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Working Group on Pesticides

REGISTRATION AND WORK SHARING

Report of the OECD/FAO Zoning Project

Fourteenth Meeting of the Working Group on Pesticides, to be held on 5-6 November at OECD Headquarters, Paris, beginning at 9h30 on 5 November

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This document is the final report of the OECD/FAO Zoning Project, which explored the possibility of developing international climate zones for pesticide residue testing. The project concluded that it would not be possible to develop such zones, but recommended other actions to promote international sharing of pesticide residue tests.

Action Required:

The Working Group on Pesticides is invited to:

(i) comment on the outcome of the Zoning Project,

(ii) agree on whether and how to publish the project report; and

(iii) consider whether the WGP should undertake any follow-up.

Report of the OECD/FAO Zoning Project

29 August 2002

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SUMMARY

In response to one of the recommendations of the workshop in York (1999) on "Developing Minimum Data Requirements for Estimating MRLs and Import Tolerances", the OECD Working Group on Pesticides and the FAO Pesticide Management Group invited a small group of residue experts from OECD and FAO Member countries to develop the concept of a global zoning scheme to define areas in the world where pesticide trials data could be considered comparable, and therefore where such trials could be used within each zone for MRL-setting purposes, irrespective of national boundaries.

In progressing this work, this Zoning Steering Group first developed a world map of four possible residue zones: cold; temperate wet; temperate dry and; tropical. In order to validate the applicability of the proposed zones the Group collected an extensive database of residue trials data from the FAO/WHO Joint Meeting of Experts on Pesticide Residues (JMPR) Residue Evaluations. This database was then analysed by an independent statistician to estimate residue variability associated with the proposed global zones.

Indications from this first statistical analysis suggested that the proposed zones, based on the Köppen global climate classification, were not appropriate. Nor could an analysis of the variability related to average pre-harvest climatic conditions (temperature and rainfall) for each residue trial location support a proposal for different temperature and rainfall 'bands', within which residue trials data could be considered comparable.

Both these analyses showed that the available data were not sufficient to separate out the various climatic factors that could contribute to residue variability, mostly due to the high level of residue variability found within the proposed zones.

Furthermore, there was a strong indication that pre-harvest climate may not have such a strong influence as had been previously thought. The Group considered this could reflect the common growing and climatic conditions associated with each crop, irrespective of geographic location.

The Group then considered a further analysis of the data-sets, in conjunction with additional data on residues reported at zero-days (the day of the final pesticide application, i.e. 0 days after the final application). Based on this analysis, the Group concluded that a large proportion of the residue variability at harvest could be explained by variation in residues at 'zero-days' (assumed to be largely unaffected by pre-harvest climatic conditions).

The Group noted that the analysis indicated considerable variations in zero-day residues for comparable trials (i.e. those with the same or similar Good Agricultural Practice), and suggested that much of this variability could be associated with residue sampling and laboratory analytical variability, and possibly with differences in agronomic practices and pesticide application techniques used in the trials.

The overall conclusions of the Group were that:

- there was sufficient information to indicate that a residue zoning scheme, based on climatic differences alone, could not be proposed because of the high variation in residues reported from comparable trials even within the same climatic zone;

- pre-harvest climatic conditions were not major factors influencing residue variability in comparable residue trials;

- most of the residue variability at harvest reported from comparable trials was associated with variability in residues at 'zero-days' (assumed to be largely unaffected by pre-harvest climatic conditions);

- many of the factors possibly contributing to residue variability in comparable residue trials have already been recognised, to a greater or lesser extent, in the MRL assessment procedures established at the national, regional and international level, with residue trials being designed to reflect the range of agronomic and climate situations that might be expected during the commercial use of the product.

RECOMMENDATIONS

Based on the above conclusions; that pre-harvest climatic conditions (primarily rainfall and temperature) have relatively little impact on residue levels remaining at harvest; and that a high percentage of the variability in harvest residues from comparable trials can be attributed to the residue variability at zero-days, and recognising there are significant advantages in extending the acceptability of comparable trials to include those from other countries or regions, particularly with respect to the establishment of MRLs for imported produce, for minor crops and for the elaboration of Codex MRLs, the Zoning Steering Group recommends:

1. that FAO and OECD Member countries, when considering further work in promoting the acceptability and 'transferability' of residue data from comparable trials, place less emphasis on climatic differences between countries or regions;

2. that JMPR and residue assessors at the national or regional level be encouraged to review the extent to which they use climatic differences to determine the acceptability of comparable residue trials data from other localities when establishing MRLs, taking into account the relatively small impact that pre-harvest climatic conditions appear to have on residue variability and recognising the potential advantage of being able to accept residue trials data from a larger global database of comparable trials;

3. that JMPR and residue assessors at the national or regional level consider the relevance of factors contributing to day-zero residue variability, and the extent to which these factors may influence the acceptability of residue trials from different regions, countries or localities;

4. that data-generators, when reporting supervised residue trials, ensure that adequate details are provided on potential factors that may influence residue variability, including comprehensive information on all aspects of the pesticide treatments and application techniques, and on the crop growth/behaviour and cultural/management practices, in order to facilitate the acceptance of data from other regions or localities where these details indicate that the residue trials are comparable;

5. that JMPR be invited to consider whether the current FAO guidelines on the Submission and Evaluation of Pesticide Residues Data for the Estimation of MRLs in Food and Feed may need to be revised in light of the Group's conclusions;

6. that residue assessors and data-generators in developing countries take note of the results of this Zoning project (that climate is not a major factor influencing residue behaviour in comparable residue trials) and should consider submitting residue data from comparable trials in different regions of the world to national regulatory authorities and to JMPR to support import MRLs and international MRLs respectively, for crop/pesticide combinations with the same or similar Good Agricultural Practices and comparable agronomic conditions.

1 INTRODUCTION

In September 1999, pesticide residue and regulatory experts from 20 OECD Member countries, together with some JMPR members, took part in a joint EU/OECD Workshop in York (UK). The purpose of this workshop was to establish guidance on the minimum or core data requirements for establishing MRLs, including import tolerances. The workshop participants also worked to identify the components of a minimum data package that were already harmonised and to propose measures to improve the global acceptance of common data packages.

One of the recommendations from this workshop was the proposal to initiate a joint OECD/FAO residue 'zoning' project to develop the concept of sharing residue data between countries within regions or areas where pesticide residue behaviour could be expected to be the same.

The report of the York workshop (Annex 2) and its recommendations were discussed at the February 2000 meeting of the OECD Working Group on Pesticides (WGP). The WGP agreed to initiate the zoning project, suggesting that a joint Steering Group of OECD and non-OECD Member country residue experts be established to develop this project.

This Zoning Steering Group (ZSG) first met in March 2000 and held two subsequent meetings during 2001 and 2002. During the project, experts from eight OECD Member countries, five other FAO Member countries, CropLife International, OECD and FAO Secretariats attended one or more meetings. A consolidated list of steering group members and contributors is included in Annex 1.

2 OBJECTIVE

The objective of the Zoning Project was to define and design world-wide geographic zones for conducting pesticide residue field trials, where, within each zone, pesticide residue behaviour would be expected to be comparable and therefore where residue trials data would be considered equivalent and therefore acceptable for regulatory purposes.

3 THE ZONING CONCEPT

At the first meeting of the Group (March 2000), the previous work of the York Workshop was reviewed (see Annex 2) and the Group discussed the use of other zoning schemes in Europe and North America, as well as the approaches under development in New Zealand and Australia. This provided the meeting with a general background on the factors currently used to decide the 'transferability' of residue trials data between or within regions and/or countries and on what barriers might exist to the adoption by national authorities of a more global approach to zoning for the acceptance of comparable residue trials data.

After further discussion on the feasibility of a global zoning scheme, whether it was likely to be supported by OECD and FAO Member countries and the possible benefits to developing countries, the Group expressed support for the development of a global zoning scheme and considered that such a scheme could be used:

- in national or regional registration procedures, where the submission of pesticide residue data, not necessarily generated in the country/region where registration is sought, but generated anywhere in the same zone would be accepted; and

- in regional or international work (e.g. JMPR) in evaluating residue data, where the use of zones should lead to an increase in the 'comparable' data available, even though the trials may have been generated in different parts of the world.

The Group agreed that the adoption of geographic zones for the purposes of residue data assessment would allow the use of a more extensive database of comparable residue trials. The Group also agreed that the project would have the following benefits:

- improve governments' and consumers' confidence in residue data and hence in food safety standards based on these data;
- promote mutual acceptance of residue data outside national borders;
- facilitate governments' assessment of data used to establish MRLs and import tolerances;
- facilitate international trade by increasing the acceptance of Codex MRLs by countries (because of greater confidence in the supporting residue data);
- develop more robust databases to support MRLs for minor crops;
- reduce the duplication of data world-wide (the overall number of trials required should be reduced);
- encourage governments to share the work of pesticide review for regulatory purposes (by encouraging manufacturers to submit the same supporting data to all countries within the same zone).

The beneficiaries of a zoning scheme would be:

- Governments: regulators would improve their confidence in supporting data that would be more representative; they would better use/accept reviews from other countries and thus would carry out more efficient assessments;
- Industry: a global zoning scheme would provide manufacturers with the potential for fewer trials world-wide, should generate more rapid approvals through mutual use of regulatory reviews; and would offer opportunities for a greater number of uses across a wider geographic area;
- Producers: would have more access to a greater range of pesticides, particularly for minor crops, more rapidly (as a result of more rapid approvals), and enhance trade opportunities resulting from more import tolerances being granted;
- Consumers: would have improved confidence in the scientific assessments underlying the establishment of MRLs and other food safety standards;
- International Organisations: Codex MRLs should be better accepted by national authorities because of their increased confidence in the supporting global data set; and the number of MRLs, particularly for minor crops, could be expected to increase.

During the discussions on the scope of the project, the Group recognised that pesticide applications covered a wide range of techniques, including soil-incorporation, seed treatment, banded soil treatments, trunk injections, etc. and that it would be impossible to develop a zoning scheme that catered for all the various treatment techniques available.

For this reason, the Group agreed that the initial focus on the zoning project should be on foliar/spray treatments (insecticide, fungicide and herbicide) for non-systemic pesticides, as it was recognised that these reflected the most common practice associated with the presence of residues world-wide and is also consistent with the use of just climate data in developing the residue zones.

In line with the above decision, the Group was of the opinion that different residue zones, based on climatic differences were not necessary for:

- Greenhouse/protected crops. The Group supported the view of the York workshop that residue behaviour of foliar applied non-systemic pesticides used in protected crops should not differ significantly between countries or regions, and in line with the approach taken in Europe, a single global zone would be appropriate;

- Very close-to-harvest treatments. The Group also considered that different climate-based zones would not be needed for foliar applied pesticides used close to harvest, as residue decay would not be influenced much by climate in the relatively short time between application and harvest. While this term 'very close to harvest' was not quantified, the general feeling was that this could be where pre-harvest intervals of up to 2 days were involved.

- Post-harvest treatments. While not within the scope of the proposed scheme (i.e. not involving foliar applications), the Group also confirmed the earlier opinion from the York Workshop, that residue trials for post-harvest treatments could also be considered as being from a single global zone, as again, significant differences in residue behaviour would not be expected from treatments in different countries.

- Non-systemic Seed Treatments. Similarly, the Group also supported the view of the York Workshop, that significant differences in residue behaviour would not be expected from non-systemic seed treatments in different countries, and that a single global residue zone could be supported.

4 WORK PLAN

In developing the work plan for the project, the Group noted the suggestion from the OECD Working Group on Pesticides that any global scheme should adopt a pragmatic approach, and that possible costs and resource implications associated with the development of a residue zoning scheme needed to be taken into account.

The Group discussed in more detail the preliminary approach suggested at the York workshop, and confirmed:

- that the key factor associated with the scheme should be that different zones should reflect actual differences in pesticide residue behaviour.

- that the approach to be taken in developing the zoning scheme should be pragmatic and any such scheme should be simple and workable/practicable and that the number of zones should be kept to a minimum.

- that the use of GIS (geographic information system), possibly requiring sophisticated computer techniques and databases, would not be cost-effective and was probably unnecessary (at least in the initial approach).

- that the project should make use of existing data to the extent possible, with existing climatic maps and available residue data (for validation purposes) being used as much as possible.

- that the tentative zoning scheme should take into account political realities (e.g., where possible, zone boundaries should be adjusted to align with adjacent country administrative boundaries).

The work plan developed by the Group progressed through three distinct phases.

Phase 1 was the development of a tentative zone map, the collection of suitable residue trials data and the statistical analysis of these data to validate (or adjust) the tentative zones.

Phase 2 involved the collection of more specific information on pre-harvest climatic conditions (temperature, rainfall and sunshine) during the month of harvest in the locality (country, region or state) of the residue trials, and an assessment of the relationship between these conditions and residues found at harvest.

Phase 3 was the collection of additional data on residues found at zero-days, for as many of the initial residue trials as possible, and the investigation of possible relationships between the initial (zero-days) residue levels and those present at harvest.

5 PHASE 1: ZONE MAP DEVELOPMENT AND VALIDATION

5.1 Zone Mapping Based on Climate

During the first phase of the Group's work, it was agreed to consider existing climate maps based on temperature and rainfall, as these were considered to be the two main factors influencing residue behaviour for foliar/spray treatments. However, the Group also recognised there may be a need to take into account sunshine hours at a later stage, if there was a need to refine the model.

After considering several existing climate maps and classifications, the Group agreed to use the Köppen[1] classification of climates as the basis for it's work, and an initial 'residue zones' map was developed by adjusting the boundaries of five of the major Köppen zones to reflect political boundaries.

The five zones were:

- polar
- cold
- temperate (wet), referred to in this report as 'temperate')
- temperate (dry), referred to in this report as 'dry')
- tropical

This ‘adjusted’ map of potential 'residue-equivalent' zones was considered by the Group to be a good basis for dividing the world into 4 major residue zones based on climate. The polar zone was not considered relevant for residue zoning purposes because crops are not grown there.

[1] Working paper 2: *Initial residue-zone map, based on the Köppen climate classification system*

While the Group agreed that the initial suggestion to 'marginally adjust' the zone boundaries to reflect political borders could be done without significantly affecting the integrity of the 'climate-based' zoning, it was noted there were some instances where this could not be done (e.g. USA, Chile). It was agreed that in these cases, the regional representatives of the Group would look more closely at the practicality of splitting one country into two or more zones.

After taking the above points into account, it was agreed to refine the initial zone maps by using the WINDISP 4 software (ex FAO) to generate a new 'boundary-adjusted' map based on 4 residue zones, for use in grouping the residue data sets for statistical analysis.

5.2 Collection of Existing Residue Data

The Group confirmed that an essential component of the work-plan was the validation of the tentative zones, using existing residue data, to see if the residue data reported from trials with the same or similar GAP conducted within a zone were comparable. The variability of the residue data within one zone should be less than the variability of the data between zones and if this pattern was consistent over a range of pesticides and crops, the zoning concept could be supported.

It was agreed that the major source of data should be the more recent (1990-2000) JMPR Monographs, as these provided the most representative and comprehensive data sets available from any one source.

The Group agreed that the following 'criteria' should be used to decide what residue data sets should be selected for this validation phase of the project.

- residue results should be detectable (above the Limit of Determination or Quantification);
- Good Agricultural Practice (GAP) information should be available;
- that trials could be considered comparable if the Pre-Harvest Intervals or area/dilution rates varied by less than 25% (according to EU guidance);
- geographic information on trial locations should be available, at least to the country level;
- a minimum of six residue data points (per crop/pesticide/GAP combination) should be available, with at least four such data points from any one zone;
- pesticide formulation differences should be considered with some flexibility, recognising the York Workshop's view that in the case of foliar sprays, the different commonly used formulation types are not likely to influence residue behaviour to any great extent.
- crops with the potential for being grown in more than one zone should be given some preferences (e.g. cereals and citrus);
- the residue data had been confirmed by JMPR as being 'valid' results.

The initial data sets, selected from the JMPR Monographs (1990-2000) covered about 2200 individual trial results, involving 46 pesticides, 67 commodities and 30 countries.

The data collected for each trial result included:

- the pesticide involved, the crop treated and the country/state where the trial was conducted;
- the climate zone (as identified from the tentative residue zoning map);
- Good Agricultural Practice information, specifically the application rate (kg ai/Ha) and/or the dilution rate (kg ai/100 litres), the number of treatments per season and the pre-harvest interval (between the last application and sampling);
- the residue level found (with duplicate results being included if more than one analysis was conducted);
- a reference to the source of the data (normally the JMPR Monograph and page number).

These trial results were then grouped into different data-sets, with each data-set containing those trial results that were considered to have equivalent or comparable Good Agricultural Practice. In practice, this resulted in trial results for each pesticide/crop combination being grouped in one data set if:

- the pre-harvest intervals differed by less than 10% from the 'nominal' PHI for each data-set (e.g. trial results from samples taken at days 6, 7 or 8 were grouped under a nominal PHI of 7 days, while results for days 39 to 46 were included in a 'nominal' 42-day PHI data-set);
- the dilution rates (for kiwifruit and the tree crops), or the application rates per hectare (for grapes, the vegetable and arable crops) within each data-set differed by less than 25%.

After reviewing this initial data, and noting the conclusions from an initial assessment of the data by J. H. Jowett[2], (suggesting that the data may not reflect a direct relationship between residue decline and climate) and similar comments from D MacLachlan[3], it was agreed that the data sets used for validation should be refined to include a lesser number of results where there was a greater degree of confidence in the data.

The meeting therefore agreed that the residue data-sets to be used in validating the proposed zones should be selected from the more recent JMPR Monographs (1994-2000). A listing of the refined data-sets[4], involving 1254 trials on 29 crops done in 23 countries for 16 pesticides is presented in Annex 3 (Table 1).

5.3 Methodology

The methodology used in this initial statistical analysis, intended to assess the inherent variability of the total data-sets across all zones, the variability between the proposed zones and the variability within each zone, included:

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[2] Working paper 3: *Statistical analysis of some data comparing different climate zones in crop residue trials: J Jowett: . 18 March 2001*

[3] Working paper 4: *Validation of zones: D MacLachlan: 14 March 2001*

[4] Working paper 1: *JMPR residue data-sets extracted for residue zone assessment purposes*

- a preliminary examination of the distribution of the residue data using histograms and the Kolmogorov Smirnov test which showed that residues on the log scale were approximately normally distributed and supported the use of these logarithmic values in the subsequent statistical analyses; and

- an examination of the variations between zones for the range of crop/pesticide combinations using box-and-whisker plots and analysis of variance.

5.4 Results

A representative sample of the results of this initial Inter- and Intra- Zone analysis is summarised in Table 1 (below). These results reflect the best represented crops where the data had been collected for different crop/pesticide combinations in different countries and the initial climate-related zones. Further details are provided in Annex 3 and in the associated Preliminary Statistical Report[5] considered by the Group.

Table 1: Summary of representative zone comparisons

Crop / pesticide	*Significant zone comparisons*
Captan, apples	Residues from trials conducted in the 'Cold' zone were significantly higher than residues from comparable trials in the 'Temperate' zone.
Captan, grapes	Residues from trials conducted in the 'Cold' zone were significantly higher than residues from comparable trials in the 'Temperate' zone.
Dinocap, grapes	Within the Temperate zone, residues from trials conducted in Germany and France (mostly in the North), were significantly higher than residues from comparable trials in Greece and Italy.
Fenbuconazole, apples	No significant differences
Tebufenozide, apples	No significant differences between residues from comparable trials conducted in the 'Cold' zone and the 'Temperate' zone, although the Australian results were higher than the rest
2,4-D, wheat forage	Residues from trials conducted in the 'Cold' zone were significantly lower than residues from comparable trials in the 'Temperate' zone

5.5 Discussion

The Group noted that this preliminary statistical analysis showed that residue trials conducted in the 'Cold' zone generally reported higher residues than those reported in comparable trials conducted in the 'Temperate' zone. However, there was a higher level of residue variability within zones than between zones with a substantial proportion of the residue variability being explained by between country variation, possibly related to climate differences.

Conclusions: The results of this initial analysis suggested that the differences in residue behaviour between the proposed residue zones were inconsistent and that the use of a residue zoning scheme based on refinements of existing climate maps could not be validated using the available data.

6 PHASE 2: PRE-HARVEST CLIMATIC CONDITIONS

Subsequently the Group discussed the idea that a given crop requires certain climatic conditions to grow, irrespective of location. Climate may not be the most important factor influencing the variability of residues measured 'at harvest' from comparable residue trials.

The Group noted that in practice, the climatic conditions under which crops were grown can influence the pest or disease pressure, thus affecting the 'Good Agricultural Practice' (e.g. the application rates, the pre-harvest intervals, the spray frequency and timing) required by growers to achieve effective pest and disease control. However, this climatic influence was of more relevance in determining the comparability of the residue trials, rather than the variability of the residue results within a group of comparable trials.

The initial zone analysis (see section 5) showed that it would be difficult to define clear statistical relationships between the residue behaviour and the Köppen-based residue zones. The Group therefore agreed to refine the approach and look more closely at the climatic conditions (temperature, rainfall and sunshine hours) occurring during the immediate pre-harvest period (i.e. during the average month of harvest of the crop), as this was considered to be of greater relevance with respect to residue depletion.

6.1 Methodology

The analysis of the relationship between pre-harvest climatic conditions and residue variability at harvest was conducted in two parts.

The first of these analyses involved the collection of information on rainfall, temperature, and in some cases, sunshine hours during the typical harvest month for each country/crop combination and the generation of box plots showing the residues for each crop/pesticide combination across zones (or countries where all data were from one zone), with the values being compared using analysis of variance of the log transformed values. The log transformation was used to achieve variance homogeneity and normality of the distributions and normality was checked using the Kolmogorov Smirnov test.

Where appropriate, crops were combined into a single analysis of variance, which took account of the crop/pesticide/GAP differences, to establish any common trends in patterns not significant in the smaller data sets.
Linear regression based on log residues, with independent variables temperature, rainfall and their interaction, plus application rate and PHI where appropriate, was used to assess the effects of the climate variables on residues.

The log transformation of the residues was used (a) to ensure positive residues are predicted from any model and (b) in order that statistical inferences based on normal distribution theory would be soundly based. Q-Q plots were used to check normality.

In this analysis, a selection of the available data-sets were used (about 60% of the total JMPR data-sets), generally reflecting the availability of information on expected rainfall and temperatures during the pre-harvest period. Crops included in this analysis covered 10 different forage crops, apples and pears, together with German data for cyfluthrin on four other crops where specific trial-related weather information was available.

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[5] Working paper 6: *Preliminary Statistical Report to the Sub-team of the ZSG. A Gould. 16 August 2001*

In addition, an analysis was conducted on 253 US trials on apples, pears, grapes, lettuce and seven forage crops, where information was available on rainfall, temperature and sunshine hours related to the month of harvest for each crop.

The contribution of the climate variables was assessed using the p values for the climate terms in the analysis, as well as the change in the value of R^2 statistic[6]. The Group noted that the change in R^2 must be used with caution where the number of trials available was small, since over-fitting of the relationship could occur, and could lead to 100% of the variation being spuriously explained in extreme cases.

Except in the case of wheat forage, where there were enough residue values, interactions between factors were not included in the regressions to avoid overfitting and drawing spurious conclusions.

In cases where several crops occurred in combinations with the same pesticide, a combined analysis was carried out to assess the overall effect of climate factors and to provide more powerful inferences. Interactions between climate factors were included in these analyses.

6.2 Results

The initial analysis of the selected data-sets indicated a significant correlation between temperature and residue behaviour in only one instance (2,4-D in wheat forage).

Figures 2(a) to 2(f) in Annex 3 show a selection of results illustrating the general conclusions from the analysis and Table 2 (below) summarises the relationships found.

Full details of this analysis are provided in the statistician's report[7] on the climate factor analysis, presented to members of the Group in September 2001.

[6] Weisberg S *Applied Linear Regression* 1980. Wiley, New York

[7] Working paper 7: *Statistical Analysis of the Relationship between Climate Factors and Pesticide Residues: Anne Gould, 28 September 2001*

Table 2: Summary of representative climatic condition-related analyses

Crop / pesticide	*Temperature*	*Rainfall*
Captan, apples	Not significant	Wetter conditions associated with lower residues
Cyfluthrin, apples	Warmer temperatures associated with lower residues	Not significant
Fenbuconazole, apples	Not significant	Wetter conditions associated with lower residues
Tebufenozide, apples	Warmer temperatures associated with higher residues	Not significant
Fenbuconazole, sugarbeet tops	Not significant	Wetter conditions associated with lower residues
2,4-D, wheat forage	Warmer temperatures associated with higher residues	Wetter conditions associated with higher residues

A more refined analysis was also conducted on 253 residue values from US trials (involving 14 crop/pesticide combinations) where pre-harvest climatic conditions were available. Table 3 below summarise the results of the seven crop/pesticide combinations where the climatic factors were shown to be significant, Annex 3 provides more detailed information on this analysis and full details are provided in the related statistical report[8].

Table 3: Pre-harvest climatic conditions regression analysis (US Data)

Crop	*Pesticide*	*Variation explained by climate factors*	*Reliability of the relationship**	*Climate significant (at 5% level)?*
Apples	Chlorpyrifos	50%	Moderate	(Yes)
Grapes	Chlorpyrifos	68%	Moderate	(Yes)
Clover (forage)	Parathion	95%	Poor	
Soya (green forage)	Cyfluthrin	80%	Poor	
Sugarbeet tops	Fenbuconazole	52%	Moderate	(Yes)
Wheat forage	2,4-D	37%	Good	Yes
Wheat straw	Fenbuconazole	57%	Moderate	(Yes)

* Based on residual degrees of freedom: 5 or less = Poor; 6 – 20 = Moderate; Over 20 = Good

[8] Working paper 10: *Statistical Analysis of the Relationship between Climate Factors and Pesticide Residues: Analysis of Data from the USA: A Gould, 5 February 2002*

6.3 Discussion

When discussing the results of the first analysis, the Group noted that in a number of cases, temperature, rainfall and sunshine data from close to the trials sites were not available, and that less appropriate average climate information had been used. Also, in some cases, because there was insufficient 'regional' climate information to analyse the forage crop data sets for variability associated with 'pre-harvest' conditions, the initial climate-based zoning system had been used.

Recognising these constraints, the Group noted that while this analysis (of about 1250 trials on 29 crops) produced some statistically significant relationships between pre-harvest climatic conditions (or zone-based climate) and residues at harvest, these relationships were not sufficiently consistent or strong enough to support a zoning scheme based on climate.

When considering the results of the more refined analysis of the US data, the Group noted that only in the case of 2,4-D / wheat forage was there reliable evidence of a pre-harvest climate effect on the residues (with these climate factors explained only 37% of the residue variation). However, since 2,4-D was considered a systemic pesticide, the Group was of the opinion that this effect was of lesser relevance in the context of the Group's work.

In other cases, the residual degrees of freedom were relatively low, implying spuriously good fits. In addition, the significant effects of climate were not consistent across crop/pesticide combinations.

Conclusion: That the results of this analysis indicated a general lack of significant correlation between the pre-harvest climatic conditions and residues at harvest reported in comparable residue trials, and in the few cases where significant effects were observed, these effects were inconsistent.

7 PHASE 3: ZERO-DAYS VARIABILITY

After considering the results of the pre-harvest climate-related variability, the Group proposed that the third phase of the work programme should investigate the effect of non-climatic factors on residue behaviour, and suggested that crop management and agronomic practices could be among the factors that may have a significant impact on pesticide residue levels.

It was therefore agreed that an analysis of zero-days residue data should be conducted to compare the residue variability immediately after the last pesticide application (zero-days) where climatic factors should not have much influence, with the variability of residues "at-harvest".

7.1 Methodology

Additional information on residue levels reported at zero-days in the JMPR Evaluations were collected for as many of the trials as possible, to provide the statistician with a reference data base on which to estimate the relationship between residue variability at day-zero and the residue variability at harvest.

The data used for this analysis of zero-days variability were from 379 trials, many of which included several harvest dates. These trials covered eight fruit crops, six vegetable crops; three forage crops and involved 14 pesticides.

Multiple linear regression was used to examine the relationships between residues at harvest and residues measured immediately after the last application. For each crop / pesticide combination, the relationship between the zero-days residue and the harvest residue was examined using scatter plots and linear regression. Separate lines were fitted for each pre-harvest interval (PHI) value where necessary. The logarithms of the residue values were used to stabilise the variance and hence allow valid statistical inference based on normal distribution theory. The percentage of variation in the harvest residue values explained by the zero-days value was expressed using the R^2 statistic.

In this analysis, the additional, subsequent, effect of climate factors was also investigated, using multiple linear regression. The contribution of the climate variables after allowing for the zero-days variation was assessed using the p values for the climate terms in the analysis, as well as the change in the value of R^2.

7.2 Results

In 14 crop/pesticide combinations, the percentage variation in the residues at harvest explained by the zero-days residue variation (R^2) was at least 70%. In 20 crop/pesticide combinations, the R^2 value was at least 50% and only in five cases was the percentage of variation explained by zero-days residues less than 30%.

There were seven crop/pesticide combinations where climate variables improved the percentage of variation explained by a statistically significant amount (at the 5% level). In most of these cases, the relative increase in R^2 was small; i.e. the effect of the zero-days variation was much greater than the additional effect of the climate variables.

In two of the three cases where climate variables appeared to have a considerable effect (Brussels sprouts/cyfluthrin and cabbage/tebufenozide), the levels of statistical significance were marginal.

The results of this analysis of zero-day variation, and the added contribution of climatic factors are presented in Table 4, with further details summarised in Annex 3 and the associated statistician's report[9].

7.3 Discussion

The Group noted that the variation associated with the zero-days residue values was high and that there was a very consistent and strong relationship between the variation in the residues measured at zero-days and the variation in residues at harvest.

The data showed that up to about 70% of the variation in harvest residues could be explained by variation in residue levels found at zero-days, and that the additional contribution of pre-harvest climatic conditions to this variability was relatively small, about 10-20% on average.

Conclusions: A large proportion of the variation in residues at harvest can be explained by variation in zero-days residue values (assumed to be largely unaffected by pre-harvest climatic conditions), with the added contribution of these climatic factors generally being very small.

[9] Working paper 9: *The Contribution of Zero-day Residue values to the Variability of Residues measured at harvest: A Gould, 7 March 2002*

Table 4: Summary of zero-days and climate-contribution variability analysis

Crop	*Pesticide*	*No of Trials*	*R^2 (zero-days)*	*R^2 (zero-days + climate)*	*Climate contribution*
Apples	Bitertanol	20	72%	79%	Not significant
	Captan	7	45%		
	Chlorpyrifos	6	49%		
	Cyfluthrin	15	82%	89%	Yes (7%)
	Fenbuconazole	13	54%	64%	Not significant
	Fenpyroximate	8	67%	78%	Not significant
	Kresoxim methyl	10	74%	88%	Yes (14%)
	Parathion	12	38%		
	Tebufenozide	13	87%	90%	Yes (3%)
Bananas (unbagged)	Fenpropimorph	12	76%		
Broccoli	Tebufenozide	8	78%	79%	Not significant
Brussels sprouts	Cyfluthrin	8	10%	70%	Yes (Marginal)
Cabbage	Tebufenozide	11	47%	74%	Yes (Marginal)
Cherries	Bitertanol	6	38%		
Cherry, sour	Cyfluthrin	8	74%	88%	Not significant
Clover (forage)	Parathion methyl	13	20%	81%	Not significant
Grapes	Captan	8	41%		
	Dinocap	31	77%	90%	Yes (13%)
	Kresoxim methyl	16	12%	28%	Not significant
Lettuce (head)	Cyfluthrin	12	74%	83%	Not significant
Maize (forage)	Parathion	17	56%	61%	Not significant
Mandarins	Chlorpyrifos	10	77%	85%	Yes (8%)
Mustard greens	Tebufenozide	9	42%	49%	Not significant
Peaches	Bitertanol	5	41%		
	Chlorpyrifos	12	12%	17%	Not significant
Pears	Bitertanol	12	65%		
	Captan	12	75%		
	Cyfluthrin	6	67%	69%	Not significant
	Tebufenozide	10	91%	91%	Not significant
Savoy cabbage	Cyfluthrin	12	49%	63%	Not significant
Strawberries	Fenbuconazole	7	17%		
	Myclobutanil	3	95%		
Tomatoes	Chlorpyrifos	12	60%	74%	Yes (14%)
	Kresoxim methyl	4	91%		

8 APPLICATION FACTOR VARIABILITY

Recognising that the much of the residue variability in residues at harvest was associated with the variation already present immediately after the last pesticide application (i.e., at zero-days), the Group considered there would be merit in examining the extent to which application factors contributed to the residue variability at harvest.

8.1 Methodology

In this study, involving seven pesticides and five crops, together with additional results from cyfluthrin data-sets on six crops, multiple linear regression was used to examine the dependency of residue at harvest (on the log scale) on all trial factors supplied in the data set, i.e.: the pesticide concentration, the water rate per hectare, the number of sprays and the pre-harvest interval.

First, the percentage of variation accounted for by the GAP- equivalent groups was calculated. Next, the additional variation accounted for by the other application factors was calculated. Following this, the effect of country in addition to the application parameters was calculated and finally the effect of climate in addition to the application parameters was also calculated.

8.2 Results

In this analysis, up to about 70% of the variation in residues reported at harvest from comparable trials was explained by variations in the application factors used in the trials, (pesticide concentration, water rate, number of sprays and pre-harvest interval). In six of the 15 groups of trials examined, the proportion was at least 50%, and in only three of the groups was it below 10%. The median percentage explained was 40%.

The variation explained by pre-harvest climatic conditions in addition to application factors was less than 25% in all but three groups of trials, and the highest percentage explained by climate was 45%. The median percentage was 22%.

The remaining variation (up to about 40%), was explained by a combination of 'other factors', including those captured by the analysis of the zero-days data as well as weather and measurement error.

These results are summarised in table 5 below, with further details being presented in Annex 3 and reported more extensively in the associated statistician's report[10].

[10] Working paper 11: *The Relationship between Application Parameters and Residues Measured at Harvest: A Gould, 21 June 2002*

Table 5: Variation associated with application parameters, country and climatic conditions

Pesticide	*Crop*	*Variation explained by application parameters (zero day)*	*Variation in addition to application parameters explained by country*	*Variation in addition to application parameters explained by climate*
Bitertanol	Apples	56%	22%	14%
	Pears	55%	(All Germany)	
Captan	Apples	40%	16%	19%
	Grapes	50%	Country / climate highly correlated with application parameters	
	Pears	2%	Country / climate highly correlated with application parameters	
	Tomatoes	6%	Country / climate highly correlated with application parameters	
Chlorpyrifos	Apples	22%	3%	6%
	Mandarins	32%	17%	25%
Dinocap	Grapes	70%	5%	1%
Fenbuconazole	Apples (USA)	1%	0%	15%
	Apples (non USA)	55%	10%	3%
Fenpyroximate	Apples (non USA)	0%	26%	45%
Tebufenozide	Apples (USA)	64%	All US	22%
	Apples (non USA)	24%	44%	39%
	Grapes	51%	20%	22%

8.3 Discussion

The Group noted that these results indicated that a large proportion of residue variation at harvest (up to 70%) appeared to be linked to variations in the application parameters associated with the residue trials (application rate, concentration, number of sprays and pre-harvest interval), with the additional contribution from climatic factors being generally less than 25%.

With respect to the remaining variability (up to about 40%), not explained by either the above application factors or the pre-harvest climatic factors (temperature and rainfall), the Group noted that the available data were insufficient to identify what was contributing to this variability.

It was suggested that different treatment intervals, formulation types and application techniques used in the trials could be involved (with the effect of these factors being captured by the zero-day analysis of variability). In addition, it was considered that different residue sampling methods and laboratory techniques and possibly, different crop management or agronomic practices in different regions or localities, could also contribute to this variability.

Conclusion: Application factors such as spray concentration, treatment rate, number of sprays and pre-harvest interval explain a large proportion of the variation in residues at harvest, the additional effect of pre-harvest climate is relatively small, and 'other factors' likely to be of more importance.

9 CONCLUSIONS

In reaching the following conclusions, the Group recognised that pesticide applications cover a wide range of techniques and that it would be impossible to develop a zoning scheme that catered for all the various treatment techniques available.

However, since the Group considered that foliar/spray treatments of non-systemic pesticides were the most commonly used group of pesticides associated with the presence of residues in food (and hence requiring Maximum Residue Limits), the initial work on residue zoning should concentrate on this area of pesticide use, and if successful, could be expanded to other treatment methods at a later stage.

In addition, the group noted that while the residue data summaries in the JMPR monographs were the most comprehensive data-sets available, there were some limitations in the range of counties/regions represented, in the number of different crops for which sufficient trials were available and in the completeness of the information on treatment details.

Despite these limitations, the Group was confident that the data-sets finally selected for use in the validation phase of the project, and particularly in the statistical analysis of the residue variability, were sufficiently robust, at least for the pesticide/crop combinations that were assessed, to establish that:

- pesticide residue levels detected at harvest are highly dependent on the initial residue levels present immediately after the last application (i.e. at zero-days). Indications from the available data suggest that up to 70% of residue variability at harvest in comparable residue trials can be attributed to the variability of residues reported at zero-days.
- the additional effect of pre-harvest climatic conditions is relatively small, possibly contributing less than 10-20% of the residue variability at harvest.
- a significant proportion of the residue variability at harvest, (possibly up to about 40%), is not attributable to either the specific application parameters recorded in the data-sets or to the pre-harvest climatic conditions,

9.1 Geographic Zones

Based on the above, the Group concluded that a consistent relationship between climatic zones and residue behaviour cannot be quantified, and therefore that a geographic zoning scheme, based on climate, cannot be validated.

9.2 Zero-days Variability

After considering the results of the various statistical analyses of the available residue data-sets, the Group also concluded that most of the variation in residues at harvest could be explained by the variation in residue levels found immediately after treatment, when the influence of rainfall, temperature, sunshine should be insignificant.

9.3 Pre-harvest climatic conditions

The Group also noted that the influence of pre-harvest climatic conditions on residues at harvest was considerably less that had been expected, and in general could be given a much lower priority when assessing the comparability of residue trials.

9.4 Other factors

The Group recognised that there appeared to be a significant proportion of the variation in residues at harvest that could not be attributed to the specific application parameters recorded in the data-sets (pesticide concentration, water rate, number of sprays and pre-harvest interval). The Group considered that these sources of variability may include factors such as different treatment intervals, different application techniques used in the trials, sampling/laboratory variability and different agronomic practices.

When considering the relevance of these factors, the Group noted ongoing work in the estimation of variability associated with sampling methods and with laboratory analysis, and was of the opinion that while this sampling/analysis variability could make up a large part of this 'other factor' variability, it was already taken into account during the residue assessment process at both the national and international level.

9.5 Minimum data requirements

While not part of the Group's objective, there was clear agreement that national boundaries should not be a barrier to the acceptance of comparable residue trials for MRL-setting purposes at the national, regional or international level. Although the Group could not identify geographic boundaries to zones where residue trials could be considered comparable, factors leading to variability and the large variability in residues generated globally were noted.

Hence, when widespread global use is expected, the Group considered that with respect to the required number of trials proposed by the York Workshop (Annex 2) as being the minimum number needed to support the setting of an MRL, (See Table 6 below), the proposed zone-based differences in minimum trial numbers may not be relevant.

Table 5: Residue trials showing required totals and numbers of decline trials in brackets

	Number of zones where GAP exists	Insignificant in diet	Significant in diet
Insignificant in trade	1 zone	3 (1)	6 (2)
	2-3 zones	4 (1)	8 (2)
	> 3 zones	5 (1)	10 (3)
Significant in trade	1 zone	6 (2)	8 (2)
	2-3 zones	8 (2)	12 (3)
	> 3 zones	10 (3)	16 (3)

ANNEX 1

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ANNEX 2

Minimum Data Requirements for Establishing Maximum Residue Limits (MRLs) including Import Tolerances

on 6-8 September 1999

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Contents

Background

In March 1998, PSD was awarded a contract by the European Commission to develop guidance for establishing guidelines on the minimum or core data requirements for establishing MRLs, including import tolerances. The work remit was outlined in the proposal presented and agreed by the November 1996 OECD Pesticide Forum. The primary objective was to examine those areas of guidance which represent the greatest obstacles to the establishment of national import tolerances and the acceptance of international MRLs.

The aims of the project were to:

- underpin the work of the JMPR in proposing international MRLs and to support the scientific and technical basis of Codex MRLs as reference limits within the SPS agreement;

- facilitate work of national registration authorities in granting of import tolerances;

- facilitate the work of national regulatory authorities in the granting of national registrations and MRLs.

The programme was organised as a set of three preparatory meetings held in York (November 1998, January 1999 and April 1999). During these meetings, agreements were reached **at a scientific level** on which areas relating to the setting of MRLs that were most and least harmonised. A workshop held in York in September 1999 was attended by 38 delegates representing Member States (except Greece, Italy and Luxembourg), Commission officials, OECD member country representatives (Australia, Canada, New Zealand, Norway, Republic of Korea, Slovak Republic, Slovenia), OECD secretariat, FAO and GCPF representatives. A list of delegates is given in Annex 1.

The least harmonised areas (approaches to geographical/climatic regions for residue trials ('zoning'), criteria for determining the minimum number of residue trials and acceptable extrapolation/mutual support of residue trials data between crops) formed the basis of the main presentations and the discussions in the small working groups and the plenary sessions. Other areas which are near harmonisation or where good commonality exists (plant metabolism, farm animal metabolism, farm animal feeding studies, processing studies, the effect of formulation types, residues over different years and glasshouse trials) were the subjects of short presentations and discussion generally in the plenary only.

Reports from the working groups were adopted during the workshop.

Summaries of discussions and recommendations

General

Comparisons of data requirements were carried out to determine where common requirements already existed. The main documents examined were those from FAO, Canada, USA, Australia, New Zealand and the EU [1-6]. These comparisons were used as the basis for discussions.

Where agreement could not be reached or further work is required, this is indicated in italics.

It was recognised that import MRL requirements should be consistent with the national registration requirements so that additional data were not unnecessarily required. It was hoped that the work on minimum data requirements for the setting of international MRLs could be used by national governments for a basis for import MRL data requirements.

The meeting noted the different perspective of Codex/JMPR, which does not have the registration function of national authorities or the economic interests of national governments, and evaluates data on a scientific basis, not taking into account economic matters. Codex/JMPR are able to set a MRL if there is a supported GAP where as governments need to set the MRL on the basis of the critical GAP.

Plant metabolism

A comparison of the data required for assessing metabolism in plants in the different countries showed a high degree of conformity. The minimum requirements were agreed as:

Information required: Identity and quantities of metabolites, and distribution of metabolites (surface, leaves, stems, edible root crops);

Number of studies required: one study for each crop group; extrapolation from 3 studies on different groups to all crops, provided that metabolism is similar;

Crop groupings: root vegetables; leafy crops; fruits; pulses and oilseeds; cereals;

Material used: radiolabelling (C-14, P-32, S-35);

Dosage rate: at least equal to intended use (normally up to a maximum of 10x);

Identification and characterisation: Residues should be characterised and identified if these are > 0.05 mg/kg or > 10% of TRR, characterised if these are between 0.01 and 0.05 mg/kg, normally neither characterised nor identified if these are < 0.01 mg/kg, in the case of unextractable residues neither characterised nor identified if these are < 0.05 mg/kg or < 25% TRR and a significant portion (> 75%) has been identified.

Residue definition: The “marker compound concept” should be used for enforcement and “toxicological relevant compounds” should be used for risk assessment.

These recommendations concur with the requirements laid down in the FAO manual [(1)].

Farm animal metabolism

The requirements for metabolism studies in farm animals are an area where good commonality exists. The differences between the data requirements in several OECD countries and the FAO manual were small.

Circumstances when studies required: when significant residues remain in crops or commodities used in animal feed, in forage crops or in any plant parts used in animal feed.

A definitive conclusion on when studies were required was not reached. It was noted that the trigger value expressed in terms of mg/kg feed on a dry matter basis would lead to a study being required in almost all circumstances especially where a low percentage dry matter commodity was being considered. It was recommended that a trigger value based on an animal intake per kg bw would be more appropriate but further work would be required to define these levels.

Species: ruminants (normally lactating goats, lactating cows acceptable) and poultry (chickens). Studies using pigs to be conducted if metabolism in rat is different from that of goat and/or chicken.

Duration of dosing: dosed daily for at least 3 consecutive days.

Information required: Milk, eggs, meat, liver, kidney (ruminants and pigs only) and fat should be collected. Residues should be characterised and identified if these are > 0.05 mg/kg or > 10% of TRR, characterised if these are between 0.01 and 0.05 mg/kg, normally neither characterised nor identified if these are < 0.01 mg/kg, in the case of unextractable residues neither characterised nor identified if these are < 0.05 mg/kg or < 25% TRR and a significant portion (> 75%) has been identified.

It was recommended that it was not necessary to analyse excreta in animal metabolism studies however it was noted that this may be important from an environmental perspective and if metabolism appears to be different in the rat.

Dose rate: at the level of expected exposure but in practice not normally lower then 10 mg/kg.

Material used: Normally parent compound should be used. In cases where parent compound is not detected in plant metabolism studies, the main plant metabolite(s) should be used. Where plant and animal metabolism differ, a study with a unique plant metabolite may be required if this unique plant metabolite is of toxicological significance.

Farm animal feeding studies

The requirements for livestock feeding studies are an area where good commonality exists. The differences between the data requirements in several OECD countries and the FAO manual are small.

Further work was considered necessary to harmonise an animal feed component table for calculation theoretical dietary burdens by animals. Consideration should be given to not including crops that do not contribute regularly to animal feedingstuffs.

Circumstances when studies required: when significant residues occur in crops or commodities fed to animals and livestock metabolism studies indicate that significant residues (above the LOQ) may occur in edible tissues. Potential for bioaccumulation should also be considered.

A definitive conclusion on when studies were required was not reached. It was noted that the trigger value expressed in terms of mg/kg feed on a dry matter basis would lead to a study being required in almost all circumstances especially where a low dry matter commodity was being considered. It was recommended that a trigger value based on an animal intake per kg bw would be more appropriate but further work would be required to define these levels.

Species: ruminants (normally lactating cows) and poultry (chickens). Trials with pigs are only required if metabolism differs significantly in the pig as compared to ruminants. Only those species where intake is significant should be studied.

Number of animals and duration of dosing: A minimum of 3 dairy cows and of 10 chickens should be dosed for at least 28 days or until plateau is reached in milk or eggs.

Information required: meat, fat, liver, kidney (ruminants and pigs only), milk and eggs should be collected and analysed.

Dose rate: use three dose groups (level of expected exposure (1X), 3 to 5 times the level of expected exposure (3-5X), 10 times the level of expected exposure (10X)) and control group.

Material used: usually parent compound. In cases where parent compound is not found in plant metabolism studies, the main plant metabolite(s) should be used. Where plant and animal metabolism differ, a study with a unique plant metabolite may be required if this unique plant metabolite is of toxicological significance.

It was noted that for lipophilic compounds, variable residues can occur in different fat depots and it was considered important to take this into account when taking fat samples.

Processing studies

The need for processing studies has become more important since changes in guidelines for predicting dietary exposure have indicated that adjustments for processing should be taken into account at the first stage of the NEDI or IEDI calculations. In some cases, they are also taken into account for setting MRLs in traded, processed commodities such as oils. It was considered that current guidelines necessitate the generation of too many studies from too many crops/commodities. The requirements for processing studies is an area where less harmonisation of requirements exists. The USA uses standard concentration factors for some processes but it was unclear how these were derived.

It was agreed that there was a necessity to know the nature of the residue in processed commodities. Generally, data should be requested where residues in the raw agricultural commodity exceed 0.1 mg/kg. However, consideration should be given to the processes involved: where these do not involve heating and/or change of pH, assessment of the nature of the residue may not be required.

For some crops and commodities such as hops and beer, residue levels may be predictable by the use of dilution factors.

Data on the transfer of residues into processed commodities are required where residues exceed 0.1 mg/kg and the intakes based on the individual NEDI (STMR x consumption/body weight) for any one crop exceeds 10% of the ADI or the total NEDI exceeds 100% of the ADI.

A minimum of 2 studies/commodity would be required.

The recommendations for the minimum requirements were as shown in table 1.

Table 1 Minimum requirements for processing studies

Major crops	Processed food	Extrapolation
apple	peel, juice, wet and dried pomace	pome fruit
apricot/peach	preserves (jam, dried)	stone fruit
grape	juice, wine	soft fruit and berries
citrus*	peel, pulp, juice, dried	
sub tropical fruits*	peel, pulp, dried	
wheat	flour, bran, bread	rye, maize, sorghum, oats
rice	polished, flour	
carrot	peel, juice, preserved	others tubers, peel
tomato	juice, preserved	other vegetables
peas, beans	without pod	
oilseed**	meal, oil	all other oilseeds
olive**	virgin oil	
tea	brewed tea	

* studies not required where no detectable residues in pulp
** take account of fat solubility of residue

The need for studies on sugar beet was questioned. Whilst this would give useful information, it was considered that efforts should be concentrated on minimum requirements.

<u>The effect of formulation types</u>

Data were presented comparing residue levels from trials on identical plots and crops using different formulations. It was agreed that different formulations are equivalent in terms of residues if they are used in the same way, for example as a high volume foliar spray. Aerially applied and ground applied low-volume treatments were considered equivalent for residue purposes. Aerially applied ULV may not be the same as ground applied ULV. If the change in formulation leads to a changed application technique (e.g. from foliar to soil applied granular) then it should be decided on the basis of available information (e.g. bridging trials) whether residues would be lower or higher than the previously accepted use. If residues are higher, a full data package is required. Case-by-case decisions will be necessary. For example, in moving from foliar sprays to soil applied granular treatments, root vegetables are the crops likely to produce higher residues and should be examined first. It was agreed that it was not possible to extrapolate other formulation residue data to support the use of slow-release formulations, which will need bridging data as a minimum requirement.

<u>Residues trials carried out over different years</u>

Comparisons of residue levels from different years indicated that this did not significantly affect the ranges seen. If trials covered a range of geographic locations, data from more than one season would not be required.

<u>Glasshouse trials</u>

It was agreed that protected crops (glasshouse, plastic tunnel where the environmental conditions can be controlled) should be treated as a single zone for Europe. Since this is predominantly a European practice, little data are available to show that this was true for the rest of the world. Cultural conditions were essentially optimised to suit the protected crop and it should be possible with further work (comparison of crop/growing conditions) to consider whether glasshouses could be considered as a single zone on a world-wide basis.

Post-harvest treatments

Post-harvest treatments were considered as a "single zone" for the purposes of decisions on numbers of trials.

Post-harvest treatments on cereals should generally produce a homogeneous and predictable residue. Where the residue is persistent or where the required storage interval is small, the MRL may be set at the application rate without residue trials data. However, it is should be noted that processing studies with incurred residues were likely to be necessary as a result of post-harvest treatments.

Post-harvest treatments on potatoes should also produce a predictable residue, but much less homogeneous than for cereals and trials will be required. Post-harvest spraying or dipping of fruits and vegetables produces a less predictable residue, but possibly more homogeneous than for potatoes and trials will be required.

The trials requirements for post-harvest treatments except where the residue is predictable and homogeneous (cereals) were agreed and are shown in table 2.

Table 2 The trials requirements for post-harvest treatments except where the residue is predictable and homogeneous

	Insignificant in diet	**Significant in diet**
Insignificant in trade	3	6
Significant in trade	6	8

Significance of commodities in the diet

0.5% of the total diet was agreed as the trigger value to differentiate between significant and non-significant in the diet. The 'diet' is the relevant WHO Regional Diet (currently 5 diets; mean consumption for the whole population).

Significance in trade

A definition of significant in trade was not agreed. This was primarily due to the lack of availability of useable statistics. Economic indicators for crop importance were discussed and it was agreed that the most convenient would be the % of cultivation area per relevant zone. This factor was chosen because it is less likely to fluctuate, compared to factors such as tonnage of production. No information was available to choose a suitable trigger value; 0.5% was suggested but the value should only be finalised after checking to see what value differentiates major crops from others. It was noted that % cultivation area was probably not a good indicator for glasshouse production.

More work is required to define crops significant/insignificant in trade.

Minimum residue trial requirements

The report from the working group is given in Annex 2. The main recommendations were:

- the absolute minimum number of trials required should be 3;
- the minimum number of trials required would depend on the significance of the crop in the diet and in trade and also the number of zones where GAP exists; this would range from 3 to 16;

- decline studies are only required in those situations where the pesticide is applied late in the season and when the final crop commodity to be harvested has formed and developed into its final form;
- single composite samples are adequate for supervised trials;
- zero residues may be predicted in some cases from crop metabolism studies and the physico-chemical properties of the pesticide. In such situations, 3 trials are required for commodities significant in the diet and no trials are required for commodities insignificant in the diet.

Extrapolation

The report from the working group is given in Annex 3. The main recommendations were:

- it was agreed that the ± 25% rule could be used when comparing GAPs;
- the primary crops within a group/subgroup must have a robust database prior to an extrapolation or group tolerance being considered;
- the main criterion for extrapolation when the edible part of the crop had started to form was crop morphology;
- *consideration was given to the definition of comparability when differences are seen in the residue profile of the main crops within a group. No agreement could be reached in setting an appropriate factor;*
- for tropical and subtropical fruit GAPs, morphology and cultural practices for these crops are so dissimilar that it makes extrapolation difficult;
- no recommendations were made for feed items since there are very few in international trade. However, for the purpose of MRL setting for products of animal origin, animal feed crops and fodder are important and residues data are required.

Leafy vegetables were not considered. Further work is required to define acceptable extrapolations for this group.

The possibility of increasing recommendations for group tolerances was examined. It was noted that the main obstacle was often incompatible GAPs within the group. It was also noted that if groups were too large, difficulties may arise in estimating realistic levels of consumer exposure.

The meeting noted that it had only been possible to recommend a limited number of extrapolations for minor crops.

Zoning

The report from the working group is given in Annex 4. Whilst the benefits of using the concept of zoning were acknowledged, specific recommendations could not be made. However, the benefits, beneficiaries, key parameters for defining zones and a proposal for developing a global zoning concept were proposed.

Further work will be required before a global zoning concept can be developed.

Conclusions

A set of positive recommendations was made as a result of comparing and contrasting global data requirements. A high degree of similarity of requirements for plant and farm animal metabolism and farm animal residue studies was noted. Recommendations for a reduced set of core data for predicting the transfer of residues into processed products were made. Situations were identified where extrapolations could be made for foliar applied sprays using different formulation type. It was agreed that residues data were only required from one seasons studies where data covered a range of geographic locations. Glasshouses in Europe and post-harvest treatments were considered single zones. Where crops treated post-harvest give rise to homogenous and predictable residues, residues data would not be required. Recommendations were made for developing a global zoning concept. Recommendations on the minimum number of residues trials and extrapolations were developed. These reduce requirements both nationally and internationally without affecting the reliability of the data sets.

Acknowledgements

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Abbreviations/Glossary of terms

ADI	Acceptable daily intake
CCPR	Codex Committee on Pesticide Residues
EC	European Commission
EU	European Union
FAO	Food and Agriculture Organisation
GAPs	Good Agricultural Practice
GATT	General Agreement on Tariffs and Trade
GCPF	Global Crop Protection Federation
GIS	Geographic Information Systems
IEDI	international estimate of dietary intake
JMPR	Joint Meeting on Pesticide Residues
LOQ	limit of quantification
MRL	Maximum Residue Limit
NAFTA	North American Free Trade Association
NEDI	national estimate of dietary intake
OECD	Organisation for the Economic Co-operation and Development
PMRA	Pest Management Regulatory Agency
PSD	Pesticides Safety Directorate
SPS Agreement	Sanitary and Phyto-sanitary agreement
STMR	supervised trials median residue
TRR	total radioactive residue
UK	United Kingdom
ULV	ultra low volume
UN	United Nations
USA	United States of America
WHO	World Health Organisation
WTO	World Trade Organisation

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Annex 2 Report from the Working Group on Minimum Residue Trial Requirements

The Working Group first agreed on a set of headings to cover the topic and then discussed each in turn and made recommendations.

Scientific basis for the required number of trials

The Working Group agreed that importance of a commodity in the diet was a scientific basis for influencing the required number of residue trials.

The importance of the commodity in trade was also discussed as influencing the required number of trials. Indicators of importance could be its area of production or area to be treated with the product, the tonnage produced or the monetary value of the trade.

The importance in trade is more of an economic basis than a scientific basis for the minimum number of residue trials, but is a legitimate concern of national governments. Some crops products such as processed animal feed, hop extract and sugar are minor in the diet but are major in trade.

The Working Group noted the different perspective of Codex/JMPR, which does not have the registration function of national authorities or the economic interests of national governments, and evaluates data on a scientific basis, not taking into account economic matters. Codex/JMPR are able to set a MRL if there is a supported GAP where as governments need to set the MRL on the basis of the critical GAP.

Trigger values

The Working Group chose 0.5% of the total diet as the trigger value to differentiate between significant and non-significant in the diet. The diet is the relevant WHO Regional Diet (currently 5 diets) which are the mean consumption for the whole population.

The Working Group discussed the economic indicators for crop importance and decided that the most convenient would be the % of cultivation area per relevant zone. This factor was chosen because it is less likely to fluctuate, compared to factors such as tonnage of production. No information was available to the Group to choose a suitable trigger value; 0.5% was suggested but the value should only be finalised after checking to see what value differentiates major crops from others. It was noted that % cultivation area was probably not a good indicator for glasshouse production.

Absolute minimum number of trials

The Working Group agreed that the absolute minimum number of required trials was 3. This requirement should be kept as low as possible to minimise the number of “minor crop” situations where it is uneconomic to produce the trials data.

Minimum data requirements for establishing Maximum Residue Limits (MRLs) and import tolerances (Doc. 2734/SANCO/99)

Range of number of trials

The Working Group incorporated significance in diet, significance in trade and the geographic zone concept into a matrix of required number of trials. In this case the GAP in the different zones is the same.

Required residue trials

The minimum number of residue trials required was as shown in table 3.

Table 3 Minimum residue trials requirements

	Number of zones where GAP exists	Insignificant in diet	Significant in diet
Insignificant in trade	1 zone	3	6
	2-3 zones	4	8
	> 3 zones	5	10
Significant in trade	1 zone	6	8
	2-3 zones	8	12
	> 3 zones	10	16

Significance in diet and trade: see *Trigger values*.

If the GAP is significantly different from one zone to another, a full package may be required by the national authority for the maximum GAP situation.

Number of seasons necessary

The aim is to cover the range of possible production conditions occurring in practice. More than one year's trials are unnecessary if the aim can be realised by distributing trials in different zones, in the one zone at different locations with a possibility of different conditions, early season and late season variation and different growing seasons within the one year where this is possible.

Number of sampling occasions during residue trials

The Working Group broadened the scope of the original "decline trials" topic to take into account all the situations where sampling is needed on more than one occasion during a residue trial:

(a) decline studies – 4 sampling intervals, i.e. 5 samples.
Decline information (residue depletion half-life) is needed in residue evaluation to decide on the range of trial PHIs acceptably close to GAP PHI and to assist in determining the influence of numbers of applications on the final residue.

Decline studies are only required in those situations where the pesticide is applied late in the season and when the final crop commodity to be harvested has formed and developed into its final form.

The Working Group agreed that, in these situations, the number of trials required as decline trials would be 1, 2 or 3 as shown in table 4. Decline trials are required only in defined situations.

Table 4 Residue trials showing required totals and numbers of decline trials in brackets

	Number of zones where GAP exists	Insignificant in diet	Significant in diet
Insignificant in trade	1 zone	3 (1)	6 (2)
	2-3 zones	4 (1)	8 (2)
	> 3 zones	5 (1)	10 (3)
Significant in trade	1 zone	6 (2)	8 (2)
	2-3 zones	8 (2)	12 (3)
	> 3 zones	10 (3)	16 (3)

(b) forage commodities where immature crops are taken for feed – usually 2 samples during the growing of cereals and other field crops to provide information on residues when they are likely to be consumed by farm animals grazing the crop.

(c) *systemic pesticides* - tracing build-up and dissipation of systemic pesticides in the commodity resulting from soil or foliar treatment. Examples are translocation of a soil-applied pesticide to fruits and translocation of a foliar applied pesticide to peanuts. Information on the timing of residue build-up and decline is needed for proper MRL evaluation. Plant and soil metabolism studies should be examined to decide on the necessary sampling strategy in the residue trials, but the number of sampling occasions should be adequate to define the time when residues reach a maximum in the commodity.

The Working Group agreed that the number of such studies required for systemic pesticides used in the circumstances described is the same as defined for decline studies.

Necessity of replicates or multiple composite samples from an individual trial site

The Working Group agreed that single samples are adequate for supervised residue trials. However, the variation between replicate field composite samples from a trial may be used as an aid to defining unit-to-unit variation, where unit-to-unit variation information is needed for the purposes of acute dietary intake assessment.

Number of trials in the case of changes in formulation

The Working Group agreed that different formulations are equivalent in terms of residues if they are used in the same way, for example as a high volume foliar spray. Aerially applied and ground applied low-volume treatments were considered equivalent for residue purposes. Aerially applied ULV may not be the same as ground applied ULV.

If the change in formulation leads to a changed application technique (e.g. from foliar to soil applied granular), then we should decide on the basis of available information (e.g. bridging trials) if residues are lower or higher than the previously accepted use. If residues are higher, a full data package is required.

Case-by-case decisions will be necessary. For example, in moving from foliar sprays to soil applied granular treatments, root vegetables are the crops anticipated to perhaps produce higher residues and should be examined first.

Minimum data requirements for establishing Maximum Residue Limits (MRLs) and import tolerances (Doc. 2734/SANCO/99)

The Working Group agreed that it is not possible to extrapolate other formulation residue data to support the use of slow-release formulations, which will need a full data package.

Number of trials in the case of a zero residue situation

Zero residues may be predicted in some cases from crop metabolism studies and the physico-chemical properties of the pesticide. Examples are:

- seed treatments where metabolism data show that no translocation occurs;
- early applications where plant metabolism data show rapid decline of residues with no residues at harvest;
- edible portion is not present at time of application and no translocation of residues into edible portion occurs.

The Working Group noted examples where residues were predicted not to occur from metabolism studies but still may occur because of the methods of production or harvesting. Residues of a non-translocated foliar applied pesticide may occasionally occur in potatoes because part of a potato may be exposed to the direct spray. Pesticide may be physically transferred from the outside of tree-nut shells to the kernels during the cracking process and similarly from the pods of peas to the peas themselves during shelling.

The Working Group agreed that 3 trials are needed for commodities significant in the diet and no trials are needed for commodities insignificant in the diet.

Number of trials where residues are below LOQ

This situation is distinguished from the zero residue situation in that residues are expected to be present but at levels too low for the analytical method. For example, the residues may be seen to decline below the LOQ by the time of harvest, or exaggerated application rates produce detectable residues.

The Working Group noted that it was difficult to know that residues would be below LOQ until the full data set was produced. However, if the situation was found to apply to a major crop it would assist in ready extrapolation to the group, i.e. relaxing requirements on subsequent commodities within the group. In general where it is an LOQ situation much broader extrapolations should be possible.

Number of trials necessary for group tolerances

Full data packages for two representative crops would be required before a group tolerance could be established. Precedence should be given to the recommendations from the extrapolation group.

Number of trials in the case of protected crops

The Working Group agreed that protected crops (glasshouse, plastic tunnel with controlled environmental conditions) should be treated as a single zone for Europe but there were no data available to show that this was true for the rest of the world. Conditions are essentially optimised to suit the protected crop and it should be possible with further work to define this as one zone for the world. When a pesticide has both a field use and a glasshouse use, a full data package is needed for the critical GAP. Examples where the glasshouse use is clearly the critical GAP are for relatively volatile pesticides and those subject to photolytic breakdown as the main degradation pathway.

Required residue trials for protected crops

The Working Group agreed that for protected crops, the minimum number of trials required would be 1 as shown in table 5. Decline trials are required only in defined situations.

Table 5 Minimum number of trials required for protected crops

	Insignificant in diet	Significant in diet
Insignificant in trade	3	6
Significant in trade	6	8

Significance in trade is defined as the significance of the whole crop (field + protected) in the region with the official glasshouse GAP. See "trigger values" for discussion on significance of crops.

Number of trials in the case of post-harvest treatments

The Working Group considered post-harvest treatments as a "single zone" for the purposes of decisions on numbers of trials.

Post-harvest treatments on cereals should generally produce a homogeneous and predictable residue. Where the residue is persistent or where the required storage interval is small the MRL may be set at the application rate without residue trials. The Working Group drew attention to the requirement for processing studies on aged residues, not to be confused with the treatment and storage of the raw commodity. It is likely however, that trials will be required to produce aged residues for use in processing studies.

Post-harvest treatments on potatoes should also produce a predictable residue, but much less homogeneous than for cereals and trials will be required.

Post-harvest spraying or dipping of fruits and vegetables produces a less predictable residue, but possibly more homogeneous than for potatoes and trials will be required.

The Working group agreed on the trials requirements for post-harvest treatments except where the residue is predictable and homogeneous (cereals) as shown in table 6.

Table 6 Minimum residues trials requirements for post-harvest treatments

	Insignificant in diet	Significant in diet
Insignificant in trade	3	6
Significant in trade	6	8

Minimum data requirements for establishing Maximum Residue Limits (MRLs) and import tolerances (Doc. 2734/SANCO/99)

Significance in trade is defined as the significance of the crop in the region with the official post-harvest GAP. See “trigger values” for discussion on significance of crops.

Residue data not conforming with GAP

Residue data not conforming to GAP may be directly used under some circumstances. In the nil residue situation data from trials may be used to support a GAP where:

- application rates in the trials exceed the GAP rate;
- PHIs in the trials are less than the GAP PHI and residues are expected to decline with time;
- the numbers of treatments in the trials exceeds the maximum number specified by GAP.

Trials on the isomeric mixture of a pesticide should support the GAP for a single isomer, where it may be predicted that the residues of the single isomer will be proportional to the isomeric mixture, taking into account the residue definition or expression of residue.

Annex 3 Report from the Working Group on Extrapolations

Introduction

The group decided to accept the recommendations of the third preliminary meeting as a starting point for their discussions. The following items were discussed:

- pre-requisite for extrapolation (comparability of GAP);
- tabulating extrapolation when edible crop part has started to form;
- special attention was made to the tropical sub-tropical group;
- tabulating of post harvest extrapolations;
- considerations of extrapolation for animal feed items.

The tables should be considered as a starting point for extrapolations, which can be added to in the future.

Discussion and agreement on major points

It was agreed that the ± 25% rule could be used when comparing GAPs. This can be applied to either the application rate or the number of applications. To consider the affects of changing the pre harvest interval, decline curves should be utilised. Deviations from this rule can be considered on a case by case basis.

The group considered that extrapolation could be made between different formulation types such that all formulations (except encapsulated products) that are used as a spray will lead to comparable residues.

The primary crops within a group/subgroup must have a robust database prior to an extrapolation or group tolerance being considered. This was defined as having both quantitatively and qualitatively enough data at the GAP to set a MRL for the primary crop(s) in its own right.

It was agreed that the main criterion for extrapolation when the edible part of the crop has started to form was crop morphology. But it was also agreed that other parameters such as the physical and chemical properties of the active substance could be of importance.

The Codex crop groupings were used as a starting point and modified where necessary. Only the crops considered significant in international trade were included in the list. In addition to this their importance in the diet was also considered.

Consideration was given to the definition of comparability when differences are seen in the residue profile of the main crops within a group. No agreement could be reached to set a factor.

When the group considered the tropical and subtropical fruit it became clear that the GAPs, morphology and cultural practices for these crops are so dissimilar that it makes extrapolation difficult. The group also considered extrapolation into this group from other fruit and vegetable categories but again this was difficult due to GAP, morphology and cultural practice differences and of course climatic conditions.

For feed items the group considered that there were very few in international trade. However, for the purpose of MRL setting for products of animal origin feed animal feed crops and fodder are important and residues data are required. No recommendations were made by the group.

Leafy vegetables were not considered due to time constraints.

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Table 7 Commodity groups and proposal for extrapolations and group tolerances for applications after the consumable part of the crop has started to form.

Commodity	Group tolerance	Other extrapolations
Citrus		
Oranges *Grapefruits* Lemons Limes *Mandarins* (including clementines and similar hybrids) Others	Oranges/grapefruit and mandarins/lemons to the whole citrus group on a case by case basis. The commodities were picked to cover the large and the small fruit in the group.	Oranges to grapefruit. Mandarins to limes, lemons, clementines. Again these extrapolations are based on fruit size.
Pome fruit		
Apples *Pears* Quinces Crab apples Medlars Nashi Others	Apples and pears up to 50 % of the trials can be on pear. The justification for this is that apple and pears are by far the major commodities in trade and in the diet.	Apples and pears to whole group
Stone fruit		
Peaches *Apricots* *Plums* Nectarine (and similar hybrids) Cherries* Others	Peach or apricot or plum with a minimum of 50 % peach trials. ‘Group’ tolerance for peach, apricot, nectarine and plum.	
Berries and small fruit		
*Strawberry**	Data on strawberry will be required, as there are no other crops with a similar morphology.	
*Grapes**		Wine grapes to and from table grapes
<u>Cane fruit</u> *Blackberry* Loganberries *Raspberries*	Any *Rubus* spp. to any other *Rubus* spp.	

Table 7 continued

Commodity	Group tolerance	Other extrapolations
Other small fruit Bilberries Cranberries *Currants* *Blueberries*	Currants or blueberry to the crops listed.	-
Cereals		
Wheat *Barley* Rye Oats Triticale	Wheat and barley, at least 50 % barley but no more than 70 %. To wheat, barley, rye, oats and triticale.	
Millet *Sorghum* Rice* Maize*		Sorghum to millet.
Oilseeds		
Oilseed rape (canola) Linseed Poppy* Sesame* Sunflower Cotton* Mustard Safflower Peanut*		Oilseed rape to mustard and linseed. Sunflower to safflower.
Bulb vegetables		
Fennel Garlic Leek Bulb onion Shallot Spring onion		Bulb onions to garlic and shallots. Leek to spring onion.

Minimum data requirements for establishing Maximum Residue Limits (MRLs) and import tolerances (Doc. 2734/SANCO/99)

Table 7 continued

Commodity	Group tolerance	Other extrapolations
Fruiting vegetables		
Solanacea		
Peppers (sweet and chilli) Aubergine Okra *Tomato* (including cherry tomatoes)		Tomato and peppers to aubergine or okra. If chilli pepper or cherry tomatoes consideration should be given to possible residues, due to the difference in surface area to weight ratio.
Sweetcorn		Immature maize to sweetcorn.
Cucurbits edible peel		
Cucumber *Courgette (zucchini)* Gherkin Summer squash Others	Cucumber and courgette with a minimum of 50 % cucumber trials to the group.	
Cucurbits inedible peel		
Melons Watermelon Winter squash Pumpkins Others	Melon to the group.	
Pulses		
Beans *Peas* Lentils Soyabean*	Beans and/or peas to the group (excluding soyabean).	
Legume vegetables		
Pea (with pod) Pea (without pod) Bean (with pod) Bean (without pod)	Peas and beans to the group	Pea (with pod) to and from bean (with pod) Pea (without pod) to and from bean (without pod)

Table 7 continued

Commodity	Group tolerance	Other extrapolations
Root and tuber vegetables		
Beetroot Carrot Cassava Celeriac *Potato* Radish Sweet potato Yams	Carrot and potato to the group.	
Tropical and sub-tropical fruit		
Edible peel		
Carambola* Date* Fig* Kumquats* Olives* Persimmon*		
Inedible peel		
Avocado Banana* Cherimoya* Durian* Guava* Kiwifruit* Litchi* Tamarillo* Mango Papaya* Passion fruit* Pineapple* Pomegranate*		Avocado to mango *It was considered that there could be no extrapolation to these crops.

i) The major crops in each group are in Italics.
ii) * = crops where there are no extrapolations.
iii) When ‘or’ is used in the tables it means that the data can be provided on either of the crops in any proportion unless otherwise stated.
iv) ‘Others ‘ refers to unlisted crops in the Codex crop group. The ‘Others’ category has been included where possible.

Minimum data requirements for establishing Maximum Residue Limits (MRLs) and import tolerances (Doc. 2734/SANCO/99)

Table 8 Extrapolations and group tolerances for post harvest applications.

Commodity	Group tolerance	Other extrapolations
Citrus		
Oranges Grapefruit Lemons Limes *Mandarins* (including clementines and similar hybrids) Others	Oranges, mandarins or lemons to the whole group. At least 50 % of the trials should be on smaller fruits.	
Pome fruit		
Apples Pears Quinces Crab apple Medlar Nashi Others	Apples to the whole group.	-
Stone fruit		No extrapolation necessary since post harvest treatment is only applicable to peaches.
Berries and small fruit		Not applicable.
Cereals		
Wheat Barley Rye Oats Triticale Millet *Sorghum* Rice (unpolished) Maize Others	Any one commodity to the group.	
Oilseeds		Not applicable
Bulb vegetables		Not applicable
Fruiting vegetables		Not applicable
Pulses		
Beans *Peas* Lentils Soyabean	Beans or peas to the group.	

Table 8 continued

Commodity	Group tolerance	Other extrapolations
Legume vegetables		Not applicable
Root and tuber vegetables		Not applicable
Tropical and sub-tropical fruit		
Edible peel		
Carambola Date Fig Kumquats Olives Persimmon		Extrapolations may be made on a case by case basis and will mainly depend on the surface area to weight ratio of the fruit.
Inedible peel		
Avocado Banana Cherimoya Durian Guava Kiwifruit Litchi Mango Tamarillo Papaya Passion fruit Pineapple Pomegranate		Extrapolations may be made on a case by case basis and will mainly depend on the surface area to weight ratio of the fruit.
Nuts	From one type of nuts to all others except coconut. The justification for this was that it will be the nature of the commodity (i.e. high oil content) that will influence the residue and not the individual commodity.	
Commodity	Group tolerance	Other extrapolations
Dried fruit	Dried fruit to other dried fruit. It was considered that the moisture content of dried fruit was important. It was concluded that the fruit that will be treated would normally have the same moisture content. If the moisture content is very low then treatment would be unnecessary anyway.	

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i) The major crops in each group are in Italics.
ii) When ‘or’ is used in the tables it means that the data can be provided on either of the crops in any proportion unless otherwise stated.
iii) ‘Others ‘ refers to unlisted crops in the Codex crop group. The ‘Others’ category has been included where possible.

Annex 4 Report from the geographic zoning working group

Introduction

The Working Group considered the utility and possible approaches to mapping the world into geographic zones within which pesticide residue behaviour would be expected to be comparable. This would allow the scientific comparison of data from residue trials within a particular zone to be considered equivalent and could support GAP for any country or region containing the same zone. This should help in assessing data in support of the establishment of MRLs and import tolerances.

When considering the reports of the Preliminary Meetings, the group noted that this zoning concept was already operating in a number of countries, either on a formal basis (e.g. NAFTA, EU) or more informally at an operational level (e.g. Australia, New Zealand), and that the opportunity existed to extend and harmonise these approaches into a single global zoning system.

In discussing possible approaches to zoning, the group noted the points made at the Preliminary Meetings:

- on the importance of climatic data (with other relevant data also being taken into account);
- that the use of the powerful GIS technique may not be strictly necessary;
- the need to keep the number of zones to a minimum necessary for the purposes of residue trial comparability.

Benefits

The group supported the zoning concept as a means of:

- promoting mutual acceptance of residue data from trials conducted within a particular zone;
- improving confidence in the supporting data reflecting potential residues in food, and thus the enhancement of food safety assurances based on these data;
- reducing the duplication of data on a world-wide basis (fewer trials required);
- facilitating international trade by supporting the establishment of Import Tolerances based on data developed anywhere within the same zone;
- increasing the opportunity to establish MRLs for minor crops by accepting data from the same zone that has been produced in a different part of the world;
- providing an incentive for manufacturers to develop (where possible) a common GAP for all countries within a particular zone and to generate a single supporting data package for all of these countries.

Beneficiaries

The working group agreed that the proposed zoning scheme would have advantages for:

- Manufacturers: potential for fewer trials world-wide; more rapid approvals through the mutual use of regulatory reviews; opportunity for a greater number of uses across a wider geographic area;
- Producers: greater range of pesticides available, particularly for minor crops; more rapid access to pesticides as a result of more rapid approvals; enhanced trade opportunities arising from more Import Tolerances being granted;
- Regulators: improved confidence that the supporting data are more representative; greater opportunity to accept regulatory reviews from other countries and thus more efficient assessments;
- Consumers: improved confidence in the scientific assessments underlying the establishment of MRLs;
- International Organisations: greater acceptance of Codex MRLs by national authorities because of increased confidence in the supporting global data set; increased number of MRLs, particularly for minor crops.

Approach

The Working Group considered a number of approaches towards designing global zone maps. These included the simple overlaying of publicly available maps as well as the complex computerised GIS system.

Key Parameters for Defining Zones

The Working Group considered the key parameters worthy of consideration in defining geographic zones with equivalent biophysical conditions relevant to the residue behaviour. It agreed that climate (predominantly rainfall, sunshine and temperature), altitude and to a lesser extent soil characteristics should be the major components to be investigated, and that crop distribution data would be of benefit in confirming or refining the boundaries between the different zones.

Proposal for developing the global zoning concept

Proposed approach

The Working Group suggested that to develop a global zoning system, the following steps would be necessary:

1. identify and collect available national and/or global data on the ‘key’ parameters used in the NAFTA approach. Data gaps should be identified;
2. develop a preliminary set of global geographic zones using the NAFTA approach to the extent possible. Identify those zones/areas where the full data sets are not available;
3. assess the relative importance/impact of the various data sets used in determining the different zones.

Rationale: It is anticipated that not all the data sets will be available globally. It would therefore be useful to know the relative importance/impact of the different data sets in determining the zones, and whether a simpler approach, using fewer parameters would be acceptable.

4. Compare the results of Steps 2 and 3 with the other existing zoning schemes already in operation (e.g. EU, Australia, New Zealand), i.e. the number and location of zones, and refine the approach as necessary.

Rationale: The Working Group recognised the need for the zoning approach to be as simple as possible but as complex as necessary, such that the total number of zones are kept to the minimum needed for the purpose of residue trial comparability. It was considered that a system that resulted in more than 20-30 zones world-wide would not be acceptable. Difficulties would also arise if a system identified many more zones in a particular country or region than those already in use. For example, the EU currently use 2 zones, and the introduction of many more would not be practicable.

5. Conduct a verification study of the proposed zoning approach developed in Step 4 by comparing residue trial data summaries for a selection (e.g. 6?) of pesticide/commodity combinations. This would involve a comparison of (1) residue data from trials conducted within the same zone, but at different locations around the world, and (2) residue data from trials conducted in different zones. JMPR Monographs and/or manufacturers' registration submissions could be used in this study.

Rationale: It was agreed that the zones should be selected such that the anticipated variation in residue levels between zones is likely to be significant relative to factors affecting the variation in residue levels within a zone.

6. From the outcome of Step 5, revise the proposed approach as necessary.

   Propose a global zoning system for approval and use by interested parties (e.g. OECD, EC, JMPR, Codex, NAFTA countries).

7. Review the approach in 5-10 years time by conducting a further verification study based on all data available which should be considerably more than that available during the earlier verification described in Step 5. At this time, modifications to the zone map could be considered.

Rationale: The group agreed that continued support for the zoning system at the national and international level would depend on verification of the approach, and considered that an ongoing verification would be an integral part of the development process.

Proposed mechanism

It is proposed that the development of the global zoning system be done as a joint activity of OECD and FAO.

It is proposed that an OECD/FAO Steering Group be established to manage the development of the system. The Steering Group should include representatives from interested countries, relevant international organisations and industry. For the outcome of the project to be widely accepted and applied, the involvement of key players from an early stage is vital. However, the Steering Group should not be too large (e.g. 10-15 persons maximum).

The Steering Group should include people with policy and/or technical expertise in pesticide registration, cropping systems and in MRL setting. Since much of the work, particularly in the early phases, will be of a very technical nature (i.e. GIS, mapping, agronomy etc.), it will be necessary for the Steering Group to identify and use additional expertise (e.g. consultants).

The Steering Group would report on progress to OECD, EC, JMPR, and Codex.

Constraints

The group recognised that the development and adoption of the zone concept has significant resource implications, particularly in the collection and analysis of the biophysical data underpinning the delineation of the various zones and may take a number of years.

Special Factors

The working group agreed there could be a number of instances where the use of the proposed geographic zoning system may not be appropriate. Examples included:

- greenhouse/protected crops ;
- post-harvest treatments;
- seed treatments (non-systemic);
- very close-to-harvest treatments;
- pre-harvest desiccation.

Related activities

The Working Group recommended that any further work in this area should take account of other environmental data gathering initiatives involving collection of similar data e.g. EUROSEISMIC, contractor. This should avoid duplication of effort and reduce costs.

ANNEX 3

Quantics

OECD / FAO ZONING STEERING GROUP: PESTICIDE RESIDUES

FINAL STATISTICAL REPORT

Ann Gould PhD, CStat

16 AUGUST, 2002

1 AIM OF PROJECT

The original aim of the project was:

> To identify geographic zones within which pesticide residue behaviour would be expected to be comparable and subsequent residue trial data would be considered equivalent.

Report of First Meeting of Zoning Steering Group 12-13 September 2000, Geneva. Page 2

The Zoning Steering Group (ZSG) agreed to concentrate on pre harvest spray applications; for residue trial behaviour to considered equivalent, Good Agricultural Practice (GAP) would have to be comparable.

2 DATA AND METHODS

2.1 Trials data

Initially, residue data from supervised trials held in the JMPR database were selected by a sub group of the ZSG. The measured residues were provided for analysis, along with details of the crop, pesticide, location (country, state, zone), application factors (kg ai/ha, kg ai/hl, water rate /ha, number of sprays), and the PHI.

The ZSG subgroup provided a grouping of equivalent trials according to GAP parameters for the purposes of the analysis. Table 1 shows the numbers of trial results for each crop in the data set.

Subsequently, at the point where the zero day residues were required, some further trial results had become available and these were included in the remaining analyses; it was judged unnecessary to re-do the original analyses.

2.2 Climate data

As the JMPR database does not include any weather or climate data, these had to be collected from other expert sources. Climate data were provided by country experts in Australia, Chile, Germany, New Zealand and UK. For cyfluthin trials in Germany, the actual location and date of harvest were provided, with accurate climate data.

For the remaining countries, climate data were extracted from FAOCLIM 2 [11] based on month of harvest for the crop in question. For trials from the USA, the months of harvest were provided by experts for each crop/state combination. For remaining trials, the months of harvest were taken from the FAO World Harvest Calendar, or estimated by OECD.

[11] FAOCLIM 2 - *World wide agroclimatic database* FAO – agrometry group, Rome 2000.

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For some trials, the location was identified in the JMPR database exactly enough for appropriate climate data to be found. For trials where the 'state' was not specified, average climate data over the country were used, except for Canada.

Data for hours of sunshine were in many cases unavailable.

Table 1 Crops

Group	**Crop**	***Number of trial results***	***Number of pesticides***	**Zones represented**			
				Cold	*Dry*	*TEmperate*	*TRopical*
Forage	alfalfa (fresh)	15	1	✓	✓	✓	
	clover (forage)	22	2	✓		✓	
	maize (forage)	24	1	✓	✓	✓	
	mustard greens	10	1		✓	✓	
	soya, green forage	10	1		✓	✓	
	sugarbeet tops	16	1	✓	✓	✓	
	sweet corn forage	20	1	✓	✓	✓	
	wheat forage	88	1	✓	✓	✓	
	wheat, straw	29	1		✓	✓	
Pome	apples	372	10	✓	✓	✓	
	pears	111	5	✓		✓	
Other	banana (unbagged)	12	1			✓	✓
	blackcurrants	14	1			✓	
	broccoli	11	1		✓	✓	
	brussels sprouts	8	1			✓	
	cabbage	12	1	✓	✓	✓	
	cherries	6	1			✓	
	cherry, sour	8	1			✓	
	grapes	175	5	✓		✓	✓
	kiwifruit	12	1			✓	
	lettuce (head)	44	2	✓		✓	
	lettuce (leaf)	24	1	✓	✓	✓	
	mandarins	25	1			✓	
	peaches	20	2			✓	
	peppers (sweet)	9	1			✓	
	plums	4	1			✓	
	savoy cabbage	12	1			✓	
	strawberries	48	3			✓	
	tomatoes	93	3	✓		✓	
Total		*1254*					

2.3 Statistical methods

A preliminary analysis of the proposed zones was carried out by JH Jowett [12], with the aim of assessing the within – zone variation in residues compared with the between zone variation. Both parametric and non parametric approaches were used, and results were combined across all crop / pesticide combinations to give an overall assessment of the performance of the proposed zoning. All remaining analyses were carried out by Quantics (A Gould) as follows.

1. A preliminary examination of the distribution of the residue data using histograms and the Kolmogorov Smirnov test showed that residues on the log scale were approximately normally distributed. Thus all parametric statistical inference was based on analysis of the residues on the log scale.

2. The variations across zones were examined within crop / pesticide combinations using box plots and analysis of variance.

3. Multiple linear regression was used to examine the relationships between residues and climate factors; scatter plots were used to illustrate these relationships. The contribution of climate factors to the variation in residues was expressed as the percentage of variation explained: R^2.

4. Multiple linear regression was also used to examine the relationships between residues at harvest and residues measured at day zero of the trial. The contribution of zero day residue values to the variation in harvest residues was expressed as the percentage of variation explained , R^2. The additional, subsequent, effect of climate factors was expressed as the percentage of the variation explained by the zero day values plus the climate factors, less the percentage already explained by the zero day values.

5. For the analysis of the contribution of the variation in measured application parameters, the multiple regression methodology described in (4) was used.

3 RESULTS

3.1 Comparison of zones[13]

The temperate (TE) zone was by far the best represented, with 78% of the trial results.

The differences among zones were inconsistent (residues in the Temperate zone being sometimes higher and sometimes lower than those in the Cold (C) zone, for example). However there was a suggestion that residues might be related to climate (e.g. for dinocap, residues were lower in Spain and Italy than in France (mainly Northern) and Germany). A further observation was that residues in Australia seemed consistently higher than elsewhere.

Figures 1a to 1f illustrate the results of the comparisons among zones. Table 2 summarises the comparisons.

Because it is clearly the climate (or more directly the weather) during the period between spraying and harvest) that is important, the conclusion was that classifying a country (or state)

[12] JH Jowett: *Statistical analysis of some data comparing different climate zones in crop residue trials* 18 March 2001

[13] A Gould: *Preliminary statistical report to the sub-team of the ZSG* 16 August 2001

into a climate zone based on the average over the whole year was not reasonable for the purpose of the project's aims.

It was proposed that the next step should be to examine the relationship between residue and climate for the trial location at the time of harvest of the particular crop. The subgroup of the ZSG recommended that pome crops and forage crops should be examined in the first instance.

Table 2 Summary of representative zone comparisons

9..5.1.1.1 Crop / pesticide	***Significant zone comparisons***
a) Captan, apples	C > TE
b) Captan, grapes	C > TE
c) Dinocap, grapes	(all TE) Greece, Italy significantly lower residues than France (mostly N), Germany
d) Fenbuconazole, apples	no significant differences
e) Tebufenozide, apples	TE ~ C; Australia values higher than the rest
f) 2,4-D, wheat forage	C < TE

3.2 Examination of climate factors[14,15]

There were statistically significant relationships between climate factors and residues in some of the crop/pesticide combinations examined. Figures 2a to 2f show a selection of results which illustrate the general conclusions from the analysis. Table 3 summarises the relationships.

[14] A Gould: *Statistical analysis of the relationship between climate factors and pesticide residues* 28 September 2001, revised 16 August 2002

[15] A Gould: *Statistical analysis of the relationship between climate factors and pesticide residues*: *analysis of data from the USA* 5 February 2002 , revised 16 August 2002

Table 3 Summary of representative climate analyses

Crop / pesticide	***Temperature***	***Rainfall***
a) Captan, apples	Not significant	Wetter = lower
b) Cyfluthrin, apples	Warmer = lower	Not significant
c) Fenbuconazole, apples	Not significant	Wetter = lower
d) Tebufenozide, apples	Warmer = higher	Not significant
e) Fenbuconazole, sugarbeet tops	Not significant	Wetter = lower
f) 2,4-D, wheat forage	Warmer = higher	Wetter = higher

For apples, both captan and tebufenozide had higher residues recorded for Australia than elsewhere. The climate at the Australian locations at apple harvest was hotter than the other locations.

The relationships with climate factors were not consistent; the ZSG decided that the case for acquiring better climate data was not convincing. It was agreed that the next step should be to examine the relationship between zero-day residues and harvest residues, in order to explore the variation explained very early, before climate could have had an appreciable effect.

3.3 Examination of zero day factors (plus climate factors)[16]

The variation in the zero day values was high and there was a very consistent and strong relationship between zero day values and harvest residues. Figures 3a to 3d show some examples of these relationships. In crop/pesticide combinations accounting for 43% of the trials, at least 70% of the variation was accounted for by the residue at day zero. In five crop/pesticide combinations the percentage of variation accounted for by zero day residues was less than 30%. There were only two examples where the additional effect of climate was considerable, and in neither case were there enough trials to be convincing.

The conclusions from this analysis were that:

1. A large proportion of the variation in harvest residues is accounted for by the variation in zero day values of the residues, which are assumed to be largely unaffected by climate, and
2. The contribution of climate factors to the variation, after allowing for zero day values, is generally very small.

[16] A Gould *The contribution of zero-day residue values to the variability of residues measured at harvest* 7 March 2002, revised 16 August 2002

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3.4 Examination of application factors (plus climate factors)[17]

Four independent application parameters were available in the database:

1. Concentration of pesticide (kg ai / hl)
2. Water rate (l / ha)
3. Number of sprays
4. PHI

Their specific contributions to the variation in harvest residues were examined.

The variation explained by the application factors ranged from 0% to 70%. In 6 of the 13 groups of trials examined, the proportion was at least 50%, and in only 3 of the groups was it below 10%. The median percentage explained was 40%.

The variation explained by climate factors in addition to application factors was less than 25% in all but three groups of trials, and the highest percentage explained by climate was 45%. The median percentage was 22%.

4 CONCLUSIONS

This study has shown that the residues are highly dependent on the variations that arise very early on in the trial, the effects of which can be measured at day zero. The additional effect of climate factors is relatively small.

The remaining variation (approximately 40% on average) is explained by a combination of other factors. These are likely to include the application parameters unavailable for this analysis (treatment interval, formulation and application technique), whose effect was captured by the analysis of zero day data, as well as weather, measurement error and variations in local practices.

Geographic zoning alone will therefore not achieve the stated aims of

- Comparable pesticide trial residues
- Equivalence of trial data.

[17] A Gould *The relationship between application parameters and residues measured at harvest: analysis of selected crop / pesticide combinations* 21 June 2002

Figure 1 Comparisons of zones

The plots represent the data for the zone or country. In cases where there all, or nearly all, the data come from a single zone, data from the individual countries are shown.

Each rectangle is bounded by the upper and lower quartiles; the median is marked. Where there are more than 2 data points, the maximum and minimum are shown extended from the rectangles. Outliers are marked separately.

Blocks of different colours relate to different PHIs. Hence comparisons should be made by examining the differences between blocks of the same colour

Figure 1a: Captan, apples
(Canada Cold; others Temperate)

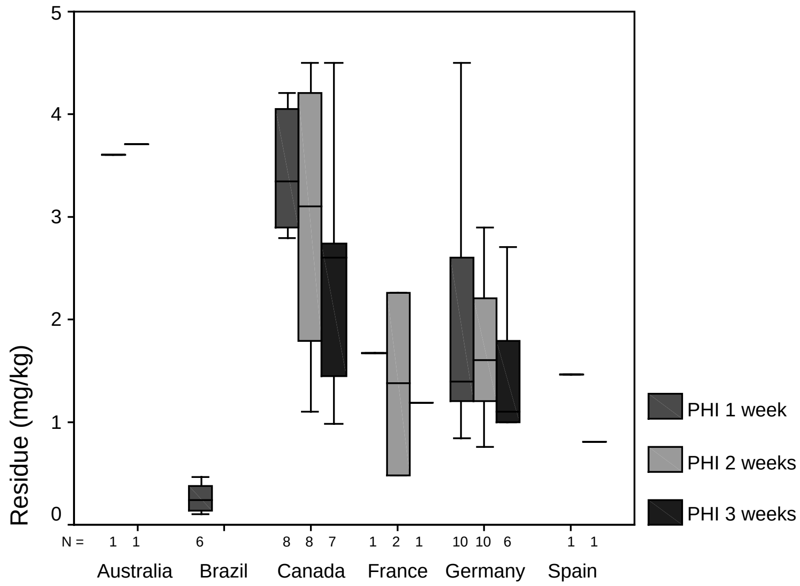

Figure 1b: Captan, grapes

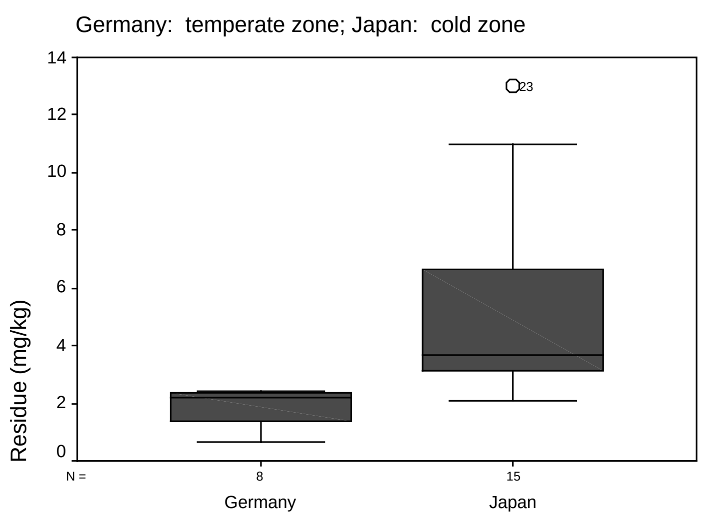

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Figure 1c: Dinocap, grapes

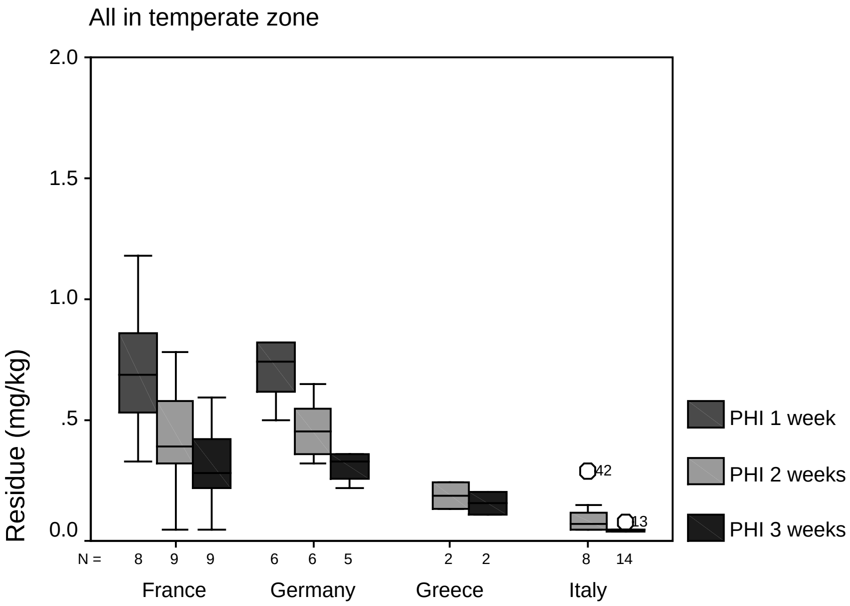
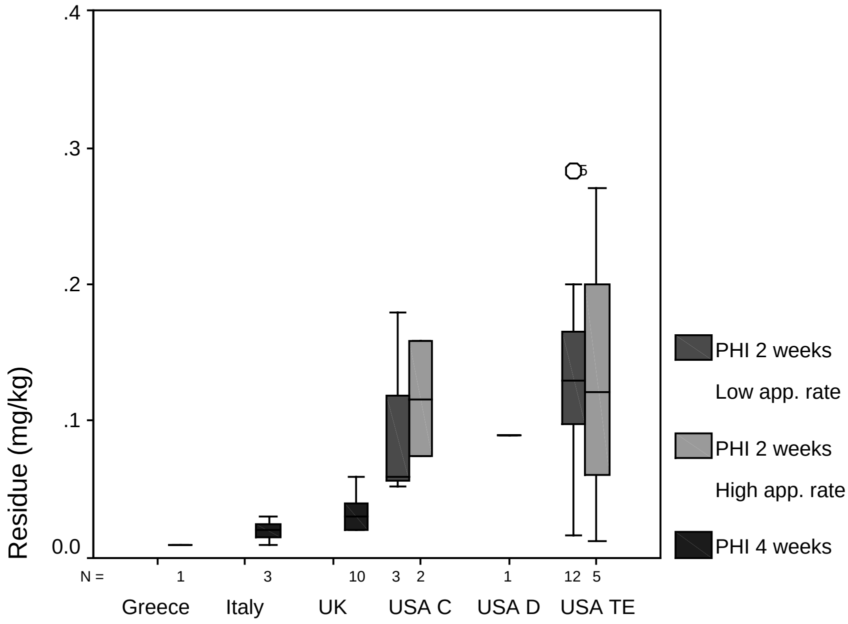


Figure 1d: Fenbuconazole, apples


.4
.3
.2
.1
0.0
Residue (mg/kg)
N =
1
3
10
3
2
1
12
5
Greece
Italy
UK
USA C
USA D
USA TE
PHI 2 weeks
Low app. rate
PHI 2 weeks
High app. rate
PHI 4 weeks

Minimum data requirements for establishing Maximum Residue Limits (MRLs) and import tolerances (Doc. 2734/SANCO/99)

Figure 1e: Tebufenozide, apples

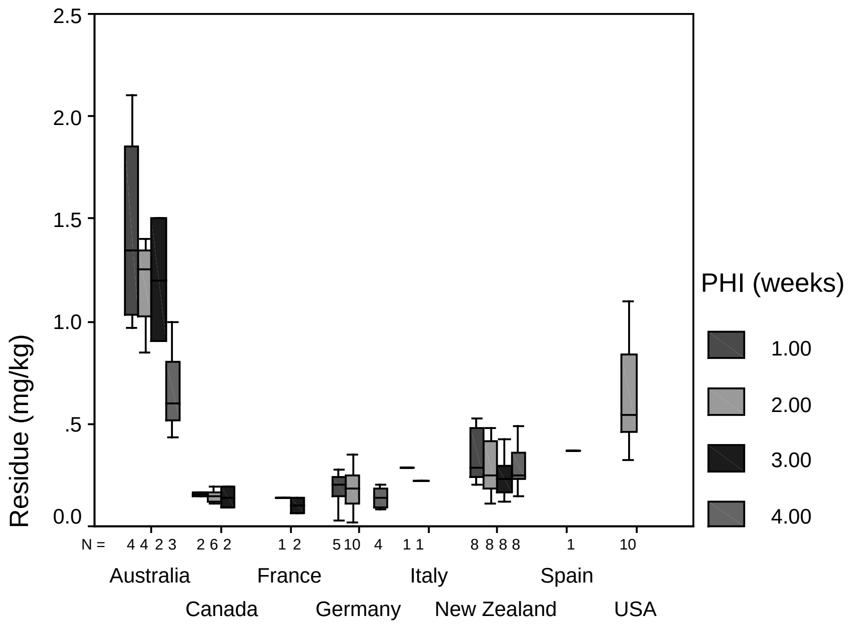


Figure 1f: 2,4-D, wheat forage

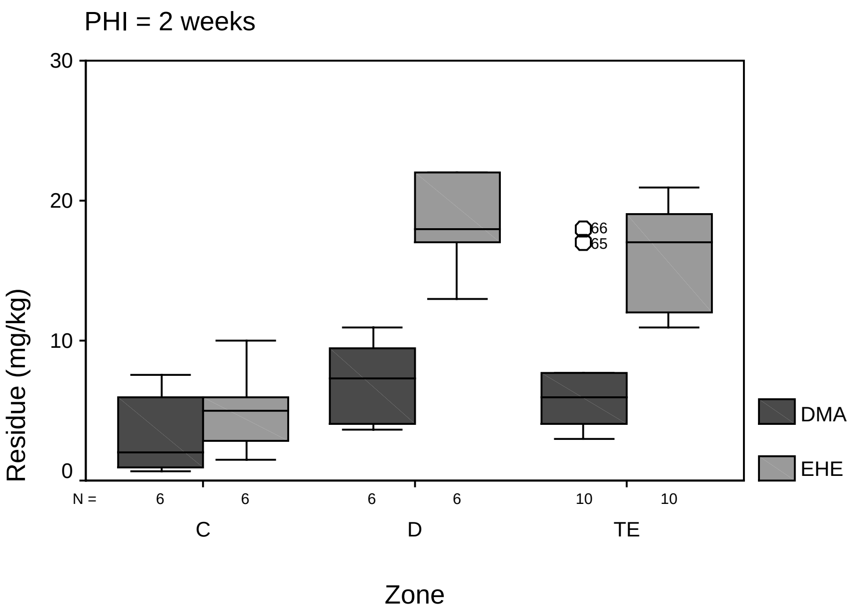


Figure 2 Analysis of climate

The plots represent the data separated by PHI. The residues are plotted on the log scale.
Only climate variables which showed a statistically significant ($p < 0.05$) relationship with residue are included.

Figure 2a: Captan, apples

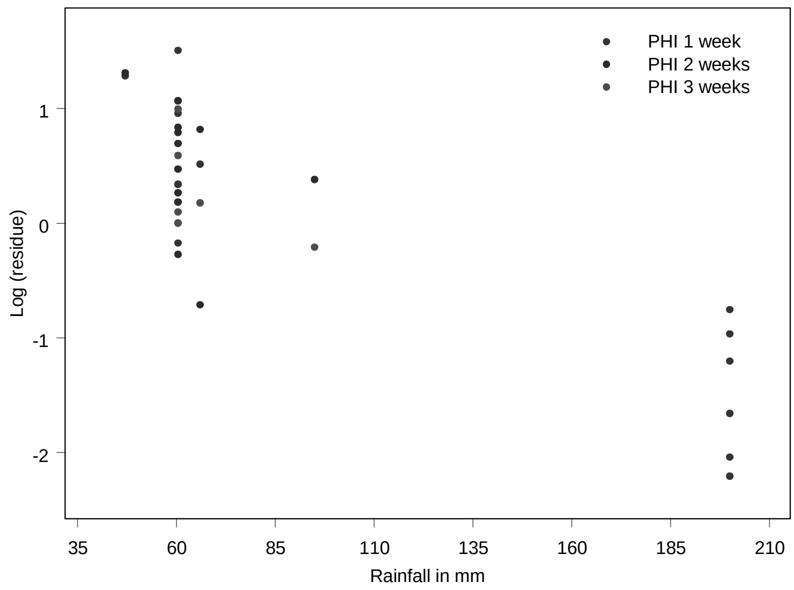
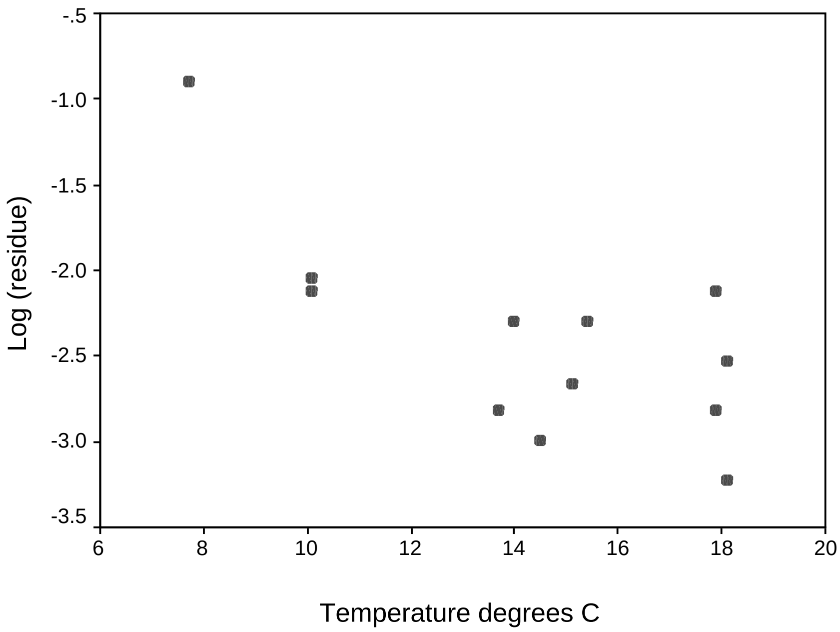


Figure 2b: Cyfluthrin, apples



Minimum data requirements for establishing Maximum Residue Limits (MRLs) and import tolerances (Doc. 2734/SANCO/99)

Figure 2c: Fenbuconazole, apples

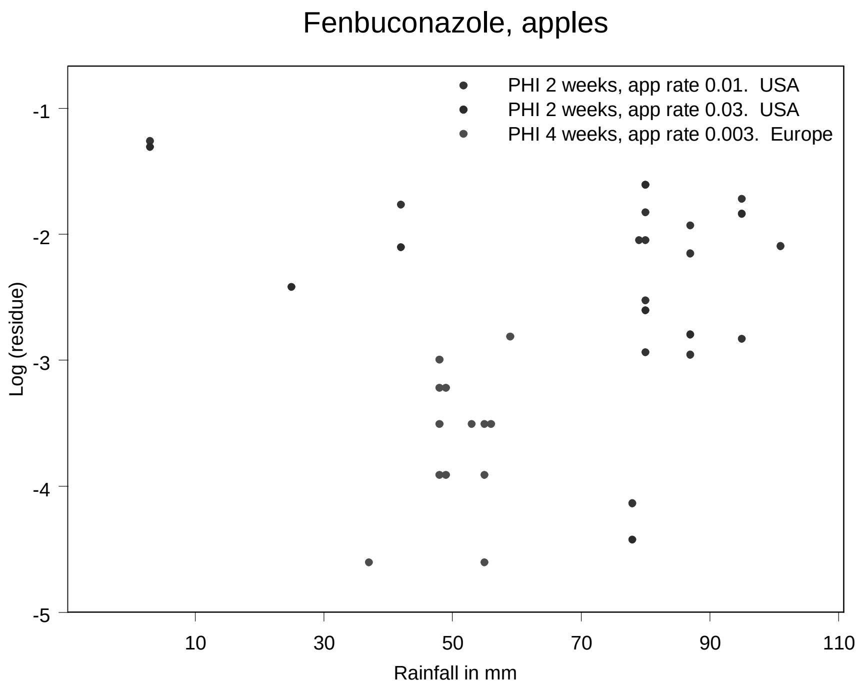


Figure 2d: Tebufenozide, apples

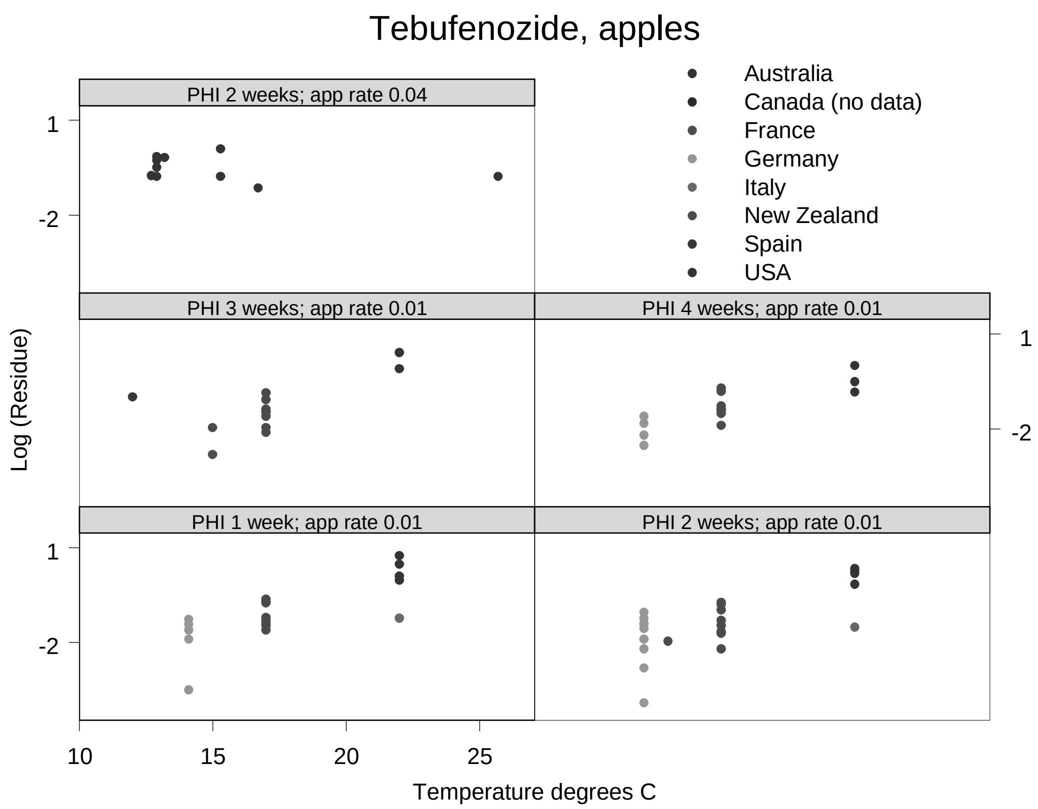


Figure 2e: Fenbuconazole, sugarbeet tops

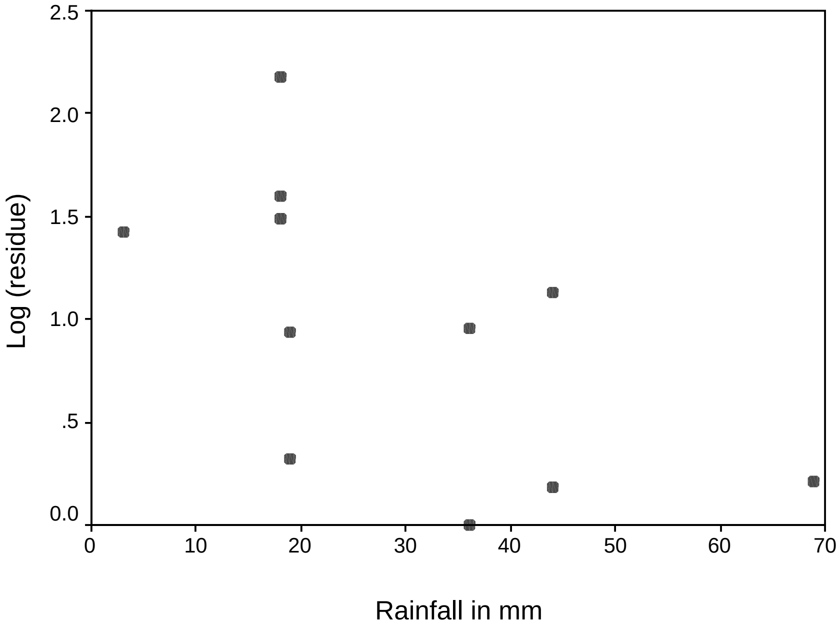
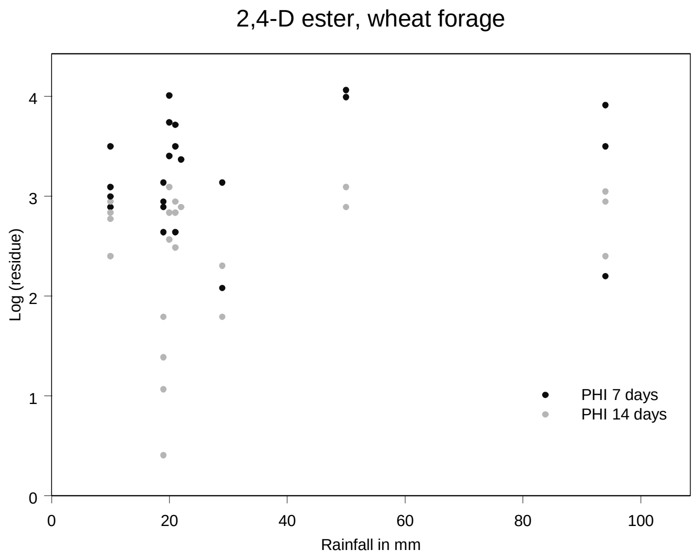
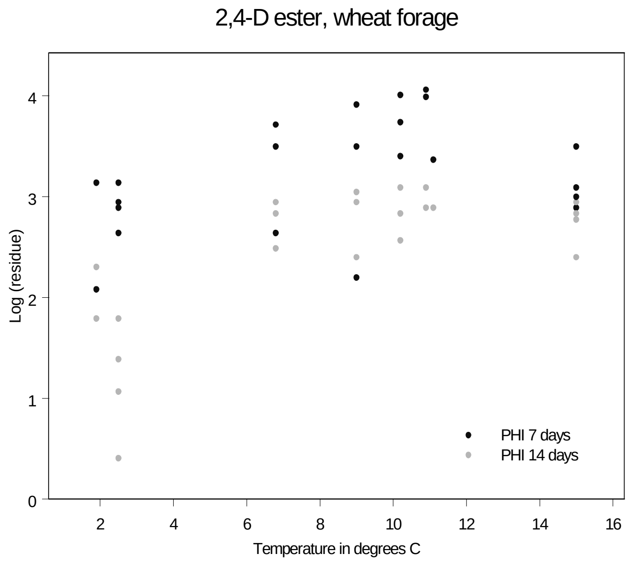


Figure 2f: 2,4-D ester, wheat forage





Minimum data requirements for establishing Maximum Residue Limits (MRLs) and import tolerances (Doc. 2734/SANCO/99)

Figure 3 Analysis of zero day residues

The plots represent the data separated by PHI. The zero day and harvest residues are plotted on the log scale.

Figure 3a: Captan, apples

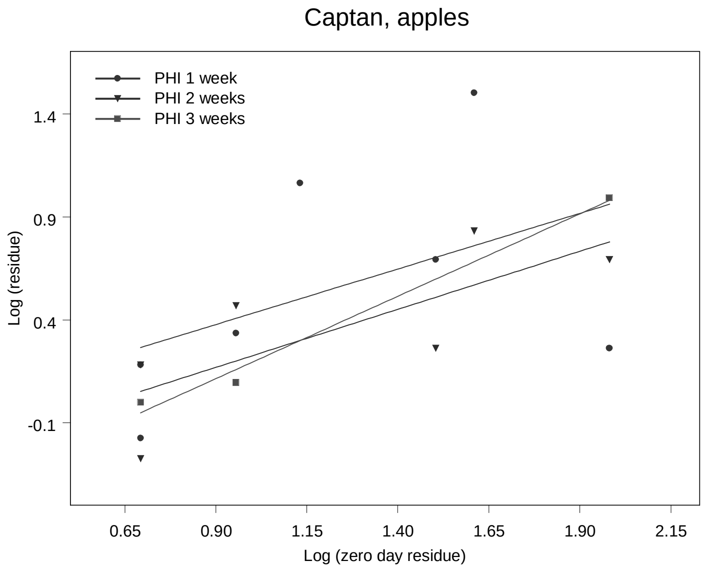


Figure 3b: Dinocap, grapes

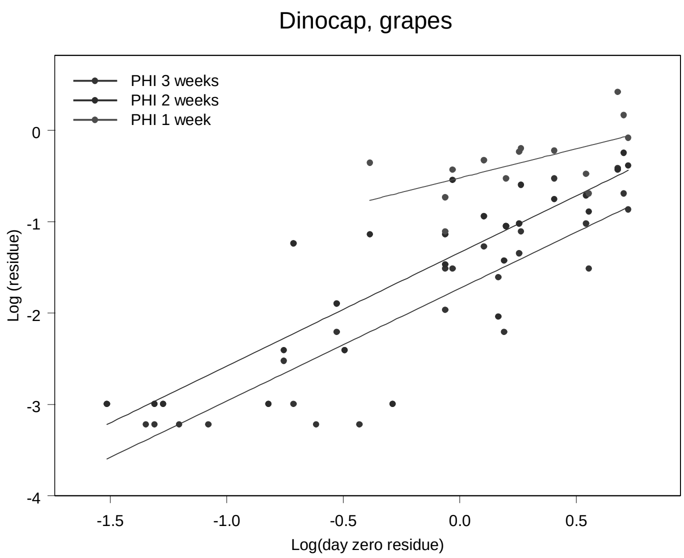


Figure 3c: Fenbuconazole, apples

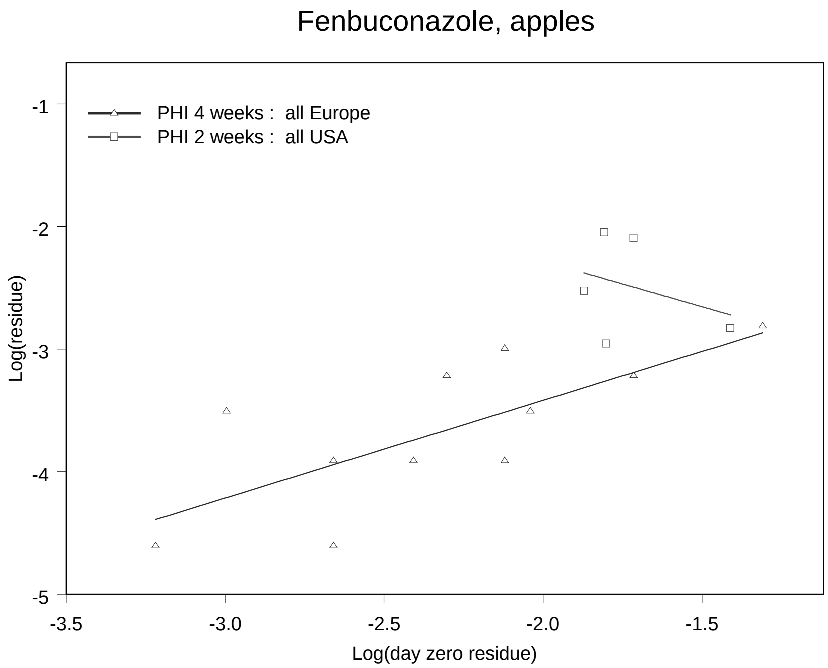


Figure 3d: Tebufenozide, apples