意見交換会で提示した「たたき台」

○作物残留性試験テストガイドラインの改正

・減衰試験と１点分析試験に関する試験方法を規定する方向で検討。
（現在は減衰試験のみ）

・TGの国際調和の観点から所要の改正。

○試験例数の検討

現行：2例以上。
改正案 原則として8例。
・作物の生産量、リスクの程度などに応じて例数を要求する。
具体的には、
主要作物は8例（うち減衰試験は2例）、
準主要作物は4例（同2例）、
マイナー作物は2例（同2例）。

○作物残留性試験の検査基準

・適正な使用方法（ＧＡＰ）に基づいた試験成績か（試験条件は適切か）についても厳密な検査を実施。

・標準的な使用方法が幾つかある場合は、その中で残留量が一番多くなると思われる使用方法で実施。

○試験成績の読み替え等（1）

・FAOﾏﾆｭｱﾙ、米国EPAｶﾞｲﾄﾞﾗｲﾝ、EUｶﾞｲﾄﾞﾗｲﾝを参考に検討。

検討項目
①製剤、②試験条件、③作物群、④主要作物
⑤マイナー作物、⑥例数の増減、⑦特殊要因
⑧海外データ、⑨既登録剤の例数適用

○試験成績の読み替え等（2）

①製剤

水で希釈して散布する製剤（ＭＣ剤は除く）において、使用時期が収穫７日以前までの場合、代替を認める（EUｶﾞｲﾄﾞﾗｲﾝ）。

○試験成績の読み替え等（3）

②試験条件
・散布量又は散布濃度：申請における使用量又は使用濃度の±３０％以内（FAOﾏﾆｭｱﾙ）。
・使用回数　申請における散布回数の±２５％以内（EUｶﾞｲﾄﾞﾗｲﾝ）。
・収穫前日数　申請における収穫前日数の±２５％以内（EUｶﾞｲﾄﾞﾗｲﾝ）。

○試験成績の読み替え等 (4)

③作物群
・作物の分類学上の類縁性、可食部の形態、使用方法、残留値において同等と確認された作物間においては、合わせて評価することが可能。

例　りんごとなしに申請する場合各４例ずつの試験成績でも可能となる場合がある。

○試験成績の読み替え等 (5)

④主要作物等
・主要作物（生産量概ね３万トン以上）とそれ以外の作物（マイナー作物）は現行どおり。

ただし、主要作物のうち栽培地域が限定されている作物（てんさい、さとうきび等）は準主要作物とすることを検討。

○試験成績の読み替え等 (6)

⑤マイナー作物
・適用農作物ごとに２例以上で、公的試験機関での分析も可。
・生産量が特に少ない作物については、より高く残留する作物で代替可能は継続。

○試験成績の読み替え等 (7)

⑥例数の増減
・休眠期散布、水稲用除草剤のように収穫時に明らかに残留が認められない場合減衰試験は省略できる。
・減衰試験で２例とも検出限界以下の場合は１点分析試験は省略できる。

○試験成績の読み替え等 (8)

⑦特殊要因
・農産物のくん蒸（倉庫くん蒸）等の比較的均一な試験結果が得られると見込まれる場合や、大規模な面積を必要とする試験（空散）については、試験例数の減少は可能。

○試験成績の読み替え等 (9)

⑧海外データの扱い
・ＯＥＣＤ、諸外国での検討状況を踏まえて今後対応を検討。

○試験成績の読み替え等 (10)

⑨既登録剤の例数適用

・科学的に評価した経口摂取による健康リスクの程度などに応じた優先度をつけて、計画的に行う仕組みを検討。

※これらの代替方針の決定に当たっては、厚生労働省との調整が必要。

→　今後実施

Submission and evaluation of pesticide residues data for the estimation of maximum residue levels in food and feed

(抜粋)

Food and Agriculture Organization of the United Nations

Rome, 2002
First edition

the trial conditions and the established GAP. The procedure for estimating and recommending Codex MRLs may be somewhat different from that applicable at national level as Codex MRLs cover residues derived from authorized uses worldwide and therefore reflect a variety of agricultural practices and environmental conditions. See also Chapter 6, "Definition of independent supervised residue trials and selection of one residue value from each trial".

An awareness of the expected variability of residues is necessary. If the data truly reflect the range of conditions, application methods, seasons and cultural practices likely to be encountered commercially, then considerable variation in the resulting residue levels is expected. Where copious data are available, consideration of the spread and variability of the residues helps to avoid misleading interpretations of small differences in estimates of the maximum level. Where only limited data are available, the interpretation of fine differences is not valid. It is not a criticism to say that the data are widely spread and variable. If results have been obtained at a number of places over some years they are likely to be a better approximation to commercial practice and will be widely spread. In addition to the variability of residues within a confined area which can be considered uniform regarding climate, agricultural practices, pest situation and use recommendations, there may be an even greater variation of residues among areas of widely differing conditions (e.g. countries in temperate, Mediterranean and tropical zones). The differences in use conditions can be so large that they result in different residue populations (see Chapter 6 section "Combining of populations of data for the calculation of STMRs").

Frequently the situation is complex even when copious data and information are available. There are alternative interpretations, and judgement is required to arrive at an estimate that is realistic, practical and consistent.

Although supervised residue trials are conducted according to the GAP prevailing at the time, GAP is often subsequently modified by changing the rate of application, type of formulation, method of application, number of applications and PHI. Judgement is then required in order to determine whether the trial conditions are still close enough to GAP to be relevant. (See also Chapter 6 section "Comparability of supervised trial conditions to GAP.")

Rate of application

The nominal rate of application in a trial would normally be considered still consistent with GAP when it is within approximately ± 30% of the GAP rate, which includes the probable variation in commercial practice. When little or no residue is present, data from higher application rates may be important.

Formulations

In many situations different formulations would cause no more variation than other factors, and data derived with different formulations would be considered comparable. Experience from trials demonstrates that EC, WP and SC formulations (see Appendix III) lead to similar residues. On the other hand, controlled-release formulations would be expected to lead to more persistent residues and would not be comparable to others.

Application method and number

The method of application can be quite influential on residue levels. For example, directed application is not comparable to cover spray, and aerial application may not be comparable to ground application.

For a non-persistent pesticide the number of applications is unlikely to influence residue levels. For a persistent pesticide the number of applications would be expected to influence residue levels. The nature of the crop should also be considered. Where the interval between the flower and the harvest of the resulting fruit is only a few days, e.g. summer squash, residues of a non-systemic pesticide applied before flowering would be expected to be low and the number of applications should have little influence on the residue level.

Pre-harvest interval

The pre-harvest interval usually, but not always, influences residue levels. (See Chapter 6 section "Comparability of supervised trial conditions to GAP").

Non-detectable residues

Some pesticide uses, such as seed treatments and pre-emergence herbicide treatments, usually lead to non-detectable residues in the final harvested crop; but when many results are provided residues may be detected in occasional samples. While residues resulting from use according to GAP are most likely to be undetectable, the occasional detectable residues should not be ignored when a maximum residue level is estimated. Phorate on potatoes and residues arising from the pre-planting application of glyphosate are two examples.

Climate

Greater certainty that the climatic conditions are properly reflected in the supervised trials is afforded when the trials are carried out in a country with established GAP. Trials conducted in other countries with similar climatic conditions may be acceptable on a case-by-case basis. An assessment of those conditions is difficult, and a critical evaluation is needed as only some difference in conditions, such as temperature or intensity of sunlight, may be of great importance for the persistence of many pesticides and consequently for the residue level.

Crop description

The trials should be carried out with the same crops as those specified in the national GAPs. The proper description of the crops used in the supervised trials is important for deciding if crops referred to in GAP information are in accordance with those for which trials have been carried out. Codex Classifications should be used for describing harvested commodities. A crop description such as "beans" is difficult to interpret because of the wide variety of beans grown. A more specific description is needed. Foliar application to head lettuce and leaf lettuce may produce different residue levels, so it may not be possible to use trials for a crop described as "lettuce".

Crop groups such as leafy vegetables, cole crops and grain legumes on national labels may not have precisely the same meaning as the Codex commodity groups. It is necessary to check the crops included in a national label crop grouping.

Commodity of trade and edible portion

Codex establishes MRLs on commodities as they move in trade to enable the control of compliance with and enforcement of GAP. Consequently, the maximum residue levels are estimated on a whole commodity basis (see Appendix VI) as far as practical.

In addition to residues in or on the whole commodity, the JMPR is also interested in residues in the edible part of the crop. Residues of systemic pesticides may be expected to be present in all parts of the crop, while residues of non-systemic pesticides are not always present or may

Appendix III

CIPAC CODES FOR PESTICIDE FORMULATIONS

AB	Grain bait
AE	Aerosol dispenser
AL	Other liquids to be applied undiluted
AP	Other powders to be applied undiluted**
BB	Block bait
BR	Briquette
CB	Bait concentrate
CF	Capsule Suspension for Seed Treatment**
CG	Encapsulated granule
CL	Contact liquid or gel**
CP	Contact powder**
CS	Capsule suspension
DC	Dispersible concentrate
DP	Dustable powder
DS	Powder for dry seed treatment
DT	Tablet for direct application**
EC	Emulsifiable concentrate
ED	Electrochargeable liquid
EG	Emulsifiable Granule**
EO	Emulsion, water in oil
EP	Emulsifiable powder**
ES	Emulsion for seed treatment
EW	Emulsion, oil in water
FD	Smoke tin
FG	Fine granule
FK	Smoke candle
FP	Smoke cartridge
FR	Smoke rodlet
FS	Flowable concentrate for seed treatment
FT	Smoke tablet
FU	Smoke generator
FW	Smoke pellet
GA	Gas
GB	Granular bait
GE	Gas generating product
GF	Gel for Seed Treatment**
GG	Macrogranule
GL	Emulsifiable gel
GP	Flo-dust
GR	Granule
GS	Grease
GW	Water soluble gel
HN	Hot fogging concentrate
KK	Combi-pack solid/liquid*
KL	Combi-pack liquid/liquid*
KN	Cold fogging concentrate
KP	Combi-pack solid/solid*
LA	Lacquer
LS	Solution for seed treatment
LV	Liquid vapouriser**
MC	Mosquito coil**
ME	Micro-emulsion**
MG	Microgranule
MV	Vapourizing mats**
OF	Oil miscible flowable concentrate (oil miscible suspension)
OL	Oil miscible liquid
OP	Oil dispersible powder
PA	Paste
PB	Plate bait
PC	Gel concentrate or paste concentrate
PO	Pour-on
PR	Plant rodlet
PS	Seed coated with a pesticide
RB	Bait (ready to use)
SA	Spot-on
SB	Scrap bait
SC	Suspension concentrate (= flowable concentrate)
SD	Suspension concentrate for direct application**
SE	Suspo-emulsion
SG	Water soluble granule
SL	Soluble concentrate
SO	Spreading oil
SP	Water soluble powder
SS	Water soluble powder for seed treatment
ST	Water soluble tablet**
SU	Ultra-low volume (ULV) suspension
TB	Tablet
TC	Technical material
TK	Technical concentrate
TP	Tracking powder***
UL	Ultra-low volume (ULV) liquid
VP	Vapour releasing product
WG	Water dispersible granule
WP	Wettable powder
WS	Water dispersible powder for slurry seed treatment
WT	Water dispersible tablet**
XX	Others

* Special two-letter codes for twin-packs

** Manual on Development and Use of FAO and WHO Specifications for Pesticides, FAO/WHO Joint Meeting on Pesticide Specifications (JMPS), Rome, 2002

*** Discontinued term – refer to CP (Contact Powder)

CHAPTER 6

ESTIMATION OF RESIDUE LEVELS FOR CALCULATION OF DIETARY INTAKE OF PESTICIDE RESIDUES

CONTENTS

INTRODUCTION

The JMPR evaluates the possible risks to consumers from pesticide residues in foods by assessing available residue data and then using this information to estimate the short-term and long-term dietary intakes of residues. This chapter deals with the residue data assessment and the following chapter will deal with estimating dietary intakes. This chapter should be read in the context of the "Estimation of maximum residue levels" section in Chapter 5. The same principles apply to selection of supervised trials data for maximum residue levels, supervised trials median residue levels and highest residue levels.

The following guidelines are provided for selecting data that support supervised trials median residue (STMR) levels. The same data are used for estimating the HR (highest residue in edible portion of composite sample).

It is not necessary to estimate HR values for compounds where the JMPR has concluded that an acute RfD is unnecessary.

COMPARABILITY OF SUPERVISED TRIAL CONDITIONS TO GAP

Residues data are evaluated against the GAP in the country of the trials or a neighbouring country with similar climate and cultural practices.

In identifying the STMR and HR values, the trials values selected should be comparable with the maximum registered use (i.e. maximum application rate, maximum number of treatments, minimum pre-harvest interval (PHI)) on which the MRL is based.

The application rates in the trials should generally deviate no more than ±30% of the maximum application rate. Deviations from this should be explained in the appraisal.

The latitude of acceptable intervals around the PHI depends on the rate of decline of residues of the compound under evaluation. The allowable latitude should relate to a ±30% change in residue level and may be estimated from residue decline studies. If the decline is assumed to be first order it may be shown that the acceptable intervals are PHI + 0.51 × $t_{1/2}$ (half-life) and PHI - 0.38 × $t_{1/2}$. When the PHI is more than a few days, the estimation of half-life should exclude the data from day 0 (day of application) because the initial decline of residues is generally much faster than the later decline.

Consideration of whether the number of treatments reported in trials is comparable to the registered maximum number of treatments will depend on the persistence of the compound and the interval between applications. Nevertheless, when a large number of treatments are made in the trials (more than 5 or 6), the residue level should be considered very little influenced by further treatments unless the compound is persistent or the treatments are made with unusually short intervals. Residue data are sometimes provided from just prior to the final treatment as well as after it, which is direct evidence of residue contributions from previous applications to the final residue. Also, treatments from more than about 3 half-lives (obtained from residue decline trials) prior to the final treatment should not make a significant contribution to the final residue.

In establishing comparability of residue trials data in which more than one parameter (i.e. application rate, number of treatments or PHI) deviate from the maximum registered use, consideration should be given to the combination effect on the residue value which may lead to an underestimation or overestimation of the STMR. For example, a trial result should not normally be selected for the estimation of the STMR if both the application rate is lower (perhaps 0.75 kg/ha in the trial; 1 kg ai/ha GAP) than the maximum rate registered and the PHI is longer (perhaps 18 days in the trial, 14 days GAP) than the minimum registered PHI, since these parameters would combine to underestimate the residue. When results are selected for the estimation of STMRs and HR values, despite combination effects, the reasons should be explained in the appraisal.

If a residue value is lower than another residue value from the same trial which is within GAP, then the higher residue value should be selected in identifying the STMR and HR values. For example, if the GAP specified a minimum PHI of 21 days and the residue levels in a trial reflecting GAP were 0.7, 0.6 and 0.9 mg/kg at 21, 28 and 35 days respectively, then the residue value of 0.9 mg/kg would be selected.

Interpretation tables for supervised trials data

When residue data are available from several countries the results may be tabulated to show the comparison of trial conditions with GAP to assist with interpretation. In the example in Table XI.1 (Appendix XI) residue data on tomatoes from 6 countries are compared with GAP. Note that some countries specify application rate (kg ai/ha) while others specify spray concentration (kg ai/hl) in their GAP. Italian trials may be evaluated against the conditions of Spanish GAP.

The interpretation table provides the set of residues that match maximum GAP from the various countries. The next step is to decide if the residues constitute a single population or different populations.

EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate E – Safety of the food chain
E3 - Chemicals, Contaminants, Pesticides

SANCO 7525/VI/95 - rev.8
1 February 2008

GUIDANCE DOCUMENT
Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs

(抜粋)

Appendix D

Revision history

When	What
Rev. 8 of 1.02.2008	Extrapolation tables (tables 3 to 6)

If, however, in situations where non-relevant residues can be expected with a high degree of probability, then as an exception to the basic rules it may be possible for all trials to be carried out within one growing season. However caution must be used in generating only one seasons data for outdoor crops particularly if relevant residues occur in related crops since differences in residue profiles can occur between seasons. In any case, if contrary to expectations relevant detectable residues should be found, results must be obtained in a second growing season.

When the residues of an active substance are foreseen to be under the LOD and at least2 residue trials confirm this then no further trials are normally necessary. In the case of relatively unstable residues, this interval should be checked.

3 **Changes in the trial parameters**

The following guidelines presuppose that in each case the original situation is sufficiently well documented

If, when changes are made to the trial parameters, the obtaining of further residue results is considered not to be necessary, then thorough justification for this must be submitted. A justification could be, for instance, that existing trial results show that relevant residues are unlikely to occur.

3.1 Changes in formulation

Ideally, and as a general principle, residue trials should be carried out using the formulation to which the authorization applies, or for which the application has been made. If there is a significant change in formulation, therefore, new residue trials are, in principle, necessary It has proved sufficient to carry out four comparative trials on each crop selected. Data are not needed for all crops, but should be generated for approximately 3 major crop groups which may be treated - data for a single representative crop for each group should be generated, e.g. a leafy crop, a root crop, a soft fruit, a tree fruit, a seed crop etc. The trials should preferably be carried out on crops that would be expected to show high levels of residues. The timing of treatment is also important in this situation. Where treatments are made to the soil or to the seed the formulation is not important and where treatment is to a very young crop the effect of co-formulants is likely to be minimal. In cases of minor changes in formulation, which would not be expected to have any influence on efficacy and residue behaviour, additional trials may be waived.

Nothwithstanding the above, experience shows that EC, WP, WG, and SC formulations usually produce comparable residues (especially if the last application is more than seven days prior to harvest) and well-justified and documented departures from the above could be considered.

Changes in formulations on the basis of a change in the content of formulants need to be evaluated on a case by case basis. Special consideration should be given to changes in the content of adjuvants like wetting agents which lead to a better penetration of the active substance into the plant particularly where the PHI is less than 7 days

3.2 Changes in application rate

In order to encompass the least favourable trial conditions, the trials must as a matter of principle be carried out using the highest rate (e.g. kg/ha) of application. In the case of active substances which act via the soil (e.g., pre-emergence herbicides), the application rate appropriate for the particular type of soil should be used. In the case of increases or reductions of up to 25% in the rate of application of the active substance under otherwise identical conditions, experience suggests that the residue results can be assumed to be comparable. However, if residue trials with a higher application rate than the indended uses indicate that no detectable residues are to be expected, the number of trials can be reduced

3.3 Changes in number of applications

In order to encompass the least favourable trial conditions, the trials must as a matter of principle be carried out using the maximum number of application provided for in the registered GAP. It is generally the last application prior to harvest that is crucial to residue behaviour in the harvested crop The number of applications prior to

flowering, on the other hand, is generally of lesser importance. In the case of relatively persistent residues in plants, the results can be assumed to be comparable if the number of applications are increased or reduced by not more than 25 % (e g , 4 ± 1 or 8 ± 2 applications). In the case of relatively non-persistent residues in plants, the results can also be assumed to be comparable if the number of applications are increased or reduced by more than 25 %. Persistence should be defined on a case-by-case basis on the basis of residue-decline studies.

3 4 Changes in application method

Different application methods, such as spraying, drenching, dusting, misting and granule spreading, will as a rule not produce comparable residue results, and must therefore be documented separately. The results from normal spraying and low-volume spraying may be comparable for a comparable rate of application for the active substance per ha. However where both, low-volume and normal spray applications, are the usual methods, both methods of application ought to be documented according to standard application practice in the basic data set submitted.

In tall crops one should take note of the fact that the application rate may depend on the surface area of the leaves For this reason in former times the amount applied was given in kg ai per hl. In such cases residue trials should be carefully planned. In certain circumstances it may be necessary to explain that a residue trial result fall within a given GAP.

3.5 Changes in timing of application; changes in pre-harvest interval

The stage of development of the crop at the time of application and the time intervals between applications, especially between the last two applications, are important factors influencing the level of residues. Because the least favourable residue situation is the determining factor when establishing maximum residue limits (MRLs), then applications at later stages of development will encompass applications made at earlier stages of development, just as applications at shorter intervals before harvesting will encompass applications at longer intervals before harvesting (but note Section 2.1).

In the case of changes in pre-harvest interval of not more than 25 %, experience has shown that the residue results can be assumed to be comparable.

3.6 Area of application (outdoors, under glass, in store, protective covering)

The results of outdoor trials are not normally comparable with the results of trials carried out under other conditions of application The climatic conditions, above all, under glass, under plastic, or in climate-controlled chambers or in stores, but also the other parameters that differ from those in outdoor trials, generally create markedly different residue situation than that found in outdoor testing. Therefore, separate studies are necessary for each area of application unless a 'worst case' can be clearly identified.

3.7 Simultaneous changes in several trial parameters

The 25 % rule (mentioned in Sections 3.2, 3.3 and 3.5 for purposes of comparability) only applies where just one of the parameters is changed. Where more than one parameter is changed at the same time, the effects may be cumulative, or may cancel each other out.

Thus, for example, increasing the application rate by 20 % while at the same time reducing the number of applications from 4 to 3 will probably result in a comparable residue behaviour. If, however, the number of applications were instead increased from 4 to 5, it would be likely that the residue behaviour would no longer be comparable. The stability of the active substance and the timing of applications and intervals between applications naturally also play a crucial part in this.

If more than two trial parameters are changed at the same time, experience suggests that it is then no longer possible to assume a comparable residue behaviour with any sufficient degree of certainty

4 Comparable climatic zones/weather influences