ASSESSING PESTICIDE RISKS TO NON-TARGET TERRESTRIAL PLANTS

SECTION SIX: OPTIONS FOR TESTING AND RISK ASSESSMENT

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Contents of Section 6

6.1 INTRODUCTION

The aim of this section is to review key elements of existing proposals for testing and risk assessment, and consider alternatives. The approach taken was to start by summarising the existing proposals in a series of tables, which were used as the basis for one part of the round-table discussion between the project team and PSD on 5 August 1998. This section draws on the implications of other sections of the report, plus the issues discussed at the meeting, to reach conclusions on approaches to testing and risk assessment. It also includes revised versions of the summary tables (the more lengthy ones are in Appendices 6.1 - 6.3).

Ultimately, risk assessment is a means of deciding between the options available to regulators and registrants. Therefore two issues are of fundamental importance in considering alternative approaches for risk assessment:

- what are we trying to protect?
- what options are available for risk management?

These two issues are dealt with in detail in sections 1-4 and 7 respectively and their implications are considered below, primarily in the sections on what to protect and on exposure scenarios.

The potential to use data generated for efficacy purposes is also important, because of the need to avoid unnecessary testing, so this is also discussed separately below.

We also need to take account of the regulatory context. For the UK, this is determined by EU Directive 91/414 which states that risks of pesticides to the environment should be assessed. It also defines the environment as including wild species of flora and fauna and any relationship between them and with other living organisms. However, virtually no further guidance is given on how to assess risks to non-target plants: the Annexes to the Directive simply state that a summary of available data should be submitted together with a statement of its relevance to potential impacts.

Future approaches to risk assessment for non-target plants are likely to be influenced strongly by work which is underway in two international fora: small working groups under the auspices of the Organisation for Economic Cooperation and Development (OECD) and the European and Mediterranean Plant Protection Organisation (EPPO).

Independently, schemes for assessing risks to non-target plants have been developed by the US Environmental Protection Agency (USEPA) and the Canadian Wildlife Service (CWS). Finally, the Global Crop Protection Federation (GCPF), an industry association, has developed proposals which it submitted to the OECD Working Group and which are currently being revised by Joe Dulka of Dupont (pers. comm.). All these approaches are likely to influence the development of future practices to some extent.

The USEPA and CWS proposals are in final form, but the other 3 are at an earlier stage of development (apparently the Canadian authority PMRA is using the USEPA approach rather than CWS one, C Boutin pers. comm.). The latest available versions of these 5 proposals have been reviewed for this project and are summarised in the tables below. They are identified in the remainder of this Section by their initials, as defined above (OECD, GCPF, EPPO, USEPA, CWS).

There are also some new initiatives which are relevant. First, the USEPA has commissioned the Risk Science Institute (RSI) in Washington DC to coordinate a series of reviews on the assessment risks pesticides, especially low-dose high-potency pesticides, to non-target plants. A steering committee identified key scientific issues and commissioned relevant experts to produce 5 detailed review papers. Details of the issues to be addressed by the 5 papers are given in Appendix 6.4 but the working titles for the papers are as follows:

1. Overview of New Compounds: Low-Dose, High Toxicity Herbicides
2. Exposure to Low-Dose, High Toxicity Herbicides
3. Unintended or Nontarget Aquatic Plant Effects of Herbicides
4. Unintended or Nontarget Terrestrial Plant Effects of Herbicides
5. Problems Associated with Risk Characterization of the Impacts of Herbicides on Nontarget Plants

These papers will form the basis for a workshop involving a full range of 'stakeholders' (government, industry, academia, public interest groups). The final output of the project will be a report of the workshop plus revised versions of the 5 papers, which may then influence future USEPA policy in this area.

Second, there are a number of initiatives exploring the use of probabilistic methods in pesticide risk assessment. The most substantial is the USEPA ECOFRAM project, with two sub-groups working respectively on risks to aquatic organisms and terrestrial organisms (the latter focussing mostly on birds). The EPPO panel on risks to terrestrial vertebrates has also briefly considered these methods in a recent meeting. Though the current ideas from these groups are very tentative (and may or may not appear as firm proposals) they have some relevance here and are discussed briefly in the section on 'alternative approaches'.

6.2 WHAT ARE WE TRYING TO PROTECT?

Sections 1-4 show that a number of plant species can be identified as important to man (in supporting beneficial invertebrates) and to wildlife (in providing food or habitat structure). Priority might be given to protecting those species which contribute most to these benefits, if they could be reliably defined. Work done for this project suggests that it might be possible to identify, for example, ten species as being particularly important to birds, mammals and invertebrates. If it were necessary only to protect such a small number of 'key' species this would have major implications for risk assessment, as it would be reasonably practical to conduct toxicity tests with all the species of concern. However, (a) it is not likely that the contribution of all other species could be disregarded, and (b) as the key species would vary from country to country, an impractical number of species might require testing overall. Furthermore, plant biodiversity can be considered important in its own right, as was agreed at the round-table meeting for this project. This would imply a need to protect a much wider range of species, though not necessarily every species nor every individual of a species.

Priority is often given to protecting those species which are already rare. However, restrictions on pesticide use are not likely to be effective as a means of protecting rare plant species, and this is more effectively achieved through targetted conservation plans. At the round table discussion it was concluded that this argued against giving any special emphasis to rare species in risk assessment. It is also true that rare species are unlikely to be providing an important resource to other species (unless those are also rare), though they may have done so in earlier times if they were more widespread.

Of the existing proposals, only the USEPA explicitly mentions ferns, mosses, liverworts and conifers (in field studies at Tier III, see Appendix 6.1). These species were also excluded from the list agreed with PSD for consideration in the present study.

Conclusions:

- Some species of plants can be identified as particularly important, but these are not the only ones which require protection. It is impractical to test all the species which require protection, so it will be necessary to test a limited number and extrapolate to the others.

- Nevertheless, it may be desirable to ensure that the most important of the common species are given particular consideration in risk assessment. This could be achieved by (a) including them in toxicity testing, and/or (b) conducting species-specific risk assessments. This would probably be restricted to those pesticides for which a preliminary, generic assessment indicates a significant potential for risk.

- Consideration should be given to including species such as ferns, mosses, liverworts and conifers in risk assessment.

6.2.1 Definition of non-target plants

Species which are considered important may sometimes be the target of herbicide use, depending on where they are growing. The definition of non-target plants is therefore crucial, but it varies markedly between the existing schemes (see Table below). Note that, taken literally, the GCPF definition excludes plants in hedgerows and in the outer 5m or so of non-crop habitats (e.g. woodlands).

Most mammals and birds depend primarily on species outside the cropped area, but some species currently obtain significant amounts of food in the cropped area and/or use it as nesting habitat (Section 3). Furthermore, it is conceivable that appropriate regulation of pesticide use could increase the value of the cropped area to wildlife without adversely affecting crop performance. This implies that some importance may be attached to non-crop plants within cropped areas, as well as outside.

Conclusion:

- Risk assessment should consider desirable species inside the target area as well as outside. However, the level of risk which is acceptable will generally be higher in the crop, due to the need to control pests and weeds there.

Scheme	**Definition of non-target plants**
OECD Working Group	Not defined
GCPF Proposal	'Those plants which are outside the agricultural area.' Agricultural area is defined as 'the cultivated area plus a small zone (e.g. 5 m) typically necessary for commercial farming operations'.
EPPO Draft Scheme	Plants outside the treatment area.
USEPA Public Draft	Vascular and nonvascular plants, algae and fungi which are 'not considered to be pests in the area in which they are growing'. Includes 'desirable or pest host plants such as crops or ornamentals within the target area, and desirable plants outside the target area'.
CWS Proposal	'...plants occurring in nontarget areas and may include desirable species occurring in target areas and aquatic sites where total vegetation control is not intended.'

6.2.2 What types of effects to consider

In theory, pesticides could have many types of effects on plants which might damage their value to man and other wildlife:

- they may affect the adult plant, flowering and seed formation, seed viability, seed germination or seedling establishment,
- they may be temporary or long-term.

Effects that influence recruitment in the plant community may be the most significant. This may be the reason why existing schemes concentrate on tests of germination, establishment and early growth (see Table below). For species with a large seed-bank, reductions in seed production may be unimportant unless they are protracted or occur repeatedly. In some cases, however, seed production may be important. Furthermore, recruitment is also achieved by vegetative spread. However, no standard methods exist for tests on mature plants, though one is under development by ASTM (Kapustka, in prep.). Some of the existing risk assessment schemes mention the possibility of measuring a wider range of effects but only at higher tiers, in special tests or field studies (USEPA and CWS, see Table below and Appendix 6.1). Currently there is little evidence for growth enhancement effects and sublethal effects in the field, but this does not necessarily mean they are unimportant (see Section 5).

Scheme	**Types of effects considered**
OECD Working Group	• Phytotoxicity, including germination/emergence and vegetative vigour (growth, injury, mortality) • Reproduction and F1 germination - to be considered later.
GCPF Proposal (April '97)	• Phytotoxic response - defined as 'adverse effects on growth habit, yield, and quality of plants or their commodities'
EPPO Draft Scheme	• Phytotoxicity ('negative effects e.g. chlorolosis, growth')
USEPA Public Draft	• Adverse effects (measures include growth, injury, mortality) • Special protection for critical habitats of endangered or threatened plants listed by US Department of Interior. • Objectives of Tier II tests refer to importance of plants as food and shelter for wildlife, in controlling erosion, and filtering air pollution.
CWS Proposal	• Detrimental effects on plants (vegetative growth, seedling establishment), including endangered species. • Special single species tests at Tier III provide scope for assessing reproduction, entire life cycle, genotoxicity, translocation, bioaccumulation. • Rationale section refers to importance of plants in nutrient cycling, in primary production, and as food and habitat for other organisms.

Although tests are conducted with individual plants of particular species, the goal of risk assessment is ultimately to protect plant populations or communities, or animals which depend on plants. In principle this implies a need to extrapolate from effects measured on individuals to effects at these higher levels. However, this would require the use of complex

single and multi-species population models. It seems more practical in the short term to focus the risk assessment on predicting effects at the individual level, as is done for other taxonomic groups.

Finally, it must be remembered that pesticide effects in plant communities may be quite different to those in artificial tests (see Section 5). This provides a source of uncertainty which needs to be taken into account in risk assessment (see later).

Conclusion:

- Initially effort should focus on developing methods to predict effects on individual plants, rather than attempting to predict effects at plant populations or communities, or indirect effects on animals.

- Research would be needed to confirm whether effects on mature plants are important and frequent enough to merit specific consideration in risk assessment and, if so, whether they can be predicted by extrapolation from tests of germination, establishment and early growth or whether tests with mature plants are required.

6.3 EXPOSURE ASSESSMENT

Some of the existing schemes are structured around a small number of exposure scenarios, while in the OECD and CWS documents exposure scenarios are not defined (see Table below).

Scheme	**Exposure Scenarios**
OECD Working Group	Not defined
GCPF Proposal	• Exposure of seeds following application to soil • Exposure of emerged plants to spray drift
EPPO Draft Scheme	• Exposure to drift during application • Exposure to vapour after application • Scheme includes aquatic plants
USEPA Public Draft	• Direct exposure to pesticide application in treated area • Indirect exposure e.g. runoff, soil erosion, spray drift • Long-range transport a concern for some pesticides but not part of standard assessment
CWS Proposal	• Not defined • Scheme includes aquatic plants

There is clearly a major distinction to be made between the cropped and uncropped areas, as exposure is much higher in the former and there are different mechanisms of exposure. For this reason, it seems sensible to consider these two scenarios separately in risk assessment. For the *in-crop scenario*, the exposure routes may be effectively simulated by a test in which pesticide is applied in the recommended manner (e.g. spraying). It does not seem necessary to make calculations of the concentration expected in the soil, unless differences between soil concentrations in the lab and field situations are thought to be substantial.

For the *out-of-crop scenario*, drift of droplets at the time of application probably accounts for the majority of exposure and may be assessed by comparison with the effects seen for a direct spray at a suitable fraction of the in-crop application rate. There are a range of options for deriving this fraction. The CWS scheme uses a figure of 10%, USEPA 5%, EPPO uses figures from the Dutch USES database, and the GCPF use the Ganzelmeier drift estimates at 5m (due to their definition of non-target area), multiplied by 2 (the reason for the factor of 2 is not explained).

Other routes of exposure may need to be considered additionally for the out-of-crop scenario, but probably contribute less than droplet drift in most cases. Vapour drifts further than droplets and is easily assimilated by plants, but vapour drift is too complex to include in standard assessment procedures (Section 5). We therefore suggest that it might be considered only in cases where the physico-chemical properties of the pesticide indicate the potential for high vapour concentrations outside the crop, based on expert judgement. The USEPA scheme assesses run-off exposure as between 1 and 5% of the application rate, depending on the water solubility of the pesticide. One possibility is to include a standard uncertainty factor to account for the contribution of routes other than droplet drift, rather than make a specific assessment. Note that if exposure via droplet drift and runoff are estimated

separately, then some way must be found of aggregating them with other routes of exposure before comparing total exposure with toxicity. This is not straightforward, as they enter the plant in different ways (vapour and uptake from soil), and are not directly comparable with toxicity tests with doses defined in terms of amount applied per unit area.

There is also a need to consider the life stage at which exposure occurs. In principle it would be possible to use the results of germination/establishment and early growth tests in a single assessment predicting the overall probability of producing a plant of a certain size or growth stage from each seed, but this is complicated because the treatment is applied to seeds in one test and young plants in the other. In the field, exposure might occur at any point (or several) in the life cycle. It therefore seems sensible to consider exposure at the two life stages separately in risk assessment. If it were decided to conduct tests with mature plants this would comprise a third life stage to consider separately.

Another issue which requires consideration is how to take account of cumulative exposure from repeated applications of the same pesticide (and from different pesticides, if the regulatory process provides for regulating combined effects). There was insufficient time to address these issues in this project.

Conclusions:

- Combining the factors of location (in/out of crop) and life stage (seed, young plant) implies the need to consider a total of 4 exposure scenarios separately in each risk assessment (6 if mature plants are considered). For pesticide applications prior to the emergence of the crop, the 'young plant/in crop' scenario would presumably not require assessment, but the 'young plant/out of crop' scenario probably would.

- Assessments should be based on effects measured in tests at the actual application rate (in-crop scenarios) or a suitable fraction of it (out-of-crop scenario, based on droplet drift only). For consistency with European assessments for aquatic organisms, it would seem sensible to use the Ganzelmeier estimates for the drift fraction as a function of distance.

- Vapour drift only needs to be considered separately for the out-of-crop scenario, and perhaps only in cases where where the physico-chemical properties of the pesticide indicate the potential for high vapour concentrations. Further consideration should be given to appropriate ways of allowing for the contribution of runoff and vapour drift to total exposure.

- Further consideration should be given to how to take account of cumulative exposure from repeated applications of pesticides.

6.4 TOXICITY ASSESSMENT

6.4.1 Exploiting efficacy screening data

An important influence on the existing schemes for risk assessment is the desire to make maximum use of data which is already available from studies with plants, conducted as part of the efficacy assessment for new chemicals. According to the CWS, efficacy studies are typically assessed in a four-tier process: single-dose screening; preliminary dose-response with crop and weed plants; refined dose-response; and small plot field trials to determine exact rates of application and assess options for formulation and adjuvants.

The USEPA scheme is notable for excluding the use of screening data. This is based on a number of concerns which were listed in a presentation for the OECD working group on non-target plants:

- test species and methods differ between companies,
- measurement endpoints, data analysis and reporting not standardised,
- visual assessments are variable and subjective,
- seedling emergence and vegetative vigour tests are not always done,
- final formulation often not available for early efficacy tests.

In contrast the CWS philosophy is to allow the use of screening studies, provided they meet the CWS's minimum criteria. This is more consistent with the EU regulations, where Annexes 2 and 3 to Directive 91/414 both state that a summary of relevant 'preliminary tests' should be submitted.

Two contrasting types of screening are used in the efficacy assessment in Europe, particularly for herbicides. To assess risks to *succeeding crops*, a requirement under EC Directive. 91/414, a screen of activity against a range of crop plants in soil is required. The growth effect at various doses must be examined, usually to produce a no adverse effect concentration in soil. Seedling emergence and growth is normally examined. To examine risk to *adjacent crops*, particularly for highly biologically actives, a post-emergence screen is carried out. This is against a range of crops species at various doses. The methodology for both screens has not been standardised internationally but various national methods are available.

It is interesting to note that no routine role is given to efficacy data in risk assessments for non-target invertebrates, although this may be because more relevant data is usually available from IOBC tests which would often be done anyway to establish compatibility with IPM.

Conclusion:

- On balance it seems efficient to make use of efficacy screening data as far as possible. Given the variable extent and quality of the data as pointed out by the USEPA there is a need to define the minimum type and quality of data required at each stage of the risk assessment, or adopt the CWS specifications if appropriate. There is also a need to establish guidance on how to decide whether additional data is required, to avoid unnecessary testing and ensure consistency.

6.4.2 Test design

Detailed aspects of the design of germination/establishment and early growth tests are discussed in Appendix 6.3.

Note that the existing proposals all employ challenge tests in the lower tiers of assessment (one treatment level, at or above the field application rate), and dose-response tests at higher tiers. This seems an efficient approach. Interestingly, challenge tests are not used routinely for birds at present, even though the cost saving through using only a single dose would presumably be greater for birds and there is the additional factor of animal welfare to consider. Dose-response tests for plants are clearly necessary at higher tiers, however, to enable comparison with exposure levels which vary both between and within exposure scenarios (e.g. in-crop, out-of-crop).

At the round-table meeting it was noted that rate of leaf extension is generally more sensitive than plant weight. It was concluded that a choice between these and other endpoints would ideally be based on comparative experiments to assess their relative sensitivity and repeatability. Consideration should also be given to their relative ecological significance.

Tests using seeds on filter paper in Petri dishes under controlled conditions have the advantage of high repeatability. However, they are restricted to examining effects on germination itself and very early growth. More seriously, it may be difficult to relate the exposure in the test to that in the field. A seed on filter paper corresponds to a seed on the soil surface rather than below, and the filter paper provides no opportunity for leaching of the pesticide away from the seed. Both germination and seedling establishment can be assessed in pot tests, or the effects of exposure of young plants. The use of a standard soil is preferred, being a more realistic substrate than inert materials. Existing schemes give various specifications for the types of soil to be used, and it may be possible to vary this according to the areas in which the pesticide will be used (Appendix 6.3).

The USEPA favour the use of typical end-products as test substances, whereas GCPF and CWS provide for the use of either formulation or technical grade active substance. Flexibility is important in lower-tier assessments to permit maximum use of existing data (e.g. screening studies). However, formulations of herbicides generally have higher toxicity than technical grade. This needs to be borne in mind when active substance data are used in the initial assessment: consideration could be given to applying an uncertainty factor if the scale of the difference in toxicity between active substance and formulation were reasonably consistent between pesticides. In higher tier assessments where additional studies are carried out specifically to assess risks to non-target plants, the formulation should be used.

The USEPA favour bottom-watering to prevent washout of the pesticide from the pot, whereas the GCPF consider it more important to water the soil surface to simulate the movement of water through the soil profile. Another factor to consider is the risk of waterlogging from bottom-watering, which can affect growth rate and reduce the sensitivity of the test to treatment effects. It may be preferable to water well before dosing, to the field capacity of the soil. This makes it possible to withold watering for several days after treatment, after which top-watering will be less problematic as residues are less likely to leach.

Conclusion:

- It seems sensible to make use of challenge tests in the initial stages of risk assessment, but in refined assessment dose-response tests are essential to predict effects at varying levels of exposure. Further work is required to identify the best test endpoints in terms of their sensitivity and repeatability, as well as ecological relevance. The use of a standard soil is preferred to inert materials. Studies with technical active substance or experimental formulations could be included in the initial stages of risk assessment, but the end-use formulation is strongly preferred for higher tier assessments. Further work may be required to determine appropriate methods of watering. Additional issues of test design appear in Appendix 6.3.

6.4.3 Tests with mature/reproducing plants

As already stated, there are no standard methods for mature plants, although one is being developed for ASTM (Kapustka, 1997). Test protocols for mature plants need to be repeatable, relevant to field use conditions and exposure patterns, relevant to the modes of action of the active (e.g. phloem-mobile pesticides are likely to have higher risk to non-targets, than others), and realistic or at least interpretable from an ecological viewpoint.

Such a test needs to examine three types of effect: growth of the adult plant, seed production and vegetative propagation. The first is fairly straightforward, as mortality, shoot height and weight, a visual rating of damage etc. can be measured. The second and third effects require plants to grown on for a considerable period. Nevertheless, if seed production effects (and effects on the viability of seed produced) are important then they need to be tested.

Conclusion:

- If effects on mature plants are considered important, they could be tested in pots kept in the glasshouse. Pesticide application should be related to use patterns, usually applied by methods similar to field applicators. Growth effects can be measured for a minimum period of 28 days, except where seed production is to be assessed. Seed production may need to be assessed over 12 months. Collected seed should be tested for viability, in comparison with untreated controls. Vegetative propagation measurement will also require the test to be continued for up to 12 months, so that perennation can be assessed.

6.4.4 Extrapolation of toxicity

We concluded above that it would be necessary to test some species and extrapolate from these to others. The approach to this problem varies between the existing proposals (Appendices 6.1 and 6.2). The traditional approach has been to specify the number (and sometimes the taxonomic composition) of species required with the aim of ensuring that they represent the sensitivity of non-target plants in general. The number of species varies between 6 (GCPF, OECD), 10 (USEPA, EPPO) and 30 (CWS). In addition to requiring more species, the CWS apply a safety factor of 10 as a further allowance for variation in sensitivity between species.

All of the above approaches were presumably based on expert but largely subjective judgement about patterns of variation in plant sensitivity to pesticides. A more objective approach is to base decisions about the number and composition of species to test on a statistical analysis of those patterns. Celine Boutin has attempted this using existing data held by the CWS and USEPA (pers. comm.). The data confirm that sensitivity varies widely between species. For the most part there are no consistent patterns of differences between species or between chemicals, which makes it unlikely that reliable predictions can be made from one to another. However, grasses show more consistent responses than broadleaves:

this suggests that more broadleaves than grasses should be tested if it is desired to characterise the range of variation for a particular chemical. Boutin found that the ratio between the maximum and minimum toxicity increases as more species are tested, and that this relationship continues beyond 30 species tested (although in the figure we have seen, it appears to level off after about 20 species). She concluded from this that more than 10 species should be tested, but the ideal number could not be determined.

Another approach to dealing with variation in sensitivity is to characterise the shape and breadth of the distribution of sensitivity and use this to predict the 95-percentile. This is sometimes interpreted as the dose which would be hazardous to the most sensitive 5% of species (the 'HD5'). If it can be shown that the shape and breadth of the distribution is consistent between pesticides, then existing data can be used to characterise the standard distribution. Standard factors can then be derived for extrapolating from one or a few test results to the HD5 for new pesticides. This approach has been developed for birds and mammals (Luttik and Aldenberg, 1997) and is likely to be used in the next revision of the EPPO Guideline for terrestrial vertebrates. Robert Luttik (pers. comm.) states that the fact that it has not yet been proposed at ECCO meetings does not imply any lack of confidence by Dutch regulators.

Boutin is currently assessing whether the HD5 approach can be applied to existing data for non-target plants (pers. comm.). Preliminary results suggest that the data are poorly fitted by the log-logistic distribution (used for birds and mammals). Other distributions are being tried: as long as it fits consistently it matters little which one is used. It is also worth checking whether different distributions may be required for different taxonomic groups (e.g. grasses vs. broadleaves).

In addition, Boutin recently carried out some studies in Denmark, generating new data by testing 15 plant species with 6 herbicides representing different modes of action. Early indications are that results confirm sensitivity is less variable among grasses than other species (confirming the need to test more of the latter). It also appears that most non-crop species are less sensitive than the most sensitive crop species, both pre- and post-emergence, however firm conclusions should not be drawn until a detailed report of the results is available.

Boutin's data should provide an excellent basis for testing whether standard distributions can be established for extrapolating toxicity between plant species. It should also provide definitive evidence on differences in sensitivity between crop and non-crop species, that would help in deciding how much reliance can be placed on screening studies with crop species. If the distibution-based approach is successful, it will provide a clear basis for deciding which and how many species should be tested and could become a central feature of the risk assessment process.

Forbes and Forbes (1993) have criticised the use of distribution-based methods in ecotoxicology. Their objections may be dispensed with as follows:

- they state that it is dangerous to make untested assumptions about the shape of distributions - this is correct, but we propose that the distributions should be tested;
- they state that the sensitivities of tested species must provide an unbiased measure of the variance and mean of the sensitivity distribution for all species - this can be ensured by appropriate selection of test species, which may need to be random rather than focussing on species of particular interest (e.g. 'key species', see earlier);

- they state it is dangerous to assume that communities and interactions among species can be protected by protecting individual species - the same assumption is currently made in non-distributional approaches as well, so this is not a reason to prefer them;
- they suggest that there is no difference in the outcome compared to using traditional safety factors - but their statistical comparison is based on a very limited (aquatic) dataset;
- they imply that distributional methods offer no clear advantage over traditional safety factors - but in fact they provide an explicit, objective and quantitative basis for dealing with uncertainty, whereas the traditional methods are (on Forbes and Forbes' own admission) arbitrary.

An alternative to using distribution methods is to carry out toxicity tests with species of ecological concern, such as those identified in other Sections of this report. This suffers from two major disadvantages: extrapolation to other species remains necessary unless all species of concern are tested, and some of these species may not be practical for use in routine tests. A possible solution is to rely on routine tests and extrapolations in basic risk assessments, and incorporate special tests with key species of concern in more refined (higher tier) assessments. This joint approach could simultaneously provide a high level of certainty about risks to key species, and a lower but adequate level of certainty about risks to non-target species in general. Consideration could be given to including some of the 'key' species in the list for routine testing in lower tier assessments, provided they were practical to work with. However, a final decision on this requires further work to check whether the species concerned are unusually sensitive or insensitive to pesticides in general, in which case they might bias the extrapolation methods for other species.

Conclusion:

- Statistical approaches to extrapolating toxicity between species, such as the HD5, have a more objective basis than alternatives. Their applicability for plants should be carefully assessed using Boutin's database of existing studies and also the new studies she is currently undertaking. Particular attention should be paid to specifying how test species should be selected so as to provide unbiased estimates of the distribution of sensitivities.
- In more refined (higher tier) assessments, toxicity tests might be conducted with particular species on the grounds of their ecological importance. Further work would be needed to determine how best to integrate this with statistical extrapolation for other species.

6.5 OVERVIEW OF EXISTING RISK ASSESSMENT SCHEMES

All of the existing proposals are based on a tiered approach to risk assessment (See Table below). This has advantages in (a) matching the amount of resources required for testing and assessment to the level of need (potential risk), and (b) providing a standard sequence of assessment so that regulators and registrants are clear about what is required at each stage.

In all of the existing proposals, the tier structure is based around:

- extracting maximum value from existing screening data (except in the USEPA approach),
- use of challenge tests and dose-response tests at separate, intermediate tiers,
- use of special tests at higher tiers.

As already noted, it seems sensible to make maximum use of existing data, from both challenge and dose-response tests. If additional toxicity data is required and if dose-response tests cost little more than challenge tests, then it may be sensible to conduct dose-response tests as standard as these can be used to assess risk under the range of exposure levels expected at different distances outside the crop (as noted above). At higher tiers, special tests are likely to focus on measuring effects in the more complex exposure scenarios which occur in the field. In view of the potential differences between pot tests and effects in the field (Section 5), mesocosm or full field experiments may be appropriate in these cases (but see also the next section).

Three existing proposals require no assessment for uses with certain types of exposure scenario. Of these the more flexible EPPO definition seems most reasonable: this simply requires the assessor to determine whether exposure is possible.

<table>
<tr><th></th><th>OECD</th><th>GCPF</th><th>EPPO</th><th>USEPA</th><th>CWS</th></tr>
<tr><td>PRE-SCREENING CRITERIA</td><td>-</td><td>-</td><td>No exposure</td><td>Food crops & other uses</td><td>Closed systems</td></tr>
<tr><td>SCREENING/ EFFICACY DATA</td><td>0</td><td>I</td><td rowspan="2">I</td><td></td><td>I & II*</td></tr>
<tr><td>CHALLENGE TESTS</td><td>I</td><td>II</td><td>I</td><td>I*</td></tr>
<tr><td>DOSE-RESPONSE TESTS</td><td>II</td><td>III</td><td>II</td><td>II</td><td>II*</td></tr>
<tr><td>REFINED ASSESSMENT</td><td>-</td><td>IV - case by case</td><td>Persistence in soil</td><td>III - Field Study</td><td>III.3 - single species
IV - multi-species</td></tr>
</table>

* The CWS scheme is designed to allow existing efficacy data to be used in tiers I and II, but additional tests might be necessary to cover the required number of species.

Three factors favour flexibility in the assessment scheme:

- the desire to make use of existing data, which varies in type and quantity between pesticides
- the existence of multiple exposure scenarios which may not all need assessment every time
- the existence of a number of possible complications such as vapour drift and run-off, which may only need assessment in special cases.

Conclusion:

- It seems sensible to adopt a flexible risk assessment structure built around starting with existing screening data, then conducting additional standard tests using dose-response methods, then conducting specialist studies if required. No testing would be required for special pesticide uses for which exposure is assessed as negligible.

6.6 ALTERNATIVE APPROACHES TO RISK ASSESSMENT

6.6.1 Probabilistic methods

Recently there has been increasing interest in using 'probabilistic' methods for assessing pesticide risks. The USEPA ECOFRAM Project is specifically tasked with developing probabilistic approaches, and the EPPO Panel on terrestrial vertebrates is considering similar methods. The defining feature of a 'probabilistic' assessment is that at least one of the input variables is a distribution rather than a fixed value and, generally, so is the output. In simple cases the input variable is a specified point from a distribution, rather than a whole distribution. This would be true if we were to use the HD5 in plant risk assessment, or the Ganzelmeier 95 percentiles for spray drift. Both values are point estimates based on distributions, so the output of the risk assessment would also be a point estimate (i.e. a toxicity-exposure ratio for the 95 percentile species and 95 percentile exposure).

A more refined probabilistic assessment can be made by using the whole distributions for the input variables rather than just one point on the distribution. Thus the inputs would be (a) a distribution of toxicity, and (b) a distribution of exposure. There are a number of ways of expressing the resulting risk:

- graphically, by plotting the cumulative decreasing distribution of exposure on the same graph as the cumulative increasing distribution of toxicity. The extent of overlap between the two distributions would provide an index of the probability of exposure exceeding the hazardous dose.
- calculating a distribution of toxicity-exposure ratios (TERs), by using a computer program to repeatedly select values at random from the input distributions for exposure and toxicity, calculate the TER, and store them until a distribution of TERs is developed. This could be used to assess the frequency with which the TER falls below any given threshold.
- using a computer program to simulate the exposure of a large number of individuals to pesticide, taking values at random from the input distributions, and assigning each individual as dead or alive depending on the extent to which its exposure exceeds its sensitivity. The output could be used to assess how often mortality would occur and what proportion of individuals it would affect. In principle, the results could also be fed into higher level models to predict changes in populations and communities.

These methods allow the user to take account of 3 sorts of uncertainty:

- uncertainty due to natural variability, such as differences in sensitivity between individuals of the same species, and between different species;
- uncertainty due to measurement error, for example in measuring the level of residues or a toxicity endpoint;
- uncertainty due to things which are unknown, or not included in the model underlying the risk assessment, for example uncertainty about the influence of vapour drift if this is not being assessed.

Each of these can be quantified in a probabilistic assessment, if ways can be found to measure or estimate the relevant distributions (this is particularly difficult for the third category, as by definition little is known about them).

These methods are unfamiliar and require the use of new computational methods, however a reasonable level of expertise can be developed fairly quickly with the software which is

available (e.g. @Risk and CrystalBall, both of which are add-ons to Microsoft Excel). The additional complexity seems justified by the two major advantages of probabilistic methods:

- They enable uncertainties in the risk assessment to be dealt with explicitly, objectively and quantitatively, as stated earlier. This seems fundamentally better than previous approaches, which tend to use arbitrary or poorly-justified safety factors for some types of uncertainty, and to ignore others (particularly those about which least is known).
- They can be used to produce results in terms of the frequency and magnitude of effects, e.g. the probability of killing a given proportion of the population, or a given proportion of species. These should provide a much improved basis for deciding the acceptability of risk than current methods.

It might be argued that as there is currently little or no risk assessment for non-target plants, it would be appropriate to start with a simple method similar to those used which have been used for other taxa in recent years. The alternative view would be that we should not limit ourselves to simple methods if better ones are becoming available.

Conclusion:

- Consideration should be given to using probabilistic methods for assessing risks to non-target plants. It would be useful to undertake some case studies using existing data, to compare these approaches with more conventional, deterministic ones.

6.6.2 Levels of refinement in probabilistic assessment

It is apparent from the preceding sections that several options exist for quantifying toxicity and exposure for non-target plants, and that these can be organised into 3 or 4 levels of increasing refinement, moving from simple point estimates to distributions and from generic estimates to data specific to the pesticide, species and scenario under assessment. Options for presenting the outputs of the risk assessment can similarly be arranged into levels of increasing sophistication, moving from simple TERs to predicted frequencies of mortality.

This diversity of options raises two questions:

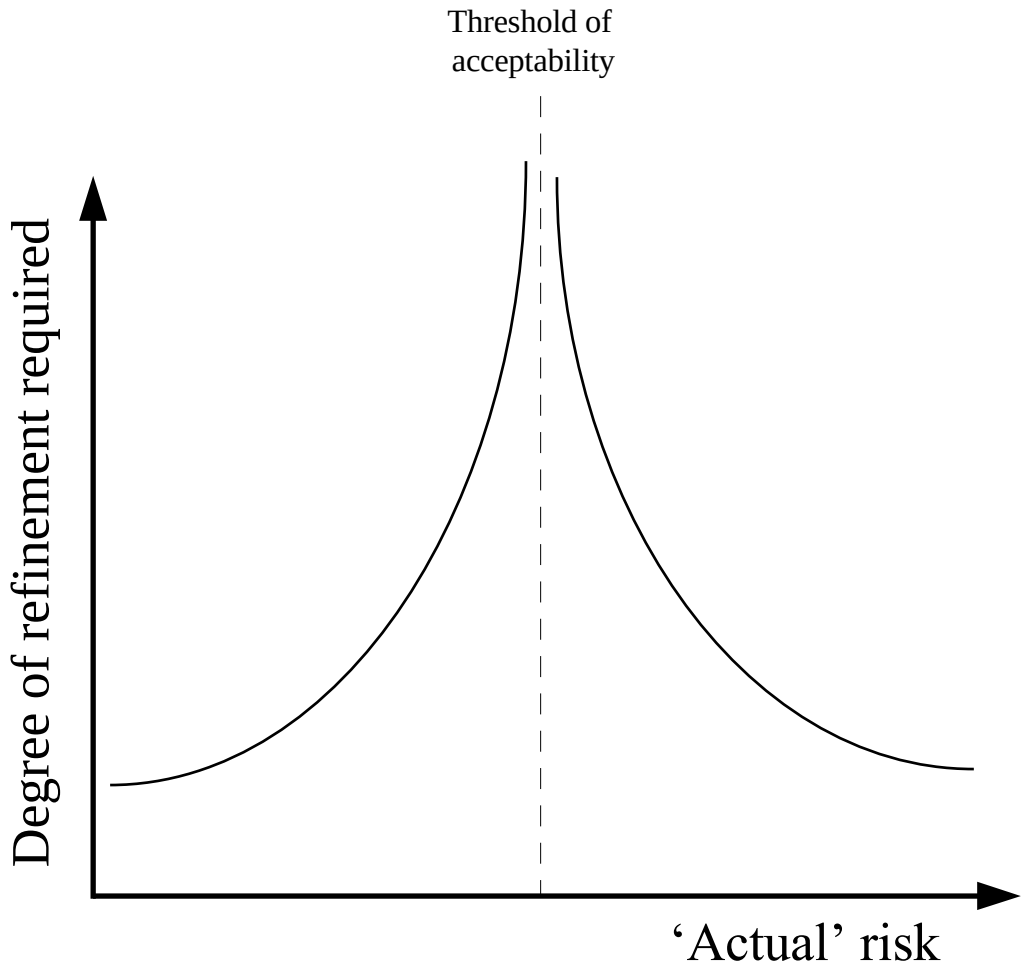
- how far to refine the assessment?
- which parameters to refine?

6.6.2 How far to refine the assessment

Refining the assessment costs registrants money and takes time (potentially delaying the entry of a new pesticide or pesticide use to the market). Regulators also incur extra costs at higher levels of refinement, as the submitted studies take more time to evaluate. Therefore it is in the interests of both parties to refine the assessment no more than is necessary for a regulatory decision to be taken with adequate certainty. If the actual risk is much higher, or much lower than the acceptable level, this may be apparent from a relatively simple, initial assessment. Although the risk prediction includes a high level of uncertainty, it is sufficiently far from the threshold for acceptability that a decision can be made with adequate certainty.

The closer the actual risk is to the threshold, the more precision is required in the risk assessment to enable a decision to be made. Consequently, *the degree of refinement required depends on how close the actual risk is to the threshold of acceptability*. This relationship is illustrated in Figure 1. The problem for the registrant and regulator is how to optimise the risk assessment process so as to achieve adequate certainty with minimum cost and time.

Figure 1. The closer the actual risk is to the threshold of acceptability, the more the assessment has to be refined for a regulatory decision to be taken with adequate certainty.



6.6.4 Which parameters to refine

The choices available for refining the risk assessment are illustrated in Table 6.1. At any point in the assessment, toxicity and exposure will have been addressed at some level of refinement (note it is not necessary for both to be assessed at the same level). Assuming that the assessment requires further refinement, either or both could be refined in the next phase of the assessment. Sometimes it may be most efficient to skip a level altogether.

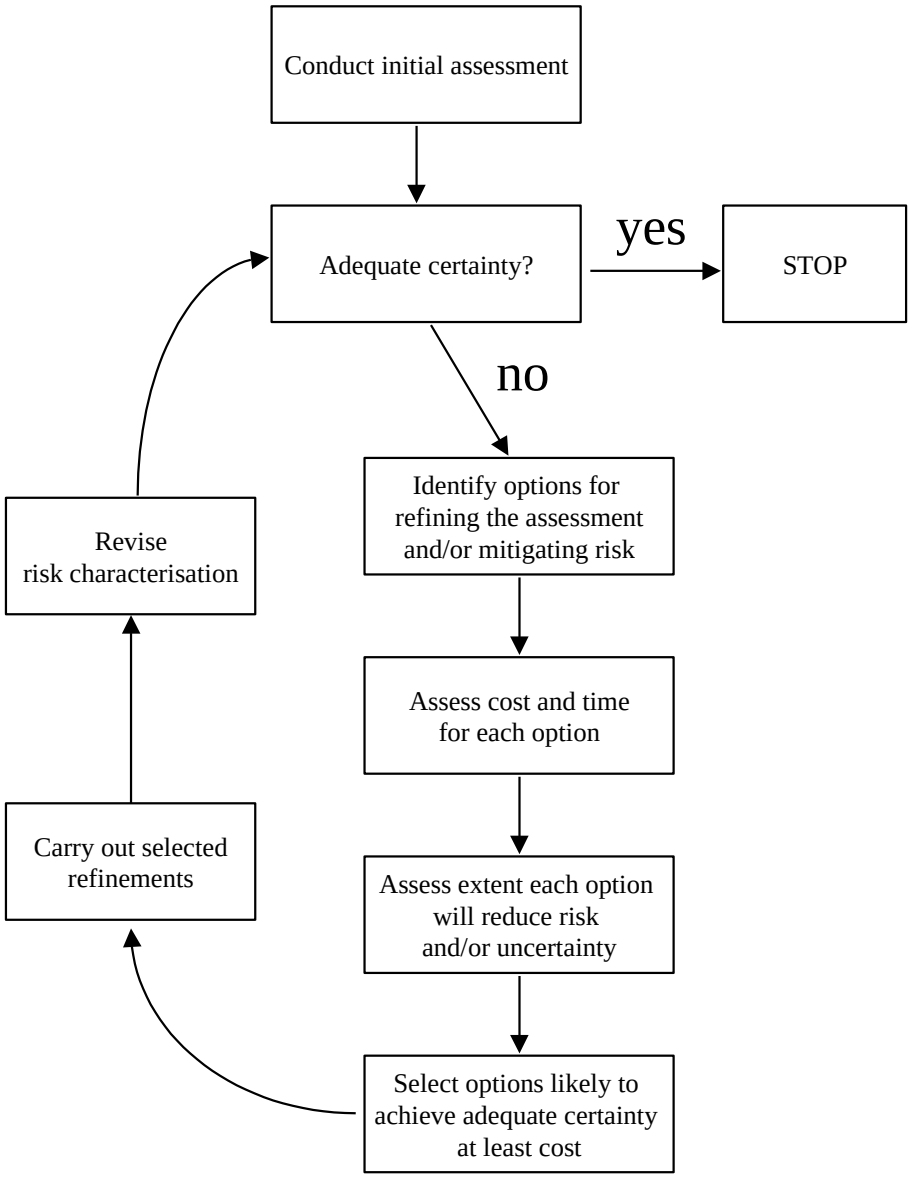
Table 6.1. Illustration of choices available for refining the risk assessment. Ticks represent the levels of refinement of each variable in the initial assessment in a particular case (note it is not necessary for all variables to be assessed at the same level). Question marks indicate the simplest choices for refining the assessment, one or more of which might be pursued simultaneously. In some cases it might be preferable to skip a level for one or more variables.

	Level I	Level II	Level III	Level IV
Toxicity	□	?		
Exposure	□	□	?	
Risk output	□	?		

A simple approach to deciding how to progress might be as follows:
1. assess how much each option will contribute to reducing uncertainty (U),
2. assess how much each option will cost (£, including the financial costs of time taken),
3. choose the option which has the highest ratio of U to £.

The selected options would then be implemented in the next phase of assessment, producing a refined estimate of risk. If it was concluded that there was still too much uncertainty, then the cycle could be repeated to identify options for a further phase of refinement. Thus the overall process would be an interative refinement of the assessment which would stop when the result was sufficiently certain for a regulatory decision to be made (Figure 2). Note that the registrant might prefer to consider risk mitigation options at any stage in the process, if the earlier results suggested that the result of refining the risk was likely to be unacceptable. This option is also illustrated in Figure 2.

Figure 2. Possible approach for optimizing the risk assessment sequence.



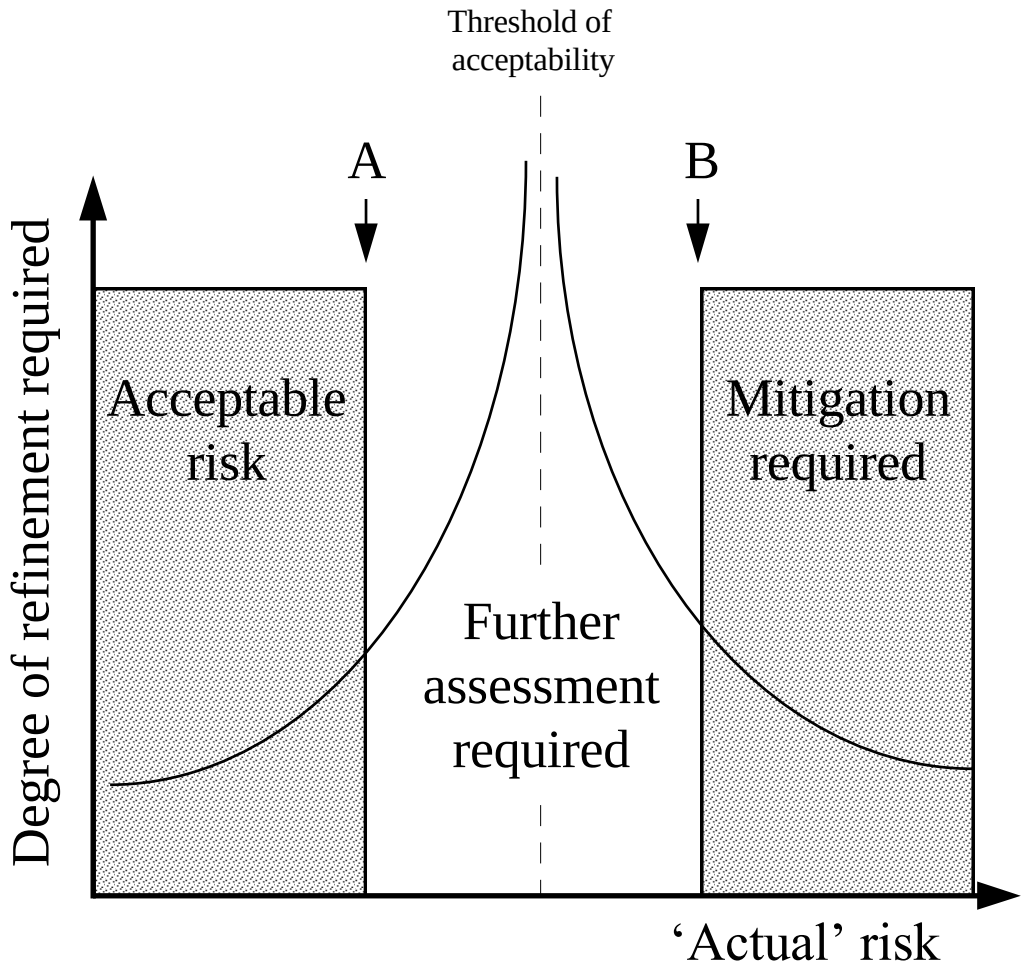
6.6.5 Tiered approach to risk assessment

As already mentioned, tiering is a common feature of pesticide risk assessment schemes, whether explicit or implicit, because it provides a clear structure for registrants and regulators and helps to match the level of refinement to the needs of each case. A general feature of the EPPO schemes for various taxa is that the initial tier (though not described as such) seeks to separate pesticide uses into three categories which are described as high, medium and low risk. The intent is to identify as simply as possible those uses which:

- are sufficiently low risk that they can be judged acceptable without refined assessment
- are sufficiently likely to cause unacceptable effects to warrant risk mitigation or non-approval
- are intermediate such that refined assessment is required to reach a decision.

This is a very attractive approach because it provides a very simple way of focussing effort on those pesticides which require it (Figure 3).

Figure 3. Illustration of the use of a first tier or initial assessment to focus effort on those pesticide uses for which it is most required. 'A' and 'B' represent the 'triggers' for deciding whether to proceed to a higher tier assessment.



The challenge is to find appropriate criteria for defining the high, medium and low risk categories. Because the actual risk is never known, this takes us to the heart of what risk assessment is about: assessing uncertainty. Using conventional risk assessment methods this has been very difficult, as there has been no objective or quantitative way to deal with uncertainty. As a result, the criteria for the risk categories are often defined in an arbitrary way, and indeed it has not been possible to give any definite rationale for them (see for example the justification offered in Note 12 of the EPPO scheme for terrestrial vertebrates).

The probabilistic approach offers a more objective and quantitative solution to this problem. The key idea is to calculate not just a *worst-case* TER in the initial assessment (as in most current schemes), but also a '*most-likely'* TER. The most-likely TER would be based on average or typical estimates of toxicity and exposure, rather than worst-case estimates. If the most-likely TER is less than one, this suggests that a large proportion of individuals in a large proportion of species will be affected under conditions which are common in the field. For many taxonomic groups (e.g. birds) this would be clearly unacceptable. For this category of pesticide uses, risk mitigation would be required before it would be worth refining the assessment. The interpretation of the worst-case TER is the same as at present: if it is high then it can be concluded that even under worst case conditions no adverse effects are likely. This category of pesticide uses can be considered acceptable without further refinement of the assessment. For the intermediate group, the risk assessment must be refined before it can be decided with adequate certainty whether the risk is acceptable.

Underlying this approach is the recognition that there is no single value for the actual risk of a pesticide. Rather, a distribution of effects will occur depending on the circumstances of each application. Furthermore, the actual shape and position of this distribution is unknown. To determine it would require a detailed and costly probabilistic assessment. What the proposed approach does is to estimate roughly where the upper limit and median of the distribution lie, and use these to decide whether it is necessary to determine the distribution more closely. This is illustrated in Figure 4.

Note that the 'triggers' have been given as 1 in both cases. This contrasts with the current EU approach where triggers are set at higher values (5, 10, 100). Clearly, if we set the triggers at 1 then the assumptions on which the TERs are calculated need to be defined in a suitable way. In the case of the worst-case TER, this means using a more conservative value for toxicity (e.g. the HD5) or exposure, or both. Setting the triggers equal to one has the following advantages:

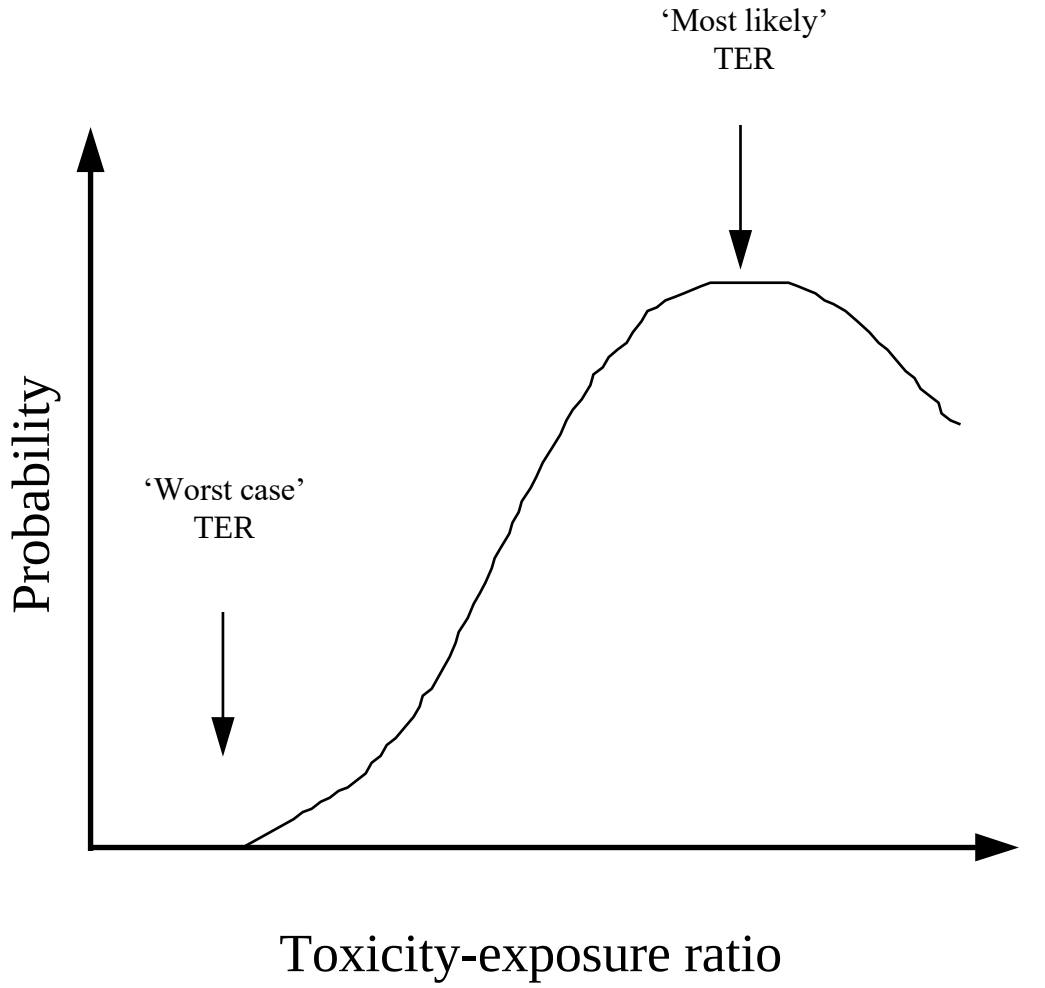
- it focusses the interpretation of the TER on whether effects are expected or not
- it forces the risk assessor to identify sources of uncertainty and include them explicitly in the calculation of the TER, rather than lumping them all into the safety factor which is implicit (but rarely explained) in the higher trigger value.

This approach therefore offers a direct, explicit and objective approach to dealing with uncertainty in the first tier of risk assessment. The advantage of this over current approaches seems obvious. Caution is required, because the concept is very recent (it was first proposed at a meeting of the EPPO Sub-panel on Terrestrial Vertebrates on 10-11 September 1998) and requires more development to assess whether it will fulfil this potential. However, it seems sensible to consider this as an option for plant risk assessment, especially as it can be made much simpler here than in assessments for other taxa where there are more variables to consider (e.g. birds).

Conclusion:

- Risk assessment schemes should focus effort on those cases which require it. Consideration should be given to whether this can be achieved by a novel approach based on the use of worst-case and most-likely TERs in the initial assessment.

Figure 4. This illustrates the concept of using two different TERs in the initial assessment to estimate the upper limit and median of a hypothetical distribution of TERs for the pesticide under assessment, and how these can be used to decide whether a refined (higher tier) assessment is necessary. Note that for the criteria shown to apply, the TERs must be based on suitable assumptions (e.g. worst case must be sufficiently conservative).



6.6.6 Application of tiering to non-target plants

The approach outlined in the preceding section could be implemented for non-target plants in a number of ways. However, we have already concluded that:

- it is desirable to make use of existing efficacy screening studies, where possible
- it is necessary to assess a number of alternative exposure scenarios which require different treatment and possible different criteria for acceptable risk
- it may be desirable to focus to some extent on particular species identified as being important, especially in more refined (higher tier) assessments
- risk assessment should be a flexible process, focussing additional testing at higher tiers on the specific issues which need refining in order to reach a decision.

One possible implementation of tiering, which takes these factors into account, is shown in Table 6.2 (below). It comprises five tiers which can be characterised as follows:
0 - potential for exposure
I - preliminary screening tier using efficacy studies
II - initial assessment using worst-case TER
III - initial assessment using most-likely TER
IV - refined assessment where required, including special studies and attention to key species.

Tiers 0-II serve to identify low-risk pesticides which require no further assessment, Tier III serves to identify high-risk pesticides which are likely to require risk mitigation, and Tier IV refines the assessment for pesticides of intermediate risk potential.

Note that the top tier contains a wide range of options and that no attempt is made to structure these. This is appropriate because the methods have yet to be developed and are likely to be case-specific. It is also consistent with many existing approaches to risk assessment, which leave higher tier methods to be defined case-by-case.

Table 6.2 is offered only as a starting point for discussion. It is clear that before this type of approach could be adopted, many of the components would require significant further work (shown in italics in the Table). However, alternative approaches (even those following conventional patterns) would also require development work (e.g. to achieve a consensus on the number and identity of species to be tested). In fact, if alternative approaches require less development it is likely to be because they assume that some issues can be covered by safety factors, whereas our suggestion requires them to be addressed directly. There is a paradox here: in order to be sure that an issue could be covered by a safety factor, it would be necessary to address it directly. Thus either way the issues really need to be addressed directly at some point.

This leads us to consider issues which are not explicitly addressed in Levels I-III in Table 6.2. The toxicity column does not identify the type of test to be conducted: it is assumed that separate assessments will be carried out for germination/emergence and young plants, using appropriate tests, as mentioned earlier. Other types of effect (including those on mature plants) could either be addressed directly (using appropriate tests) or indirectly, by applying an uncertainty factor to the toxicity data. Of course, such a factor should be based on some knowledge about the likely relationship between different types of effect (or at least an assessment of the worst-case relationship). The exposure column implies that exposure is presumed equal to the maximum application rate or a fraction of it (for out-of-crop scenarios) and does not address routes such as vapour drift and run-off. Again, uncertainty factors

might be developed to take account of these. This is particularly important for the worst-case TER (Level II), as it is proposed that pesticides which clear the trigger at this tier will be presumed safe. Note that this approach is forcing us to identify the various uncertainties and deal with them explicitly, an advantage mentioned previously.

It is important to note that this type of approach can and should be used in a flexible way, to meet the needs of each assessment. For example, screening data in Tier I together with other information (e.g. mode of action) could be used to focus testing at higher tiers on particular types of species (e.g. monocot/dicot) and particular growth stages, as appropriate to the pesticide concerned. More limited testing against other species and growth stages could be carried out to ensure there are no unexpected effects.

Conclusion:

- Consideration should be given to implementing a tiered approach to the initial assessment, incorporating probabilistic methods, along the lines presented in Table 6.2. Most of the components will require development work, as indicated in the Table. When defining the worst-case TER, particular attention should be paid to dealing with factors which are not addressed directly in the assessment, such as the importance of vapour drift, effects on mature plants, etc. As the approach is novel, some preliminary case studies should be conducted to test its feasibility before committing to detailed development.

Table 6.2. Suggested approach to tiered risk assessment for non-target plants, incorporating probabilistic methods. Note that Levels I-IV are repeated for each exposure scenario which is relevant to the case in hand. Work required to develop these approaches is shown in italics.

Level	Toxicity	Exposure	Assessment criteria
0	-	Qualitative assessment of whether exposure is possible.	If yes, proceed to next level.
I	Existing challenge and dose-response tests conducted for efficacy screening studies. *Work required to define minimum standards for acceptance of such studies for this purpose.*	Simple worst-case estimate. In-crop: maximum application rate. Out-of-crop: 95 percentile of Ganzelmeier estimates? *Work required to define percentile to use for out-of crop exposure.*	Estimate probability that an unacceptable proportion of species (e.g. 5%) are sensitive to the worst-case estimate of exposure. If probability is acceptable then no further assessment required, otherwise go to Level II. *Work required to develop this method and define acceptable proportions.*
II	Sufficient dose response tests to estimate the HDx with appropriate level of precision, including existing efficacy studies if conducted to the defined standard (see above). *Work required to develop method for HDx and define appropriate level of precision.*	As Level I.	If the worst case exposure is less than the HDx then conclude risk is acceptable, no further assessment of this exposure scenario required. Otherwise proceed to Level III. *Work required to decide percentile to use in HDx to achieve an appropriate level of protection (e.g. HD5).*
III	Use same toxicity data as Level II but take a more central value (e.g. HD50).	Simple estimate of 'most likely' exposure. In-crop: mean application rate if several are used. Out-of-crop: median of Ganzelmeier estimates? In both cases, a factor (0-1) might be used to allow for the fact that only a proportion of the population will be exposed. *Work required to define percentile to use for out-of crop exposure, and methods for the proportion exposed.*	If 'most likely' exposure exceeds HD50, conclude many species will be affected under typical conditions. The acceptability of this may differ between in and out-of-crop scenarios. If clearly unacceptable, refuse approval or consider risk mitigation. Otherwise, proceed to level IV (risk is neither clearly acceptable or unacceptable, so refined assessment is required).

IV	Refined toxicity assessment. Develop case by case but may include: • dose-response tests with additional species to improve characterisation of toxicity distribution • special tests for additional types of effects or exposure routes (e.g. vapour, runoff). • semi-field or field tests (but these must include parallel exposure assessment) • tests with particular species of concern. *Work required to develop suitable methods.*	Refined exposure assessment. Develop case by case but may include: • use whole Ganzelmeier distribution • use models for additional exposure routes (vapour, runoff, etc) • measure distribution of exposure in semi-field or field tests (but these must be carried out under a representative range of conditions) • exposure estimates for particular species of concern. *Work required to develop suitable methods.*	Refined risk characterisation methods, for example: • compare distributions of toxicity and exposure graphically • use Monte-Carlo methods to generate a distribution of risk quotients or TERs • use Monte-Carlo methods to generate estimates of the proportion of individuals and/or species affected • conduct separate risk assessment for particular species of concern (using any of the above methods). *Work required to develop suitable methods.*

6.7 REFERENCES

Forbes, TL & VE Forbes. 1993. A critique of the use of distribution-based models in ecotoxicology. Functional Ecology, 7: 249-254.

Kapustka, L. 1997. Standard guide for conducting terrestrial plant bioassays. Draft of 13 January 1997 prepared for ASTM Technical Committee E-47. ASTM, Philadelphia, USA.

Luttik, R & T Aldenberg. 1997. Extrapolation factors for small samples of pesticide toxicity data: special focus on LD50 values for birds and mammals. Environmental Toxicology and Chemistry, 16: 1785-1788.

APPENDIX 6.1 OVERVIEW OF EXISTING SCHEMES

N.B. The USEPA and CWS proposals are in final draft form, but the others are at an earlier stage of development.
ND = not defined

OECD Working Group

Tier	Toxicity	Exposure	Assessment criteria	Comments
0	'Screening and efficacy data' ≥ 6 spp. (3 monocot, 3 dicot), 4 families	≥ max. field application rate	If potentially phytotoxic, go to next Tier	
I	• Germination/ emergence test • Vegetative vigour test	'one dose based on application rate to demonstrate safety'	ND	Test design not yet decided Number and choice of species not yet decided Can skip this tier if Tier II data available
II	• Germination/ emergence test • Vegetative vigour test Dose-response tests	ND	ND	Test design not yet decided Number and choice of species not yet decided

GCPF Proposal

Tier	Toxicity	Exposure	Assessment criteria	Comments
I	Existing data from efficacy screens. ≥ 6 spp. (3 monocot, 3 dicot), 4 families. Separate tests for emergence and vegetative vigour.	ND	Go to next Tier if 50% or greater effect on any species at max field appliation rate, or if no efficacy data available.	
II	Challenge Test at dose/rate equal to 2 x PEC. Six species. Separate tests for emergence and vegetative vigour.	2 x PEC outside agricultural area, i.e. crop plus 5m boundary. Use Ganzelmeier data at 5m for reasonable worst-case spray drift. Zero for granulars?	Go to next Tier for those species where 50% or greater effect is seen at 2 x PEC.	
III	Dose-response test to obtain EC50s for species which showed 50% or greater effects in Tier II. Separate tests for emergence and vegetative vigour.	ND	Go to Tier IV for pesticides 'identified as potentially hazardous to non-target plants'.	Unclear whether assessment criterion is based on 2 x PEC as in Tier II.
IV	More refined tests and information, e.g. duration and extent of effects, slope of dose-response curves	More refined information, including distribution and frequency of plants	Options include: • ecological significance of effects at PEC • probability of effects based on distributions of toxicity and exposure	Test and assessment methods based on expert judgement

EPPO Draft Scheme

Tier	Toxicity	Exposure	Assessment criteria	Comments
		Use pattern	Go to Tier I if the possibility of direct and indirect exposure cannot be ruled out.	
1	Single dose test ≥ max. application rate on at least 10 species from 6 families.	Test at ≥ max. application rate.	If phytotoxicity observed in one or more species, go to Tier 2.	
2	Dose-response tests on at least 6 species including 3 monocot and 3 dicot species (at least 1 of each to be noncrop) in both soil and foliar exposures.	PEC estimated as fraction of application rate. Standard estimates provided for both drift and vapour exposure for pre- and post-emergence applications in various situations (based on Dutch USES database).	Calculate Exposure-toxicity ratio, ETR = PEC/EC50. If ETR < 0.1 for all species, categorise as low risk. If ETR > 0.1 for ≥ 50% species, categorise as high risk. If ETR > 0.1 for 1-49% species, go to Tier 3.	Assess separately for drift and vapour exposures, using different PEC estimates. Criterion of 0.1 implies x10 safety factor for EC50 effects. Scheme lists options for risk management in high risk cases.
3	No new data	DT50 in soil.	If soil application and DT50 > 60 days, categorise as high risk, otherwise categorise as medium risk.	This tier can be invoked for either or both of drift and vapour exposures. Expert judgement of degradation & bioavailability required in this Tier.

USEPA Public Draft

There is some confusion in the current USEPA regulations about the uses for which non-target plant assessment is required. Future revisions are likely to require a minimal Tier I set of terrestrial and aquatic plant studies using the maximum label dosage for all non-phytotoxicants with outdoor uses; and will require dose response studies for all known phytotoxicants with outdoor uses (Petrie, pers. comm.).

Tier	Toxicity	Exposure	Assessment criteria	Comments
I	Standard US screening tests. Seedling emergence test for runoff exposure. Vegetative vigour test for spray drift exposure. More than 10 species including corn, soybean, a root crop (6 spp of ≥4 dicot families + 4 spp of ≥2 fams monocots). Suitable non-standard screening tests may be accepted.	Test at max. label rate or 3 x estimated environmental concentration (EEC).	Go to Tier II for respective test type (emergence or vigour) if >25% adverse effect occurs in ♍1 species.	Herbicides, dessicants, defoliants and plant regulators skip to Tier II (no Tier I tests required). Additional seed germination tests exist for Tier I but generally waived.
II	Dose-response testing. Species as in Tier I. Use lowest EC05 or NOEC for endangered species risk assessment. Otherwise most sensitive EC25.	Solubility factors to determine runoff (1-5%). Assume 5% spray drift. Models under development: • PLANTEEC model of adsorption to soil. • Spray Drift Task Force - drift as % application rate.	Calculate risk quotient, RQ = EEC / toxicity. Go to Tier III if RQ > 1.	Additional seed germination tests exist for Tier II but generally waived.
III	Terrestrial Plants Field Study under field-use conditions. Test species to include dicots (3 families), monocots (3 fams.), ferns (2 fams.), mosses or liverworts (1 sp, for wetland uses only), conifer (1 sp.).	Tests to be conducted at doses representing the range of realistic exposures, same as Tier II tests.	Not specified - expert judgement?	Use to 'broaden knowledge of detrimental effects and evaluate mitigation methods'. Field study may need repeating in different regions/biomes.

CWS Proposal

Tier	Toxicity	Exposure	Assessment criteria	Comments
I	Challenge tests at ≥max. field rate. Herbicides: 30 spp. in 10 families. Non-herbicides: 10 spp. from 6 families; if any effects in these or algal tests then expand to 30 spp. in 10 families. Test design not specified (use existing screening data).	Test at or above max. label rate	Go to Tier II if effect >25% or statistically significant for any species.	Some confusion in CWS document whether extra challenge tests for nonherbicides are in Tier I or Tier II. Mostly implies Tier II but
II	Dose-response test for all species which showed >25% effect on any endpoint in Tier I. Seed germination and root elongation test on inert substrate (USEPA guideline). Vegetative vigour test design not specified (use existing data).	For seed germination or root elongation, EEC = conc. in soil resulting from max. rate applied to 3cm column of soil with bulk density of 1.5 g/cm^3. For veg. vigour, EEC = 100% of max label rate for overspray, 10% for drift.	Compare EEC to toxicity for each species. Go to Tier III/IV if EEC > EC25/10 for 25% of spp or 50% of families. Note uncertainty factor of 10, justified by reference to variation in toxicity between species.	Inert substrate preferred for standardisation. Note: seed guideline is one recommended by USEPA for toxics other than pesticides.
III	Special single species tests may apply to terrestrial species. No set test method.	ND	Go to Tier IV if EEC > EC25/10.	Guideline slightly ambiguous: Tier III.3 is for terrestrial species.
IV	Microcosm, mesocosm or field testing. Multiple species per test. Designed case-by-case to address concerns from lower Tiers. Ecologically relevant endpoints.	Micro/mesocosm tests at range of concentrations spanning no-effect and EC50s. Field tests at max. label rates.	'Advisory options' include no registration and restricted registration (including soils, crops, applic. method, buffers, timing, frequency)	Registrants can opt to omit Tiers I-III.

APPENDIX 6.2 OPTIONS FOR RISK ASSESSMENT

This Table summarises options for the design of the risk assessment procedure excluding test design, which follows in the next section. An important influence on the existing schemes for risk assessment is the desire to make maximum use of data which is already available from studies with plants, conducted as part of the efficacy assessment for new chemicals. According to the CWS, efficacy studies are typically assessed in a four-tier process: single-dose screening; preliminary dose-response with crop and weed plants; refined dose-response; and small plot field trials to determine exact rates of application and assess options for formulation and adjuvants.

Issue	Options	Comments
Which pesticides/uses require assessment?	• All crop protection products require bottom tier - GCPF • All plant protection chemicals require testing unless it can be shown exposure will not occur - EPPO • Intended phytotoxicants start at Tier II - USEPA • All non-domestic and outdoor domestic, except closed system greenhouses - CWS	The EPPO criterion seems to capture the key point: only necessary to test hazard where exposure is possible. CWS is similar in intention but the definition may be too restrictive?
Number and definition of tiers	• Initial assessment of potential for exposure - EPPO • Screening tier - OECD, GCPF, EPPO, CWS • Challenge test tier - OECD, GCPF, EPPO, USEPA • Dose-response test tier - OECD, GCPF, EPPO, USEPA, CWS • Top tier for refined assessment / additional studies - GCPF, USEPA, CWS	Number of tiers identified depends on : • whether initial exclusions are counted as a tier • how tiers accommodate use of existing data and standard challenge tests • whether there is a tier for refined assessments
Stepping criteria	• See Scheme summary tables for details • Can skip over intermediate tiers - OECD • Skip to Tier II if no screening data - GCPF • Herbicides, dessicants, defoliants and plant regulators skip to Tier II - USEPA	

Options for risk assessment (continued)

Issue	Options	Comments
Use of existing studies	• Screening/efficacy data - OECD, GCPF, EPPO, CWS • Suitable non-standard screening tests may be accepted - USEPA	Assess: • general preferences for test design (see next section) • needs of individual assessments.
Number and choice of species to test	• Specified minimum number of species - OECD, GCPF, EPPO, USEPA, CWS • Specify minimum number of families - OECD, GCPF, EPPO, CWS • Specify particular families - EPPO • Specify particular groups (e.g. monocot and dicot) - OECD, GCPF, EPPO • Specify crop and non-crop - OECD, GCPF, EPPO • Lists of suggested species for initial and additional testing - GCPF, CWS • Specify particular species - USEPA • At higher tiers, test only those species which showed effects at lower tiers - GCPF • Additional species at registrants discretion - GCPF • Specify cultivars? • Relevant to use pattern - CWS • Submit all efficacy screening data - CWS	• Consider practical issues - worldwide availability, ease of rearing, measurability and reproducibility of endpoints, plant uniformity • See summaries of existing schemes for numbers used at each Tier, also GCPF summary for number and choice of species specified in various test guidelines • Statistical analysis of existing data (Boutin and Rogers, draft paper).

Options for risk assessment (continued)

Issue	Options	Comments
How to combine multiple test results	• Use most sensitive species - GCPF, EPPO, USEPA • Proceed to Tier II for all species showing effects in Tier I - CWS, GCPF • Base assessment on % of species exceeding criterion - EPPO, CWS	• Investigate applicability of HD5 concept.
How to extrapolate toxicity between species	• Use most sensitive species tested - GCPF • Apply safety factor of 10 - CWS • Apply variable safety factor, depending on number of species tested • Calculate HD5 • Use most sensitive species to identify 'low risk' pesticides - EPPO • Implied assumption that test species are representative - EPPO	
Methods to quantify exposure	• Lower tiers based on max. field application rate - OECD, GCPF, EPPO, USEPA, CWS • Estimate PEC as percentage of application rate - GCPF, EPPO, CWS • Use of Ganzelmeier tables - GCPF • Use of RIVM estimates and EPPO air scheme - EPPO • Estimate EEC as conc. in soil - CWS	Depends on exposure scenarios and routes considered. Little to choose between alternative drift assessment methods? (Section 5).
Role of special tests	• special single species tests at Tier III, may include formulation studies, reproduction, entire life cycle, genotoxicity, translocation, bioaccumulation - CWS • multispecies microcosm/ mesocosm test at Tier IV - CWS • field tests at top tier - USEPA, CWS	Use if required to resolve uncertainties remaining after standard tests at lower tiers. Can more use be made of information on mode of action to decide when special tests are needed?
Role of incident data	• ND - OECD, GCPF, EPPO, USEPA, CWS	Limited by lack of data and difficulties in reporting, diagnosis and analysis of incidents (Section 5).

Options for risk assessment (continued)

Issue	Options	Comments
Methods for dealing with uncertainty	• Application rate - use maximum - OECD, GCPF, EPPO • Interspecies - specify minimum number and type of species - OECD, GCPF, EPPO, USEPA • Base assessment on 2 x PEC - GCPF • Use distributions of toxicity and exposure in top Tier - GCPF • Uncertainty factor of 10 - CWS	

APPENDIX 6.3 OPTIONS FOR TEST DESIGN

Tests of seedling establishment

Note differences in test design between tiers.

Issue	Options	Comments
Measurement endpoint: (a) what to measure	• Time to emergence - OECD • Number or % emerged - OECD, GCPF, USEPA • Number or % survived - OECD, GCPF • Shoot height - OECD, GCPF, USEPA • Shoot weight - OECD, GCPF, USEPA • Percent injury (visual rating) - OECD, GCPF, USEPA • Number and % germinated - CWS • Dry weights specified - USEPA • Root measurements for known root inhibitors - USEPA • Mean root length - CWS	Consider: • Ecological significance • Accuracy and precision • Reproducability of subjective measures Germination, root length *and* shoot length should be measured. Some actives suppress root growth, while others suppress only shoot elongation.
Measurement endpoint: (b) what to report	• To be decided - OECD • EC50 - GCPF, EPPO, USEPA • EC25 - USEPA, CWS • EC05 - USEPA • NOEC/NOEL - USEPA, CWS • LOEC • x % effect • 95% confidence limits on EC50 and EC25 - USEPA	Factors to consider: • reliability of estimation • ecological significance • endpoints available from existing data e.g. efficacy Slope of probit and standard error may also be useful for probabilistic assessment.

Tests of seedling establishment (continued)

Issue	Options	Comments
Test environment	• ND - OECD • Any system suitable for test species - GCPF, USEPA • Petri dish - CWS • Growth chamber - GCPF, USEPA • Phytotron - GCPF • Glasshouse - GCPF, USEPA • Semi-field/small plot - GCPF, USEPA • Field - GCPF • Monitor CO_2? • CO_2, RH, light, temperature specified in Tier II - USEPA • In Tier II, report soil K_d, K_{OC}, pH, type and texture and daily conditions - USEPA	Test conditions need to be maintained within limits relevant to the species and use scenario. Also desirable to use conditions which enable fairly rapid relative growth, to facilitate detection of treatment effects.
Test substrate/soil type	• Soil: OM 1-3%, pH 5-8, sandy loam to clay loam, untreated for ♍ 2 yrs - OECD • Soil typical of intended use area - GCPF • Soil ♋ 3% OM, sandy loam or clay loam - GCPF, USEPA • Sand, glass beads, rockwool etc not recommended - USEPA • Inert material covered with filter paper - CWS • Artificial soil • Filter paper	Issues to consider: • realism (favours soil) • standardisation (favours artificial soil or other substrates) Realism more important.
Exposure conditions	• Apply to soil surface - OECD • Use calibrated sprayer - GCPF • In field studies, use simulated or actual commercial equipment - USEPA • Minimum recommended spray volume - USEPA • Mix into soil • Multiple applications? • Spray or mix in according to intended use - USEPA	relate to actual exposure scenarios

Tests of seedling establishment (continued)

Issue	Options	Comments
Test duration	• ND - OECD • Typically 14 to 21days - GCPF, EPPO • At least 14 days - USEPA	Consider potential for delayed effects although this is unusual and for some pesticides recovery may occur.
Test substance	• ND - OECD • Formulation *or* active substance *or* technical grade - GCPF, CWS • Typical end-use product preferred - USEPA	Need flexibility to allow use of existing data. However, formulations of herbicides generally have higher toxicity than technical grade, so it is important to use the final formulation in additional tests.
Use of toxic reference compound	• To be decided. Choice of reference compound may vary with mode of action of test substance - OECD • Required - CWS	Consider using only if test conditions are difficult to control.
Number of treatment levels	• One at lower tiers - OECD, GCPF, EPPO, USEPA • Not decided at top tier - OECD • Multiple at Tier III, e.g. 5 levels - GCPF • At least 5 at Tier II - USEPA	For dose-response tests, base number and level of treatments on statistical assessment of requirement to estimate chosen endpoint.
Choice of treatment levels	• ♍ field rate at lower tiers - OECD, GCPF, EPPO, USEPA • ND at higher tiers - OECD • Geometric progression or chosen to encompass the EC50 - GCPF, USEPA • Include <EC50 and a nontoxic level - USEPA, CWS	

Tests of seedling establishment (continued)

Issue	Options	Comments
Replicates per treatment	• ND - OECD • At least 3 - GCPF • 3 - USEPA • 4 - CWS	Base on statistical assessment of test power.
Seeds per replicate	• ND - OECD • Typically 10 - GCPF • At least 10 per pot - USEPA • At least 15 to germinate in each control replicate - CWS	Need to increase replication for species with low germination rates.
Container type and size	• ND - OECD • Non-porous, avoid peat or clay containers - GCPF, USEPA • Plant densities suggested for different spp. - USEPA	Avoid materials likely to absorb pesticides. Size determined by number of plants per container and needs of test species - GCPF list suggestions for 9 species. Essential to report densities: note potential for shading from spray at high densities.
Pretreatment with pesticides	• Avoid confounding pesticide treatments - OECD, GCPF, USEPA	
Watering	• From above, simulating movement of pesticide through soil profile - GCPF • From bottom to prevent washout - USEPA	Consider: • needs of test species • effects on pesticide fate • rain in field conditions
Temperature control	• ND - OECD • Suit to test species - GCPF, USEPA	

Tests of plant growth and development

Many features are common between these and the seedling establishment tests and are not repeated here. Again, note the differences between tiers. Also, note that the CWS proposal does not give detailed specifications at Tier I or Tier II in order to allow use of all existing screening data, but instead requires detailed reporting of methods.

Issue	Options	Comments
Measurement endpoint: (a) what to measure	• Shoot/plant height - OECD, GCPF, USEPA • Shoot/plant weight - OECD, GCPF, USEPA • Percent injury/abnormal growth and development (visual rating) - OECD, GCPF, USEPA, CWS • Mortality - USEPA • Chlorosis - EPPO, CWS • Stand or plant population • Plant diameter - USEPA • Lodging - USEPA • Root weight for known root inhibitors - USEPA • Entire plant length • Entire plant weight	
Measurement endpoint: (b) what to report	• As for germination/ emergence tests	
Test substrate/soil type	• As for germination/ emergence tests (excluding inert substrates)	
Exposure conditions	• 'even spraying on all plant surfaces' - OECD • Representative of standard field equipment - OECD • Base application rate on amount per unit area, not concentration - GCPF, USEPA • Spray volumes in range of normal field practice - GCPF • Methods for indoor tests include hand-held atomisers or track sprayers - GCPF • Outdoor tests use simulated farm equipment - GCPF • Spray ensuring even and thorough contact with plant surfaces - USEPA	relate to actual exposure scenarios

Tests of plant growth and development (continued)

Issue	Options	Comments
Age of plant at treatment	• Early growth stages (2-4 leaf depending on species) - GCPF • 4-6 weeks Tier I, 2-4 weeks Tier II - USEPA	
Test duration	• 14 days after emergence - OECD • extend if delayed effects are expected - OECD, USEPA • 14 to 28 days - EPPO • min. 14 days - USEPA	
Toxic reference compound	• Not required - CWS	
Replicates per treatment	• Min. 4 recommended - CWS	
Plants per replicate	• Typically 5 - GCPF	
Watering	• Bottom watering preferred, or on soil under foliage - GCPF, USEPA	Avoid washing pesticide off foliage.

APPENDIX 6.4. REVIEW OF NON-TARGET PLANT ISSUES FOR THE US ENVIRONMENTAL PROTECTION AGENCY

OUTLINE PROPOSAL FROM RSI (Risk Sciences Institute)

IMPACTS OF PESTICIDES ON NONTARGET PLANT SPECIES

In 1982, the first FIFRA guidelines were published that addressed tests needed for nontarget plant toxicity risk assessments. Currently, nontarget plant risk assessments are conducted for pesticides that have the potential to drift or move from a treated site to adjacent, and sometimes distant, nontarget vegetation, following the 1982 guidelines. Herbicides, which account for approximately 75% of all pesticides used on agricultural crops, pose particular challenges for risk assessment of nontarget plant toxicity. Movement of herbicide residues from treated crops to adjacent crops, and into terrestrial and aquatic ecosystems, is well documented. With the introduction and increasingly widespread use of "low-dose," high toxicity herbicides, short, intermediate, and long range transport of herbicide residues in air, water, and on soil particles have become significant concerns. A complicating factor regarding "low-dose" herbicides is that many cannot be detected chemically using existing detection methods. These and other issues make it difficult to predict risks and to identify the cause of damage to nontarget plants in field incidents.

Other scientific questions raised in the advent of increasing concern over nontarget plant impacts include: what types of effects are occurring; what constitutes "unacceptable adverse effects," particularly on economically or ecologically important nontarget plants, and threatened and endangered plant species; and how should adverse effects be assessed within the context of quantitative risk assessment?

RSI proposes a set of activities to respond to these issues and questions. Initially, a small steering committee of government, academia, private industry, and public interest group representatives will be identified and convened by RSI. The steering committee will provide guidance to RSI on the content, organization, and development of up to five manuscripts from experts in the field addressing the critical scientific issues in nontarget plant risk assessments. Subsequent to the completion of the manuscripts, a workshop will be held for individuals from government, academia, private industry, and public interest groups, and any other interested and affected parties, to disseminate and discuss the completed manuscripts. The steering committee will also be asked to provide guidance on issues to be addressed and discussed at the workshop. Manuscripts may be revised as a result of workshop deliberations. Upon conclusion of the workshop and completion of the manuscripts, RSI will compile the manuscripts and report of the workshop for publication in the peer reviewed literature, as a stand-alone text, or monograph by an appropriate publisher.

CHARGES TO MANUSCRIPT AUTHORS FOR RSI REVIEW

RSI have commissioned five papers covering issues identified by the Steering Group. The working titles of the five papers and the issues they are charged to address are listed below.

Overview of New Compounds: Low-Dose, High Toxicity Herbicides

- Provide a history of why these compounds were developed (e.g., regulatory pressures, scientific advances, economic advantages, etc.), the agricultural desirability of the compounds, and how/why their use is on the increase.
- Discuss the mechanism of action of these compounds and why their potency is of unique importance with regard to unintended or non-target plant impacts.
- Identify and discuss particular or unique problems posed by these compounds for nontarget plants.
- Identify and briefly discuss alleged incidents of unintended effects and impacts associated with use of these compounds and discuss the lack of detection methods (and other unique impediments) to validate the cause.
- Discuss the importance of chemical detection in resolving legal disputes between landowners regarding chemical drift and the current status of low dose, high toxicity herbicides.
- Summarize and discuss the scientific evidence presented in the herbicide registration documents, especially with respect to effects on plant reproduction in both target and nontarget plants.

Exposure to Low-Dose, High Toxicity Herbicides

Identify and discuss issues associated with exposure assessment of unintended or nontarget plants to these compounds:

- Discuss aspects of routes of exposure of nontarget plants to these compounds (e.g., during application via irrigation systems and spray drift, and post-application via volatilization, adherence to soil particles, movement in soil and water, environmental persistence, etc.). Whenever possible, relate the factors listed to specific physicochemical characteristics of the compounds.
- Briefly outline methodology for exposure assessment (e.g., models, monitoring, sentinels).
- Discuss current and potential new chemical, physical, and biological detection methods for these compounds (e.g., tissue culture, immunoassay). Include a financial evaluation of the feasibility of adding new chemical or biological detection methods to current assays conducted by State, Federal, and private labs.
- Discuss monitoring off-target movement through the use of collection devices and/or markers (tracers) used as pesticide additives.

Unintended or Nontarget Aquatic Plant Effects of Herbicides

Identify and discuss unique issues associated with effects or dose/response assessment of nontarget aquatic plants to these compounds such as:

- What do we know about acute, chronic, and reproductive effects associated with these compounds? What should we know? Are there potential chronic effects that do not translate into a reproductive response, yet are of interest ecologically? Are the reproductive tests conducted on plants consistent with those conducted on other

organisms? Are life cycle testing methods feasible and appropriate for plant studies?

- Identify and discuss how results from laboratory studies (e.g., greenhouse) are or are not extrapolated to the field. What are the limitations of this process? Are there novel ways that exist or could be developed to improve this process? Can we extrapolate from tests in the laboratory to potential community or ecosystem level responses in the field?
- Discuss the adequacy of existing methods to evaluate herbicide effects on different taxonomic divisions and/or plants with different structural or physiological features. How might methods be modified among plant classes? Discuss ways to interpret findings from experiments in which different exposure methods were used.
- Identify and discuss what constitutes adverse effects on a population or community and on ecosystem structure and function.

Unintended or Nontarget Terrestrial Plant Effects of Herbicides

Identify and discuss unique issues associated with effects or dose/response assessment of nontarget terrestrial plants to these compounds such as:

- What do we know about acute, chronic, and reproductive effects associated with these compounds? What should we know? Are there potential chronic effects that do not translate into a reproductive response, yet are of interest ecologically? Are the reproductive tests conducted on plants consistent with those conducted on other organisms? Are life cycle testing methods feasible and appropriate for plant studies?
- Discuss considerations for what constitutes adverse effects on nontarget crops versus nontarget native vegetation.
- Identify and discuss how results from laboratory studies (e.g., greenhouse) are extrapolated to the field. What are the limitations of this process? Are there novel ways that exist or could be developed to improve this process? How do laboratory tests conducted on seedlings relate to herbicide drift onto mature flowering plants in the field? Can we extrapolate from seedling tests in the laboratory to potential community or ecosystem level responses in the field?
- How should field tests be conducted to evaluate potential adverse effects of pesticides on nontarget plants growing under different environmental conditions across the U.S.?
- Discuss the adequacy of existing methods to evaluate herbicide effects on different taxonomic divisions and/or plants with different structural or physiological features. How might methods be modified among plant classes? Discuss ways to interpret findings from experiments in which different exposure methods were used.
- Identify and discuss what constitutes adverse effects on a population or community and on ecosystem structure and function.

Problems Associated with Risk Characterization of the Impacts of Herbicides on Nontarget Plants

Identify and discuss unique issues associated with risk characterization of these compounds. Suggested topics may include, but are not limited to:

- Describe and discuss current methods for characterizing the risks to nontarget plants from the use of herbicides, including, but not exclusively, the low-dose, high toxicity compounds. How do we combine effects and exposure analyses into characterization? Are these methods sufficient for low-dose, high toxicity herbicides? For pesticides in general? Why or why not?
- Describe and discuss novel methods and issues associated with this type of risk

characterization.

- Identify and discuss what and how new technology might be implemented to better characterize the risks. How can we evaluate and characterize interactions of various chemical stressors? How do/can we estimate the impacts of interactions of chemical and nonchemical stressors, such as temperature and pest infestation?
- How do/can we extrapolate risks, not from the greenhouse to the field, but to populations and community structure? How do/can we evaluate impacts to ecosystem function?
- What is the potential crop loss, in dollars, to farmers brought about by chemically undetectable levels of high toxicity herbicides?
- How can or should the performance of newly released pesticides be monitored to ensure that they behave in the environment as predicted during the registration process?
- Describe and discuss the "perfect" risk characterization and offer an example or two of the type of risk characterization that would be nice to achieve.