HEALTH AND ENVIRONMENTAL HAZARD CLASSIFICATION OF PESTICIDES

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Classification by hazard has been at the heart of many regulatory decisions on pesticides worldwide but achieving a degree of uniformity in approach and criteria has not been easy. The publication, in July 1999, of a new EU Directive concerning the Classification, Packaging and Labelling of Dangerous Preparations[1], presents an opportunity to review the development and role of hazard classifications.

Introduction

In order to reduce risks arising from the transport, use and disposal of pesticides, and preparations containing them, it is necessary to take into account:

- a knowledge of the HAZARDS presented by a substance and its preparations, leading to proposals for classifying these hazards
- the EXPOSURE to the substance and the subsequent assessment of the RISKS to the user and others, and the environment
- various options available to minimise the risks through the introduction of safe packaging, informative labelling, safety data sheets and, if appropriate, control of availability and use.

Many legislative and advisory bodies have approached these issues over a period of 50 years with the objective of achieving some degree of uniformity and harmonisation and avoiding conflicting regulations, labelling and advice. Part of the difficulty is historical and has arisen from the miscellany of organisations involved and their objectives, and part from the limitations on the subject matter each has tackled. Pesticides have a very special place in the wide range of chemical substances and their commercial uses, since they have formed the basis of much of the work on dangerous substances over the years. This text identifies the main trends that have contributed to the present position in the hazard classification of pesticides.

Early background

The major risks from dangerous substances may arise from:

- physical hazards — based on *physico-chemical* properties
- health hazards — based on *toxicological* properties
- environmental hazards — based on *ecotoxicological* properties

Table 1. Early history of pesticide classification

1948	'Standard Safety Regulations for Government and other Industrial Establishments', prepared by the International Labour Organisation (ILO) approved in Geneva
1950	Chemical Industries Committee of the ILO adopted a resolution on the classification, labelling and international symbols for dangerous, harmful and toxic chemical substances.
1955	Social Committee of the Brussels Treaty Organisation (no longer exists) published a list of toxic and dangerous chemical substances and proposals concerning their labelling, using the symbols proposed by the ILO Chemical Industries Committee.
1958	A subsequent edition of the 1955 list published under the auspices of the Western European Union (WEU), successor to the Brussels Treaty Organisation.

This review looks only at health and environmental hazards which are highly significant for the classification of pesticides.

Recommendations or legislation governing the supply and use of dangerous chemicals are not new. Although the often-quoted EU directive 67/548[2] – the '67 directive – is regarded in Europe as a landmark on this subject, it was based on over 20 years of international work (Table 1).

Council of Europe's 'Yellow Book'

In 1960, when the social and public health activities of the WEU were transferred to the Council of Europe (C of E), the work was continued by the Industrial Safety and Health (Chemical Questions) Subcommittee of the Social Committee under the 'Partial Agreement' arrangement and in 1962 the C of E published the first edition of a list of 500 dangerous chemicals and recommendations for their labelling, including Risk and Safety phrases, widely known as 'the Yellow Book'. The 4th edition, published in 1978, covered over 900 substances, the majority of them pesticides.[3] Class 4 in the Yellow Book dealt with health hazards and divided dangerous chemical substances into two classes, 'toxic' and 'harmful', using acute oral toxicity criteria, as in Table 2.

Council of Europe's Subcommittee on Poisonous Substances in Agriculture

Originally set up in 1956 as a Working Party of the Subcommittee of Health Control of Foodstuffs, this subcommittee carried out much 'pioneering work' on various aspects of

Table 2. Classification of technical substances in the Council of Europe's 'Yellow Book'

Class	acute oral toxicity to the rat (LD_{50}) (mg/kg)	Symbol	Label
Toxic	0–200	T	Skull and crossbones
Harmful (or irritant)	200–2000	X_n(or X_i)	St Andrew's cross

Table 3. Council of Europe's Classification Criteria for Formulated Pesticide Products in Resolution AP (71) 4.[4]

Class	Acute oral LD_{50} (mg/kg) of the formulation to the rat	Label
Ia	All products with active substance 0–25	Skull and crossbones and
Ib	Other products 0–200	POISON
II	200–2000	St Andrew's Cross and HARMFUL
III	2000–5000	PRECAUTIONS
IV	>5000	–

the safe use of pesticides. Early studies included, for example, maximum daily intakes and residues in food, later taken up by FAO/WHO in their Joint Meetings on Pesticide Residues. It also made a study of the principles and procedures for the classification of pesticides and this resulted in the publication of Resolution AP (71)4 "On the Classification of Formulated Pesticide Products" for member countries to consider adopting into their national practices (Table 3).

C of E's booklet "Pesticides", (7th edition 1992)[5], also contains a chapter on "Guidance on the classification and safety labelling of formulated pesticide products", although since the 5th edition in 1981 it has endorsed the more comprehensive WHO Recommended Classification (see later).

The present position – classification criteria in current use

The objectives and relationships of the four major 'players' in the development of classification criteria are outlined in Figure 1. For practical purposes, however, there are only three international systems which significantly affect pesticide regulatory decisions worldwide. Although there are similarities there are also significant differences.

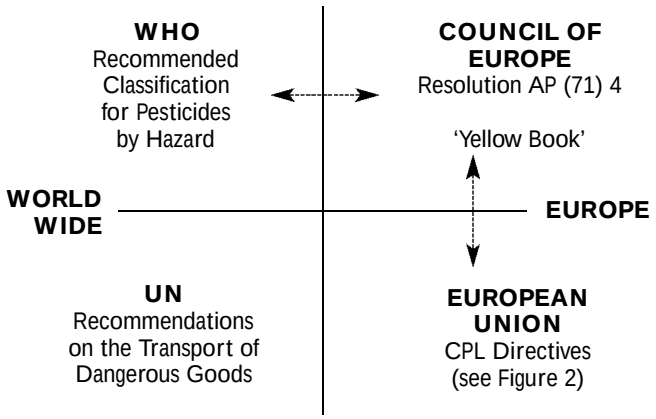
The Transport of Dangerous Goods (The United Nations Criteria for the Classification of Pesticides for Transport)

For many years the international organisations responsible for establishing Codes of Practice for the transport of dangerous goods by the various modes of transport have classified pesticides with the ultimate intention that there should always be suitable packaging and appropriate segregation of hazardous substances and foodstuffs during transport.

In earlier years these organisations devised the classification criteria for their codes and regulations independently, with the result that some pesticide packages travelling by several modes of transport could be required to carry conflicting labels. The recommendations of the United Nations Committee of Experts on the Transport of Dangerous Goods on classification[6], however, have been adopted by all transport organisations and the hazard labelling requirements are now harmonised. Toxic substances are grouped, according to the packaging requirements, into three packaging groups in Class 6.1 using the criteria in Table 4. Other miscellaneous dangerous substances are placed in Class 9. The publication should be consulted for details of the packaging and transport requirements.

Classification of the full range of pesticide active substances and preparations

Criteria limited to acute health effects (oral and dermal) with provision for *adjustments*.



Classification limited by definitions of *dangerous* chemical substances and preparations.

Criteria include inhalation hazard and other special health and environmental effects.

Figure 1. **Objectives and relationships of the four major 'players' in classification criteria.**

Table 4. UN criteria for grouping substances according to toxicity.

UN Packaging Group		Oral toxicity LD_{50} mg/kg	Dermal toxicity LD_{50} mg/kg	Inhalational toxicity by dusts and mists LC_{50} mg/l (1 hr)
I		>5	>40	<0.5
II		5–50	40–200	0.5–2
III	solids	50–200	200–1000	2–10
	liquids	50–500		

Although there are similarities between the UN and WHO criteria (Tables 4 and 5), the UN system fails to distinguish between the hazards of solids and liquids except in the case of oral toxicity for Packaging group III. On the other hand, it must be remembered that the use of the classification is quite different since the WHO system looks at hazards of pesticides to the user whilst the UN system is concerned with hazards in transport.

The continued retention of the oral toxicity criteria of <5, 5–50 and 50–500 mg/kg (for liquids) in the UN classification is probably a reflection of a strong United States lobby in the International Transport Regulations, since these criteria are favoured in US regulations.

The WHO Recommended Classification of Pesticides by Hazard[7]

The WHO Classification was approved by the 28th World Health Assembly in 1975 and has since gained wide acceptance. It is specifically designed for pesticides and based primarily on the acute oral and dermal toxicity of a substance or preparation to the rat since these determinations are standard procedures in toxicology and generate apparently quantitative data which may then be compared with set criteria.

The criteria recommended by WHO (Table 5) are realistic, being developed from a detailed examination of toxicological data of pesticide active substances and preparations and the experience gained from their practical use. They share main criteria of the C of E's Resolution AP (71)4 for the more hazardous liquid materials but, in addition, propose dermal criteria to supplement the basic oral criteria and also allow for the lesser hazards from solids compared with liquids.

Although there cannot be great precision in comparative hazards, the use of simple arithmetical ratios can make the system pragmatic and 'user-friendly'. *E.g.*, liquids are ×4 as hazardous as solids and oral exposure is ×2 as hazardous as dermal exposure.

In practice, the majority of pesticide classifications will be made on the acute oral LD_{50} value with a lesser number based on dermal data, reflecting the risk from a high dermal absorption in occupational exposure. With few exceptions, pesticides have low volatility and the use of inhalation criteria will only occasionally affect the classification. The exceptions are volatile fumigants and some preparations which contain relatively volatile solvents. The final classification is flexible and there is recognition that health effects other than oral and dermal toxicity may occasionally result in an 'adjusted' classification.

Table 5. Classification criteria recommended by WHO.

Class	LD50 for the rat (mg/kg body weight) Oral		Dermal	
	solids	liquids	solids	liquids
1a Extremely hazardous	<5	<20	<10	<40
1b Highly hazardous	5–50	20–200	10–100	40–400
II Moderately hazardous	50–500	200–2000	100–1000	400–4000
III Slightly hazardous	>500	>2000	>1000	>4000

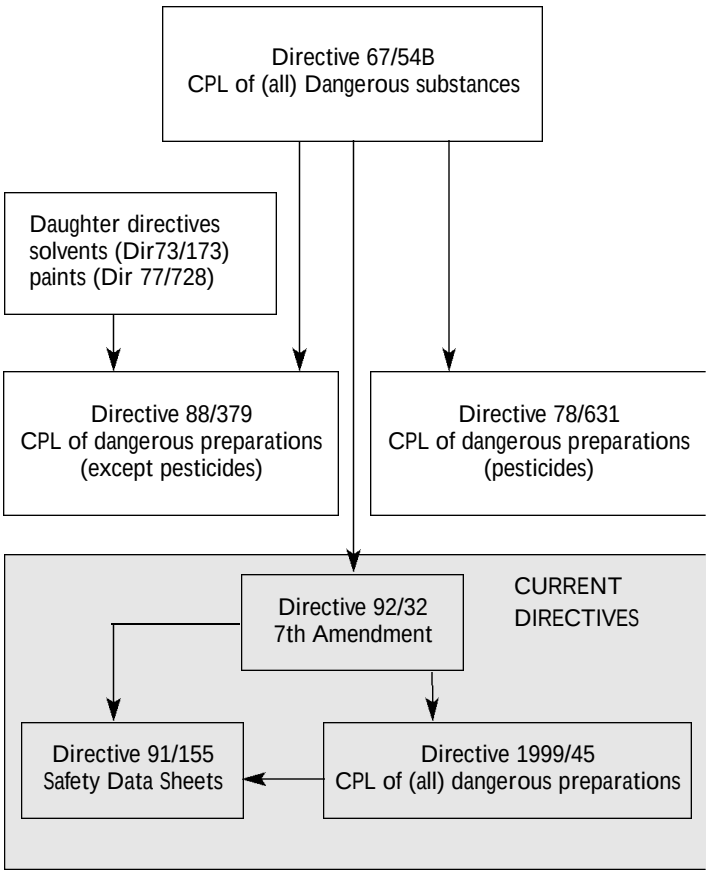


Figure 2. **The 'family' of CPL Directives in the EU. (See also Ref. 8)**

The WHO Classification is open-ended but the guidelines accompanying the classification additionally identify those pesticides that are *unlikely* to present any acute hazard in normal use – a deficiency in those classifications which are limited to the legal definition of 'dangerous substances'. This point of 'negligible' acute hazard is assumed to be at an oral LD_{50} of 2000 mg/kg for solids and 3000 mg/kg for liquids.

EU Directives on the Classification, Packaging and Labelling of Dangerous Substances and Preparations (CPL Directives)

It is now 33 years since the publication of the original '67 Directive on the Classification, Packaging and Labelling of Dangerous Substances (CPL Directive). This has been amended 7 times and there have been over 20 adaptations for Technical Progress. Several 'daughter' directives, those on solvents, paints and pesticides, have come and gone. Figure 2 outlines the family of CPL directives which are relevant to the current situation on the classification of pesticides in the EU.

The '67 Directive originally contained classification criteria for acute health effects adopted from the C of E 'Yellow Book' (compare Tables 2 and 6), although substances and preparations with an acute oral LD_{50} <25 mg/kg were given a special sub-class of *very toxic* but with the same hazard label [compare C of E Resolution AP (71)4]. Dermal criteria were added which reflected that oral hazard was ×2 the dermal hazard – the same ratio as that

Table 6. Classification criteria for acute health effects in Directives 92/32, Annex VI (substances) and 1999/45 (preparations).

Class		oral LD_{50} rat (mg/kg)	dermal LD_{50} rat (mg/kg)	Inhalation LC_{50} rat (mg/l)
Very toxic	T+	<25	<50	<0.25
Toxic	T	25–200	50–400	0.25–1
Harmful	X_n	200–2000	400–2000	1–5

recommended by WHO. Inhalation toxicity criteria were added later.

The criteria in Directive 67/548 were later extended to Directive 88/379 on the classification of dangerous preparations – but not to Directive 78/631 on the classification of pesticides which, until the new Directive 1999/45 on *all dangerous preparations*, used the WHO criteria.

Although the 6th Amendment to the 1967 Directive, which came into force on 18 September 1981, was known for its introduction of the pre-marketing notification requirement of new chemicals, it was not until the 7th Amendment, Directive 92/32[9], that significant changes were made to the criteria for hazard classifications. By re-defining 'dangerous' (Article 2) to include substances and preparations which exhibited special health effects such as serious damage to health on prolonged exposure, carcinogenicity, mutagenicity, toxicity for reproduction as well as dangerous for the environment, new criteria or approaches were needed to classify substances for these properties. These are presented in detail in the 18th Adaptation of Technical Progress of the '67 Directive, Commission Directive 93/21 and its Annexes,[10] together with hazard symbols and indications of danger and labelling requirements in the form of Risk (R) and Safety (S) phrases. The 22nd Adaptation, Commission Directive 96/37, refines 'dangerous' even further by introducing a new aspiration hazards phrase, R65 Harmful: May cause lung damage if swallowed.

The new 'Dangerous Preparations' Directive 1999/45[1] now becomes (implementation date 30 July 2002) the only directive available to Member States for the classification, packaging and labelling of pesticide products.

It is worth noting, however, that the potential health hazard of a preparation is allowed to be assessed by one or other of two methods

- by calculation from the properties of the active substance, accepting a dilution effect (the conventional method)
- by determination of the toxicological properties of the preparation

Default values which provide a possible escape from classification for health hazard are given in Annex II, Part B to the directive and Table 7 gives examples of these. Considering the two options for arriving at a figure to represent the potential acute health hazard of a preparation and the default values in Table 7, there is a clear degree of flexibility which could lead to 'discrepancies' in the final classification of a preparation.

Table 7. Some concentration limits to be used in the calculation of acute health hazards of preparations.†

Classification Of substance	Classification of preparation		
	T	X_n	No classification
T with R23	concn. >25%	concn. >3%	concn. <3%
X_n with R22, R21	–	concn. >25%	concn. <25%

†this table is intended to show how the hazard classifications of substances can be reduced as they are diluted in preparations; *e.g.* if a substance with classification T with R23 is used at <3% in a preparation it requires no classification at all.

Environmental hazards

Rapidly gaining importance, especially in the problems it creates, is the introduction of the category 'N Dangerous to the Environment' with the symbol of the 'dead tree and fish' (Figure 3) in Directive 92/32, which marked a significant change in the scope of hazard classification. The primary objective of classifying substances dangerous to the environment is to alert the user to the hazards these substances present to ecosystems, with criteria for fish, *Daphnia* and algae, it is recognised that certain substances may also affect other ecosystems whose constituents may range from soil microflora and microfauna to primates. There is even provision for a risk phrase 'Dangerous for the ozone layer' although this is not expected to be used for pesticides; methyl bromide could be a candidate, but is being withdrawn from future pesticide use.

Since the EU directives only classify on the basis of hazard there is the potential for a majority of pesticide (and biocide) formulations to be classified and labelled as *Dangerous to the environment* even if their use does not bring them into contact with soil or water. Since Member States are required, under Directives 91/414 and 98/8, not to approve plant protection products or biocides unless they are satisfied that there will be no harm to man, animals or the environment, the environmental hazard warnings on many product labels will lead to considerable confusion, to say the least.

However, 'generic default limits' have been set to allow the interpretation of substance hazard to generate an overall classification for the preparation (Table 8). These enable progressive dilutions of a very toxic substance to be labelled with Risk phrases of relatively increasing leniency.

Principal uses of classification

Since the urge to classify anything and everything has been a human passion for centuries it could be assumed that the classification of pesticides was just another manifestation of this passion to introduce order from chaos. There are several practical and valuable uses, however, for the classification of pesticides (and all dangerous chemicals).

Control of supply

Pesticides, like all potentially hazardous substances, produce

Table 8. Default values for classification of preparation based on acute aquatic toxicity of the active substance.†

Classification Of substance	Classification of preparation			
	N, R50 + R53	N, R51 + R53	N, R52 + R53	UNCLASS
N, R50 + R53	>25%	2.5% – 25%	0.25% – 2.5%	<0.25%

R50 = very toxic to aquatic organisms
R51 = toxic to aquatic organisms
R52 = harmful to aquatic organisms
R53 = may cause long-term adverse effects in the aquatic environment.

†this table is intended to show how the hazard classifications of substances can be reduced as they are diluted in preparations; e.g. if a substance with classification N, R50 + R53 is used at 0.25–2.5% in a preparation it can be classified as N, R52 + R53

the greatest injury in those who are the most heavily exposed to them. Although it has been considered advisable in certain countries, in recent years, to ban, withdraw or restrict the use of certain hazardous pesticides (*e.g.* WHO Class 1a substances), it is but a short step to a planned policy of *pesticide management* with recommended restrictions on the availability of the more hazardous chemicals. Such management can link the hazard, identified through classification, to the risk, identified by the responsibility, skill and experience of the user.

Table 9 outlines a typical framework for such a system which reflects part of C of E Resolution (81)3 which recommends that only formulated products with an acute oral LD_{50} for the rat greater than 2000 mg/kg should be available for purchase for domestic use and which forms part of a number of national systems of the control of supply.

Table 9. The use of classification in the control of supply and use. [11]

Class	Simplified criteria Acute oral LD_{50} (mg/kg)	Degree of hazard and control	User group
I	<20	Severe occupational hazard. Permit required.	professional pesticide applicator
II	20–200	High occupational hazard. Controlled sales.	as above plus licensed farmers
III	200–2000	Moderate occupational hazard. General sales	general farmer use
IV	>2000	Slight hazard	general public home and garden use.

Hazard symbol

Highly flammable (F)

Toxic (T)

Harmful (Xn)
Irritant (Xi)

Dangerous for the Environment

Figure 3. **International Hazard Symbols and indications of danger in current use on pesticide labels.**

Hazard/risk labelling

All the systems of classification discussed here include appropriate hazard symbols and indications of danger as direct consequences of classification. (Figure 3).

However, the EU directive 92/32 Annex VI, however, goes further and lists 59 standard risk (R) phrases and 62 standard safety (S) phrases for use, as appropriate, in conjunction with the hazard warnings on labels. It is a very complex document and requires careful study in its interpretation.

Safety data sheets (SDS)

Article 27 of Directive 92/32 refers to the requirement for an SDS, which must contain the information necessary for the protection of man and the environment, to be communicated to the professional user of a dangerous substance before its first delivery. SDSs are intended to supplement a hazard label and clearly, since a correct classification must be the starting point for a correct SDS, this depends on an understanding of the issues involved in arriving at a correct classification.

Some problems – discussion

Obtaining data for hazard classification

Almost all the basic data used to classify health and environmental hazards are derived from acute animal studies which often present difficulties in interpretation. For example, an LD_{50}, being a calculated (rather than a determined) value, is always accompanied by some estimate of the error of the value, such as the confidence limits. There are even several methods of calculating LD_{50}'s. Thus an LD_{50} close to any particular criterium limit could legitimately result in classification in either of the adjoining classes. Consequently, it must be recognised that hazard assessment is not a precise science.

Comparing the criteria of the classification systems

Some years ago, there was considerable optimism that an apparent 'window of opportunity' existed for harmonising the different classification systems and their criteria. There were several encouraging signs. The EEC had adopted the C of E's Yellow Book classification for dangerous substances with one minor modification, for its '67 Directive.

The WHO Classification of Pesticides (1972) developed the C of E's Resolution AP (71)4, by adding dermal criteria and distinguishing the lesser hazards of solids compared with liquids. The classification of dangerous preparations (pesticides) was defined in the EU directive 78/631 by transferring the criteria for WHO classes Ia, Ib and II, (with minor modifications to align two limit numbers with the '67 directive).

Harmonisation seemed possible and, more importantly, there was recognition that because of well-established pesticide registration procedures, later standardised through Directive 91/414 for plant protection products and Directive 98/8 for biocides, there was enough justification to classify pesticides separately from other dangerous preparations.

The EU, however, has now abandoned Directive 78/631, choosing to ignore the pragmatic WHO criteria and some 25 years of valuable experience. Instead, in a retrograde step, it has aligned pesticides with all other dangerous preparations in Directive 1999/45 using the criteria of the '67 Directive which fails to distinguish between the hazards from solids and liquids.

In the Transport of Dangerous Goods Regulations the hazard assessment is used to specify hazard labelling requirements based on the principle that exposure, and risk, results from accidental spillage. Since decisions on hazard or relative hazard are normally based on arbitrary criteria set with a particular objective in mind, classification criteria for *transport* were always likely to differ from other criteria set for the *use* of dangerous substances. The criteria in the UN Recommendations reflect these different objectives.[7]

Inhalation toxicity criteria and their use

Criteria for inhalation toxicity are included only in the UN and EC systems, both of which focus on potentially dangerous chemical substances. The inhalation of dusts (particulates); mists (aerosols); gases and vapours are obviously of concern in possible accidents in transport, or exposure in use, and the criteria in both Directive 92/32 Annex VI and the UN system carefully define the physical forms to which they apply.

Annex VI also states, para 3.1.4 '*when the classification is to be established from experimental results obtained in animal tests the tests should have validity for man in that the tests reflect, in an appropriate way, the risks to man*'.

It follows that pesticide active substances should be classified for inhalation hazard only if they exist as, or produce dusts, gases or vapours and can be tested as such, reflecting the risks to man in their use. It is clearly unrealistic to classify liquid pesticide active substances with very low volatility using experimental results from animal tests which do not reflect the risks to man – *i.e.*, by creating an artificial mist of the substance in a solvent. Inhalation risks from pesticide preparations in use are a separate issue and should be dealt with by evaluation in registration procedures. Poor interpretation of the Directives and guidelines has also led to misleading inhalation toxicity data being included in safety data sheets for active substances.

Safety Data Sheets (SDS)

The EU Safety data sheet directives 91/115[12] and 93/112 require that a safety data sheet must be supplied to all professional users of chemical substances or preparations that have been *classified as dangerous for supply* using the criteria in the Dangerous Substances (67/548) and Dangerous Preparations (1999/45) Directives.

The aim of the safety data sheet is to provide these users with *the information needed for safe handling within the workplace or the environment.* The requirement for the content of a SDS is detailed in Directive 91/115 laying down 16 obligatory headings under which information should be provided. It does not, however, prescribe the format or obligatory information that has to be provided. This lack of clear direction has been partly responsible for a considerable variation in the quality of SDSs in recent years. In addition, the extensive commercial practice of using SDSs (and Material SDSs) as short *summary data sheets* to provide data exchange between companies has lead to the inclusion of all kinds of technical data of varying relevance to the main objective, and not needed for the clear transfer of vital information on safe handling. There is also increasing evidence that many SDSs also containing inaccuracies, including wrong classifications, suggesting that the whole SDS system is in need of urgent review.

Conclusions

It is generally agreed that the potential hazards presented by *all* chemical substances and their preparations to workers, others and the environment should be identified and, if possible, quantified. Despite the detailed and complex EU directives and legislation in Member states, however, there are still problems in relating these potential hazards to risk. Hazard labelling has a certain attraction but requires users to carry out their own risk assessment based on interpretation of exposure. Evidence from many comparable situations indicates that the equation:

$risk = hazard \times exposure$

is poorly understood by most people and additional complex labelling requirements do nothing to clarify already over-labelled pesticide products. Quite the reverse, the prospect of label phrases on *potential* environment hazards conflicting with environmental risk assessments appears to strengthen the suggestion that pesticides preparations need some form of special consideration, both in hazard classification and in the clarity of label information.

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Ray Bates has participated in many aspects of UK and international control of pesticides for about 40 years. He was the consultant for the WHO Classification of Pesticides by Hazard in 1972 and has participated in many European discussions on the classification of pesticides.