metabolism studies conducted on apples, cucumbers, peanuts, and a supple-mentary study on wheat. On the basis of existing metabolism studies, the HED Metabolism Assessment Review Committee (MARC) concluded that both trifloxystrobin and the free form of its acid metabolite CGA-321113 are of concern for both regulatory and risk assessment purposes for plant commodities, and also concluded that additional metabolism studies would be needed to support possible future uses on leafy vegetables, cereals or crops other than fruits, fruiting vegetables, cucurbit vegetables, and peanuts. In the interim, the MARC concluded that trifloxystrobin and the free form of its acid metabolite CGA-321113 are of concern in wheat for both regulatory and risk assessment purposes but that additional metabolism data on wheat are required for a full Section 3 registration. In the previous petition (PP#9F5070), RAB3 concluded that the nature of the residue in almond, hops, fruiting vegetables, tuberous and corm vegetables, and sugar beet is understood, and trifloxystrobin and the free form of its acid metabolite CGA-321113 are of concern for both regulatory and risk assessment purposes in these plant commodities.*

*In the current petition, Novartis submitted two sugar beet trifloxystrobin metabolism studies. Sugar beets were treated three times with 1x or 5.5x trifloxystrobin, labeled at the [glyoxylphenyl-(U)-14C] or [trifluoromethylphenyl-(U)-14C] position (GP-labeled and TFMP-labeled,*

*respectively). Results for the two radiolabels were comparable. Total residues at all intervals were much greater in the tops than in the roots, and in the soil samples were generally similar to or lower than in the roots. In the tops and roots, the majority of the radiolabel was present as parent compound at all intervals (23.9-96.3% TRR), whereas the most abundant soil metabolite was CGA-321113 (29.3-84.3% TRR). The roots were shown to contain ~ 5.9% of the TRR incorporated into saccharose, 0.4% into cellulose, 2.4% into lignin, and 1.5% into pectin. In addition to the parent CGA-279202 and its two isomers (CGA-331409 and CGA-357262), nine metabolites were identified by TLC and/or HPLC in the sugar beet tops. Seven of the 9 metabolites were also found in the roots and soil. Mass spectrometry confirmed or suggested the identity of most of the compounds. Trifloxystrobin metabolism involves several routes, including cis/trans isomerization, methyl ester cleavage, hydroxylation of the trifluoromethylphenyl ring, glucose conjugation, oxidation of the 2-ethylideneaminooxymethyl group, and cleavage of the methyl ester bond of the parent compound and addition of three hydroxyl groups. Based on these studies, the nature of trifloxystrobin in/on sugar beet is adequately understood, and the major residues include the parent and metabolite CGA-321113. However, the sugar beet metabolism studies do not fulfill the wheat metabolism data requirement because the two crops are too dissimilar.*

*<u>Residue definition plant commodities for enforcement and risk assessment:</u> Trifloxystrobin and CGA 321113, expressed as trifloxystrobin*

<u>Comments</u>

The studies sent by the applicant were critical reviewed. The results were presented in a report in a review format including new created tables.

Although the petitioner proposed the regulation of trifloxystrobin only, it was clearly stated that both trifloxystrobin and the free form of CGA-321113 are of concern for both regulatory and risk assessment purposes for plant commodities.

### 4.4.5 JMPR

<u>Studies submitted by the applicant and evaluated by the JMPR</u>

- Gross, D. 1997. Distribution and degradation of CGA 279202 in field grown spring wheat after treatment with (CF3-phenyl-(U)-) CGA 279202 labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR15/97, Edition Number: MO-01-015761. Unpublished.
- Gross, D. 1997. Metabolism of [CF3-phenyl-(U)-14C]CGA 279202 in field grown spring wheat. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR18/97, Edition Number: MO-01-001658. Unpublished.
- Kiffe, M. 1997. Metabolism of CGA 279202 in greenhouse grown apple trees after application of [trifluoromethyl-phenyl-(U)-14C]labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR12/97, Edition Number: MO-01-010615. Unpublished.
- Kiffe, M. 1997. Metabolism of CGA 279202 in greenhouse grown apple trees after application of [glyoxyl-phenyl-(U)-14C] labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR13/97, Edition Number: MO-01-001686. Unpublished.
- Kiffe, M. 2000. Behaviour and metabolism of [glyoxyl-phenyl-(U)-14C] CGA 279202 in field grown sugar beets. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 99MK10, Edition Number: MO-01-015673. Unpublished.

- Kiffe, M. 2000. Behaviour and metabolism of [trifluoromethyl-phenyl-(U)-14C] CGA 279202 in field grown sugar beets. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 99MK09, Edition Number: MO-01-015671. Unpublished.
- Reiner, H. and Bongartz, R. 2002. Metabolism of [trifluoromethyl-phenyl-UL-14C]trifloxystrobin in spring wheat. Bayer AG, Bayer CropScience, Monheim, Germany. Bayer CropScience AG, Report No.: MR-027/02, Edition Number: MO-02-009343. Unpublished.
- Reiner, H. and Bongartz, R. 2002. Metabolism of [glyoxyl-phenyl-UL-14C]trifloxystrobin in spring wheat. Bayer AG, Bayer CropScience, Monheim, Germany. Bayer CropScience AG, Report No.: MR-028/02, Edition Number: MO-02-009727. Unpublished.
- Rezaaiyan, R. 1997. Uptake and metabolism of CGA-279202 in field grown peanuts after spray treatment with phenyl (A)-14C-CGA-279202 and phenyl (B)-14C-CGA-279202. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97084, Edition Number: MO-01-016005. Unpublished.
- Stingelin, J. 1997. Behaviour and metabolism of CGA 279202 in field grown spring wheat after treatment with [Glyoxyl-Phenyl-(U)-14C] labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR04/97, Edition Number: MO-01-012305. Unpublished.
- Stingelin, J. 1997. Metabolism of [glyoxyl-phenyl-(U)-14C] CGA 279202 in field grown spring wheat. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR25/97, Edition Number: MO-01-001675. Unpublished.
- Stingelin, J. 1997. Behaviour and metabolism of CGA 279202 in greenhouse grown cucumbers after treatment with [CF3-phenyl-(U)-14C]labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR23/97, Edition Number: MO-01-001692. Unpublished.
- Stingelin, J. 1997. Behaviour and metabolism of CGA 279202 in greenhouse grown cucumbers after treatment with [glyoxyl-phenyl-(U)-14C]labelled material. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR22/97, Edition Number: MO-01-001695. Unpublished.

Studies submitted to other participants and not reviewed by JMPR
none

Result

The evaluation was made by the FAO Panel the JMPR in 2004. A detailed monograph including the metabolism of trifloxystrobin in apples, cucumbers, peanuts, sugar beet and wheat was prepared. Information on the test conditions, analytical methods, total radioactive residues, characterisation and identification of metabolites and storage stability of residues were presented in detail under point plant metabolism. The reports prepared by Australia, Canada, the EU and the USA as well as the dossier submitted by the applicant were used. The conclusions presented in the appraisal for plant metabolism are quoted below.

> *The metabolism of trifloxystrobin in plants was investigated in wheat, apples, cucumbers, sugar beet and peanuts using [glyoxylphenyl-U-$^{14}$C]-trifloxystrobin and [trifluoromethylphenyl-U-$^{14}$C]-trifloxystrobin by spray applications. Although there were differences in the number of metabolite fractions in the different plants, the metabolic pathways for all the crops are comparable.*
>
> *In mature wheat, the highest levels of radioactivity (TRR) were found in straw (3.85 mg/kg trifloxystrobin equivalents), followed by husks (0.14 mg/kg equivalents) and grain (0.02 mg/kg equivalents). The composition of the TRRs was complex; trifloxystrobin and its isomers constituted less than 5% of the TRRs.*

*Studies on wheat showed that trifloxystrobin absorption by plants was quite rapid, with about 15% of the TRR within the first 24 hours, 29% of the TRR within 3 days, and 44% of the TRR in 14 days. Characterisation of the surface radioactivity in wheat revealed that trifloxystrobin is relatively stable to photodegradation, with the parent compound accounting for up to about 80% of the surface radioactivity after 14 days. In contrast to the residue found on the crop surface, the absorbed residue appears to undergo quite rapid degradation: the trifloxystrobin concentration declined exponentially, with an apparent half-life of 12 hours. Up to 35 metabolite fractions were found in wheat, most of which constituted less than 1% of the TRR.*

*In apples, 14 days after treatment, the main residue component was the parent compound trifloxystrobin (E,E- isomer), which, together with its Z,Z-, Z,E- and E,Z- isomers, constituted about 92% of the residue.*

*In the leaves and fruits of cucumbers, the residue consisted of trifloxystrobin (80 to 93% of the TRR), isomers of trifloxystrobin (2.3 to 3.8% of the TRR), and the carboxylic acid derivative of trifloxystrobin, CGA 321113 (0.9 to 4.2% of the TRR).*

*In sugar beet, the main compounds found, with both labels, in the tops and roots were trifloxystrobin and its E,Z- and Z,Z- isomers. They accounted for up to 69% of the TRR in tops (1.1 mg/kg trifloxystrobin) and 52% in roots (0.02 mg/kg trifloxystrobin). CGA 321113 was found up to 5.2% (0.073 mg/kg) and up to 11% (0.012 mg/kg) of the TRR in the tops and roots respectively.*

*In peanuts, many metabolite fractions containing only one moiety of the parent molecule were detected, generally similar to those found in wheat. Extensive formation of sugar and malonyl sugar conjugates was found in most metabolite fractions. In vines the percentage of extractable radioactive residues (acetonitrile/water) amounted to 91% of TRR. In mature hay extractable residues were up to 74% and in nutmeat up to 53%. The unextracted residues were solubilised by hot extraction and sequential hydrolyses with cellulase, protease, HCl and NaOH. Radioactive residues remaining unextracted under the exhaustive conditions were <10% of TRR.*

*In general, the metabolism of trifloxystrobin in crops is complex owing to isomerization of the parent compound and its metabolites. Overall, the metabolism of trifloxystrobin is similar in all crops:*

- *Cis/trans isomerization of trifloxystrobin (E,E- isomer) to its E,Z-, Z,Z and Z,E- isomers*
- *Hydrolysis of the methyl esters of the parent and its isomers to carboxylic acids*
- *Cis/trans isomerization of the E,E-carboxylic acid CGA 321113*
- *Hydroxylation of the trifluoromethylphenyl ring, followed by sugar conjugation*
- *Oxidation of the methyl of the 2-ethylideneamino group with subsequent sugar conjugation*
- *Cleavage of the N-O bridge, followed by oxidation of the trifluoromethylphenyl moiety to form the acetophenone derivative with subsequent sugar conjugation*
- *Cleavage of the N-O bridge, followed by oxidation of the glyoxyl-phenyl moiety with eventual formation of phthalic acid*
- *Formation of unextracted residues.*

*<u>Definition of the residue for plant commodities (for compliance with MRL)</u>: trifloxystrobin.*
*<u>Definition of the residue for plant commodities (for estimation of dietary intake):</u>*
*sum of trifloxystrobin and CGA 321113, calculated as trifloxystrobin.*

Comments:

The studies sent by the applicant were critical reviewed.

The metabolism of trifloxystrobin in plants occurs primarily *via* cleavage of the methyl ester group to form CGA 321113, but the main component of the radioactivity is parent trifloxystrobin. The Meeting agreed that the residue definition for enforcement purposes for plant commodities should be trifloxystrobin *per se*.

The metabolite CGA 321113 does comprise a significant portion (about 30%) of the terminal residue in raw plant commodities like strawberries, leek, Brussels sprouts, flowerhead brassicas, carrots, barley, wheat, maize, rice, hops, peanut fodder, barley straw, maize fodder and rice straw. Furthermore, trifloxystrobin will be hydrolysed to CGA 321113 under conditions of processing. In these cases, the nature of residue in the processed product may be partly different from that found in the raw agricultural commodity. For that reason, CGA 321113 should be included in the residue definition for risk assessment for plant commodities. The Meeting agreed that the residue definition for consideration of dietary exposure should consist of parent compound plus CGA 321113 (expressed as trifloxystrobin equivalents).

### 4.4.6 Results – plant metabolism

The participants of the work sharing project did not receive the same studies caused by the differences in the dates of evaluation with regard to the times of finishing the studies. Studies on apples, cucumber and several wheat studies (apples CMR-12/97, apples CMR-13/97, cucumbers CMR-22/97, cucumbers CMR-23/97, wheat CMR-15/97, wheat CMR-18/97, wheat CMR-25/97) were evaluated by all participants. The peanut study ABR-97084 and the sugar beet studies 99MK09 and 99MK10 were not evaluated by Australia, Canada and the EU but by the USA and the JMPR. The wheat study CMR-04/97 was evaluated by Australia, the EU and the JMPR, but not by Canada and the USA. The 2002 wheat studies MR-027/02 and MR-028/02 were only evaluated by the JMPR.

The results of the evaluation - the residue definition - are identical for the evaluations carried out by Australia, Canada and the USA. The residue of concern for plant commodities both for enforcement and risk assessment was defined as the parent and the acetic acid metabolite (CGA 321113).

The EU concluded not to include CGA 321113 into the residue definition for plants both for enforcement and risk assessment for the reason that "*it is not of toxicological concern at the levels present in crops as a result of trifloxystrobin being applied at rates comparable with those of proposed GAPs*" (in the EU).

The JMPR agreed with the EU that the residue definition for enforcement purposes for plant commodities should be trifloxystrobin *per se* but, like Australia, Canada and the USA, the JMPR included the metabolite CGA 321113 into the residue definition for risk assessment.

## 4.5 Nature of residues under processing conditions

### 4.5.1 Australia

Studies submitted by the applicant and evaluated by Australia
none

Studies submitted to other participants and not reviewed by Australia
Morgenroth, U. 2000. Hydrolysis of [Glyoxyl-phenyl-U-14C]-CGA 279202 under processing conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Study Report Number: 00MO02, Edition Number: MO-01-005601. Unpublished.

Result

The study 00MO02 was not submitted by the applicant and could not be included into the evaluation. The absence of the study was not addressed by the Australian agency as deficiency.

Comments

none

### 4.5.2 Canada

Studies submitted by the applicant and evaluated by Canada
none

Studies submitted to other participants and not reviewed by Canada
Morgenroth, U. 2000. Hydrolysis of [Glyoxyl-phenyl-U-14C]-CGA 279202 under processing conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Study Report Number: 00MO02, Edition Number: MO-01-005601. Unpublished.

Result

The study 00MO02 was not submitted by the applicant and could not be included into the evaluation.

Comments

The absence of the study was not addressed by the Canadian agency as deficiency.

### 4.5.3 EU

Studies submitted by the applicant and evaluated by the EU
none

Studies submitted to other participants and not reviewed by the EU
Morgenroth, U. 2000. Hydrolysis of [Glyoxyl-phenyl-U-14C]-CGA 279202 under processing conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Study Report Number: 00MO02, Edition Number: MO-01-005601. Unpublished.

Result

The study 00MO02 was not submitted by the applicant and could not be included into the evaluation. The EU addressed this open point in their evaluation under B.7.8.4 on page 330 as follows:
*"Hydrolysis is not specific to any one process and therefore may represent all processes. Since there is evidence that trifloxystrobin is stable in microwave studies and since CGA 321113 has been well*

*characterised in crops and is of no greater toxicity than trifloxystrobin, the nature of the residues following processing is considered to have been adequately addressed."*

Comments

The absence of the study was addressed by the EU as deficiency.

### 4.5.4 USA

Studies submitted by the applicant and evaluated by the USA
none

Studies submitted to other participants and not reviewed by the USA
Morgenroth, U. 2000. Hydrolysis of [Glyoxyl-phenyl-U-14C]-CGA 279202 under processing conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Study Report Number: 00MO02, Edition Number: MO-01-005601. Unpublished.

Result

The study 00MO02 was not submitted by the applicant and could not be included into the evaluation.

Comments:

The absence of the study was not addressed by the Canadian agency as deficiency.

### 4.5.5 JMPR

Studies submitted by the applicant and evaluated by the reviewer
Morgenroth, U. 2000. Hydrolysis of [Glyoxyl-phenyl-U-14C]-CGA 279202 under processing conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Study Report Number: 00MO02, Edition Number: MO-01-005601. Unpublished.

Studies submitted to other participants and not reviewed by the JMPR
none

Result

The evaluation was made by the FAO Panel of the JMPR in 2004. A detailed monograph including the description of the effect of processing on the nature of residues of trifloxystrobin was prepared. The experiment was carried out with radioactive [glyoxyl-phenyl-U-$^{14}$C]-trifloxystrobin in buffered water under laboratory conditions, which were representative for processing operations of raw agricultural commodities (RAC) like pasteurisation, baking and sterilisation. An appraisal including the conclusions is presented and quoted below.

> *The Meeting received information on the fate and nature of trifloxystrobin residues during different conditions of hydrolysis. Trifloxystrobin will be partially hydrolysed to CGA 321113 under conditions representative for baking, brewing and boiling (2.6%) and sterilisation (22.5%). Under conditions representative for pasteurisation trifloxystrobin was found to be stable. Any*

*possible effects of hydrolysis on the nature of the residue during processing are covered by the fact that the only relevant metabolite (CGA 321113) is analysed in all residue and processing trials.*

Comments

Based on the study sent by the applicant the JMPR stated that acid metabolite CGA 321113 is relevant for the residue definition for dietary intake.

### 4.5.6 Results - nature of residues in processing

The national/regional agencies did not receive the hydrolysis study 00MO02 which was submitted to the JMPR only.

The absence of the study was not addressed by Australia, Canada and the USA as deficiency. The EU addressed this open point in their evaluation as follows *"... the nature of the residues following processing is considered to have been adequately addressed."*

Based on the hydrolysis study 00MO02, the JMPR stated that the acid metabolite CGA 321113 is relevant for the residue definition for dietary intake.

## 4.6 Environmental fate in soil and water-sediment systems

Many studies were submitted to the agencies participating on the work sharing project with the aim to prepare a specific environmental fate evaluation report. The comparison by the work sharing project is limited to the subjects hydrolysis and residue degradation in water-sediment systems because of JMPR's decision in 2003 to evaluate only specific environmental fate studies with regard to the residue behaviour of the pesticide depending on the proposed uses.

### 4.6.1 Australia

Studies submitted by the applicant and evaluated by Australia

- Kitschmann, P. 1996.Hydrolysis of (U)-14C-phenyl-glyoxylate-labeled CGA 279202 under laboratory conditions. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 94PK01, Edition Number: MO-01-001565. Unpublished.
- Ulbrich, R. 1997. Hydrolysis of (trifluormethyl-phenyl-(U)-14C)-labeled CGA 279202 under laboratory conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 94UL04, Edition Number: MO-01-001568. Unpublished.

Studies submitted to other participants and not reviewed by Australia

- Manuli, P. J. and Jacobson, B. 2000. Aquatic field dissipation of CGA-279202 under field conditions with rice in Arkansas. Waterborne Environmental, Inc., Leesburg, VA, USA. Bayer CropScience AG, Report No.: 242.40, Edition Number: MO-01-005846. Unpublished.
- Widmer, H. 1997. Thermal decomposition of CGA 321113 and CGA 373466 to CGA 357276 and the corresponding nitrile of CGA 373466. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 97WI40, Edition Number: MO-01-001570. Unpublished.

Result

The evaluation was made by the APVMA in 2000. A monograph entitled *Environmental Assessment Report* was prepared. Information on hydrolysis was presented in detail on pages 6 – 7. A summary discussion is presented on page 7 and quoted below.

> *Kitschmann, 1996 (*94PK01*): The main degradation product which was generated at pH >5 was identified as the acid CGA 321113 and confirmed using mass spectrometry. This made up 28.3% of radioactivity at pH 7 (25°C) with the parent compound making up 61.4% at the end of the incubation time. At pH 9 (25°C), the metabolite accounted for around 97% of radioactivity. The half lives of CGA 321113 were determined at pH 9 and pH 13 at 60°C to be 742 and 452 days, respectively. Therefore, at environmentally relevant pH values and temperatures, this acid is expected to be hydrolytically stable.*
>
> *Ulbrich, 1997 (*94UL04*): As with Kitschmann (1996) above, at pH >5 the acid CGA 321113 was the major metabolite accounting for some 41.4% of radioactivity at pH 7 and 95.6% at pH 9 (25oC) after about 800 hours. The half lives for this acid were determined by a pseudo first order kinetic model based on consecutive reactions at 60°C as 72.3 days, 85.7 days and 155.2 days for pH 7, pH 9 and pH 13, respectively. Breakdown rates at environmentally relevant temperatures would be far slower than this, again suggesting this primary degradation product would be hydrolytically stable.*

Comments

Australia evaluated the studies by Kitschmann (1966) 94PK01 and Ulbrich (1997) 94UL04 for hydrolysis of trifloxystrobin. The study by Widmer (1997) 97WI40, explaining an artefact in the study by Ulbrich (1997) and the aquatic field dissipation study for rice by Manuli and Jacobson (2000) 242.40, were not submitted by the applicant.

### 4.6.2 Canada

Studies submitted by the applicant and evaluated by Canada
no information received

Studies submitted to other participants and not reviewed by Canada

- Kitschmann, P. 1996.Hydrolysis of (U)-14C-phenyl-glyoxylate-labeled CGA 279202 under laboratory conditions. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 94PK01, Edition Number: MO-01-001565. Unpublished. also filed: 1.2.9
- Manuli, P. J. and Jacobson, B. 2000. Aquatic field dissipation of CGA-279202 under field conditions with rice in Arkansas. Waterborne Environmental, Inc., Leesburg, VA, USA. Bayer CropScience AG, Report No.: 242.40, Edition Number: MO-01-005846. Unpublished.
- Ulbrich, R. 1997. Hydrolysis of (trifluormethyl-phenyl-(U)-14C)-labeled CGA 279202 under laboratory conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 94UL04, Edition Number: MO-01-001568. Unpublished. also filed: 1.2.9
- Widmer, H. 1997. Thermal decomposition of CGA 321113 and CGA 373466 to CGA 357276 and the corresponding nitrile of CGA 373466. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 97WI40, Edition Number: MO-01-001570. Unpublished.

Result

No information on the environmental fate part (hydrolysis etc.) was received by PMRA.

Comments

none

### 4.6.3 EU

Studies submitted by the applicant and evaluated by the EU

- Kitschmann, P. 1996. Hydrolysis of (U)-14C-phenyl-glyoxylate-labeled CGA 279202 under laboratory conditions. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 94PK01, Edition Number: MO-01-001565. Unpublished.
- Ulbrich, R. 1997. Hydrolysis of (trifluormethyl-phenyl-(U)-14C)-labeled CGA 279202 under laboratory conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 94UL04, Edition Number: MO-01-001568. Unpublished.
-

Studies submitted to other participants and not reviewed by the EU

- Manuli, P. J. and Jacobson, B. 2000. Aquatic field dissipation of CGA-279202 under field conditions with rice in Arkansas. Waterborne Environmental, Inc., Leesburg, VA, USA. Bayer CropScience AG, Report No.: 242.40, Edition Number: MO-01-005846. Unpublished.
- Widmer, H. 1997. Thermal decomposition of CGA 321113 and CGA 373466 to CGA 357276 and the corresponding nitrile of CGA 373466. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 97WI40, Edition Number: MO-01-001570. Unpublished.

Result

The evaluation was made by the United Kingdom as EU Rapporteur Member State in April 2000. A monograph entitled *Draft Assessment Report* was prepared (11343c/ECCO/BBA/00). Information on hydrolysis was presented on page 330 under point B.7.8.4 and is quoted below.

> *Hydrolysis studies were performed with [14C-TP]- and [14C-GP]- trifloxystrobin in aqueous solution under a range of pHs (1-13) at temperatures of 25-60°C. Results indicated trifloxystrobin to be stable at pH 5 under the range of temperatures. No isomerisation of the parent compound occurred. In neutral and alkaline conditions, CGA 321113 was the major metabolite. This metabolite was found to be stable under alkaline conditions at temperatures of 60°C.*
>
> *Hydrolysis is not specific to any one process and therefore may represent all processes. Since there is evidence that trifloxystrobin is stable in microwave studies and since CGA 321113 has been well characterised in crops and is of no greater toxicity than trifloxystrobin, the nature of the residues following processing is considered to have been adequately addressed.*

Comments

The studies sent by the applicant were critical reviewed. The EU evaluated the studies by Kitschmann (1966) 94PK01 and Ulbrich (1997) 94UL04 for hydrolysis of trifloxystrobin. The study by Widmer (1997) 97WI40, explaining an artefact in the study by Ulbrich (1997) as well as the aquatic field dissipation study for rice by Manuli and Jacobson (2000) 242.40, were not submitted by the applicant.

### 4.6.4 USA

Studies submitted by the applicant and evaluated by the USA
no information received

Studies submitted to other participants and not reviewed by the USA
- Kitschmann, P. 1996.Hydrolysis of (U)-14C-phenyl-glyoxylate-labeled CGA 279202 under laboratory conditions. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 94PK01, Edition Number: MO-01-001565. Unpublished.
- Manuli, P. J. and Jacobson, B. 2000. Aquatic field dissipation of CGA-279202 under field conditions with rice in Arkansas. Waterborne Environmental, Inc., Leesburg, VA, USA. Bayer CropScience AG, Report No.: 242.40, Edition Number: MO-01-005846. Unpublished.
- Ulbrich, R. 1997. Hydrolysis of (trifluormethyl-phenyl-(U)-14C)-labeled CGA 279202 under laboratory conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 94UL04, Edition Number: MO-01-001568. Unpublished.
- Widmer, H. 1997. Thermal decomposition of CGA 321113 and CGA 373466 to CGA 357276 and the corresponding nitrile of CGA 373466. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 97WI40, Edition Number: MO-01-001570. Unpublished.

Result

No information on the environmental fate part (hydrolysis etc.) was received by the US EPA.

Comments

none

### 4.6.5 JMPR

Studies submitted by the applicant and evaluated by the JMPR
- Kitschmann, P. 1996.Hydrolysis of (U)-14C-phenyl-glyoxylate-labeled CGA 279202 under laboratory conditions. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 94PK01, Edition Number: MO-01-001565. Unpublished.
- Manuli, P. J. and Jacobson, B. 2000. Aquatic field dissipation of CGA-279202 under field conditions with rice in Arkansas. Waterborne Environmental, Inc., Leesburg, VA, USA. Bayer CropScience AG, Report No.: 242.40, Edition Number: MO-01-005846. Unpublished.
- Ulbrich, R. 1997. Hydrolysis of (trifluormethyl-phenyl-(U)-14C)-labeled CGA 279202 under laboratory conditions. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 94UL04, Edition Number: MO-01-001568. Unpublished.
- Widmer, H. 1997. Thermal decomposition of CGA 321113 and CGA 373466 to CGA 357276 and the corresponding nitrile of CGA 373466. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 97WI40, Edition Number: MO-01-001570. Unpublished.

Studies submitted to other participants and not reviewed by JMPR
none

Result

The evaluation was made by the FAO Panel of the JMPR in 2004. A detailed monograph including the description of hydrolysis and residue degradation in water-sediment systems of trifloxystrobin was prepared. The conclusions were presented in an appraisal and are quoted below.

> *Because trifloxystrobin is used for foliar spray treatment and on paddy rice, only studies of hydrolysis and degradation in water-sediment systems were considered.*
>
> *Trifloxystrobin is relatively stable hydrolytically under sterile neutral and weakly acid conditions whereas under alkaline conditions hydrolytic degradation increases with increasing pH. The acid CGA 321113 formed under alkaline conditions is not degraded hydrolytically. No ring cleavage is observed at pH ≥5.*
>
> *In biologically active aquatic systems such as a paddy rice plot trifloxystrobin was rapidly degraded in both flooding water and paddy soil, with a maximum half-life of about 2-5 days. As in sterile hydrolysis the principal product in a paddy rice field was the acid CGA 321113. While stable to sterile hydrolysis, CGA 321113 was rapidly degraded in the rice plot with degradation half-lives of 7-8 days in flooding water and paddy soil. Besides CGA 321113 formed by biotic hydrolysis, isomerization of the parent compound and CGA 321113 occurred, resulting in the formation of the parent Z,E- isomer CGA 357261 in minor amounts and the acid Z,E- isomer CGA 373466 in major amounts. CGA 373466 showed rapid degradation in the water layer with a half-life of 4.2 days. A half-life with reasonable significance could not be estimated for CGA 357261 owing to the very low concentrations in the range of the LOQ.*
>
> *Experimental photolytic half-lives of trifloxystrobin in sterile aqueous buffered solutions at 25°C under a Xenon arc light (12 hours light / 12 hours dark cycle) were found to be 20.4 hours at pH 5 and 31.5 hours at pH 7. Corresponding predicted environmental half-lives under summer sunlight at a geographical latitude of 40°N were 1.1 and 1.7 days at pH 5 and pH 7 respectively.*

Comments

The JMPR stated that trifloxystrobin and its main metabolite CGA 321113 are rapidly degraded in the paddy rice field.

### 4.6.6 Results - environmental fate in soil and water-sediment systems

No information on the subject environmental fate (hydrolysis etc.) was received by the Canadian PMRA and the US EPA. Australia and the EU evaluated two hydrolysis studies. The hydrolysis studies and a residue degradation study in water-sediment systems were evaluated by the JMPR. The JMPR stated that trifloxystrobin and its main metabolite CGA 321113 are rapidly degraded in paddy rice fields.

## 4.7 Crop rotation

### 4.7.1 Australia

Studies submitted by the applicant and evaluated by Australia
none

Studies submitted to JMPR and not reviewed by Australia

- Gross, D. 1997. Outdoor confined accumulation study on rotational crops after bareground application of (CF3-Phenyl-U-14C) labelled CGA 279202. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR26/97, Edition Number: MO-01-015715. Unpublished.
- Hayworth, C. G. 1999. CGA - 279202 - Field accumulation in rotational crops. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 109-97, Edition Number: MO-01-017324. Unpublished.
- Kennedy, E. T. 1997. 14C-CGA-279202: Uptake and distribution of residues in confined rotational crops. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97087, Edition Number: MO-01-015714. Unpublished.
- Stingelin, J. 1997. Outdoor confined accumulation study on rotational crops after bareground application of [glyoxyl-phenyl-(U)-14C]-CGA 279202. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR24/97, Edition Number: MO-01-002816. Unpublished.

Result

No information on the rotational crop subject was received by the Australian APVMA.

Comments:

none

### 4.7.2 Canada

Studies submitted by the applicant and evaluated by Canada
- Hayworth, C. G. 1999. CGA - 279202 - Field accumulation in rotational crops. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 109-97, Edition Number: MO-01-017324. Unpublished.
- Kennedy, E. T. 1997. 14C-CGA-279202: Uptake and distribution of residues in confined rotational crops. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97087, Edition Number: MO-01-015714. Unpublished.

Studies submitted to other participants and not reviewed by Canada
- Gross, D. 1997. Outdoor confined accumulation study on rotational crops after bareground application of (CF3-Phenyl-U-14C) labelled CGA 279202. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR26/97, Edition Number: MO-01-015715. Unpublished.
- Stingelin, J. 1997. Outdoor confined accumulation study on rotational crops after bareground application of [glyoxyl-phenyl-(U)-14C]-CGA 279202. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR24/97, Edition Number: MO-01-002816. Unpublished.

Result

The evaluation was made by the PMRA ARLA in 2000 and 2001. A *review* prepared each for residues in confined rotational crops (2001) and field accumulation in rotational crops (2000) by the reviewer Monique Thomas gives detailed information on materials and methods, total radioactive residues and results. The conclusions are presented in the respective report on page 23 (confined rotational crops) and page 10 (field accumulation) and are quoted below.

*Confined rotational crops*

*The submitted confined rotational crop study is adequate. Total radioactive residues (TRRs) accumulated at levels greater than 10 ppb in/on the following rotational commodities planted 30 days after treatment (DAT) and 120-DAT to silt loam soil with [ 14 C]trifloxystrobin (uniformly labelled in the glyoxyl (GP) or trifluoromethylphenyl (TFMP) ring) at 2.24 kg a.i./ha: turnip leaves (11-64 ppb); turnip roots (5-18 ppb); spinach (16-264 ppb); wheat (25% and 50% mature, 21-282 ppb); wheat straw (42-200 ppb) and wheat grain (29-69 ppb). Overall, TRRs in crops planted in [TFMP-14 C]-labelled trifloxystrobin treated soil were higher than those planted in [GP-14 C]-labelled trifloxystrobin treated soil. The available data suggest that trifloxystrobin is not readily taken up by secondary crops. The TRRs in rotational crop matrices were extracted using acetonitrile:water (8:2, v:v) and the resulting extracts were partitioned with dichloromethane. For wheat grain and straw, non-extractable residues were subjected to acid and/or base reflux and/or enzyme hydrolysis to release additional radioactivity. The majority of the extractable radioactivity in rotational crops was aqueous soluble. The TFMP-specific metabolite, trifluoroacetic acid (TFA), accounted for the majority of the radioactivity in the [TFMP-14 C]-labelled aqueous soluble fractions of the rotational crops from both plant-back intervals (PBIs), while the [GP-14 C]-labelled aqueous soluble fractions constituted predominantly acidic aglycones and their conjugates. The major metabolites observed in the [GP-14 C]-labelled and [TFMP-14 C]-labelled organosoluble fractions included parent (CGA-279202), the diastereomers of parent (CGA-331409 and CGA-357262) and CGA-321113, with lower concentrations of CGA-373465 and CGA-373466. In addition, the organic fractions of the [GP-14 C]-labelled plant samples also contained minor amounts of lactone (CGA-320299) and phthalic acid. Nonextractable residues following extraction and hydrolysis procedures accounted for less than 40 ppb. Based on the submitted data, the analytical methods used were adequate to determine the identity of major residue components in rotational crops.*

*Field accumulation*

*No measurable residues of trifloxystrobin and CGA 321113 (<0.02 ppm/analyte) were detected in the raw agricultural commodities of the secondary crops (leaf lettuce, turnips and wheat) planted 30 days following application to soil or a primary crop (cucumber or squash) at a maximum seasonal application rate of 1140 g ai/ha. Therefore, the rotational crop restrictions on the FLINT 50WG and STRATEGO 250EC labels should state immediate plantback of any crop listed on the label and a 30-day plantback interval for all other crops.*

Comments:

The studies sent by the applicant were critical reviewed. The PMRA evaluated the US study by Kennedy (1997) ABR-97087, as well as the US field rotational crop study using unlabeled trifloxystrobin by Hayworth (1999), 109-97.

The two studies by Gross (1997) CMR 26/97 and by Stingelin (1997) CMR 24/97, for outdoor confined accumulation of trifloxystrobin on rotational crops were not submitted by the applicant for evaluation.

The PMRA stated that the metabolic pathway of trifloxystrobin in rotational crops was qualitatively similar to the pathway observed in apples, wheat and cucumbers with the exception that TFA is detected in rotational crops and not in target crops.

### 4.7.3 EU

Studies submitted by the applicant and evaluated by the EU

- Gross, D. 1997. Outdoor confined accumulation study on rotational crops after bareground application of (CF3-Phenyl-U-14C) labelled CGA 279202. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR26/97, Edition Number: MO-01-015715. Unpublished.
- Stingelin, J. 1997. Outdoor confined accumulation study on rotational crops after bareground application of [glyoxyl-phenyl-(U)-14C]-CGA 279202. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR24/97, Edition Number: MO-01-002816. Unpublished.

Studies submitted to other participants and not reviewed by the EU

- Hayworth, C. G. 1999. CGA - 279202 - Field accumulation in rotational crops. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 109-97, Edition Number: MO-01-017324. Unpublished.
- Kennedy, E. T. 1997. 14C-CGA-279202: Uptake and distribution of residues in confined rotational crops. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97087, Edition Number: MO-01-015714. Unpublished.

Result

The evaluation was made by the United Kingdom as EU Rapporteur Member State in April 2000. A monograph entitled *Draft Assessment Report* (DAR) was prepared (11343c/ECCO/BBA/00). Information on rotational crops was presented on pages 237 – 249 under point B.7.1.3. A summary is included in Point B.7.1.6 on page 255 and is quoted below.

> *Metabolism of trifloxystrobin was investigated in rotational crops (lettuce, radish wheat) planted 30, 120, 174 and 365 days after treatment, by applying [14C-GP] trifloxystrobin and [14C-GP] trifloxystrobin to bare soil at a rate of 500 g a.s./ha. At harvest in 31 day crops, total mg/kg residues (expressed as trifloxystrobin) were lettuce (0.025 mg/kg), radish tops and roots (0.041, 0.031 mg/kg), spring wheat at 50% maturity (0.060 mg/kg)and grain (0.059 mg/kg) and straw (0.075 mg/kg). The TRR in the 0-10 cm soil layer decreased from 0.375 mg/kg to 0.262 mg/kg over 31 days, corresponding to a half life of TRR of approximately 81 days, assuming pseudo first-order decay. Trifloxystrobin decreased from 86.7% to 3.6%TRR and hydrolysis acids CGA 321113 (E,E-isomer) plus CGA 373465 ( E,Z-isomer) increased from 2.5% to 46.2% corresponding to a half life of CGA 321113 plus CGA 373465 of approximately 72 days. This was the major fraction at each rotational planting.*
>
> *Trifluoroacetic acid was the major metabolite, accounting for up to 65.7% of the TRR (0.016 mg/kg) in radish tops at 120 day rotation and for 23% and 12% respectively of residues in 31 day wheat grain and straw, however is not of toxicological concern at these levels. Trifloxystrobin + isomers were detected in immature wheat (10.5%TRR; 0.006 mg/kg) and radish roots (15.0%TRR; 0.005 mg/kg). CGA 321113 was detected in radish roots (7.5%TRR; 0.001 mg/kg) and wheat straw (2.3%TRR; 0.003 mg/kg).*

Comments

The studies sent by the applicant were critical reviewed. The EU evaluated the two studies by Stingelin (1997) CMR 24/97 and Gross (1997) CMR 26/97 for outdoor confined accumulation of trifloxystrobin on rotational crops. No further studies are required (statement on page 333 of the DAR).

The US study by Kennedy (1997) ABR-97087, as well as the US field rotational crop study using unlabeled trifloxystrobin by Hayworth (1999) 109-97, were not submitted by the applicant.

### 4.7.4 USA

Studies submitted by the applicant and evaluated by the USA

- Hayworth, C. G. 1999. CGA - 279202 - Field accumulation in rotational crops. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 109-97, Edition Number: MO-01-017324. Unpublished.
- Kennedy, E. T. 1997. 14C-CGA-279202: Uptake and distribution of residues in confined rotational crops. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97087, Edition Number: MO-01-015714. Unpublished.

Studies submitted to other participants and not reviewed by the USA

- Gross, D. 1997. Outdoor confined accumulation study on rotational crops after bareground application of (CF3-Phenyl-U-14C) labelled CGA 279202. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR26/97, Edition Number: MO-01-015715. Unpublished.
- Stingelin, J. 1997. Outdoor confined accumulation study on rotational crops after bareground application of [glyoxyl-phenyl-(U)-14C]-CGA 279202. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR24/97, Edition Number: MO-01-002816. Unpublished.

Result

The evaluation was made by the US EPA in 1999 and in 2002.

The 1999 *Memorandum (PP#8F04955, 7/22/99 review, DP Barcodes D257888 and D254208)* including the evaluation of the US study by Kennedy (1997), ABR-97087, was prepared by the reviewer Fred Ives. Information on the test conditions, analytical methods, total radioactive residues, characterisation/identification of metabolites and storage stability of residues were presented in detail on pages 188 – 202 under point 35. Summary discussions are presented on pages 16 to 17 and are quoted below.

> *The submitted confined rotational crop study is adequate. Total radioactive residues (expressed as trifloxystrobin equivalents) accumulated at levels greater than 0.01 ppm in/on the following rotational commodities planted in silt loam soil that has been treated with [14C]trifloxystrobin (GP or TFMP label) at 2.0 lb ai/A (2x the maximum proposed seasonal rate): turnip leaves (0.011-0.064 ppm); turnip roots (0.005-0.018 ppm); spinach (0.016-0.264 ppm); wheat forage (0.021-0.282 ppm); wheat straw (0.042-0.200 ppm); and wheat grain (0.029-0.069 ppm). Total radioactive residues in/on commodities from the TFMP-label treatment were higher than the GP-label treatment.*
>
> *The study adequately characterized/identified the majority of radioactive residues in/on all commodities harvested from all plantback intervals. The predominant metabolite identified was trifluoroacetic acid (20.1-93.6% TRR). HED does not consider this residue to be of concern at the 0.2 ppm levels observed. Intact parent was identified only as a minor (#0.001 ppm) component. The following additional metabolites were detected at low concentrations (<0.01 ppm each): CGA-279202, CGA-331409, CGA-357261, CGA-357262, CGA-321113, CGA-373465, CGA-373466, CGA-320299, and phthalic acid.*

*In consideration of the 2x rate used in the study and because quantifiable residues of trifloxystrobin and CGA-321113 in/on crops rotated at a 30-day plantback interval are not likely to be detected at the LOQ (0.02 ppm) of the proposed enforcement method, limited confined rotational field trials (OPPTS GLN 860.1900) will not be required. Proposed plantback restrictions for the revised WDG label for use on pome fruits, grapes, cucurbit vegetables and the WG Twin-pak label (trifloxystrobin a.i. + propiconazole a.i.) are adequate for trifloxystrobin uses and no rotational crop tolerances must be proposed at this time.*

The 2002 *Memorandum (PP#0F06121, 1/17/02 review, DP Barcodes D267787 and D272054)* including the evaluation of the US field rotational crop study using unlabeled trifloxystrobin by Hayworth (1999), 109-97, was prepared by the reviewer Leung Cheng. Information on the test conditions, analytical methods, total radioactive residues, characterisation/identification of metabolites and storage stability of residues were presented in detail on pages 84 – 88. A summary discussion is presented for plant metabolism from pages 12 to 13 and is quoted below.

*The petitioner did submit new data on field accumulation in rotational crops. Trifloxystrobin (as CGA-279202 50 WG) was applied to squash or cucumbers as a post-foliar spray four times at 7-day intervals at 0.25 lb ai/A/application for a maximum rate of 1.0 lb ai/A/ season. The last application occurred on the day of primary crop harvest. Rotational crops were planted 30–31 and 120 days after the last application. The following rotational crops were planted: leaf lettuce, turnips, and wheat. Crops were grown under normal agricultural conditions. Samples of the appropriate RACs were collected at normal harvest maturity, frozen, and maintained frozen (approximately –20°C) until analysis using method AG-659A. The LOQ for both analytes were 0.02 ppm. Residues of trifloxystrobin and its acid metabolite CGA-321113 were all less than the LOQ in all crops planted at 30–31 days after the last application. Since all the 30-day samples were <0.02 ppm, no analysis was performed for the 120-day plantback interval samples.*

Comments

The studies sent by the applicant were critical reviewed. The US EPA evaluated the US study by Kennedy (1997) ABR-97087, as well as the US field rotational crop study using unlabeled trifloxystrobin by Hayworth (1999) 109-97.

The two studies by Gross (1997) CMR 26/97 and by Stingelin (1997) CMR 24/97, for outdoor confined accumulation of trifloxystrobin on rotational crops were not submitted by the applicant for evaluation.

The US EPA decided the proposed plant back restrictions for trifloxystrobin pesticides Flint™ and Stratego™ are adequate and no rotational crop tolerances need to be proposed.

### 4.7.5 JMPR

Studies submitted by the applicant and evaluated by the JMPR

- Gross, D. 1997. Outdoor confined accumulation study on rotational crops after bareground application of (CF3-Phenyl-U-14C) labelled CGA 279202. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR26/97, Edition Number: MO-01-015715. Unpublished.
- Hayworth, C. G. 1999. CGA - 279202 - Field accumulation in rotational crops. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 109-97, Edition Number: MO-01-017324. Unpublished.

- Kennedy, E. T. 1997. 14C-CGA-279202: Uptake and distribution of residues in confined rotational crops. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97087, Edition Number: MO-01-015714. Unpublished.
- Stingelin, J. 1997. Outdoor confined accumulation study on rotational crops after bareground application of [glyoxyl-phenyl-(U)-14C]-CGA 279202. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: CMR24/97, Edition Number: MO-01-002816. Unpublished.

Studies submitted to other participants and not reviewed by the JMPR
none

Result

The evaluation was made by the FAO Panel of the JMPR in 2004. A detailed monograph including crop rotation was prepared. Information on the test conditions, analytical methods, total radioactive residues, characterisation/identification of metabolites and storage stability of residues were presented in detail under point environmental fate – residues in rotational crops. The reports prepared by Canada, the EU and the USA as well as the dossier by the applicant were used by the JMPR to prepare the evaluation of this subject. The conclusions are presented in an appraisal and are quoted below.

> *The Meeting received data from confined crop rotation studies with both glyoxyl-phenyl-U-$^{14}$C-labelled and trifluoromethyl-phenyl-U-$^{14}$C-labelled trifloxystrobin and from crop rotation trials using unlabelled trifloxystrobin. In some trials a first crop was treated with trifloxystrobin while in others bare ground was directly treated with trifloxystrobin as an extreme case for residues in the soil from the first crop. The normal rotation was a first crop followed in rotation by a root crop (radish, turnip), a vegetable (lettuce, spinach) and a cereal (wheat). The rotation crops were sown or planted from approximately 30 days to 1 year after the final treatment of the first crop or bare ground.*
>
> *In a study with the exaggerated application rate of 2.2 kg ai/ha to bare soil turnips, spinach and wheat were planted and components of each were analysed at 30 and 120 days after application. Trifloxystrobin-equivalent residues were higher for the trifluoromethylphenyl label than the glyoxylphenyl label. Trifluoromethylphenyl label TRRs (as trifloxystrobin equivalents) after 30/120 days were turnip leaves 0.06/0.04 mg/kg, turnip roots 0.02/0.02 mg/kg, spinach 0.25/0.26 mg/kg, 25% mature wheat fodder 0.28/0.19 mg/kg, mature wheat fodder 0.14/0.10 mg/kg, wheat straw 0.17/0.20 mg/kg and wheat grain 0.07/0.06 mg/kg. Generally with the glyoxylphenyl label only a small proportion of the TRR was identified or characterised, with trifloxystrobin being <2%. CGA 321113 was higher, up to 8.5% of the TRR in turnip leaves and 17.5% in turnip roots (0.003 mg/kg). With the trifluoromethyl-phenyl-U-$^{14}$C label 37-100% of the TRR was identified or characterised. Trifloxystrobin, its conformational isomers and the acid CGA 321113 and its isomers were reported, all <0.01 mg/kg. Trifluoroacetic acid (TFA) was found as a major degradation product in all crops, especially in wheat (up to 0.23 mg/kg in immature fodder and 0.12 mg/kg in straw), demonstrating breakdown of the trifluoromethylphenyl ring. As trifluoroacetic acid was hardly observed as a plant metabolite in target crops after foliar application, it is likely that its precursor is formed in the soil or rhizosphere of the plants.*
>
> *In the unconfined rotational studies with unlabelled trifloxystrobin, no residues of trifloxystrobin (<0.02 mg/kg) or CGA 321113 (<0.02 mg/kg) in any of the rotational crops at the 30 days plant back intervals, except in wheat straw and grain from one trial, were detected.*

*The rotational crop studies suggest that trifloxystrobin itself and the acid CGA 321113 will not occur in rotational crops at levels ≥0.01 mg/kg.*

Comments

The JMPR stated that trifloxystrobin and its main metabolite CGA 321113 will very rarely occur as residues in rotational crops and then at levels <0.01 mg/kg.

### 4.7.6 Results - Crop rotation

No information on rotational crops was received by the Australian Agency. The Canadian PMRA and the US EPA evaluated two US studies and the EU evaluated two studies carried out in Europe. All four studies available were evaluated by the JMPR.

Generally, the metabolic pathway of trifloxystrobin in rotational crops was qualitatively similar to the pathway observed in apples, wheat and cucumbers with the exception of trifluoroacetic acid (TFA) that was detected in rotational crops but not in target crops. The rotational crop studies suggest that trifloxystrobin itself and the acid metabolite CGA 321113 will very rarely be occuring as residues in rotational crops and at levels <0.01 mg/kg.

## 4.8 Analytical methods

Only analytical methods for the determination of trifloxystrobin residues in plants and animal commodities were considered by the work sharing project.

### 4.8.1 Australia

Studies submitted by the applicant and evaluated by Australia

- Kissling, M. 1996. CGA 279202: Determination of parent compound by HPLC, fruits, vegetables and liquid processed commodities - Residue method including validation. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.02, Edition Number: MO-01-002940. Unpublished.
- Kissling, M. 1996. CGA 279202: Determination of parent compound and of metabolite CGA 321113 by GC -- cereals, bananas. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.03, Edition Number: MO-01-002944. Unpublished.
- Kissling, M. 1996. Validation of Method REM 177.03: Validation by analysis of fortified specimens and determination of recoveries (including efficiency of extraction and accountability tests). Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 141/96, Edition Number: MO-01-013697. Unpublished.
- Peterson, S. M. 1999. Determination of CGA 279202 and CGA 321113 in plant material by HPLC. Novartis Animal Health Australasia Pty. Limited, Kemps Creek, NSW, Australia. Bayer CropScience AG, Report No.: 265A.00, Edition Number: MO-01-009051, Method Report No.: 99/5/1647. Unpublished.
- Peterson, S. M. 1999. Validation of analytical method 265A.00. Novartis Animal Health Australasia Pty. Limited, Kemps Creek, NSW, Australia. Bayer CropScience AG, Report No.: 99/5/1647, Edition Number: MO-01-009054. Unpublished.

Studies submitted to other participants and not reviewed by Australia

- Bandong, G. Q. 1998. Independent laboratory validation of the analytical method for the determination of residues of CGA-279202 and the acid metabolite, CGA-321113, in crops and animal substrates by gas chromatography. The National Food Laboratory, Dublin, CA, USA. Bayer CropScience AG, Report No.: 279202/564, Edition Number: MO-01-012334. Unpublished.
- Bruns, G. and Hunka, K.1997. Independent Laboratory Validation for the Analytical Method (AG-654A) for the Determination of CGA-279202 and 5 Metabolites by HPLC/UV: Lab Project No: ETL97NV03.PRO: 416-97: AG-654A. Unpublished.
- Campbell, D. D. 1997. Analytical method for the determination of residues CGA 279202 and the acid metabolite, CGA 321113, in crops and animal substrates by gas chromatography. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: AG-659, Edition Number: MO-01-002956. Unpublished.
- Campbell, D. D. 1998. Analytical method for the determination of residues CGA-279202 and the acid metabolite, CGA-321113, in crops and animal substrates by gas chromatography. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: AG-659A, Edition Number: MO-01-011370. Unpublished.
- Eudy, L. W. and Ediger, K. 1999. CGA-279202 - summary of recovery data for analytical method AG-659A. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 756-99, Edition Number: MO-02-006422. Unpublished.
- Haan, R. A. de 2002. Analytical method for the determination of residues of trifloxystrobin ( Flint) and trifloxystrobin acid in/on tomatoes and peppers by LC-MS/MS. Bayer Corporation, Stilwell, KS, USA. Bayer CropScience AG, Report No.: 200177, Edition Number: MO-02-017364. Unpublished
- Hamilton, L. S. 1998. Independent laboratory validation of Novartis analytical method No. AG-659A, analytical method for the determination of residues CGA 279202 and the acid metabolite, CGA 321113, in crops and animal substrates by gas chromatography. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-98013, Edition Number: MO-01-014672. Unpublished.
- Kaijun, L., CGA 279202: Determination of CGA 279202 and its Metabolite, CGA 321113 by the US Food and Drug Administration Multiresidue Methods, Novartis Crop Protection, Inc. Greensboro, NC, Report No. ABR-97043. November 24, 1997. Unpublished.
- Kissling, M. 1997. Determination of parent compound (CGA 279202) by GC and of metabolite CGA 321113 by HPLC, hops (green and dry cones). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.04, Edition Number: MO-01-014692. Unpublished.
- Kissling, M. 1997. Validation of method REM 177.04 - Validation by analysis of fortified specimens and determination of recoveries. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 161/97, Edition Number: MO-01-014687. Unpublished.
- Kissling, M. 1997. CGA 279202: Determination of parent compound and of metabolite CGA 321113 in body fluids (urine, blood) by GC. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.05, Edition Number: MO-01-013702. Unpublished.
- Kissling, M. 1997. Validation of Method REM 177.05: Validation by analysis of fortified specimens and determination of recoveries. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 164/97, Edition Number: MO-01-013703. Unpublished.
- Lin, K. 1997. Determination of CGA-279202 and its Metabolite, CGA-321113 by the U.S. Food and Drug Administration Multiresidue Methods: Lab Project No. ABR-97043: 204-96. Unpublished.
- Nuesslein, F. 2002. Method 00742 for the determination of residues of trifloxystrobin (parent compound) and CGA 321113 (metabolite) in/on sample materials of carrot, brussels sprouts, cabbage, tomato, red pepper and lettuce by HPLC-MS/MS. Bayer AG, Leverkusen, Germany. Bayer CropScience AG, Report No.: 00742, Edition Number: MO-02-006453, Method Report No.: MR-078/02. Unpublished
- Nuesslein, F. 2003. Supplement E001 of the method 00742 for the determination of residues of Trifloxystrobin and CGA 321113 in/on the additional sample materials bean, broccoli, cauliflower,

cherry, cucumber, currant, leek, melon, plum and strawberry. Bayer CropScience AG, Report No.: 00742/E001, Edition Number: MO-03-005110, Method Report No.: MR-052/03. Unpublished.

- Weber, H. and Pelz, S. 2002. Enforcement method 00086/M040 for the determination of the residues of trifloxystrobin in cucumber (fruit), citrus (fruit), wheat (grain), almond (seed), hop and leek. Dr. Specht & Partner, Chemische Laboratorien GmbH, Hamburg, Germany. Bayer CropScience AG, Report No.: 00086/M040, Edition Number: MO-02-003267. Method Report No.: BAY-0018V. Unpublished.

Result

The evaluation was made by the APVMA in 2000. A monograph entitled *Residues Evaluation Report* was prepared. Information on analytical methods was presented in detail on pages 25 – 26. A summary discussion is presented on page 6 and quoted below.

> *Trifloxystrobin and the metabolite CGA321113 are quantified in plant material using HPLC method number 265A.00. The method involves extraction of residues from macerated solid samples (grapes and apples) with acetonitrile/water, and analysis by reverse phase HPLC with UV detection at 250 nm. Liquid samples such as juice and wine are not treated in any way prior to analysis. The limits of detection of available methods ranged from 0.011 mg/kg to 0.017 mg/kg for trifloxystrobin and CGA321113, while the limits of quantitation for both analytes were 0.02 mg/kg.*
>
> *Trifloxystrobin and CGA321113 are extracted from animal tissues with acetonitrile and water, then partitioned into hexane followed by solid phase extraction cleanup. Residues are quantified using GC with nitrogen-phosphorous detection (NPD). The LOQ for both analytes was 0.02 mg/kg in all samples except milk, where the LOQ was 0.01 mg/kg.*

Comments

APVMA decided that the analytical method for plant material is acceptable. Extraction efficiency data for the methods using radiolabelled samples from metabolism studies were not reported. In the case of methods for animal products, full details of the analytical methods used to determine trifloxystrobin residues in animal tissues, milk and eggs were not submitted by the applicant to APVMA. The evaluation is incomplete.

### 4.8.2 Canada

Studies submitted by the applicant and evaluated by Canada

- Bandong, G., CGA 279202: Independent Laboratory Validation of the Analytical Method for the Determination of Residues of CGA 279202 and the Acid Metabolite, CGA 321113, in Crops and Animal Substrates by Gas Chromatography. The National Food Laboratory, Dublin, CA. Report No. CA3490. January 29, 1998. Unpublished.
- Campbell, D.D., CGA 279202: Analytical Method for the Determination of Residues of Residues CGA 279202 and the Acid Metabolite, CGA 32113, in Crop and Animal Substrates by Gas Chromatography. Human Safety Department, Novartis Crop Protection, Inc., Greensboro, NC., Laboratory Report No. AG-659A (supersedes Method No. 659), Novartis Number 276-96. January 14, 1998. Unpublished.

- Kaijun, L., CGA 279202: Determination of CGA 279202 and its Metabolite, CGA 321113 by the US Food and Drug Administration Multiresidue Methods, Novartis Crop Protection, Inc. Greensboro, NC, Report No. ABR-97043. November 24, 1997. Unpublished.
- Kissling, M., CGA 279202: Determination of the Parent Compound by HPLC in Fruits, Vegetables and Liquid Processed Commodities. Residue Analysis, Novartis Crop Protection, AG., Basel, Switzerland. Laboratory Report No. REM 177.02. June 11, 1996. Unpublished.
- Kissling, M., CGA 279202: Determination of Parent Compound and Metabolite CGA 321113 by GC in Wheat, Barley and Bananas. Novartis Crop Protection, AG., Basel, Switzerland. Laboratory Report No. REM 177.03. January 14, 1998. Unpublished.
- Kissling, M., CGA 279202: Validation of Method REM 177.03 Validation by Analysis of Fortified Specimens and Determination of Recoveries. Novartis Crop Protection, AG., Basel, Switzerland. Report No. 141/96. December 9, 1996. Unpublished.
- Kissling M, CGA 279202: Determination of Parent Compound (CGA 279202) by GC and of Metabolite CGA 321113 by HPLC. Novartis Crop Protection, AG., Basel, Switzerland. Laboratory Report No. REM 177.04. November 18, 1997. Unpublished.

<u>Studies submitted to other participants and not reviewed by Canada</u>

- Bruns, G. and Hunka, K.1997. Independent Laboratory Validation for the Analytical Method (AG-654A) for the Determination of CGA-279202 and 5 Metabolites by HPLC/UV: Lab Project No: ETL97NV03.PRO: 416-97: AG-654A. Unpublished.
- Campbell, D. D. 1997. Analytical method for the determination of residues CGA 279202 and the acid metabolite, CGA 321113, in crops and animal substrates by gas chromatography. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: AG-659, Edition Number: MO-01-002956. Unpublished.
- Eudy, L. W. and Ediger, K. 1999. CGA-279202 - summary of recovery data for analytical method AG-659A. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 756-99, Edition Number: MO-02-006422. Unpublished.
- Haan, R. A. de 2002. Analytical method for the determination of residues of trifloxystrobin ( Flint) and trifloxystrobin acid in/on tomatoes and peppers by LC-MS/MS. Bayer Corporation, Stilwell, KS, USA. Bayer CropScience AG, Report No.: 200177, Edition Number: MO-02-017364. Unpublished
- Hamilton, L. S. 1998. Independent laboratory validation of Novartis analytical method No. AG-659A, analytical method for the determination of residues CGA 279202 and the acid metabolite, CGA 321113, in crops and animal substrates by gas chromatography. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-98013, Edition Number: MO-01-014672. Unpublished.
- Kissling, M. 1997. Validation of method REM 177.04 - Validation by analysis of fortified specimens and determination of recoveries. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 161/97, Edition Number: MO-01-014687. Unpublished.
- Kissling, M. 1997. CGA 279202: Determination of parent compound and of metabolite CGA 321113 in body fluids (urine, blood) by GC. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.05, Edition Number: MO-01-013702. Unpublished.
- Kissling, M. 1997. Validation of Method REM 177.05: Validation by analysis of fortified specimens and determination of recoveries. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 164/97, Edition Number: MO-01-013703. Unpublished.
- Lin, K. 1997. Determination of CGA-279202 and its Metabolite, CGA-321113 by the U.S. Food and Drug Administration Multiresidue Methods: Lab Project No. ABR-97043: 204-96. Unpublished.
- Nuesslein, F. 2002. Method 00742 for the determination of residues of trifloxystrobin (parent compound) and CGA 321113 (metabolite) in/on sample materials of carrot, brussels sprouts, cabbage, tomato, red pepper and lettuce by HPLC-MS/MS. Bayer AG, Leverkusen, Germany. Bayer CropScience AG, Report No.: 00742, Edition Number: MO-02-006453, Method Report No.: MR-078/02. Unpublished

- Nuesslein, F. 2003. Supplement E001 of the method 00742 for the determination of residues of Trifloxystrobin and CGA 321113 in/on the additional sample materials bean, broccoli, cauliflower, cherry, cucumber, currant, leek, melon, plum and strawberry. Bayer CropScience AG, Report No.: 00742/E001, Edition Number: MO-03-005110, Method Report No.: MR-052/03. Unpublished.
- Peterson, S. M. 1999. Determination of CGA 279202 and CGA 321113 in plant material by HPLC. Novartis Animal Health Australasia Pty. Limited, Kemps Creek, NSW, Australia. Bayer CropScience AG, Report No.: 265A.00, Edition Number: MO-01-009051, Method Report No.: 99/5/1647. Unpublished.
- Peterson, S. M. 1999. Validation of analytical method 265A.00. Novartis Animal Health Australasia Pty. Limited, Kemps Creek, NSW, Australia. Bayer CropScience AG, Report No.: 99/5/1647, Edition Number: MO-01-009054. Unpublished.
- Weber, H. and Pelz, S. 2002. Enforcement method 00086/M040 for the determination of the residues of trifloxystrobin in cucumber (fruit), citrus (fruit), wheat (grain), almond (seed), hop and leek. Dr. Specht & Partner, Chemische Laboratorien GmbH, Hamburg, Germany. Bayer CropScience AG, Report No.: 00086/M040, Edition Number: MO-02-003267. Method Report No.: BAY-0018V. Unpublished.

Result

The evaluation was made by the PMRA ARLA in 2001. A *Review* prepared by the reviewer Monique Thomas (April 30, 2001) gives detailed information on principle, detailed specification, qualitative parameters and recovery results of the analytical methods. The conclusions are presented in the report on pages 2 – 3 and are quoted below.

> *This analytical method (AG-659A) was developed to analyse the residue of concern (ROC) defined as trifloxystrobin (CGA 279202) and the free form of the acetic acid metabolite (CGA 321113), based on the plant and animal metabolism studies.*
> *The analytical method AG-659A involves extraction with ACN:water (80:20, v:v) followed by a three-layer liquid-liquid partition with water saturated with sodium chloride, toluene and hexane. The middle layer is collected, partitioned with hexane and evaporated. Residues are reconstituted in 0.085% phosphoric acid:acetone (95:5, v:v) and cleaned up on a C18 solid phase extraction column eluted with 0.085% phosphoric acid:acetone (30:70, v:v). Acetone is removed by evaporation and the eluate is partitioned intomethyl tert-butyl ether (MTBE):hexane (1:1, v:v). The eluate is concentrated and residues are redissolved in 0.1% polyethylene glycol in acetone prior to analysis and quantitation by GC/NPD. The method limit of detection (LOD) for each of the analytes, CGA 279202 and CGA 321113, was established at 0.08 ng injected. The reported limit of quantitation (LOQ) is 0.02 ppm for each analyte in all matrices except milk (0.01 ppm) and peanut hay (0.05 ppm). At spiking levels of 0.02-1.0 ppm, this method was found to give good mean recoveries of 74-111% with standard deviations ranging from 6-16% for CGA 279202 and recoveries of 76-120% with standard deviations ranging from 6-15% for CGA 321113 in animal matrices. For plant commodities, mean recoveries were good, ranging from 86-107% with standard deviations of 2-23% for CGA 279202 and 71-102% with standard deviations of 3-15% for CGA 321113, when spiked at 0.02-10.0 ppm. Good linearity was observed for CGA 279202 (correlation coefficient, r = 0.99788) and CGA 321113 (correlation coefficient r = 0.99996), in the range of 0.04-0.5 ng/:L. The control chromatograms generally had no peaks above the chromatographic background and the spike sample chromatograms contained only the analyte peaks. The peaks appeared well defined and symmetrical with no apparent carryover to the following chromatograms.*
>
> *An independent laboratory method validation (ILV) was conducted to verify the reliability and reproducibility of Method AG-659, for the determination of trifloxystrobin and the acid metabolite*

*in various plant and animal matrices. When incorporating the conditioning of the GC column with control matrix, the method trials for the determination of the two analytes were successful.*
*While the ILV was conducted on method AG-659, the method recommended for enforcement of trifloxystrobin per se in all subject plant or animal commodities is method AG-659A, which supercedes AG-659. Compared to AG-659, AG-659A also includes extractability and accountability results from 14 C-CGA 279202 animal validations as well as minor changes and ILV study suggestions to improve the ruggedness of the method.*
*According to the extraction efficiency data provided, the analytical method AG-659A was not successfully validated for meat as it was not capable of extracting all the radioactivity. As indicated in the lactating goat metabolism study, the extraction of liver with ACN and ACN:water released an average of 68%, however, microwave assisted extraction released an additional 29% of the TRRs. Based on the results of the radiovalidation study and the ruminant metabolism study, a microwave extraction step should be included in the enforcement analytical method AG-659A for animal matrices to ensure that the majority of the residues are extracted. Subsequently, validation of the microwave extraction step, at spiking levels equivalent to the LOQs of 0.01 ppm (milk), 0.02 ppm (all other animal matrices), 0.04 ppm (2 x 0.02 ppm), 0.10 ppm (5 x 0.02 ppm) and 0.20 ppm (10 x 0.02 ppm) should be conducted. Accountability results appeared consistent with the results obtained in the metabolism studies for peanut nutmeat, apples and cucumbers.*
*This method was determined to be valid for plant matrices only. The enforcement analytical method for animal matrices will have to include a microwave extraction step to ensure adequate extraction of the residues.*
*Additional data gathering methods (REM 177.02, REM 177.03 and REM 177.04) were developed for the quantitation of CGA 279202 and/or CGA 321113 in plant matrices and processed products. These three methods involved extraction with ACN:water (80:20, v:v), liquid-liquid partition, SPE cleanup and analysis using HPLC with UV, GC/ECD or a combination of both. All three methods were determined to be acceptable, based on accuracy and precision. The majority of the recoveries were within the guideline requirement (70-120%) with standard deviations not exceeding 20%. The chromatograms showed well defined peaks for trifloxystrobin and the acid metabolite. The identity of the parent and the metabolite were confirmed either by GC/ECD for method REM 177.02 or GC/MS for REM 177.03, however, GC/MS confirmatory method for method REM 177.04 was incapable of confirming the identity of the parent and the acid metabolite in hops due to interfering signals. No interlaboratory method validation was performed on any of these methods.*
*The development of the enforcement analytical methodology (AG-659A) for plants is acceptable while it is unacceptable for animal matrices and does not conform with the criteria of the RCGs. The data gathering analytical methodologies (REM177.02, REM 177.03 and REM 177.04) are classified acceptable and conform with the criteria of the RCGs (Residue Chemistry Guidelines Dir98-02, Section 3).*

Comments

The PMRA decided that the enforcement method AG-659A for plants is acceptable while it is unacceptable for animal matrices. The data gathering analytical methodologies (REM177.02, REM 177.03 and REM 177.04) for plants and plant processed commodities are classified acceptable and conform with the criteria of the Canadian Residue Chemistry Guidelines Dir98-02, Section 3). Extraction efficiency data for the methods using radiolabelled samples from metabolism studies were reported.

### 4.8.3 EU

Studies submitted by the applicant and evaluated by the EU

- Bandong, G. Q. 1998. Independent laboratory validation of the analytical method for the determination of residues of CGA-279202 and the acid metabolite, CGA-321113, in crops and animal substrates by gas chromatography. The National Food Laboratory, Dublin, CA, USA. Bayer CropScience AG, Report No.: 279202/564, Edition Number: MO-01-012334. Unpublished.
- Campbell, D. D. 1998. Analytical method for the determination of residues CGA-279202 and the acid metabolite, CGA-321113, in crops and animal substrates by gas chromatography. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: AG-659A, Edition Number: MO-01-011370. Unpublished.
- Kissling, M. 1996. CGA 279202: Determination of parent compound by HPLC, fruits, vegetables and liquid processed commodities - Residue method including validation. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.02, Edition Number: MO-01-002940. Unpublished.
- Kissling, M. 1996. CGA 279202: Determination of parent compound and of metabolite CGA 321113 by GC -- cereals, bananas. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.03, Edition Number: MO-01-002944. Unpublished.
- Kissling, M. 1996. Validation of Method REM 177.03: Validation by analysis of fortified specimens and determination of recoveries (including efficiency of extraction and accountability tests). Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 141/96, Edition Number: MO-01-013697. Unpublished.

Studies submitted to other participants and not reviewed by the EU

- Bruns, G. and Hunka, K.1997. Independent Laboratory Validation for the Analytical Method (AG-654A) for the Determination of CGA-279202 and 5 Metabolites by HPLC/UV: Lab Project No: ETL97NV03.PRO: 416-97: AG-654A. Unpublished.
- Campbell, D. D. 1997. Analytical method for the determination of residues CGA 279202 and the acid metabolite, CGA 321113, in crops and animal substrates by gas chromatography. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: AG-659, Edition Number: MO-01-002956. Unpublished.
- Eudy, L. W. and Ediger, K. 1999. CGA-279202 - summary of recovery data for analytical method AG-659A. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 756-99, Edition Number: MO-02-006422. Unpublished.
- Haan, R. A. de 2002. Analytical method for the determination of residues of trifloxystrobin ( Flint) and trifloxystrobin acid in/on tomatoes and peppers by LC-MS/MS. Bayer Corporation, Stilwell, KS, USA. Bayer CropScience AG, Report No.: 200177, Edition Number: MO-02-017364. Unpublished
- Hamilton, L. S. 1998. Independent laboratory validation of Novartis analytical method No. AG-659A, analytical method for the determination of residues CGA 279202 and the acid metabolite, CGA 321113, in crops and animal substrates by gas chromatography. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-98013, Edition Number: MO-01-014672. Unpublished.
- Kaijun, L., CGA 279202: Determination of CGA 279202 and its Metabolite, CGA 321113 by the US Food and Drug Administration Multiresidue Methods, Novartis Crop Protection, Inc. Greensboro, NC, Report No. ABR-97043. November 24, 1997. Unpublished.
- Kissling, M. 1997. Determination of parent compound (CGA 279202) by GC and of metabolite CGA 321113 by HPLC, hops (green and dry cones). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.04, Edition Number: MO-01-014692. Unpublished.

- Kissling, M. 1997. Validation of method REM 177.04 - Validation by analysis of fortified specimens and determination of recoveries. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 161/97, Edition Number: MO-01-014687. Unpublished.
- Kissling, M. 1997. CGA 279202: Determination of parent compound and of metabolite CGA 321113 in body fluids (urine, blood) by GC. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.05, Edition Number: MO-01-013702. Unpublished.
- Kissling, M. 1997. Validation of Method REM 177.05: Validation by analysis of fortified specimens and determination of recoveries. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 164/97, Edition Number: MO-01-013703. Unpublished.
- Lin, K. 1997. Determination of CGA-279202 and its Metabolite, CGA-321113 by the U.S. Food and Drug Administration Multiresidue Methods: Lab Project No. ABR-97043: 204-96. Unpublished.
- Nuesslein, F. 2002. Method 00742 for the determination of residues of trifloxystrobin (parent compound) and CGA 321113 (metabolite) in/on sample materials of carrot, brussels sprouts, cabbage, tomato, red pepper and lettuce by HPLC-MS/MS. Bayer AG, Leverkusen, Germany. Bayer CropScience AG, Report No.: 00742, Edition Number: MO-02-006453, Method Report No.: MR-078/02. Unpublished
- Nuesslein, F. 2003. Supplement E001 of the method 00742 for the determination of residues of Trifloxystrobin and CGA 321113 in/on the additional sample materials bean, broccoli, cauliflower, cherry, cucumber, currant, leek, melon, plum and strawberry. Bayer CropScience AG, Report No.: 00742/E001, Edition Number: MO-03-005110, Method Report No.: MR-052/03. Unpublished.
- Peterson, S. M. 1999. Determination of CGA 279202 and CGA 321113 in plant material by HPLC. Novartis Animal Health Australasia Pty. Limited, Kemps Creek, NSW, Australia. Bayer CropScience AG, Report No.: 265A.00, Edition Number: MO-01-009051, Method Report No.: 99/5/1647. Unpublished.
- Peterson, S. M. 1999. Validation of analytical method 265A.00. Novartis Animal Health Australasia Pty. Limited, Kemps Creek, NSW, Australia. Bayer CropScience AG, Report No.: 99/5/1647, Edition Number: MO-01-009054. Unpublished.
- Weber, H. and Pelz, S. 2002. Enforcement method 00086/M040 for the determination of the residues of trifloxystrobin in cucumber (fruit), citrus (fruit), wheat (grain), almond (seed), hop and leek. Dr. Specht & Partner, Chemische Laboratorien GmbH, Hamburg, Germany. Bayer CropScience AG, Report No.: 00086/M040, Edition Number: MO-02-003267. Method Report No.: BAY-0018V. Unpublished.

Result

The evaluation was made by the United Kingdom as EU Rapporteur Member State in April 2000. A monograph entitled *Draft Assessment Report* (DAR) was prepared (11343c/ECCO/BBA/00). Information on methods of analysis for residues in plants, plant products, animal tissues, milk and eggs was presented on pages 59 - 64 under point B.5. A summary evaluation and assessment is included in Point B.5.5 on page 64 and is quoted below.

*Where information has been submitted, it fulfils the following criteria:*

*a) adequate limit of determination (plant material and products: adequate for MRLs, soil: 0.05 mg/kg, water: 0.1 µg/l);*
*b) mean recovery 70-110%;*
*c) relative standard deviation of recovery rates <20%;*
*d) interfering blanks lower than 30% of the limit of determination;*
*e) readily available equipment and reagents used.*

*Reproducibility data were minimal. Results were either submitted for a number of plant and animal matrices combined or results for a particular plant matrix from the second laboratory were only reported combined with results for the first laboratory. However the combination of reproducibility data for different matrices is considered to be 'worst case' and is, in this case, acceptable.*

Comments:

The EU decided that the analytical methods submitted are acceptable. Extraction efficiency data for the methods using radiolabelled samples from metabolism studies were not reported.

### 4.8.4 USA

Studies submitted by the applicant and evaluated by the USA

- Bandong, G., CGA 279202: Independent Laboratory Validation of the Analytical Method for the Determination of Residues of CGA 279202 and the Acid Metabolite, CGA 321113, in Crops and Animal Substrates by Gas Chromatography. The National Food Laboratory, Dublin, CA. Report No. CA3490. January 29, 1998. Unpublished.
- Bruns, G. and Hunka, K.1997. Independent Laboratory Validation for the Analytical Method (AG-654A) for the Determination of CGA-279202 and 5 Metabolites by HPLC/UV: Lab Project No: ETL97NV03.PRO: 416-97: AG-654A. Unpublished.
- Campbell, D.D., CGA 279202: Analytical Method for the Determination of Residues of Residues CGA 279202 and the Acid Metabolite, CGA 32113, in Crop and Animal Substrates by Gas Chromatography. Human Safety Department, Novartis Crop Protection, Inc., Greensboro, NC., Laboratory Report No. AG-659A (supersedes Method No. 659), Novartis Number 276-96. January 14, 1998. Unpublished.
- Haan, R. A. de 2002. Analytical method for the determination of residues of trifloxystrobin ( Flint) and trifloxystrobin acid in/on tomatoes and peppers by LC-MS/MS. Bayer Corporation, Stilwell, KS, USA. Bayer CropScience AG, Report No.: 200177, Edition Number: MO-02-017364. Unpublished.
- Kissling, M., CGA 279202: Validation of Method REM 177.04 Validation by Analysis of Fortified Specimens and Determination of Recoveries. Novartis Crop Protection, AG., Basel, Switzerland. Report No. 161/97. Unpublished.
- Kissling M, CGA 279202: Determination of Parent Compound (CGA 279202) by GC and of Metabolite CGA 321113 by HPLC. Novartis Crop Protection, AG., Basel, Switzerland. Laboratory Report No. REM 177.04. November 18, 1997. Unpublished.
- Lin, K. 1997. Determination of CGA-279202 and its Metabolite, CGA-321113 by the U.S. Food and Drug Administration Multiresidue Methods: Lab Project No. ABR-97043: 204-96. Unpublished.

Studies submitted to other participants and not reviewed by the USA

- Campbell, D. D. 1998. Analytical method for the determination of residues CGA-279202 and the acid metabolite, CGA-321113, in crops and animal substrates by gas chromatography. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: AG-659A, Edition Number: MO-01-011370. Unpublished.
- Eudy, L. W. and Ediger, K. 1999. CGA-279202 - summary of recovery data for analytical method AG-659A. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 756-99, Edition Number: MO-02-006422. Unpublished.
- Hamilton, L. S. 1998. Independent laboratory validation of Novartis analytical method No. AG-659A, analytical method for the determination of residues CGA 279202 and the acid metabolite, CGA 321113, in crops and animal substrates by gas chromatography. Novartis Crop Protection, Inc.,

Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-98013, Edition Number: MO-01-014672. Unpublished.
- Kaijun, L., CGA 279202: Determination of CGA 279202 and its Metabolite, CGA 321113 by the US Food and Drug Administration Multiresidue Methods, Novartis Crop Protection, Inc. Greensboro, NC, Report No. ABR-97043. November 24, 1997. Unpublished.
- Kissling, M. 1996. CGA 279202: Determination of parent compound by HPLC, fruits, vegetables and liquid processed commodities - Residue method including validation. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.02, Edition Number: MO-01-002940. Unpublished.
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- Kissling, M. 1997. CGA 279202: Determination of parent compound and of metabolite CGA 321113 in body fluids (urine, blood) by GC. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.05, Edition Number: MO-01-013702. Unpublished.
- Kissling, M. 1997. Validation of Method REM 177.05: Validation by analysis of fortified specimens and determination of recoveries. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 164/97, Edition Number: MO-01-013703. Unpublished.
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- Nuesslein, F. 2003. Supplement E001 of the method 00742 for the determination of residues of Trifloxystrobin and CGA 321113 in/on the additional sample materials bean, broccoli, cauliflower, cherry, cucumber, currant, leek, melon, plum and strawberry. Bayer CropScience AG, Report No.: 00742/E001, Edition Number: MO-03-005110, Method Report No.: MR-052/03. Unpublished.
- Peterson, S. M. 1999. Determination of CGA 279202 and CGA 321113 in plant material by HPLC. Novartis Animal Health Australasia Pty. Limited, Kemps Creek, NSW, Australia. Bayer CropScience AG, Report No.: 265A.00, Edition Number: MO-01-009051, Method Report No.: 99/5/1647. Unpublished.
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- Weber, H. and Pelz, S. 2002. Enforcement method 00086/M040 for the determination of the residues of trifloxystrobin in cucumber (fruit), citrus (fruit), wheat (grain), almond (seed), hop and leek. Dr. Specht & Partner, Chemische Laboratorien GmbH, Hamburg, Germany. Bayer CropScience AG, Report No.: 00086/M040, Edition Number: MO-02-003267. Method Report No.: BAY-0018V. Unpublished.

Result

The evaluation was made by the US EPA in 1999 and in 2000.

The 1999 *Memorandum (PP#8F04955, 7/22/99 review, DP Barcodes D257888 and D254208)* including the residue analytical methodology was prepared by the reviewer Fred Ives. Information on enforcement

methods, independent lab validation and multi-residue methods were presented in detail on pages 135 - 147 under point 21. Summary discussions are presented on pages 7 – 9 and are quoted below.

*Residue Analytical Method - Plant and Animal Commodities:*
*The petitioner utilized a GC/NPD method AG-659 and GC/ECD method REM 177.03 for the determination of residues of trifloxystrobin and its acid metabolite CGA-321113 in/on plant and animal commodity samples collected from the storage stability, field residue, rotational crop, feeding, and processing studies. The concurrent recovery data indicate that these methods are adequate for data collection.*
*The petitioner proposes GC/NPD method AG-659A for tolerance enforcement purposes. The reported LOQ is 0.02 ppm for each analyte in all matrices, except peanut hay at 0.05 ppm and in milk at 0.01 ppm. The reported limit of detection is reported as 0.08 ng for parent and its acid metabolite, except for hay it is 0.2 ng. Method validation recoveries indicate that this method adequately recovers residues of trifloxystrobin and CGA-321113 in/on apples, apple wet pomace, and apple juice; cantaloupe; cucumber; grapes, raisins, and grape juice; peanut nutmeat, hay, and refined oil; potato tuber, granules, and wet peel; and animal tissues (ruminant and poultry meat, fat, and liver, and cow kidney), milk, and eggs. The requirements for radio validation data are fulfilled for trifloxystrobin per se.*
*Independent laboratory validation (ILV) of Method AG-659 has been completed. With some exceptions, the ILV was adequately reported and is considered by HED to be a marginally acceptable study. There was some uncertainty as to whether the residue recoveries were corrected for control values and the significance of the negative sign recorded before some control values.*
*While the ILV was conducted on Method AG-659, the method recommended for enforcement of trifloxystrobin per se in all subject plant or animal commodities and which is recommended for an EPA petition method validation (PMV) is Method AG-659A, which supecedes Method AG-659. Compared to AG-659, AG-659A also includes extractability and accountability results from 14C-CGA-279202 animal validations as well as minor changes and ILV study suggestions to improve the ruggedness of the method. A PMV of method AG-659A has been requested for trifloxystrobin and its acid metabolite.*
*Information was requested whether or to what degree the configurational isomers of trifloxystrobin and is acid metabolite CGA-321113 are recovered and determined by the proposed enforcement method. A partial reply reported that the configurational isomer of trifloxystrobin appear as separate peaks on gas chromatographic systems. While not a comprehensive reply, this information and evidence that the configurational isomers are a relatively low percentage of expected residues provides some assurance that the methodology will measure just residues recommended for regulation. Nothing further is required regarding that inquiry.*

*Multiresidue Method:*
*The petitioner submitted data concerning the recovery of residues of trifloxystrobin and the acid metabolite CGA-321113 using FDA multi-residue method protocols (PAM Vol. I). These data will be forwarded to FDA. In summary: Trifloxystrobin gave adequate responses through protocol C; it was completely recovered from fortified apple samples when analyzed through the Section 302 multiresidue method (Protocol D); standard solutions thereof were completely recovered through Protocol E Section 303 C2 (MeCL Florisil cleanup) and recovery was complete from fortified apple samples through Protocol E Section 303 E4/C2 complete method. It was not recovered though Section 303 C1 Florisil columns (ethyl ether/petroleum ether) or Section 303 E4/C1.*
*Acid metabolite CGA-321113 methylation through protocol B was effective. Unmethylated CGA-321113 gave adequate responses only on one GC system, but the methylated derivative (trifloxystrobin) on several. CGA-321113 was completely recovered through Section 402 C1a gel permeation cleanup (Protocol B - GPC) and residues from CGA-321113 fortified apples was*

*completely recovered through Section 402 E2/C1 multiresidue method (extraction with methylene chloride).*
*While a confirmatory method was not reported, HED concludes that the multi-residue method can serve that purpose.*

The 2000 *Memorandum (PP#9F5070, 04/06/00 review, DP Barcodes D254221, D254213, D254217)* including the results of analyrical methods was prepared by the reviewer Leung Cheng. Information on the analytical methods in plants, animals and a multiresidue method were presented in detail on pages 26 - 39. A summary discussion is presented on page 5 and quoted below.

*Method AG-659A is the proposed analytical method for the enforcement of trifloxystrobin per se in all subject plant and animal commodities. It supersedes Method AG-659. Compared to AG-659, AG-659A also includes extractability and accountability results from 14C-CGA-279202 animal validations as well as minor changes and independent laboratory validation (ILV) study suggestions to improve the ruggedness of the method. Method AG-659A has been validated by the petitioner for both trifloxystrobin and its acid metabolite CGA-321113. This method adequately recovers residues of trifloxystrobin and CGA-321113, usually with a limit of quantitation (LOQ) of 0.02 ppm. EPA has completed a method validation trial of AG-659A on apples, wet apple pomace, grapes, summer squash, peanut hay, peanuts, cow liver, cow milk and raisins, and concluded that AG-659A is suitable for enforcement of trifloxystrobin (CGA-279202) and the free form of its acid metabolite (CGA-321113) in plant and animal commodities).*

*The petitioner reported on a new closely-related analytical method named REM 177.04 for the determination and quantitation of residues of trifloxystrobin and its metabolite CGA-321113 in hops (both in green cones and dry cones). Acceptable validation data from two separate laboratories in the same institution were presented. This method is designed specifically to deal with complicating interferences observed in hops. For both trifloxystrobin and CGA-321113, the LOQ for green cones is 0.10 ppm and for dry cones is 0.50 ppm. In comparison, for method AG-659A the LOQ is typically 0.02 ppm for both trifloxystrobin and CGA-321113. Extensive validation data were presented from concurrent recoveries to support the results from crop field trials and rotational crop studies. One or the other of the analytical methods AG-659, AG-659A, and REM 177.04 (AG-659A with modifications) are adequate for collecting data on residues of trifloxystrobin and its acid metabolite CGA-321113 in/on all crops associated with this petition.*

*Multiresidue Method*
*The regulable residue was tested in accordance with the Pesticide Analytical Manual, Volume I, Appendix II.*

Comments

The US EPA decided that the analytical methods submitted are acceptable. Extraction efficiency data for the methods using radiolabelled samples from metabolism studies were reported.

### 4.8.5 JMPR

Studies submitted by the applicant and evaluated by the JMPR

- Bandong, G. Q. 1998. Independent laboratory validation of the analytical method for the determination of residues of CGA-279202 and the acid metabolite, CGA-321113, in crops and animal

substrates by gas chromatography. The National Food Laboratory, Dublin, CA, USA. Bayer CropScience AG, Report No.: 279202/564, Edition Number: MO-01-012334. Unpublished.
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- Campbell, D. D. 1998. Analytical method for the determination of residues CGA-279202 and the acid metabolite, CGA-321113, in crops and animal substrates by gas chromatography. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: AG-659A, Edition Number: MO-01-011370. Unpublished.
- Eudy, L. W. and Ediger, K. 1999. CGA-279202 - summary of recovery data for analytical method AG-659A. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 756-99, Edition Number: MO-02-006422. Unpublished.
- Haan, R. A. de 2002. Analytical method for the determination of residues of trifloxystrobin ( Flint) and trifloxystrobin acid in/on tomatoes and peppers by LC-MS/MS. Bayer Corporation, Stilwell, KS, USA. Bayer CropScience AG, Report No.: 200177, Edition Number: MO-02-017364. Unpublished
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- Kissling, M. 1996. CGA 279202: Determination of parent compound by HPLC, fruits, vegetables and liquid processed commodities - Residue method including validation. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.02, Edition Number: MO-01-002940. Unpublished.
- Kissling, M. 1996. CGA 279202: Determination of parent compound and of metabolite CGA 321113 by GC -- cereals, bananas. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.03, Edition Number: MO-01-002944. Unpublished.
- Kissling, M. 1996. Validation of Method REM 177.03: Validation by analysis of fortified specimens and determination of recoveries (including efficiency of extraction and accountability tests). Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: 141/96, Edition Number: MO-01-013697. Unpublished.
- Kissling, M. 1997. Determination of parent compound (CGA 279202) by GC and of metabolite CGA 321113 by HPLC, hops (green and dry cones). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.04, Edition Number: MO-01-014692. Unpublished.
- Kissling, M. 1997. Validation of method REM 177.04 - Validation by analysis of fortified specimens and determination of recoveries. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 161/97, Edition Number: MO-01-014687. Unpublished.
- Kissling, M. 1997. CGA 279202: Determination of parent compound and of metabolite CGA 321113 in body fluids (urine, blood) by GC. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.05, Edition Number: MO-01-013702. Unpublished.
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- Nuesslein, F. 2002. Method 00742 for the determination of residues of trifloxystrobin (parent compound) and CGA 321113 (metabolite) in/on sample materials of carrot, brussels sprouts, cabbage, tomato, red pepper and lettuce by HPLC-MS/MS. Bayer AG, Leverkusen, Germany. Bayer CropScience AG, Report No.: 00742, Edition Number: MO-02-006453, Method Report No.: MR-078/02. Unpublished
- Nuesslein, F. 2003. Supplement E001 of the method 00742 for the determination of residues of Trifloxystrobin and CGA 321113 in/on the additional sample materials bean, broccoli, cauliflower,

cherry, cucumber, currant, leek, melon, plum and strawberry. Bayer CropScience AG, Report No.: 00742/E001, Edition Number: MO-03-005110, Method Report No.: MR-052/03. Unpublished.

- Peterson, S. M. 1999. Determination of CGA 279202 and CGA 321113 in plant material by HPLC. Novartis Animal Health Australasia Pty. Limited, Kemps Creek, NSW, Australia. Bayer CropScience AG, Report No.: 265A.00, Edition Number: MO-01-009051, Method Report No.: 99/5/1647. Unpublished.
- Peterson, S. M. 1999. Validation of analytical method 265A.00. Novartis Animal Health Australasia Pty. Limited, Kemps Creek, NSW, Australia. Bayer CropScience AG, Report No.: 99/5/1647, Edition Number: MO-01-009054. Unpublished.
- Weber, H. and Pelz, S. 2002. Enforcement method 00086/M040 for the determination of the residues of trifloxystrobin in cucumber (fruit), citrus (fruit), wheat (grain), almond (seed), hop and leek. Dr. Specht & Partner, Chemische Laboratorien GmbH, Hamburg, Germany. Bayer CropScience AG, Report No.: 00086/M040, Edition Number: MO-02-003267. Method Report No.: BAY-0018V. Unpublished.

Studies submitted to other participants and not reviewed by the JMPR

- Bruns, G. and Hunka, K.1997. Independent Laboratory Validation for the Analytical Method (AG-654A) for the Determination of CGA-279202 and 5 Metabolites by HPLC/UV: Lab Project No: ETL97NV03.PRO: 416-97: AG-654A. Unpublished.
- Kaijun, L., CGA 279202: Determination of CGA 279202 and its Metabolite, CGA 321113 by the US Food and Drug Administration Multiresidue Methods, Novartis Crop Protection, Inc. Greensboro, NC, Report No. ABR-97043. November 24, 1997. Unpublished.
- Lin, K. 1997. Determination of CGA-279202 and its Metabolite, CGA-321113 by the U.S. Food and Drug Administration Multiresidue Methods: Lab Project No. ABR-97043: 204-96. Unpublished.

Result

The evaluation was made by the FAO Panel of the JMPR in 2004. A monograph including residue analysis was prepared. Information on enforcement and specialized methods for plant and animal commodities was presented under point residue analysis – analytical methods. The conclusions are reported in an appraisal and are quoted below.

> *The Meeting received descriptions and validation data for analytical methods for residues of trifloxystrobin and the metabolite CGA 321113 in crops and animal commodities. The methods rely on GLC, HPLC and LC/MS/MS and generally achieve LOQs of 0.01 – 0.02 mg/kg in the crop and animal matrices except dry matrices as hay, straw (LOQ 0.05 mg/kg) and hops (LOQ 0.1 mg/kg). The recoveries were in the range of 70-120% for both analytes.*
>
> *In most of the field studies, the determination of trifloxystrobin and the metabolite CGA 321113 in plant and animal commodities is based on extraction of samples with acetonitrile and water (80 : 20, v/v), filtration, liquid-liquid partitioning with a three solvent system (sodium chloride saturated water, toluene and hexane), clean up on a C18 solid extraction column, partitioned into methyl-tert.-butyl ether/hexane, concentrated to dry, taken up in 0.1% polyethylene glycol in acetone for GC analysis with nitrogen-phosphorous detection (NPD). The LOQ was 0.02 mg/kg in all matrices except peanut hay and cereal straw at 0.05 mg/kg LOQ and milk at 0.01 mg/kg LOQ. This method (or the same except with EC detection) was used in rotational crop, storage stability and the field trial studies. The NPD-method is proposed as a monitoring method also.*
>
> *The standard multi-method DFG S 19 can be used for enforcement purposes for the determination of trifloxystrobin in plant materials except hops.*

*Extraction efficiency data for the methods using weathered radiolabeled samples from the plant metabolism studies for apples, cucumbers, peanuts, wheat grain and straw, and matrices from the animal metabolism studies were submitted. The results show that the residue extracted is in the same order as in the metabolism studies.*

Comments:

The JMPR noted that analytical methods for enforcement and risk assessment of residues of trifloxystrobin and the acid metabolite CGA 321113 are available. Extraction efficiency data for the methods using radiolabelled samples from metabolism studies were reported.

### 4.8.6 Results - analytical methods

The participants of the work sharing project did not receive the same studies.

It was decided by all participants that the analytical methods for the determination of trifloxystrobin in plant material are acceptable.

In the case of methods for animal products, full details of the analytical methods used to determine trifloxystrobin residues in animal tissues, milk and eggs were not submitted by the applicant to the Australian APVMA. Therefore, the Australian evaluation is incomplete.

The Canadian PMRA decided that the enforcement method AG-659A is unacceptable for the analysis of residues in animal matrices.

The EU, the USA and the JMPR decided that the analytical methods for enforcement and risk assessment of residues of trifloxystrobin and the acid metabolite CGA 321113 in animal matrices are acceptable.

Extraction efficiency data for the methods using radiolabelled samples from metabolism studies were reported by Canada, the USA and the JMPR.

## 4.9 Stability of pesticide residues in stored analytical samples

### 4.9.1 Australia

Studies submitted by the applicant and evaluated by Australia
none

Studies submitted to other participants and not reviewed by Australia

- Grunenwald, M. C. 1997. Report on special study 160-97 interim report after 12 months: Stability of CGA-279202 and CGA-321113 in crops and processed fractions under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 160-97, Edition Number: MO-01-006357. Unpublished.
- Grunenwald, M. C. 1997. Report on special study 301-97 interim report: Stability of CGA-279202 and CGA-321113 in meat, milk, and eggs under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 301-97, Edition Number: MO-01-006359. Unpublished.

- Grunenwald, M. C. 1999. Stability of CGA-279202 and CGA-321113 in crops and processed fractions under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 160-97, Edition Number: MO-01-006357. Unpublished.
- Grunenwald, M. C. 1999. Stability of CGA-279202 and CGA-321113 in meat, milk, and eggs under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 301-97, Edition Number: MO-01-006359. Unpublished.
- Kissling, M. 1996. CGA 279202: Determination of parent compound and of metabolite CGA 321113 by GC -cereals, bananas. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.03, Edition Number: MO-01-002944. Unpublished.
- Kissling, M. 1997. Report on special study 154/96 interim report after 12 months: Stability of residues of CGA 279202 and its metabolite CGA 321113 in deep freeze stored analytical specimens of grapes, cucumbers, potatoes and wheat (whole plant, grains and straw). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 154/96, Edition Number: MO-01-006356. Unpublished.
- Kissling, M. 1999. Stability of residues of CGA 279202 and its metabolite CGA 321113 in deep freeze stored analytical specimens of grapes, cucumbers, potatoes and wheat (whole plant, grains and straw). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 154/96, Edition Number: MO-01-006356. Unpublished.

Result

Australia did no require special studies for storage stability of residues. In the *Residues Evaluation Report* (File No. P53871) is quoted on page 7, point 2.6:

> *Aspects of storage stability are addressed in the metabolism and residues trials. There are no further requirements in relation to storage stability of trifloxystrobin residues in crop and animal matrices.*

Comments

It is a deficiency that no special storage stability data were reviewed.

### 4.9.2 Canada

Studies submitted by the applicant and evaluated by Canada
- Grunenwald, M. C. 1999. Stability of CGA-279202 and CGA-321113 in crops and processed fractions under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 160-97, Edition Number: MO-01-006357. Unpublished.
- Grunenwald, M. C. 1999. Stability of CGA-279202 and CGA-321113 in meat, milk, and eggs under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 301-97, Edition Number: MO-01-006359. Unpublished.
- Kissling, M. 1996. CGA 279202: Determination of parent compound and of metabolite CGA 321113 by GC -- cereals, bananas. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.03, Edition Number: MO-01-002944. Unpublished.
- Kissling, M. 1999. Stability of residues of CGA 279202 and its metabolite CGA 321113 in deep freeze stored analytical specimens of grapes, cucumbers, potatoes and wheat (whole plant, grains and straw). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 154/96, Edition Number: MO-01-006356. Unpublished.

Studies submitted to other participants and not reviewed by Canada

- Grunenwald, M. C. 1997. Report on special study 160-97 interim report after 12 months: Stability of CGA-279202 and CGA-321113 in crops and processed fractions under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 160-97, Edition Number: MO-01-006357. Unpublished.
- Grunenwald, M. C. 1997. Report on special study 301-97 interim report: Stability of CGA-279202 and CGA-321113 in meat, milk, and eggs under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 301-97, Edition Number: MO-01-006359. Unpublished.
- Kissling, M. 1997. Report on special study 154/96 interim report after 12 months: Stability of residues of CGA 279202 and its metabolite CGA 321113 in deep freeze stored analytical specimens of grapes, cucumbers, potatoes and wheat (whole plant, grains and straw). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 154/96, Edition Number: MO-01-006356. Unpublished.

Result

The evaluation was made by the PMRA ARLA in 2001. A report in *review* format prepared by the reviewer Monique Thomas (April 25, 2001) gives detailed information on the points *materials and methods, final summary and study deficiencies.* The executive summary (conclusions) presented in the report on page 2 is quoted below.

> *In the freezer storage stability study, samples of grapes (berries, juice), cucumbers, potatoes (tubers, granules), wheat (plant, straw and grain), apples (fruit, wet pomace), peanut (nutmeat, hay and oil) and animal matrices (liver, muscle, milk, eggs), spiked separately with trifloxystrobin and the acid metabolite (CGA 321113) at levels of 0.05 and 1.0 ppm, were stored at –18°C for a duration not exceeding 24 months. The raw agricultural commodities (RACs) and the processed fractions were analyzed for residues of trifloxystrobin and CGA 321113 using GC/NPD method AG-659. Samples of grapes, cucumbers and potatoes were analyzed using a modified version of method AG-659. The modifications involved using pure tert-butyl methyl ether instead of tert-butyl methyl ether:hexane (1:1, v:v) and using ECD instead of NPD. Samples of wheat straw, grain, and whole plant were analyzed using method REM177.03, which is essentially the same as method AG-659 except that electron capture detection (ECD) is used rather than NPD. As there was no noticeable residue degradation in any of the matrices analysed, a half life for trifloxystrobin or CGA 321113 was not calculated.*
>
> *The data presented indicated that residues of trifloxystrobin and CGA 321113 were relatively stable at –18°C for 24 months in grapes, cucumbers, potatoes, and wheat (plant, straw and grain), 18 months in apples (fruit and wet pomace), peanut (nutmeat, hay and oil), potato granules, grape juice and 12-14 months in beef liver, beef muscle, milk and eggs.*
>
> *Since the freezer storage had no apparent impact on the stability of the residues of trifloxystrobin and CGA 321113 in plant and animal matrices, the residue of concern (ROC) will not have to be redefined nor will the proposed MRLs have to be adjusted to account for residue degradation as a function of time.*
>
> *This freezer storage stability study is classified acceptable and does satisfy the guideline requirement for a freezer storage stability study (Residue Chemistry Guidelines Dir98-02, Section 5).*

Comments

The studies sent by the applicant were critical reviewed. No deficiencies were identified.

### 4.9.3 EU

Studies submitted by the applicant and evaluated by the EU

- Grunenwald, M. C. 1997. Report on special study 160-97 interim report after 12 months: Stability of CGA-279202 and CGA-321113 in crops and processed fractions under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 160-97, Edition Number: MO-01-006357. Unpublished.
- Grunenwald, M. C. 1997. Report on special study 301-97 interim report: Stability of CGA-279202 and CGA-321113 in meat, milk, and eggs under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 301-97, Edition Number: MO-01-006359. Unpublished.
- Kissling, M. 1997. Report on special study 154/96 interim report after 12 months: Stability of residues of CGA 279202 and its metabolite CGA 321113 in deep freeze stored analytical specimens of grapes, cucumbers, potatoes and wheat (whole plant, grains and straw). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 154/96, Edition Number: MO-01-006356. Unpublished.

Studies submitted to other participants and not reviewed by the EU

- Grunenwald, M. C. 1999. Stability of CGA-279202 and CGA-321113 in crops and processed fractions under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 160-97, Edition Number: MO-01-006357. Unpublished.
- Grunenwald, M. C. 1999. Stability of CGA-279202 and CGA-321113 in meat, milk, and eggs under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 301-97, Edition Number: MO-01-006359. Unpublished.
- Kissling, M. 1999. Stability of residues of CGA 279202 and its metabolite CGA 321113 in deep freeze stored analytical specimens of grapes, cucumbers, potatoes and wheat (whole plant, grains and straw). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 154/96, Edition Number: MO-01-006356. Unpublished.
- Kissling, M. 1996. CGA 279202: Determination of parent compound and of metabolite CGA 321113 by GC -- cereals, bananas. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.03, Edition Number: MO-01-002944. Unpublished.

Result

The evaluation was made by the United Kingdom as EU Rapporteur Member State in April 2000. A monograph entitled *Draft Assessment Report* was prepared (11343c/ECCO/BBA/00). Information on the stability of residues prior to analysis was presented on pages 321 – 325 under point B.7.7. A summary discussion is presented on page 325 and quoted below.

> *Residues of trifloxystrobin and CGA 321113 in grapes, cucumbers, potatoes and wheat (whole plant, grain and straw), fortified at 0.5-1.0 mg/kg and stored deep frozen (less than –18°C), were unchanged after twelve months storage. Similarly, trifloxystrobin and CGA 321113 residues in apples, apple pomace and grape juice were stable after storage at –20°C for six months. Both studies are continuing.*

*Cereal residue trial samples were stored for up to 16 months, commonly for 1 year. The storage period for grapes, cucumbers and melons has been covered by freezer stability data. Apple and pear trial samples were stored for up to 2 years, commomly for 1 year, however, only 6 months freezer stability data are available, with further data to be submitted.*

*Milk, meat, liver and eggs were fortified with trifloxystrobin and CGA 321113 at 1.0 mg/kg and stored at –20°C for three to four months. The study is scheduled to continue for 24 months. There were large differences between replicate analyses and recoveries were inconsistent, possibly due to problems with temperature control in the study. However, the results superficially indicate no decrease in residue level during 3 months storage. A repeat study is required.*

Comments

Only interim reports were evaluated in the draft assessment report which is submitted for the work sharing project. It is assumend that the final reports were provided by the manufacturer in the meantime to the EU Rapporteur Member State but no information was received.

### 4.9.4 USA

Studies submitted by the applicant and evaluated by the USA

- Grunenwald, M. C. 1997. Report on special study 160-97 interim report after 12 months: Stability of CGA-279202 and CGA-321113 in crops and processed fractions under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 160-97, Edition Number: MO-01-006357. Unpublished.
- Grunenwald, M. C. 1997. Report on special study 301-97 interim report: Stability of CGA-279202 and CGA-321113 in meat, milk, and eggs under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 301-97, Edition Number: MO-01-006359. Unpublished.
- Grunenwald, M. C. 1999. Stability of CGA-279202 and CGA-321113 in crops and processed fractions under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 160-97, Edition Number: MO-01-006357. Unpublished.
- Grunenwald, M. C. 1999. Stability of CGA-279202 and CGA-321113 in meat, milk, and eggs under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 301-97, Edition Number: MO-01-006359. Unpublished.
- Kissling, M. 1997. Report on special study 154/96 interim report after 12 months: Stability of residues of CGA 279202 and its metabolite CGA 321113 in deep freeze stored analytical specimens of grapes, cucumbers, potatoes and wheat (whole plant, grains and straw). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 154/96, Edition Number: MO-01-006356. Unpublished.
- Kissling, M. 1999. Stability of residues of CGA 279202 and its metabolite CGA 321113 in deep freeze stored analytical specimens of grapes, cucumbers, potatoes and wheat (whole plant, grains and straw). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 154/96, Edition Number: MO-01-006356. Unpublished.

Studies submitted to other participants and not reviewed by the USA

- Kissling, M. 1996. CGA 279202: Determination of parent compound and of metabolite CGA 321113 by GC -cereals, bananas. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.03, Edition Number: MO-01-002944. Unpublished.

Result

The evaluation was made by the US EPA in 1999 and in 2000.

The 1999 *Memorandum (PP#8F04955, 7/22/99 review, DP Barcodes D257888 and D254208)* including the evaluation of the storage stability was prepared by the reviewer Fred Ives. Information on the test conditions, analytical methods and storage stability of residues were presented in detail on pages 147 - 158 under point 25. The summary discussion is presented on page 9 and quoted below.

> *Interim storage stability data (3-12 months, depending on matrix, of a 24 month study) demonstrate that residues of trifloxystrobin and its acid metabolite CGA-321113 are relatively stable in/on various raw agricultural and processed commodities and animal commodities stored under frozen conditions. Fortified residues of trifloxystrobin and CGA-321113 are stable for 12 months in/on grapes, cucumber, potato, and wheat straw, grain, and whole plant, for 6 months in/on apples and apple wet pomace, for 7 months in/on grape juice, peanut nutmeat, peanut hay, peanut oil, potato granules, for 3 months in beef muscle and beef liver, and for 4 months in milk and eggs. The petitioner has indicated that the results from the 24-month storage interval will be submitted to the Agency when completed.*
>
> *The maximum storage intervals (from harvest to residue analysis) of samples collected from the field and processing studies are as follows: apple juice (2 months); apples (6 months); apple wet pomace, grape juice, raisins (7 months); banana (7.5 months); cantaloupe, peanut nutmeat, meal and refined oil, and pear (8 months); grape (9 months); and cucumber and peanut hay (13 months). The maximum storage intervals (from collection to residue analysis) of samples collected from the cattle feeding study are as follows: milk, muscle, liver, and kidney (6 months); and fat (12 months). The Agency will make regulatory conclusions concerning the adequacy of the available storage stability data when the final storage stability report has been submitted and evaluated.*

The 2000 *Memorandum (PP#9F5070, 04/06/00 review, DP Barcodes D254221, D254213, D254217)* including the results of the storage stability studies was prepared by the reviewer Leung Cheng. Information on the test conditions, analytical methods, storage stability of residues were presented in detail on pages 30 - 42. Summary discussions are presented on pages 6 and 42 and are quoted below.

> *Quotation page 6*
> *Storage stability data show that residues of trifloxystrobin and CGA-321113 are stable in cucumbers, grapes, potatoes (tubers), whole wheat plant, wheat grain, and wheat straw stored at approximately –20°C for up to 24 months, and are stable in apple fruit, apple pomace, grape juice, peanut nutmeat, peanut hay, peanut oil, and potato granules stored at approximately –20°C for up to 18.6 months. The existing storage stability database for trifloxystrobin and CGA-321113 is adequate to support the crop residue data presented in this petition.*
> *Storage stability data show that residues of trifloxystrobin and CGA-321113 are stable in beef muscle, beef liver, milk, and eggs stored at approximately –20°C for at least 12 to 13 months. The existing storage stability database for trifloxystrobin and CGA-321113 is adequate to support the animal residue data presented in this petition.*
>
> *Quotation page 39*
> *Interim storage stability data on at least some of the above plant products had been presented earlier with the promise that the final results would be submitted to the Agency when completed. It was noted that the Agency would make regulatory conclusions concerning the adequacy of the available storage stability data when the final storage stability report had been submitted and*

*evaluated (PP#8F04955, DP Barcodes: D257888 & D254208, F. Ives, 7/22/99). The results are reported above and show that trifloxystrobin and CGA-321113 in fruit or fruiting vegetables, non-oily grains, and oily crops are stable under frozen conditions for at least 18.6 months, and are stable for at least 24 months in potato. These results are adequate to support the frozen storage intervals for the crops reported in this petition: almond (4 mos), hops (4 mos), fruiting vegetables (17 mos), potato (26-30 mos), sugar beet (13 mons), and wheat (16 mos).*

*Quotation page 42*
*Interim storage stability data on the above animal products had been presented earlier with the promise that the final results would be submitted to the Agency when completed. It was noted that the Agency would make regulatory conclusions concerning the adequacy of the available storage stability data when the final storage stability report had been submitted and evaluated (PP#8F04955, DP Barcodes: D257888 & D254208, F. Ives, 7/22/99). The promised final results are reported above. These results are adequate to support the poultry product residue data reported in this petition.*

Comments

Interim reports were evaluated first. The final reports later submitted were included into the evaluation. No deficiencies were identified.

### 4.9.5 JMPR

Studies submitted by the applicant and evaluated by the JMPR

- Grunenwald, M. C. 1999. Stability of CGA-279202 and CGA-321113 in crops and processed fractions under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 160-97, Edition Number: MO-01-006357. Unpublished.
- Grunenwald, M. C. 1999. Stability of CGA-279202 and CGA-321113 in meat, milk, and eggs under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 301-97, Edition Number: MO-01-006359. Unpublished.
- Kissling, M. 1996. CGA 279202: Determination of parent compound and of metabolite CGA 321113 by GC -- cereals, bananas. Ciba-Geigy Limited, Basel, Switzerland. Bayer CropScience AG, Report No.: REM 177.03, Edition Number: MO-01-002944. Unpublished.
- Kissling, M. 1999. Stability of residues of CGA 279202 and its metabolite CGA 321113 in deep freeze stored analytical specimens of grapes, cucumbers, potatoes and wheat (whole plant, grains and straw). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 154/96, Edition Number: MO-01-006356. Unpublished.

Studies submitted to other participants and not reviewed by the JMPR

- Grunenwald, M. C. 1997. Report on special study 160-97 interim report after 12 months: Stability of CGA-279202 and CGA-321113 in crops and processed fractions under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 160-97, Edition Number: MO-01-006357. Unpublished.
- Grunenwald, M. C. 1997. Report on special study 301-97 interim report: Stability of CGA-279202 and CGA-321113 in meat, milk, and eggs under freezer storage conditions. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 301-97, Edition Number: MO-01-006359. Unpublished.
- Kissling, M. 1997. Report on special study 154/96 interim report after 12 months: Stability of residues of CGA 279202 and its metabolite CGA 321113 in deep freeze stored analytical specimens of grapes,

cucumbers, potatoes and wheat (whole plant, grains and straw). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 154/96, Edition Number: MO-01-006356. Unpublished.

Result

The evaluation was made by the FAO Panel of the JMPR in 2004. A detailed monograph including storage stability was prepared. Information on the test conditions and results was presented under point "stability of residues in stored analytical samples". The reports prepared by Canada, the EU and the USA as well as the applicant's dossier were used by the JMPR in this subject. The conclusions for storage stability are included in the appraisal and are quoted below.

> *The Meeting received information on the stability of residues of trifloxystrobin and the metabolite CGA 321113 in various substrates (crops, farm animal commodities and processed commodities) at freezer temperature for 1 – 2 years. Trifloxystrobin and CGA 321113 were generally stable for the duration of the testing, i.e. decline in residue level was not evident or was less than 30%.*

Comments

Because the JMPR evaluation was made in 2004, only the final reports were submitted by the manufacturer. No study deficiencies were identified.

### 4.9.6 Results - stability of pesticide residues in stored analytical samples

The evaluations by Australia and the EU are incomplete because the final studies were not submitted. Canada, the USA and the JMPR came to the conclusion that residues of trifloxystrobin and CGA 321113 are stable under freezer storage conditions.

## 4.10 Residue definition

### 4.10.1 Comparison of residue definitions

The residue definitions resulting on the different evaluations of the data provided on physical chemical properties, metabolism in farm animals and plants, analytical methods, storage stability data, nature of residues after processing and aspects of farm animal feeding studies are listed below.

| | Enforcement | | Risk assessment | |
|---|---|---|---|---|
| | Animals | Plants | Animals | Plants |
| Australia | Sum of trifloxystrobin and its acid metabolite CGA 321113[1], expressed as trifloxystrobin | Sum of trifloxystrobin and its acid metabolite CGA 321113[1], expressed as trifloxystrobin | Sum of trifloxystrobin and its acid metabolite CGA 321113[1], expressed as trifloxystrobin | Sum of trifloxystrobin and its acid metabolite CGA 321113[1], expressed as trifloxystrobin |
| Canada | Sum of trifloxystrobin and its acid metabolite CGA 321113[1], expressed as trifloxystrobin | Sum of trifloxystrobin and its acid metabolite CGA 321113[1], expressed as trifloxystrobin | For animal commodities except liver: sum of trifloxystrobin, and its acid metabolite CGA 321113[1], expressed as trifloxystrobin.<br>For liver only: sum of trifloxystrobin, its acid metabolite CGA 321113[1] and the taurine conjugate of CGA 32113, expressed as trifloxystrobin. | Sum of trifloxystrobin and its acid metabolite CGA 321113[1], expressed as trifloxystrobin |
| EU | Sum of trifloxystrobin and its acid metabolite CGA 321113[1], expressed as trifloxystrobin | Trifloxystrobin | Sum of trifloxystrobin and its acid metabolite CGA 321113[1], expressed as trifloxystrobin | Trifloxystrobin |
| USA | Sum of trifloxystrobin and its acid metabolite CGA 321113[1], expressed as trifloxystrobin | Sum of trifloxystrobin and its acid metabolite CGA 321113[1], expressed as trifloxystrobin | For animal commodities except liver: sum of trifloxystrobin, and its acid metabolite CGA 321113[1], expressed as trifloxystrobin.<br>For liver only: sum of trifloxystrobin, its acid metabolite CGA 321113[1] and the taurine conjugate of CGA 32113, expressed as trifloxystrobin. | Sum of trifloxystrobin and its acid metabolite CGA 321113[1], expressed as trifloxystrobin |
| JMPR | Sum of trifloxystrobin and CGA 321113[1], calculated as trifloxystrobin<br>The residue is fat-soluble. | Trifloxystrobin. | Sum of trifloxystrobin and CGA 321113[1], calculated as trifloxystrobin.<br>The residue is fat-soluble. | Sum of trifloxystrobin and CGA 321113[1], calculated as trifloxystrobin. |

[1] (E,E)-methoxyimino-[2-[1-(3-trifluoromethylphenyl)ethylideneaminooxymethyl]phenyl] acetic acid

### 4.10.2 Results - residue definitions

The residue definitions for enforcement and risk assessment of animal products by all participants are identical with the minor difference that the USA and Canada additionally included the taurine conjugate of CGA 321113 into the risk assessment for liver.

The residue definitions for enforcement of plant commodities recommended by Australia, Canada and the USA are identical but different from those recommended by the EU and the JMPR which are also identical.

The residue definitions for risk assessment of plant commodities by Australia, Canada, the USA and the JMPR are identical. The EU did, however, not include the acid CGA 3211113 into the residue definition.

A statement for the fat solubility was only made by the JMPR.

## 4.11 Level of residues in processing

### 4.11.1 Australia

Studies submitted by the applicant and evaluated by Australia

Grapes

- Dal Santo, P. and Peterson, S. M. 1999. Trials to determine the level of trifloxystrobin (CGA 279202) and its major metabolite CGA 321113 in grapes, grape juice and wine following six application of Flint to grapevines. Novartis Crop Protection Australasia Pry. Ltd, Pendle Hill, NSW, Australia. Bayer CropScience AG, Report No.: 99/5/1645, Edition Number: MO-01-010124. Unpublished.
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Barley

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Wheat

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Maize

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Rice

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Peanut

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Hops

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Result

APVMA submitted only references for grapes and not for the second intended use pome fruit or other crops to the FAO evaluator of the work sharing project. But, in the monograph entitled *Residues Evaluation Report* (File No. P53871) the processing of pome fruit and grapes was discussed on pages 72 – 73 under point 6.4. Summaries are given on page 7, point 2.7 and for processing factors on page 73 and are quoted below:

> *Quotation page 7*
> *No reliable concentration factors could be determined from the apple residue trials since no quantifiable residues were present in raw or processed apple commodities. In the absence of adequate data, no MRL can be set for apple pomace. Apple pomace from treated apples must not be used as an animal feed commodity. There was no appreciable concentration of residues in washed, pureed or dried pears.*
>
> *In grapes, trifloxystrobin and acid metabolite (CGA321113) residues were found to concentrate 2.3x in grape marc/wet pomace and 1.4x in raisins. No concentration of residues occurred in grape juice, must or wine. No MRL is necessary for dried grapes, as the MRL for grapes is adequate to cover residues in the dried fruit, allowing for the loss of moisture in the drying process. An MRL of 3 mg/kg is recommended for grape pomace (dry) [MRL for grapes 0.5 x concentration factor 2.3 x drying factor 90/40 = 2.6, rounded to 3].*
>
> *Quotation page 73*
> *Processing factors: Must 0.46 (0.07-1.2, n=25), wet pomace 2.3 (n=1), young wine 0.14 (0.03-0.28, n=9), wine 0.05 (0.01-0.13, n=6), juice raw 0.13 (0.11-0.15, n=5), juice pasteurised 0.13 (0.08-0.17, n=5), raisins 1.4 (n=2)*

Comments

The level of the concentration of trifloxystrobin and CGA 321113 after processing was evaluated by Australia for pome fruit and grapes only. Three studies only (00/5/1645, GR 45597, GR 46597) were identical with the submission to JMPR. Processing factors were derived for must, wet grape pomace, wine, juice and raisins. An MRL of 3 mg/kg is recommended for grape pomace (dry) based on the processing factor for wet pomace and a drying factor.

### 4.11.2 Canada

Studies submitted by the applicant and evaluated by Canada

Grapes

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- Ipach, R., Field and Processing Study Determination of CGD 20540F in Red Grapes, Must and Red Wine. Staatliche Lehr und Forschungsanstalt Fur Landwirtschaft (Germany). Report Number CGD 03. Novartis Agro GmbH. October 31, 1996.
- Ipach, R., Field and Processing Study Determination of CGD 20540F in White Grapes, Must and White Wine. Staatliche Lehr und Forschungsanstalt Fur Landwirtschaft (Germany). Report Number GR01196. Novartis Agro GmbH. October 20, 1997.
- Ipach, R., Field and Processing Study Determination of CGD 20540F in White Grapes, Must and White Wine. Staatliche Lehr und Forschungsanstalt Fur Landwirtschaft (Germany). Report Number GR01496. Novartis Agro GmbH. October 10, 1997.
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- Kissling, M., Magnitude of the Residues After Application of CGA 279202 as Formulation WG50 (A-9360B) in Grapes (Italy) Determination of CGA 279202, CGA 321113. Residue Analysis, Novartis Crop Protection AG (Basle, Switzerland). Report Number 2085/96. Novartis Crop Protection AG. October 7, 1997.
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- Kissling, M., Magnitude of the Residues After Application of CGA 279202 and Cymoxanil as Formulation 49 WG (A-9529A) in Grapes (Italy). Determination of CGA 279202, CGA 321113, Cymoxanil in Grapes Berries, Must, Young Wine and Wine. Residue Analysis, Novartis Crop

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Pome fruit

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Grapes

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Maize

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Wheat

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Rice

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Cotton

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Peanut

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Hops

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Result

The evaluation was made by the PMRA ARLA in 2001. A report in *review* format prepared by the reviewer Monique Thomas (June 1, 2001) gives detailed information on the points *materials and methods, storage stability, final summary, study deficiencies,* including processing schemes. Results for processing of apples and wheat were reported also without any reference. The executive summary (conclusions) presented in the report on page 3 is quoted below.

> *In the processed food/feed studies, trifloxystrobin (CGA 279202 50WG, 50% ai (96% purity) or A-9529A, 49WG, 25% ai (96% purity) or Stratego, 11.4% ai (96% purity)) was applied to tomatoes, grapes, apples, potatoes, sugar beets and wheat at rates of application equivalent to 1X-15X*

*registered US GAP. Tomatoes were processed into paste and puree, grapes were processed into juice, raisins and wine, apples were processed into juice, potatoes were processed into flakes and chips, sugar beets were processed into refined sugar and wheat was processed into germ, bran, middlings, shorts and flour. A comparison of the residues in the RAC with those in each processed fraction resulted in maximum concentration factors for trifloxystrobin and the acid metabolite CGA 321113 of 2.5x and 3.5x, respectively, for raisins and 4x and 1x, respectively, for wheat bran. These concentration factors are considerably lower that the maximum theoretical concentration factors of 4.7x for raisins and 7.7x for bran. Based on the potential for residues of trifloxystrobin and CGA 321113 to concentrate in these commodities, MRLs of 5 ppm and 0.15 ppm will be recommended for promulgation on raisins and wheat bran, respectively. These are consistent with the US tolerances. When treated according to the registered US label rates, concentration factors for all other processed commodities are not expected to exceed 1x, therefore, combined residues of trifloxystrobin and the acid metabolite CGA 321113 will be covered under the RAC MRLs. MRLs will not be established for grape pomace, apple wet pomace, potato wet peel and trimmings, sugar beet dried pulp and wheat aspirated grain fractions on the basis that these are all classified as livestock feed.*

*These processed food/feed studies are classified acceptable and satisfy the guideline requirement for a processing study (Residue Chemistry Guidelines Dir98-02, Section 10).*

Comments

The level of the concentration of trifloxystrobin and CGA 321113 after processing was evaluated by Canada for tomatoes, grapes, apples, potatoes, sugar beet and wheat but, no reference/citation is given in the review for the apple and wheat studies. One tomato study (40-97), 5 grapes studies (56-96, 2084/96, 2085/96, GR01396, GR01496), 1 potato study (55-96) and 1 study on sugar beet (35-97) were identical with the submission to JMPR. Processing factors were derived by Canada for commodities resulting from RACs with residues >LOQ as grape products (must, wet grape pomace, wine, juice, raisins), tomato puree and paste, apple juice and pomace, sugar beet products (sugar, molasses, dried pulp). The results received on apples, potatoes and wheat were also discussed although no residues above the LOQ were found in the RAC. MRLs of 5 and 0.15 mg/kg were recommended for raisins and wheat bran.

Canada reported the maximum processing factors instead of mean values. Furthermore the calculation was made for both trifloxystrobin and CGA 321113 separatly instead of the sum.

### 4.11.3 EU

Studies submitted by the applicant and evaluated by the EU

Pome fruit

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Grapes

- Beinhauer, K. and Kissling, M. Determination of CGA 279202, CGA 321113 (metabolite of CGA 279202) and cymoxanil in grapes (berries, must, young wine and wine), Germany. Study report 2174/95. Novartis Crop Protection AG, Basel, Switzerland, 27.05.97. Unpublished.
- Ipach, R. and Kissling, M. 1997. Determination of CGA 279202, CGA 321113 (metabolite of CGA 279202) and cymoxanil in grapes (berries, must, young wine and wine), Germany. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: GR01296, Edition Number: MO-01-002602. Unpublished.
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- Kissling, M. 1997. Magnitude of residues after application of CGA 279202 as formulation WG 50 (A-9360 B) in grapes (Italy). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2084/96, Edition Number: MO-01-002638. Unpublished.
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Barley

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<u>Studies submitted to other participants and not reviewed by the EU</u>

Citrus

- Eudy, L. W. 2000. CGA 279202 and CGA 245704 : Magnitude of the residues in or on crop group 10: citrus fruits. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: SAM 4474, Edition Number: MO-01-008369. Unpublished.

Pome fruit

- Kissling, M. 2000. Residue study with CGA 279202 in or on apples in France (north). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2007/99, Edition Number: MO-01-009821. Unpublished.
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Stone fruit

- Grunenwald, M. C. 2000. CGA 279202 and CGA 245704: Magnitude of the residues in or on crop group 12: stone fruits. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 149-98, Edition Number: MO-01-008382. Unpublished.
- Kuehne-Thu, H. 2001. Residue study with CGA 279202 in or on peaches in Italy. Syngenta Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2095/00, Edition Number: MO-01-020812. Unpublished.

Strawberry

- Nuesslein, F. 2003. Determination of residues of trifloxystrobin and CGA 321113 in/on strawberry (fruit washed, preserve, washings, jam) following spray application of Flint 50 WG in the field in Northern France and Germany. Bayer CropScience AG, Report No.: RA-3038/02, Report includes Trial Nos.: R 2002 0191/5, R 2002 0188/5, (0188-02, 0191-02), Edition Number: MO-03-003498. Unpublished.

Grapes

- Beinhauer, K., CGA 279202 - Trial for the Determination of Residue Levels in Bunches of Grapes and Wine CGD 20540F. Biochem GmbH Karlsruhe. BioChem project No.: 95 10 47 008. Ciba-Geigy GmbH. March 7, 1995. Unpublished.
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- Clarke, C. 2000. Residues of trifloxystrobin (CGA 279202) and its major metabolite (CGA 321113) in grapes and dried fruit following three applications of Flint to grapevines, Australia. Novartis Crop Protection Australasia Pry. Ltd, Pendle Hill, NSW, Australia. Bayer CropScience AG, Report No.: P99/49, Edition Number: MO-01-008321. Unpublished.
- Dal Santo, P. 1999. Residues of trifloxystrobin (CGA 279202) and its major metabolite (CGA 321113) in grapes, grape juice and wine following six applications of Flint to grapevines. Novartis Crop Protection Australasia Pry. Ltd, Pendle Hill, NSW, Australia. Bayer CropScience AG, Report No.: P98/42, Edition Number: MO-01-008322. Unpublished.
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- Kissling, M. Determination of CGA 279202, CGA 321113 (metabolite of CGA 279202) and cymoxanil in grapes (berries, must, young wine and wine), Germany. Study report 2175/96. Novartis Crop Protection AG, Basel, Switzerland, 5.11.97. Unpublished.
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- Kissling, M. 1997. Magnitude of the Residues After Application of CGA 279202 and Cymoxanil as Formulation 49 WG (A-9529A) in Grapes (Switzerland). Determination of CGA 279202, CGA 321113, Cymoxanil. Residue Analysis, Novartis Crop Protection AG (Basle, Switzerland). Report Number 2036/95. Novartis Crop Protection AG. April 1, 1997.
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- Kissling, M. 1998. Residue study with CGA 279202 in or on grapes in Italy. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2077/97, Edition Number: MO-01-009714. Unpublished.
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Cabbage

- Nuesslein, F. and Eberhardt, R. 2002. Determination of residues of Trifloxystrobin in/on round cabbage (head; head washed; washings; head, cooked; cooking water) following spray application of Flint 50 WG in the field in Germany. Bayer AG, Leverkusen, Germany. Bayer CropScience AG, Report No.: RA-3198/01, Report includes Trial Nos.: R 2001 0643/2, R 2001 0640/8, (0643-01, 0640-01), Edition Number: MO-02-010319. Unpublished.

Tomato

- Eudy, L. W. 1999. CGA 279202 - Magnitude of the Residues in or on Crop Group 8: Fruiting Vegetables. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 40-97, Edition Number: MO-01-008363. Unpublished.

Potato

- Vincent, T. P. 1999. CGA 279202 - Magnitude of the residue in or on crop subgroup 1C: tuberous and corm vegetables. Human Safety Department, Greensboro, USA. Bayer CropScience AG, Report No.: 55-96, Edition Number: MO-01-009856. Unpublished.

Sugar Beet

- Vincent, T. P. and Ediger, K. 1998. Propiconazole and CGA 279202 - Magnitude of the residues in or on sugar beet. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 35-97, Edition Number: MO-01-008675. Unpublished.

Barley

- Kissling, M. 2001. Residue study with CGA 279202 in or on spring barley in France (North). Syngenta Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2021/99, Edition Number: MO-01-009713. Unpublished.
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- Maffezzoni, M. 1999. Residue study with CGA 279202 + cyproconazole in or on winter barley in North of France. ADME Bioanalyses, Aigues-Vives, France. Bayer CropScience AG, Report No.: 9810502, Edition Number: MO-01-009352. Unpublished.
- Maffezzoni, M. 1999. Residue study with CGA 279202 + cyproconazole in or on spring barley in North of France. ADME Bioanalyses, Aigues-Vives, France. Bayer CropScience AG, Report No.: 9810602, Edition Number: MO-01-009328. GLP. Unpublished.

Wheat

- Kuehne-Thu, H. 2002. Resdiue study with CGA 279202 in or on wheat in france (south). Syngenta Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2106/00, Edition Number: MO-02-004873. Unpublished.
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Maize

- Vincent, T. P. 2000. Propiconazole and CGA 279202 - Magnitude of the residues in or on field corn and popcorn. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 144-98, Edition Number: MO-01-017969. Unpublished.

Rice

- Vincent, T. P. 2000. Propiconazole and CGA-279202 - Magnitude of the residues in or on rice. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 150-98, Edition Number: MO-03-012929. Unpublished.

Cotton

- Campbell, D., Joseph, T., Ediger, K. and Vincent, T. P. 2001. CGA 279202 - Magnitude of the residues in or on cotton. Syngenta Crop Protection Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 110786, Edition Number: MO-02-001953. Unpublished.

Peanut

- Vincent, T. P. 1998. CGA-279202 - Magnitude of the residues in or on peanuts. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 53-96, Report includes Trial Nos.: 07-FR-003-96, OS-FR-202-96, OS-FR-314-96, OS-FR-604-96, OS-FR-753-96, OS-FR-841-96, OS-FR-842-96, OS-FR-843-96, OS-FR-844-96, OS-FR-845-96, NE-FR-303-96, OS-FR-609-97, Edition Number: MO-01-018246. Unpublished.

Hops

- Campbell, D. D. 1999. CGA 279202 and CGA 245704: Magnitude of the residues in or on hops. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 148-98, Edition Number: MO-02-002720. Unpublished.
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Report No.: GR01796, Report includes Trial Nos.: FR11/96/72, Edition Number: MO-02-002728. Unpublished.

Result

The evaluation was made by the United Kingdom as EU Rapporteur Member State in April 2000. A monograph entitled *Draft Assessment Report* was prepared (11343c/ECCO/BBA/00). Information on the results of the processing studies was presented on pages 326 – 331 under point B.7.8. A summary discussion is presented on page 330 and quoted below.

> *Processing factors for trifloxystrobin were as follows: 0.64-1.21 (washed fruit); 2.75-18.6 (apple pomace); 0.06-0.28 (apple juice); 0.33/0.15 (apple/pear puree); 0.17/0.31 (apple/pear dried fruit); 0.06-1.17 (grape must); 0.01-0.2 (mature wine). No residues in barley grain were detected in the samples used for processing studies. The need for processing studies in wheat was not triggered.*
>
> *Results indicate some contamination of washed fruit. Factors for grape must were generally <1.0. No data on grapes processed to raisins was submitted and is required. An estimate of the processing factor to raisins from the data presented for grape must is difficult since raisins are dried and the data may underestimate raisin residues.*

Comments

The level of the concentration of trifloxystrobin and CGA 321113 after processing was evaluated by the EU for pome fruit, grapes and barley. Three studies on apples (GR01096, FR06/96/42, ABR-97074), 3 on grapes (GR01296, GR01396, GR01496) and 3 on barley (9715102, 9711601, 9711602) were identical with the submission to JMPR. Processing factors were derived by the EU for commodities resulting from RACs with residues >LOQ as apple juice, puree and dried fruit; grape products (must and wine). The studies on barley could not be used because of residues <LOQ in the RAC.

### 4.11.4 USA

Studies submitted by the applicant and evaluated by the USA

Citrus

- Eudy, L. W. 2000. CGA 279202 and CGA 245704 : Magnitude of the residues in or on crop group 10: citrus fruits. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: SAM 4474, Edition Number: MO-01-008369. Unpublished.

Plums

- Grunenwald, M. C. 2000. CGA 279202 and CGA 245704: Magnitude of the residues in or on crop group 12: stone fruits. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 149-98, Edition Number: MO-01-008382. Unpublished.

Tomato

- Eudy, L. W. 1999. CGA 279202 - Magnitude of the Residues in or on Crop Group 8: Fruiting Vegetables. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 40-97, Edition Number: MO-01-008363. Unpublished.

Potato

- Vincent, T. P. 1999. CGA 279202 - Magnitude of the residue in or on crop subgroup 1C: tuberous and corm vegetables. Human Safety Department, Greensboro, USA. Bayer CropScience AG, Report No.: 55-96, Edition Number: MO-01-009856. Unpublished.

Sugar Beet

- Vincent, T. P. and Ediger, K. 1998. Propiconazole and CGA 279202 - Magnitude of the residues in or on sugar beet. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 35-97, Edition Number: MO-01-008675. Unpublished.

Wheat

- Vincent, T. P. and Ediger, K. 1999. Propiconazole and CGA 279202 - Magnitude of the residues in or on wheat Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 43-97, Edition Number: MO-01-008519. Unpublished.

Maize

- Vincent, T. P. 2000. Propiconazole and CGA 279202 - Magnitude of the residues in or on field corn and popcorn. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 144-98, Edition Number: MO-01-017969. Unpublished.

Rice

- Vincent, T. P. 2000. Propiconazole and CGA-279202 - Magnitude of the residues in or on rice. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 150-98, Edition Number: MO-03-012929. Unpublished.

<u>Studies submitted to other participants and not reviewed by the USA</u>

Pome fruit

- Beinhauer, K. 1996. CGA 279202, WG 50, A-9360 B, pears, Germany. BioChem GmbH Karlsruhe, Cunnersdorf, Germany. Bayer CropScience AG, Report No.: GR01096, Edition Number: MO-01-001890. Unpublished.
- Beinhauer, K. 1997. Trial for determination of residue levels in apples according to BBA Guideline IV, 3-3 and 3-4 (1990). BioChem GmbH Karlsruhe, Cunnersdorf, Germany. Bayer CropScience AG, Report No.: gr00996, Report includes Trial Nos.: FR06/96/42, Edition Number: MO-01-001834. Unpublished.
- Campbell, D. D. 1997. CGA 279202 - Magnitude of the residue in or on crop group 11: pome fruits. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97074, Edition Number: MO-01-002811. Unpublished.
- Kissling, M. 2000. Residue study with CGA 279202 in or on apples in France (north). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2007/99, Edition Number: MO-01-009821. Unpublished.
- Kissling, M. 2000. Residue study with CGA 279202 in or on apples in Switzerland. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2125/99, Edition Number: MO-01-009846. Unpublished.

Stone fruit

- Kuehne-Thu, H. 2001. Residue study with CGA 279202 in or on peaches in Italy. Syngenta Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2095/00, Edition Number: MO-01-020812. Unpublished.

Grapes

- Beinhauer, K., CGA 279202 - Trial for the Determination of Residue Levels in Bunches of Grapes and Wine CGD 20540F. Biochem GmbH Karlsruhe. BioChem project No.: 95 10 47 008. Ciba-Geigy GmbH. March 7, 1995. Unpublished.
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- Beinhauer, K. and Kissling, M. Determination of CGA 279202, CGA 321113 (metabolite of CGA 279202) and cymoxanil in grapes (berries, must, young wine and wine), Germany. Study report 2174/95. Novartis Crop Protection AG, Basel, Switzerland, 27.05.97. Unpublished.
- Clarke, C. 2000. Residues of trifloxystrobin (CGA 279202) and its major metabolite (CGA 321113) in grapes, grape juice and wine following three applications of Flint to grapevines, Australia. Novartis

Crop Protection Australasia Pry. Ltd, Pendle Hill, NSW, Australia. Bayer CropScience AG, Report No.: P99/40, Edition Number: MO-01-008320. Unpublished.
- Clarke, C. 2000. Residues of trifloxystrobin (CGA 279202) and its major metabolite (CGA 321113) in grapes and dried fruit following three applications of Flint to grapevines, Australia. Novartis Crop Protection Australasia Pry. Ltd, Pendle Hill, NSW, Australia. Bayer CropScience AG, Report No.: P99/49, Edition Number: MO-01-008321. Unpublished.
- Dal Santo, P. and Peterson, S. M. 1999. Trials to determine the level of trifloxystrobin (CGA 279202) and its major metabolite CGA 321113 in grapes, grape juice and wine following six application of Flint to grapevines. Novartis Crop Protection Australasia Pry. Ltd, Pendle Hill, NSW, Australia. Bayer CropScience AG, Report No.: 99/5/1645, Edition Number: MO-01-010124. Unpublished.
- Dal Santo, P. 1999. Residues of trifloxystrobin (CGA 279202) and its major metabolite (CGA 321113) in grapes, grape juice and wine following six applications of Flint to grapevines. Novartis Crop Protection Australasia Pry. Ltd, Pendle Hill, NSW, Australia. Bayer CropScience AG, Report No.: P98/42, Edition Number: MO-01-008322. Unpublished.
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- Ipach, R. and Kissling, M. 1997. Determination of CGA 279202 and CGA 321113 (metabolite of CGA 279202) in grapes (berries, must, young wine and wine), Germany. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: GR01396, Edition Number: MO-01-002612. Unpublished.
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- Kissling, M. 1997. CGA 279202 & Cymoxanil (and metabolite CGA 321113), WG 49, A-9529 A, Grapes, Switzerland. Novartis Crop Protection AG Basel, Switzerland. Study Report No. 2036/96. 01.04.1997. Unpublished.
- Kissling, M. Determination of CGA 279202, CGA 321113 (metabolite of CGA 279202) and cymoxanil in grapes (berries, must, young wine and wine), Germany. Study report 2176/96. Novartis Crop Protection AG, Basel, Switzerland, 5.11.97. Unpublished.
- Kissling, M. Determination of CGA 279202, CGA 321113 (metabolite of CGA 279202) and cymoxanil in grapes (berries, must, young wine and wine), Germany. Study report 2178/96. Novartis Crop Protection AG, Basel, Switzerland, 5.11.97. Unpublished.
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Strawberry

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Cabbage

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Barley

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Wheat

- Kuehne-Thu, H. 2002. Resdiue study with CGA 279202 in or on wheat in france (south). Syngenta Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2106/00, Edition Number: MO-02-004873. Unpublished.

Cotton

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Peanut

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Hops

- Beinhauer, K. 1996. Trial for determination of residue levels in hops according to BBA Guideline IV, 3-3 and 3-4 (1990). BioChem GmbH Karlsruhe, Cunnersdorf, Germany. Bayer CropScience AG, Report No.: GR01796, Report includes Trial Nos.: FR11/96/72, Edition Number: MO-02-002728. Unpublished.
- Campbell, D. D. 1999. CGA 279202 and CGA 245704: Magnitude of the residues in or on hops. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 148-98, Edition Number: MO-02-002720. Unpublished.

Result

The evaluation was made by the US EPA in 2000 and in 2002.

The 2000 *Memorandum (PP#9F5070, 06/04/00 review, DP Barcodes D254221, DP254213, D254218 and D254217)* including the evaluation of processing was prepared by the reviewer Leung Cheng. Information on the test conditions, analytical methods and storage stability of residues were presented in detail on pages 103-116. The summary discussion is presented on page 12 and quoted below.

> *Processing studies were conducted on sugar beets, potatoes, tomatoes, and wheat. On the basis of these studies, it is recommended that tolerances be established at 5.0 ppm in aspirated grain fractions, 0.15 ppm in wheat bran, 0.2 ppm in sugar beet molasses, and 0.4 ppm in dried sugar beet pulp for the combined residues of trifloxystrobin and its acid metabolite CGA-321113. A revised Section F reflecting these tolerances is needed.*

The 2002 *Memorandum (PP#0F06121, 17/01/02 review, DP Barcodes D267787, DP272054)* including the evaluation of processing was prepared by the reviewer Leung Cheng. Information on the test conditions, analytical methods and storage stability of residues were presented in detail on pages 80 - 85. The summary discussion is presented on pages 11 - 12 and quoted below.

> *Citrus*
> *Residues did not concentrate in juice but concentrated in oil (average 118x) and dried pulp (average 3x). Based on the highest average field trial (HAFT) of 0.25 ppm in oranges and average concentration factors, residues in oil and in dried pulp are not expected to exceed 30 ppm in citrus oil and 0.8 ppm in dried pulp. The petitioner needs to propose a tolerance of 30 ppm for combined residues of trifloxystrobin and CGA-321113 in citrus oil and a tolerance of 0.8 ppm for combined residues of trifloxystrobin and CGA-321113 in dried pulp. A revised Section F reflecting these tolerances is required.*
>
> *Corn*
> *No concentration was observed for trifloxystrobin in the meal, grits, flour, starch, and dry milled oil; it is not possible to determine a concentration or reduction factor for the acid metabolite (all*

*<0.02 ppm in corn grain before processing and in processed fractions) in these corn fractions. From the 5x study, a concentration of 2.4x was obtained in wet milled oil. Based on the HAFT of 0.026 ppm in corn grain, residues are not expected to exceed 0.1 ppm in corn oil. The petitioner needs to propose a tolerance of 0.1 ppm for combined residues of trifloxystrobin and CGA-321113 in corn oil.*

*Aspirated grain fractions*
*From the 5x study, trifloxystrobin concentrated 40x in aspirated grain fractions; it is not possible to determine a meaningful concentration factor for the acid metabolite when the treated corn grain bore <0.02 ppm CGA-321113 before processing. The concentration factor for trifloxystrobin should cover both itself and its acid metabolite since the acid metabolite is only a fraction of the total residue. Based on the HAFT of 0.026 ppm in corn grain, residues are not expected to exceed 1.2 ppm in aspirated grain fractions. However, since there already exists a time-limited tolerance of 5 ppm in aspirated grain fractions from the use on wheat, the tolerance for aspirated grain fractions should remain at 5 ppm. The petitioner must also change the proposed commodity definition from "Corn, field, aspirated grain fractions" to "Aspirated grain fractions." The Agency does not set tolerances for the aspirated grain fractions of individual crops. A revised Section F is needed.*

*Rice*
*Trifloxystrobin and its acid metabolite together did not concentrate in polished rice and showed apparent concentration (average concentration of 1.1x) in rice bran. The mean concentration factor for rice hulls is 2.55x. Based on the HAFT of 3.0 ppm in rice grain, residues in rice hulls are not expected to exceed a tolerance of 8 ppm. The petitioner needs to propose a tolerance of 8 ppm for combined residues of trifloxystrobin and CGA-321113 in rice hulls. A revised Section F reflecting this tolerance is required.*

*Stone fruit*
*Residues of trifloxystrobin and its acid metabolite concentrated (1.4x) in dried plums. Based on the HAFT of 0.55 ppm in fresh plums, residues in dried plums are not expected to exceed the proposed crop group tolerance of 2.0 ppm. Therefore, a tolerance in dried plum is not needed.*

Comments

The US EPA evaluated processing studies on citrus, plums, tomato, potato, sugar beet, wheat, maize and rice. Processing studies for pome fruit, grapes, strawberry, cabbage, barley, cotton, peanut and hops were not submitted and therefore not included into the evaluation.

MRLs for processed commodities were recommended.

### 4.11.5 JMPR

Studies submitted by the applicant and evaluated by the JMPR
Citrus
- Eudy, L. W. 2000. CGA 279202 and CGA 245704 : Magnitude of the residues in or on crop group 10: citrus fruits. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: SAM 4474, Edition Number: MO-01-008369. Unpublished.

Pome fruit

- Beinhauer, K. 1996. CGA 279202, WG 50, A-9360 B, pears, Germany. BioChem GmbH Karlsruhe, Cunnersdorf, Germany. Bayer CropScience AG, Report No.: GR01096, Edition Number: MO-01-001890. Unpublished.
- Beinhauer, K. 1997. Trial for determination of residue levels in apples according to BBA Guideline IV, 3-3 and 3-4 (1990). BioChem GmbH Karlsruhe, Cunnersdorf, Germany. Bayer CropScience AG, Report No.: gr00996, Report includes Trial Nos.: FR06/96/42, Edition Number: MO-01-001834. Unpublished.
- Campbell, D. D. 1997. CGA 279202 - Magnitude of the residue in or on crop group 11: pome fruits. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97074, Edition Number: MO-01-002811. Unpublished.
- Kissling, M. 2000. Residue study with CGA 279202 in or on apples in France (north). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2007/99, Edition Number: MO-01-009821. Unpublished.
- Kissling, M. 2000. Residue study with CGA 279202 in or on apples in Switzerland. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2125/99, Edition Number: MO-01-009846. Unpublished.

Stone fruit

- Grunenwald, M. C. 2000. CGA 279202 and CGA 245704: Magnitude of the residues in or on crop group 12: stone fruits. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 149-98, Edition Number: MO-01-008382. Unpublished.
- Kuehne-Thu, H. 2001. Residue study with CGA 279202 in or on peaches in Italy. Syngenta Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2095/00, Edition Number: MO-01-020812. Unpublished.

Grapes

- Clarke, C. 2000. Residues of trifloxystrobin (CGA 279202) and its major metabolite (CGA 321113) in grapes, grape juice and wine following three applications of Flint to grapevines, Australia. Novartis Crop Protection Australasia Pry. Ltd, Pendle Hill, NSW, Australia. Bayer CropScience AG, Report No.: P99/40, Edition Number: MO-01-008320. Unpublished.
- Clarke, C. 2000. Residues of trifloxystrobin (CGA 279202) and its major metabolite (CGA 321113) in grapes and dried fruit following three applications of Flint to grapevines, Australia. Novartis Crop Protection Australasia Pry. Ltd, Pendle Hill, NSW, Australia. Bayer CropScience AG, Report No.: P99/49, Edition Number: MO-01-008321. Unpublished.
- Dal Santo, P. and Peterson, S. M. 1999. Trials to determine the level of trifloxystrobin (CGA 279202) and its major metabolite CGA 321113 in grapes, grape juice and wine following six application of Flint to grapevines. Novartis Crop Protection Australasia Pry. Ltd, Pendle Hill, NSW, Australia. Bayer CropScience AG, Report No.: 99/5/1645, Edition Number: MO-01-010124. Unpublished.
- Dal Santo, P. 1999. Residues of trifloxystrobin (CGA 279202) and its major metabolite (CGA 321113) in grapes, grape juice and wine following six applications of Flint to grapevines. Novartis Crop Protection Australasia Pry. Ltd, Pendle Hill, NSW, Australia. Bayer CropScience AG, Report No.: P98/42, Edition Number: MO-01-008322. Unpublished.
- Ipach, R. and Kissling, M. 1997. Determination of CGA 279202, CGA 321113 (metabolite of CGA 279202) and cymoxanil in grapes (berries, must, young wine and wine), Germany. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: GR01296, Edition Number: MO-01-002602. Unpublished.
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- Kissling, M. 1997. Magnitude of residues after application of CGA 279202 as formulation WG 50 (A-9360 B) in grapes (Italy). Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2085/96, Edition Number: MO-01-002622. Unpublished.
- Kissling, M. 1998. Magnitude of residues after application of CGA 279202 as formulation EC 125 (A-9604 A) in grapes and wine. Ciba-Geigy (Pty) Ltd., Isando, South Africa . Bayer CropScience AG, Report No.: 2204/95, Edition Number: MO-01-008867. Unpublished.
- Kissling, M. 1998. Magnitude of residues in wine after application of CGA 279202 as formulation EC 125 (A-9604 A) to grapes. Ciba-Geigy (Pty) Ltd., Isando, South Africa . Bayer CropScience AG, Report No.: 2205/95, Edition Number: MO-01-008859. Unpublished.
- Kissling, M. 1998. Magnitude of residues in wine after application of CGA 279202 as formulation EC 125 (A-9604 A) to grapes. Ciba-Geigy (Pty) Ltd., Isando, South Africa . Bayer CropScience AG, Report No.: 2207/95, Edition Number: MO-01-008863. Unpublished.
- Kissling, M. 1998. Residue study with CGA 279202 in or on grapes in Spain. Novartis Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2050/97, Edition Number: MO-01-009703. Unpublished.
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- Vincent, T. P. 1998. CGA-279202 - Magnitude of the residue in or on grapes. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 110440, Report includes Trial Nos.: OW-FR-648-96, OW-FR-647-96, OW-FR-532-96, OW-FR-531-96, OW-FR-419-96, OW-FR-418-96, OW-FR-417-96, OW-FR-416-96, OW-FR-415-96, NE-FR-826-96, NE-FR-825-96, 02-FR-025-96, Edition Number: MO-03-012175. Unpublished.

Strawberry

- Nuesslein, F. 2003. Determination of residues of trifloxystrobin and CGA 321113 in/on strawberry (fruit washed, preserve, washings, jam) following spray application of Flint 50 WG in the field in Northern France and Germany. Bayer CropScience AG, Report No.: RA-3038/02, Report includes Trial Nos.: R 2002 0191/5, R 2002 0188/5, (0188-02, 0191-02), Edition Number: MO-03-003498. Unpublished.

Cabbage

- Nuesslein, F. and Eberhardt, R. 2002. Determination of residues of Trifloxystrobin in/on round cabbage (head; head washed; washings; head, cooked; cooking water) following spray application of Flint 50 WG in the field in Germany. Bayer AG, Leverkusen, Germany. Bayer CropScience AG, Report No.: RA-3198/01, Report includes Trial Nos.: R 2001 0643/2, R 2001 0640/8, (0643-01, 0640-01), Edition Number: MO-02-010319. Unpublished.

Tomato

- Eudy, L. W. 1999. CGA 279202 - Magnitude of the Residues in or on Crop Group 8: Fruiting Vegetables. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 40-97, Edition Number: MO-01-008363. Unpublished.

Potato

- Vincent, T. P. 1999. CGA 279202 - Magnitude of the residue in or on crop subgroup 1C: tuberous and corm vegetables. Human Safety Department, Greensboro, USA. Bayer CropScience AG, Report No.: 55-96, Edition Number: MO-01-009856. Unpublished.

Sugar Beet

- Vincent, T. P. and Ediger, K. 1998. Propiconazole and CGA 279202 - Magnitude of the residues in or on sugar beet. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: 35-97, Edition Number: MO-01-008675. Unpublished.

Barley

- Kissling, M. 2001. Residue study with CGA 279202 in or on spring barley in France (North). Syngenta Crop Protection AG, Basel, Switzerland. Bayer CropScience AG, Report No.: 2021/99, Edition Number: MO-01-009713. Unpublished.
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Wheat

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Maize

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Rice

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Grapes

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Barley

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Result

The evaluation was made by the FAO Panel of the JMPR in 2004. A detailed monograph including processing was prepared. Information on the test conditions and results was presented under point “fate of residues in storage and processing – in processing”. The conclusions and the recommended processing factors are presented in an appraisal and are quoted below.

> *The effect of processing on the level of residues of trifloxystrobin has been studied in barley, cabbage, cotton, grapes, hops, maize, orange, peanut, pome fruit, potato, rice, stone fruit, strawberry, sugar beet, tomato and wheat. The processing factors (PF) shown below were calculated from total residues (sum of trifloxystrobin and CGA 321113, calculated as trifloxystrobin).*

| RAC | Processed product | No. | Mean PF |
|---|---|---|---|
| Orange | juice | 5 | <0.19 |
| | oil | 5 | 130 |
| | pulp, dry | 5 | 3.4 |
| Apple, Pear | juice | 7 | 0.16 |
| | sauce/preserve | 4 | 0.48 |
| | fruit, dried | 2 | 0.39 |
| | pomace, wet | 6 | 9.4 |
| | pomace, dried | 1 | 25.6 |
| Plum | dried prune | 4 | 1.5 |
| Peach | preserve | 1 | <0.05 |
| Grapes | juice | 14 | 0.24 |
| | must | 27 | 0.46 |
| | wine | 35 | 0.15 |
| | fruit, dried | 4 | 2.3 |
| | pomace, wet | 1 | 2.25 |
| Strawberry | preserve | 2 | 0.29 |
| | jam | 2 | 0.62 |
| Tomato | paste | 5 | 1.6 |
| | puree | 5 | 0.56 |
| Potato | flakes | 2 | <0.42 |
| | chips | 2 | <0.42 |
| | peel rest | 2 | 2.3 |
| Sugar beet | white sugar | 2 | <0.18 |
| | dried pulp | 2 | 3.4 |

| RAC | Processed product | No. | Mean PF |
|---|---|---|---|
| | molasses | 2 | 1.5 |
| Barley | beer | 1 | 0.04 |
| Wheat | bran | 2 | 2.7 |
| | germ | 1 | <0.67 |
| | meal/flour | 2 | 0.4 |
| | whole meal | 1 | 0.5 |
| | whole meal bread | 1 | 0.25 |
| Rice | polished grain | 4 | 0.18 |
| | hull | 4 | 3.2 |
| | bran | 4 | 1.4 |
| Hops | spent hops | 1 | 0.04 |
| | yeast | 1 | 0.007 |
| | beer | 1 | <0.001 |

*Oranges were processed into juice, oil and dried pulp with processing factors of <0.19, 130 and 3.4, respectively. Based on the STMR value of 0.095 mg/kg for whole citrus fruits, the STMR-Ps were 0.018 mg/kg for citrus juice and 12 mg/kg for oil.*
*Allowing for the standard 91% dry matter, the Meeting estimated a maximum residue level of 1 mg/kg and an STMR-P of 0.35 mg/kg is estimated for citrus dried pulp (dry weight).*

*Apples and pear were processed into juice, sauce/preserve, pomace wet, pomace dry, and dried fruit, with processing factors of 0.16, 0.48, 9.4, 25.6 and 0.39, respectively. Based on the STMR value of 0.11 mg/kg for pome fruit, the STMR-P for juice was 0.018 mg/kg, 0.053 mg/kg for sauce, 0.053 mg/kg for preserve and 0.043 mg/kg for dried fruits. Because there is an existing Codex commodity number for apple pomace, dry, the Meeting estimated a maximum residue level of 15 mg/kg for dried apple pomace.*
*In the FAO manual, Appendix IX, apple wet pomace is listed as animal feed only. Allowing for the standard 40% dry matter, the Meeting estimated an STMR of 2.6 mg/kg (0.11 x 9.4 x 2.5) for wet apple pomace (dry weight).*

*Plums were processed into dried prunes with a processing factor of 1.5. Based on the STMR value of 0.15 mg/kg for plums, the STMR-P was 0.225 mg/kg mg/kg for dried prunes.*

*Peaches were processed into preserve (canned fruits) with a processing factor of 0.05. Based on the STMR value of 0.34 mg/kg for peaches, nectarines and apricots, the STMR-P was 0.017 mg/kg for canned fruits of peaches, nectarines and apricots.*

*Grapes were processed into juice, must, wine and dried fruit (raisins) with processing factors of 0.24, 0.46, 0.15 and 2.3, respectively. Based on the STMR value of 0.15 mg/kg for grapes, the STMR-P for juice was 0.036 mg/kg, for must 0.07 mg/kg, for wine 0.023 mg/kg and 0.345 mg/kg for raisins (dried grapes). Based on the highest residue of 2.2 mg/kg, the Meeting recommended a maximum residue level of 5 mg/kg for raisins (dried grapes).*

*Strawberries were processed into preserve (canned fruits) and jam with processing factors of 0.29 and 0.62. Based on the STMR value of 0.10 mg/kg for strawberries, the STMR-P values were 0.029 mg/kg and 0.062 mg/kg for canned fruits of strawberries and jam, respectively.*

*Head cabbage was processed to cooked cabbage. Because residues were not detected in the raw commodity, a processing factor cannot be calculated and estimates in the processed commodity cannot be made.*

*Tomatoes were processed into paste and puree with processing factors of 1.6 and 0.56, respectively. Based on the STMR value of 0.08 mg/kg for tomato, the STMR-Ps were 0.13 mg/kg for tomato paste and 0.045 mg/kg for puree.*

*Potatoes were processed into flakes, chips and wet peel with processing factors of 0.42, 0.42 and 2.3, respectively. Based on the STMR value of 0.02 mg/kg for potatoes, the STMR-Ps were 0.008 mg/kg for potato flakes and chips.*
*In the FAO manual, Appendix IX, wet peel (processed potato waste) is listed as animal feed. Allowing for the standard 15% dry matter, an STMR-P of 0.307 mg/kg (0.02 x 2.3 x 6.67) is estimated for potato wet peel (dry weight).*

*Sugar beet was processed into white sugar, dried pulp and molasses with processing factors of 0.18, 3.4 and 1.5, respectively. Based on the STMR value of 0.02 mg/kg, the STMR-P for white sugar was 0.0036 mg/kg.*
*In the FAO manual, Appendix IX, sugar beet dried pulp (88% dry matter) and molasses (75% dry matter) are listed as animal feed. Codex commodity numbers exist for both feed items. Based on the highest residue of 0.06 mg/kg, the Meeting estimated maximum residue levels of 0.3 mg/kg (0.06 x 3.4 x 1.14) for sugar beet dried pulp and 0.2 mg/kg (0.06 x 1.5 x 1.33) for sugar beet molasses (dry weight). The estimated STMR-P values were 0.077 mg/kg (0.02 x 3.4 x 1.14) for sugar beet dried pulp and 0.04 mg/kg (0.02 x 1.5 x 1.33) for sugar beet molasses (dry weight).*

*Wheat was processed into milled by-products (bran), flour, whole meal, whole meal bread and germ with processing factors of 2.7, 0.4, 0.5, 0.25 and 0.67. Based on the STMR value of 0.02 mg/kg for wheat grain, the STMR-Ps were 0.008 for wheat flour, 0.01 for whole meal, 0.005 for whole meal bread and 0.013 for germ.*
*In the FAO manual, Appendix IX, wheat milled by-products (bran) are listed as animal feed. Allowing for the standard 88% dry matter, the Meeting estimated an STMR-P of 0.062 mg/kg (0.02 x 2.7 x 1.14) for wheat bran (dry weight).*
*Based on the highest residue of 0.2 mg/kg, the Meeting recommended maximum residue levels of 1 mg/kg for wheat bran (dry weight) and 0.1 mg/kg for wheat flour.*

*Maize was processed to meal, grits, flour and oil. Because residues were not detected in the raw commodity, processing factors cannot be calculated and estimates in the processed commodity cannot be made.*

*Rice was processed into polished rice, bran and hulls with processing factors of 0.18, 1.4 and 3.2. Based on the STMR of 0.16 mg/kg, an STMR-P of 0.029 mg/kg was calculated for polished rice.*
*In the FAO manual, Appendix IX, rice bran and hulls are listed as animal feed. Allowing for the standard 90% dry matter, the Meeting estimated STMR-P values of 0.57 mg/kg (0.16 x 3.2 x 1.1) for rice hulls and 0.25 mg/kg (0.16 x 1.4 x 1.1) for rice bran (dry weight).*
*Based on the highest residue of 3.4 mg/kg, the Meeting recommended a maximum residue level of 7 mg/kg for rice bran, unprocessed (dry weight).*

*Cotton was processed to refined oil. Because residues were not detected in the raw commodity, a processing factor cannot be calculated and estimates in the processed commodity cannot be made.*

*Peanuts were processed to meal and refined oil. Because residues were not detected in the raw commodity, processing factors cannot be calculated and estimates in the processed commodity cannot be made.*

*Hops and barley were processed into beer. For hops, a processing factor of 0.001 was calculated. Based on the STMR value of 9.95 mg/kg for hops, dry, an STMR-P value of 0.01 mg/kg was calculated for beer.*

*Barley was processed into beer with a processing factor of 0.04. Based on the STMR value of 0.04 mg/kg, the STMR-P for beer was 0.0016 mg/kg.*

*Because the STMR-P arising from residues in barley was lower (0.0016 mg/kg), the Meeting estimated an STMR-P of 0.01 mg/kg for beer, based on residues in hops.*

Comments

The effect of processing on the level of residue was extensive evaluated by JMPR. Processing factors were derived for many processed commodities and used to recommend STMR-P values for better estimate of dietary intake calculations of trifloxystrobin residues.

### 4.11.6 Results - level of residues in processing

The processing factors derived by the participants of the work sharing project were summarized in the table below.

The calculation of the factors is based on residues expressed according to the respective residue definition. Therefore, the Australian-, US- and JMPR-factors can only partially be compared with the factors derived by the EU.

Canada reported the maximum processing factors instead of mean values. Furthermore the calculation was made for both trifloxystrobin and CGA 321113 separatly instead of the sum. These values cannot be used for a comparison with the factors calculated by other participants.

For the reasons mentioned above, the possibilities for a comparison of the processing factors are limited. However, in some cases when data are available such as for orange juice, oil, dried pulp; apple juice, sauce, dried fruit, wet pomace; grape juice, must, wine, wet pomace; dried prunes, tomato paste; sugar beet dried pulp, molasses; rice polished grains, bran, hulls and final wheat bran, and when considering the limitations, the processing factors are nearly in the same order.

RAC Raw agricultural commodity
No. Number of studies
PF Processing factor (residue in the processed product ÷ residue in RAC)

**Trifloxystrobin processing factors**

| RAC | Processed product | Australia | | Canada | | EU | | USA | | JMPR | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. | Mean PF | No. | Mean PF | No. | Mean PF | No. | Mean PF | No. | Mean PF |
| Orange | juice | | | | | | | 5 | 0.34 | 5 | <0.19 |
| | oil | | | | | | | 5 | 118 | 5 | 130 |
| | pulp, dry | | | | | | | 5 | 3.02 | 5 | 3.4 |
| Apple, pear | juice | 7 | 0.13 | | | | | | | 7 | 0.16 |
| | sauce/preserve | 2 | 0.24 | | | | | | | 4 | 0.48 |
| | fruit, dried | 2 | 0.24 | | | | | | | 2 | 0.39 |
| | pomace, wet | 7 | 11.7 | | | | | | | 6 | 9.4 |

| RAC | Processed product | Australia | | Canada | | EU | | USA | | JMPR | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. | Mean PF | No. | Mean PF | No. | Mean PF | No. | Mean PF | No. | Mean PF |
| | pomace, dried | | | | | | | | | 1 | 25.6 |
| Plum | dried prune | | | | | | | 4 | 1.4 | 4 | 1.5 |
| Peach | preserve | | | | | | | | | 1 | <0.05 |
| Grapes | juice | 5 | 0.13 | | | | | | | 14 | 0.24 |
| | must | 25 | 0.46 | | | 17 | 0.42 | | | 27 | 0.46 |
| | wine | 6 | 0.05 | | | 17 | 0.058 | | | 35 | 0.15 |
| | fruit, dried | 2 | 1.4 | | | | | | | 4 | 2.3 |
| | pomace, wet | 1 | 2.3 | | | 1 | 2.13 | | | 1 | 2.25 |
| Strawberry | preserve | | | | | | | | | 2 | 0.29 |
| | jam | | | | | | | | | 2 | 0.62 |
| Tomato | paste | | | | | | | 5 | 1.76 | 5 | 1.6 |
| | puree | | | | | | | | | 5 | 0.56 |
| Potato | flakes | | | | | | | | | 2 | <0.42 |
| | chips | | | | | | | | | 2 | <0.42 |
| | peel rest | | | | | | | | | 2 | 2.3 |
| Sugar beet | white sugar | | | | | | | | | 2 | <0.18 |
| | dried pulp | | | | | | | 2 | 3.35 | 2 | 3.4 |
| | molasses | | | | | | | 2 | 1.7 | 2 | 1.5 |
| Barley | beer | | | | | | | | | 1 | 0.04 |
| Wheat | bran | | | | | | | 1 | 2.9 | 2 | 2.7 |
| | germ | | | | | | | | | 1 | <0.67 |
| | meal/flour | | | | | | | | | 2 | 0.4 |
| | whole meal | | | | | | | | | 1 | 0.5 |
| | whole meal bread | | | | | | | | | 1 | 0.25 |
| Rice | polished grain | | | | | | | 4 | 0.18 | 4 | 0.18 |
| | hull | | | | | | | 4 | 2.6 | 4 | 3.2 |
| | bran | | | | | | | 4 | 1.1 | 4 | 1.4 |
| Hops | spent hops | | | | | | | | | 1 | 0.04 |
| | yeast | | | | | | | | | 1 | 0.007 |
| | beer | | | | | | | | | 1 | <0.001 |

## 4.12 Farm animal feeding

### 4.12.1 Australia

Studies submitted by the applicant and evaluated by Australia

- Campbell, D. D. 1997. CGA 279202 - Magnitude of the residues in meat and milk resulting from the feeding of three levels to dairy cattle. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97075, Edition Number: MO-01-002792. Unpublished.

Studies submitted to other participants and not reviewed by Australia

- Hayworth, C. G. 1999. CGA-279202 - Magnitude of the residues in poultry meat and eggs. Residue Chemistry Department, Greensboro, NC, USA. Bayer CropScience AG, Report No.: 243-98, Edition Number: MO-02-002553. Unpublished.

Result

The evaluation was made by APVMA in 2000. A monograph entitled *Residues Evaluation Report* (File No. P53871) was prepared. Information on the test conditions and results of the dairy cattle feeding study was presented on pages 74 - 75 under point 6.5. The conclusion presented on page 75 is quoted below.

> *On the basis of the above animal transfer data, it is concluded that no finite trifloxystrobin residues will be detected in animal tissues/milk from animals fed commodities containing trifloxystrobin residues at up to 6 mg/kg in the diet (~0.2 mg trifloxystrobin/kg bwt/day). The intake of trifloxystrobin residues from consumption of treated produce by animals is significantly less than 6 ppm in the feed. Maximum residues in animal feed commodities are estimated at 7 mg/kg for dry grape pomace (MRL of 10 mg/kg recommended). As grape pomace (dry) may comprise up to 20% of the beef cattle diet, the expected maximum intake of trifloxystrobin residues is 1.4 ppm in the feed. Therefore, all trifloxystrobin MRLs for animal commodities should be set at or about the LOQ (ie *0.02 mg/kg for milk; *0.05 mg/kg for mammalian meat, liver, kidney and fat).*

Comments

Because of the Australian intended uses of trifloxystrobin are limited to grapes and pome fruit which are not listed as poultry feedingstuffs, the poultry feeding study was not submitted by the applicant. Only a cattle feeding study was included into the evaluation. Based on the cattle transfer study and the estimated animal dietary burden, Australia estimated MRLs at or about the LOQ for animal commodities.

### 4.12.2 Canada

Studies submitted by the applicant and evaluated by Canada

- Campbell, D. D. 1997. CGA 279202 - Magnitude of the residues in meat and milk resulting from the feeding of three levels to dairy cattle. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97075, Edition Number: MO-01-002792. Unpublished.
- Hayworth, C. G. 1999. CGA-279202 - Magnitude of the residues in poultry meat and eggs. Residue Chemistry Department, Greensboro, NC, USA. Bayer CropScience AG, Report No.: 243-98, Edition Number: MO-02-002553. Unpublished.

Studies submitted to other participants and not reviewed by Canada
none

Result

The evaluation was made by the PMRA ARLA in 2001. A report in a *review* format prepared each for dairy cattle (May 28, 2001) and laying hens (May 31, 2001) by the reviewer Monica Thomas gives detailed information on the points *materials and methods, results (anticipated dietary burden, residues of trifloxystrobin and CGA 321113 in tissues and milk, final summary and study deficiencies.* The executive summaries (conclusions) presented in the respective report on page 1 are quoted below.

> *Dairy cattle*
> *In the dairy cattle feeding study, trifloxystrobin was administered orally to 10 Holstein dairy cattle for 28-30 days. The dosages were equivalent to 2 (1X), 6 (3X) and 20 (10X) ppm, equivalent to 0.19x, 0.57x and 1.89x, the anticipated dietary burden to beef cattle and 0.32x, 0.96x and 3.2x the anticipated dietary burden to dairy cattle. The animals were sacrificed 20-23 hours following the last administered dose.*

*The feeding study indicated that no measurable residues of trifloxystrobin and CGA 321113 were detected in milk, muscle, fat, liver and kidney at the lower feeding levels of 2 and 6 ppm. At the highest feeding level of 20 ppm, residues of trifloxystrobin were detected in fat (perirenal and omental) at levels ranging from 0.03-0.06 ppm while residues of CGA 321113 did not exceed 0.02 ppm (method LOQ). In contrast, at the highest feeding level, residues of trifloxystrobin in liver and kidney were not quantifiable while residues of the acid metabolite CGA 321113 were measured at 0.04-0.09 ppm in liver and <0.02-0.02 ppm in kidney.*
*The lactating goat metabolism study was conducted at 100 ppm, equivalent to ca. 16x the anticipated dietary burden to dairy cattle. Both studies were consistent in demonstrating that total residues of trifloxystrobin and CGA 321113 were highest in fat, liver and kidney and that residues in milk and muscle were low.*
*The purpose of this submission is to establish MRLs on imported commodities, however, the petitioner has not requested MRLs on imported milk, meat and meat by-products. Therefore, the US MRLs were included in the dietary risk assessment (DRA) to account for potential imports. The US has established tolerances of 0.02 ppm for milk and 0.05 ppm for all meat and meat by-products of cattle, goats, hogs, horses and sheep. These tolerances cover the combined residues of trifloxystrobin and CGA 321113.*
*This dairy cattle feeding study is classified acceptable and does satisfy the guideline requirement for a livestock feeding study (Residue Chemistry Guidelines Dir98-02, Section 8).*

*Laying hens*
*In the poultry feeding study, trifloxystrobin was administered orally to forty five Leghorn laying hens for 28 days. The dosage levels were 1.5 (1X), 4.5 (3X) and 15.0 (10X) ppm, equivalent to 30x, 90x and 300x the anticipated dietary burden of 0.05 ppm calculated using the US tolerances for treated feed items.*
*No measurable residues of trifloxystrobin (<0.02 ppm) and CGA 321113 (<0.02 ppm) were detected in eggs, skin with attached fat, breast and thigh muscle and liver at the highest feeding level. Therefore, the treated samples from the lower feeding levels (1.5 ppm and 4.5 ppm) were not analysed.*
*The laying hen metabolism study was conducted at 100 ppm, equivalent to ca. 2000x the anticipated dietary burden. Both studies were consistent in demonstrating that total residues of trifloxystrobin and CGA 321113 were low in eggs and tissues.*
*The purpose of this submission is to establish MRLs on imported commodities, however, the petitioner has not requested MRLs on imported eggs, poultry meat and meat by-products. Furthermore, the US has not established any tolerances for eggs and poultry tissues on the basis that finite residues of trifloxystrobin and the acid metabolite CGA 321113 are not expected to occur in poultry commodities. Therefore, any contribution from these commodities were not included in the dietary risk assessment (DRA).*
*This poultry feeding study is classified acceptable and does satisfy the guideline requirement for a livestock feeding study (Residue Chemistry Guidelines Dir98-02, Section 8).*

Comments

The studies sent by the applicant were critical reviewed. No deficiencies were identified. The calculation of the animal dietary burden was based on the US feed tolerances because the Canadian uses do not include feed items. But, no MRLs for animal products were derived because the petitioner has not requested MRLs on imported milk, meat and meat by-products.

### 4.12.3 EU

Studies submitted by the applicant and evaluated by the EU

- Campbell, D. D. 1997. CGA 279202 - Magnitude of the residues in meat and milk resulting from the feeding of three levels to dairy cattle. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97075, Edition Number: MO-01-002792. Unpublished.

Studies submitted to other participants and not reviewed by the EU

- Hayworth, C. G. 1999. CGA-279202 - Magnitude of the residues in poultry meat and eggs. Residue Chemistry Department, Greensboro, NC, USA. Bayer CropScience AG, Report No.: 243-98, Edition Number: MO-02-002553. Unpublished.

Result

The evaluation was made by the United Kingdom as EU Rapporteur Member State in April 2000. A monograph entitled *Draft Assessment Report* was prepared (11343c/ECCO/BBA/00). Information on the results of the cow feeding study was presented on pages 331 – 332 under point B.7.9. A summary discussion is presented on page 332 and quoted below.

> *A dairy cattle feeding study was conducted with lactating Holstein cows using technical CGA-279202 administered daily via gelatine capsules for 28-30 days. Mg/kg treatment rates were ca 2.0 (0.8N), 6.0 (2.3N)and 20.0 (7.7N) in the diet. No residues (<0.01 mg/kg) of trifloxystrobin and its metabolite CGA 321113 were detected in milk at all dose levels and no residues (<0.02 mg/kg) were detected in meat, liver, kidney and fat at all but the highest dose rate. At the highest dose rate, residues were all <0.02 mg/kg except for the following: trifloxystrobin in perirenal fat (0.06 mg/kg) and omental fat (0.05mg/kg). CGA 321113 in liver (0.09 mg/kg) and kidney (0.02 mg/kg).*
> *No detectable residues (<0.02 mg/kg) of trifloxystrobin and its metabolite CGA 321113 would therefore be expected in cattle tissues or milk following maximum dietary incorporation of crop material or processed crop material containing residues of trifloxystrobin.*
>
> *CGA 321113 was only detected at the LOQ (0.02 mg/kg) in kidney whereas the radiolabelled study predicted this to occur at a higher level.The applicants have suggested that this difference is due to the rate and time period of dosing and the interval between last dose and sacrifice. The higher dose for a short time period and the short time to sacrifice in the metabolism studies led to incomplete elimination of CGA 321113 in the urine and hence higher residues in the kidney. Whereas in the feeding study, elimination of CGA 321113 via urine was more advanced, resulting in lower levels in the kidney.*
>
> *Exposure of poultry to trifloxystrobin residues in treated feeds (grain) was at or below 0.01 mg/kg and therefore, no hen feeding study with trifloxystrobin was undertaken. However, the theoretical maximum residues expected in poultry eggs or meat can be extrapolated from the total radioactive residues obtained from the hen metabolism studies. Expected residues in egg yolk, liver, fat and muscle are <0.02 mg/kg.*

Comments

The hen feeding study was not submitted by the applicant to the EU.

Based on the results of the dairy cattle feeding study and the animal dietary burden calculated for the intended uses of trifloxystrobin in the EU, the EU rapporteur concluded that residues in animal products are not expected to occur and did not recommend MRLs.

### 4.12.4 USA

Studies submitted by the applicant and evaluated by the USA

- Campbell, D. D. 1997. CGA 279202 - Magnitude of the residues in meat and milk resulting from the feeding of three levels to dairy cattle. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97075, Edition Number: MO-01-002792. Unpublished.
- Hayworth, C. G. 1999. CGA-279202 - Magnitude of the residues in poultry meat and eggs. Residue Chemistry Department, Greensboro, NC, USA. Bayer CropScience AG, Report No.: 243-98, Edition Number: MO-02-002553. Unpublished.

Studies submitted to other participants and not reviewed by the USA
none

Result

The evaluation was made by the US EPA in 1999 and in 2000.

The 1999 *Memorandum (PP#8F04955, 7/22/99 review, DP Barcodes D257888 and D254208)* was prepared by the reviewer Fred Ives. Information on the dairy cattle feeding (test conditions, analytical methods, storage stability of residues and animal dietary burden) was presented in detail on pages 180 - 188 under point 34. The discussion/conclusion is summarized on pages 15 – 16 and quoted below.

> *No poultry feeding data were submitted with this petition. Based on the results of the poultry metabolism study, the Agency concludes that finite residues of trifloxystrobin are not expected to occur in poultry commodities. Therefore, for the purpose of this petition, poultry feeding data and tolerances for poultry commodities are not required. The Agency notes that poultry feeding data and tolerances for poultry commodities may be required in the future if the petitioner requests additional tolerances of crops which may be utilized as poultry feed items.*
>
> *The submitted dairy cattle feeding data are adequate. Dairy cows were orally administered trifloxystrobin at levels equivalent to 2, 6, and 20 ppm in the diet (mg/kg diet on a dry weight basis) for 28-30 consecutive days. The maximum theoretical dietary burden to cattle is ca. 3-4 ppm.*
>
> *Residues of trifloxystrobin were below the analytical methods LOQs in milk, muscle (round and tenderloin), kidney, and liver at the highest feeding level of 20 ppm. At this same feeding level, residues of trifloxystrobin were detected in omental fat (0.03-0.05 ppm) and perirenal fat (0.03-0.06 ppm). At the 6 ppm feeding study one perirenal fat sample trifloxystrobin residues were reported as „0.03 ppm (<0.02 ppm)". Residues of the acid metabolite, CGA-321113, were detected in kidney (<0.02-0.02 ppm) and liver (0.04-0.09 ppm) at the highest feeding level but were below the method LOQs in milk, muscle (round and tenderloin), and fat (omental and perirenal).*
>
> *It is the current Agency policy not to establish animal commodity tolerances if the terminal residues of concern are non-quantifiable at the 10x-feeding level. Because the highest (20 ppm) feeding level utilized in the study was only 3-4x the calculated dietary burden and because residues of trifloxystrobin and the acid metabolite CGA-321113 were detected in some tissues at this feeding level, the Agency concludes that animal commodity tolerances are needed.*

*Based on LOQ's each for parent and CGA-321113 of 0.01 ppm for milk and 0.02 ppm for other animal commodities, available data support the need for a 0.02 ppm LOQ tolerance for combined residues of trifloxystrobin and the free form of its acid metabolite CGA-321113 in milk and 0.05 ppm combined residues for meat, fat and meat byproducts of cattle, goats hogs, horses and sheep. The petitioner must submit a revised Section F proposing tolerances for trifloxystrobin residues of concern in milk, and in the meat, fat and meat byproducts of cattle, goats, hogs, horses and sheep which reflect these recommendations.*

*For risk assessment purposes the liver contribution of metabolite L7a can be estimated at ca. 0.05 ppm trifloxystrobin equivalent [adjusted to a 1x feeding level from goat metabolism studies (TFMP-* $^{14}$*C label)]. Combining with the recommended 0.05 ppm tolerance for combined residues of trifloxystrobin and CGA-321113 in meat by products results in ca. 0.1 ppm trifloxystrobin equivalent residue for liver.*

The 2000 *Memorandum (PP#9F5070, 04/06/00 review, DP Barcodes D254221, D254213, D254217)* including the results of the dairy cattle and the poultry feeding study was prepared by the reviewer Leung Cheng. Information on the test conditions, analytical methods, storage stability of residues and animal dietary burden was presented in detail for poultry on pages 116 – 121 and on pages 121 – 123 for dairy cattle. The discussion/conclusion is summarized for poultry and dairy cattle on pages 7 and 123 and quoted below.

*Quotation page 7*
*Results of a poultry feeding study were presented in which groups of 15 hens were dosed with trifloxystrobin at levels of 0, 1.5, 4.5, and 15 ppm for 28 days. Trifloxystrobin and CGA-321113 were both below the LOQ at all times tested for eggs and at the end of the study in chicken skin plus attached fat, peritoneal fat, breast plus thigh, and liver. The feeding levels correspond up to 300x the maximum theoretical dietary burden of 0.05 ppm in chickens when chicken feed items associated with the current and previous petitions are considered. Based on the poultry feeding study results, RAB3 expects no transfer of finite residues to poultry. Therefore, poultry tolerances are not needed.*

*In a previously submitted cow feeding study, groups of three cows were dosed with trifloxy-strobin at levels equivalent to 2, 6, and 20 ppm for 28–30 days. Trifloxystrobin and CGA-321113 were analyzed. Residues of trifloxystrobin were below the analytical method's LOQs in milk, muscle (round and tenderloin), kidney, and liver at the highest feeding level of 20 ppm. At the feeding level of 20 ppm, residues of trifloxystrobin were detected in omental fat (<0.02–0.05 ppm) and perirenal fat (<0.02–0.06 ppm). Residues of the acid metabolite, CGA-321113, were detected in kidney (<0.02–0.02 ppm) and liver (<0.02–0.09 ppm) at the highest feeding level but were below the method LOQs in milk, muscle (round and tender-loin), and fat (omental and perirenal). When considering the animal feed commodities in both the current and previous petitions, the maximum theoretical dietary burdens for beef cattle and dairy cattle are estimated to be 9.67 and 5.56 ppm, respectively. While the new maximum theoretical dietary burdens for beef and dairy cattle are higher than the levels given in PP#8F4955, the established meat and milk tolerances are still adequate to cover the potential transfer of secondary residues resulting from the new uses.*

*Quotation page 123*
*Adequate feeding studies are available for poultry and ruminants (a study on dairy cows). The maximum theoretical dietary burdens of the combined residues of trifloxystrobin and CGA-321113 to poultry are only 0.05 ppm. Animal commodity tolerances are not needed for eggs, and the fat, meat, and meat byproducts of poultry. In comparison, the maximum theoretical dietary*

*burdens of the combined residues of trifloxystrobin and CGA-321113 to cattle are a hundred times or more higher than they are for poultry for the commodities associated with this petition. An earlier petition recommended that the tolerances be 0.02 ppm for the combined residues of trifloxystrobin and CGA-321113 in milk (i.e., the sum of the LOQs of the two analytes) and 0.05 ppm for the combined residues of trifloxystrobin and CGA-321113 in meat and meat byproducts of cattle, including fat. Taking into consideration results from metabolism studies concerning the liver contribution of metabolite L7a (taurine conjugate of trifloxystrobin), it was also recommended that a 0.1 ppm trifloxystrobin equivalent level be used for risk assessment purposes (PP#8F04955, DP Barcodes: D257888 & D254208, F. Ives, 7/22/99). Calculation of the theoretical maximum dietary burdens to beef cattle and dairy cattle from the commodities associated with the current and previous petitions indicates that there is no need for higher tolerances or higher equivalent levels for use in risk assessment than those proposed earlier.*

Comments

Based on the results of the poultry feeding study and the animal dietary burden calculated to the intended uses of trifloxystrobin, the US EPA concluded that residues in poultry products are not expected to occur and did not recommend MRLs.

In comparison, the maximum theoretical dietary burdens of the combined residues of trifloxystrobin and CGA-321113 to cattle are a hundred times or more higher than they are for poultry for the commodities associated with the petition. The recommended MRLs were 0.02 mg/kg for the combined residues of trifloxystrobin and CGA-321113 in milk and 0.05 mg/kg for the combined residues of trifloxystrobin and CGA-321113 in meat and meat byproducts of cattle, including fat.

### 4.12.5 JMPR

Studies submitted by the applicant and evaluated by the JMPR

- Campbell, D. D. 1997. CGA 279202 - Magnitude of the residues in meat and milk resulting from the feeding of three levels to dairy cattle. Novartis Crop Protection, Inc., Greensboro, NC, USA. Bayer CropScience AG, Report No.: ABR-97075, Edition Number: MO-01-002792. Unpublished.
- Hayworth, C. G. 1999. CGA-279202 - Magnitude of the residues in poultry meat and eggs. Residue Chemistry Department, Greensboro, NC, USA. Bayer CropScience AG, Report No.: 243-98, Edition Number: MO-02-002553. Unpublished.

Studies submitted to other participants and not reviewed by the JMPR
none

Result

The evaluation was made by the FAO Panel of the JMPR in 2004. A detailed monograph including farm animal feeding on dairy cattle and laying hens was prepared. Information on the test conditions and results was presented under point “residues in animal commodities – farm animal feeding studies”. The reports by Canada, the EU and the USA as well as the applicant’s dossier were used by the JMPR to prepare its evaluation. The conclusions are summarized in the appraisal and are quoted below.

*The dietary burdens of trifloxystrobin for estimating maximum residue levels and STMRs for animal commodities (residue concentrations in animal feeds expressed as dry weight) are 6.3 and 2.1 mg/kg for beef cattle, 5.2 and 1.4 mg/kg for dairy cattle, 2.5 and 0.26 mg/kg for poultry.*

*Feeding studies*

*The Meeting received information on the concentrations of residues arising in tissues and milk in dairy cows dosed with trifloxystrobin in capsules at the equivalent of 2, 5.9 or 21 ppm in the diet for 28 - 30 days.*

*The sum of trifloxystrobin and CGA 321113 was calculated and expressed as trifloxystrobin on the basis of molecular weights. A conversion factor of 1.036 is required to express the CGA 321113 residues as trifloxystrobin equivalents. Because the metabolite CGA 321113 constitutes a significant proportion of the residue in animal products, when trifloxystrobin or CGA 321113 was below its limit of quantification, the sum of trifloxystrobin and CGA 321113 was calculated according to the examples below and expressed as trifloxystrobin.*

| Trifloxystrobin (mg/kg) | CGA 321113 (mg/kg) | Total expressed as trifloxystrobin (mg/kg) |
|---|---|---|
| <0.02 | <0.02 | <0.04 |
| <0.02 | 0.03 | 0.05 |
| 0.09 | <0.02 | 0.11 |

*No residues (sum of trifloxystrobin and CGA 321113) were detectable in milk (<0.02 mg/kg), round muscle (<0.04 mg/kg), or tenderloin samples (<0.04 mg/kg) at the highly exaggerated 21 ppm feeding level. No residues of either parent or metabolite were found in liver, kidney or fat samples from the 2 ppm or 5.9 ppm dosing levels (total residue <0.04 mg/kg). Maximum residues of 0.09 mg/kg (total residue 0.11 mg/kg) and 0.02 mg/kg (total residue 0.04 mg/kg), detected as the metabolite CGA 321113 and expressed as trifloxystrobin, were found in liver and kidney respectively at the 21 ppm feeding level. Maximum residues of 0.06 mg/kg (total residue 0.08 mg/kg) and 0.05 mg/kg (total residue 0.07 mg/kg), detected as intact trifloxystrobin, were found in perirenal fat and omental fat respectively, at the 21 ppm level.*

*The Meeting received information on the concentrations of residues in the tissues and eggs of laying hens dosed with trifloxystrobin at the equivalent of 1.5, 4.5 or 15 ppm in the diet for 28 days. The hens were killed on day 29, and composite tissue samples of breast plus thigh, skin plus attached fat, peritoneal fat, and liver were taken. Eggs and tissues were analysed for trifloxystrobin and CGA 321113. No residues (total residues <0.04 mg/kg) were detected in any of the analysed eggs, tissues or organs taken from the hens at the highest treatment level of 15 ppm.*

*Maximum residue levels*

*The Meeting noted that no trifloxystrobin or CGA 321113 residues were detected in milk (<0.02 mg/kg total), muscle (<0.04 mg/kg), kidney (<0.04 mg/kg), liver (<0.04 mg/kg) or fat (<0.04 mg/kg) from animals dosed for 28 days at 5.9 ppm which was close to the maximum dietary burdens of beef and dairy cattle (8.2 and 7.4 ppm). The highest residue of trifloxystrobin was in perirenal fat at 0.06 mg/kg (total residue 0.08 mg/kg) and of CGA 321113 in liver at 0.09 mg/kg (total residue 0.11 mg/kg) in the 21 ppm group.*

*The maximum concentrations of residues expected in tissues are <0.012 mg/kg in muscle, 0.033 mg/kg in liver, 0.012 mg/kg in kidney, 0.024 mg/kg in fat and <0.005 mg/kg in milk. The mean extrapolated concentrations are <0.004 mg/kg in muscle, 0.008 mg/kg in liver, 0.004 mg/kg in kidney, 0.006 mg/kg in fat and <0.001 mg/kg in milk.*

*Taking into account the fat solubility of trifloxystrobin (the acid metabolite CGA 321113 is of low fat-solubility), the Meeting estimated a maximum residue level of 0.05 mg/kg for the sum of trifloxystrobin and CGA 321113 in meat (fat) from mammals other than marine mammals based on the residues in the trimmable fat, and a maximum residue level of 0.02* mg/kg for residues in milks. In the liver and kidney of cattle, goats, pigs and sheep, the estimated maximum residue levels are 0.05 and 0.04* mg/kg respectively.*

*The estimated STMR values are 0.006 mg/kg in fat, 0 mg/kg in muscle, 0.008 mg/kg in liver, 0.004 mg/kg in kidney and 0 in milks.*

*The Meeting noted that in the feeding study on laying hens neither trifloxystrobin nor CGA 321113 residues (total residue <0.04 mg/kg) were detected in any of the analysed eggs, tissues or organs taken from the hens at the highest feeding level of 15 ppm. As the maximum dietary burden of 2.5 mg/kg was much lower, the Meeting agreed that the expected level of trifloxystrobin and CGA 321113 residues in poultry tissues and eggs was essentially zero.*

*The Meeting estimated maximum residue levels of 0.04* mg/kg for residues in eggs, poultry meat (fat) and edible offal. The Meeting recommended that the STMR values should be 0 in eggs, poultry meat, edible offal and fat.*

Comments

Based on the farm animal feeding studies and the calculated animal dietary burden the JMPR estimated MRLs and STMRs for animal commodities.

### 4.12.6 Results - farm animal feeding

All participants of the work sharing project received the cattle feeding study. The poultry feeding study was submitted to Canada, the EU, the USA and the JMPR but not to Australia.

The results of the evaluation - the recommendation of MRLs for animal products - are not identical. MRLs were recommended by Australia, the USA and the JMPR but not by Canada and EU.

# 5 CONCLUSIONS

The FAO/WHO/OECD pilot project on work sharing was carried out to test the use of national and international evaluations of pesticide residues and toxicology by the JMPR. The 2003 CCPR selected trifloxystrobin as the first compound for the work sharing pilot project because it had been evaluated in Australia, Canada, the USA and the EU and was scheduled for evaluation by the JMPR in 2004. The project is supported by the OECD, FAO, WHO, JMPR and national and regional authorities.

The objective of the work sharing project is to use national and regional evaluations to facilitate and expedite reviews, while maintaining independence and incorporating global perspectives. Work sharing is intended to increase efficiency, resulting in a reduction of the workload.

The purpose of the pilot project is to investigate the feasibility of using the evaluations for new pesticides prepared by national or regional authorities for JMPR evaluations.

Trifloxystrobin residue data had already been assessed in Australia, Canada, USA and EU and the detailed assessment documents were provided to the JMPR evaluator, who also received full data submissions from the company, as is the normal practice.

For the residue review, the generic studies include: pesticide identity, physical and chemical properties, metabolism, environmental fate in soil and water-sediment systems, analytical methods, freezer storage stability tests, fate of residues in processing and in farm animal feeding. For these subjects, national or regional summaries of the data with their assessments were taken into account. Supervised residue trials, which constitute the major part of a residue evaluation, were not included in this pilot project.

The requirements for the work sharing project including the availability of the experts involved in the national/international reviews for consultation and the availability of complete study reports from the applicant/sponsor were fullfilled in February 2004.

The following methodological approach was made:

- As a first step, an independent JMPR evaluation and an appraisal based on the full data submission of the applicant were prepared by the FAO evaluator. The use of national/regional evaluations was limited to the comparison of findings and conclusions.

- In the second step, the national monographs/reviews were compared with each other and with the JMPR evaluation with respect to for the data submitted/evaluated and concerning their results.

The trifloxystrobin assessment documents submitted by Australia and the EU were prepared in a monograph format. In the monograph format, excerpts of the dossier prepared by the applicant may be used and copied (e.g. tables, metabolism schemes, some text paragraphs) in preparation of the monograph. The monograph does not discuss the applicant's proposals and recommendations. Independent, complete and final evaluations of a compound are conducted without direct reference to registration purposes.

The trifloxystrobin assessment documents submitted by Canada and USA were presented in a review format. In the review approach, the scientific results are first summarised and then the applicant's dossier is subjected to a critical review. This includes discussions of the applicant's proposals and recommendations regarding registration procedures of the special plant protection products.

Because of the differences in the studies submitted for trifloxystrobin at the national or regional level, it was not practical to use a national or regional monograph as a "master". Also, the sets of studies in the

dossier provided to JMPR did not always match those assessed at the national and regional levels. (The set of studies provided to the four national and regional authorities and JMPR was identical only for farm animal metabolism).

The trifloxystrobin example showed that currently there are similarities but also differences among procedures and approaches for residue evaluations used by the national and regional agencies. These result in some divergence in conclusions, such as those for residue definitions and processing factors. It should also be noted that JMPR considers the world-wide use of pesticides when recommending MRLs for food commodities in international trade and therefore its approach is not exactly the same as national and regional approaches, which operate within registration systems.

## 6 RECOMMENDATIONS

*The JMPR came to the following recommendations:*

- Further development of the project, with changes based on the experiences with trifloxystrobin, is needed before work sharing can be routinely implemented with its anticipated benefits. Currently, based on experience with trifloxystrobin, a comprehensive acceptance by the JMPR of national or regional conclusions and recommendations is not practical for the residue-supporting topics included in this pilot project.

- Work sharing should focus on the mutual use of summaries of data validated at the national, regional and international levels. This would offer a possibility of exchange of a valid database which would be timesaving and would potentially reduce the workload. This could include all areas of the residue evaluation, including supervised residue trials data.

- For further progress in international work sharing it is proposed that national and regional evaluations should separate the summary of the submitted data from the conclusions. This would facilitate the mutual exchange of data summaries.

- A use of specific assessment results, such as the definition of residue, could potentially be done on a case by case basis.

- The evaluation process, including standardization of formats, should be harmonized at the international level.

- JMPR evaluators should use national and regional evaluations as support for the independent JMPR review.

- A further pilot work sharing project should be followed in a more flexible procedure. Procedures should be revised when there is more progress in the harmonisation of formates and evaluation procedures (harmonisation of guidance documents).

- The current workload of the JMPR precludes additional time spent by FAO Panel Members on this project if it is at the expense of normal residue evaluation commitments, which are regarded by Panel Members as the priority.