Chapter 11:
REPRODUCTIVE TOXICITY

FINAL DRAFT FOR GHS WEB

DEFINITIONS

1. Reproductive toxicity includes adverse effects on sexual function and fertility in adult males and females, as well as developmental toxicity in the offspring. The definitions presented below are adapted from those agreed at the IPCS/OECD Workshop for the Harmonisation of Risk Assessment for Reproductive and Developmental Toxicity, Carshalton, UK, 17-21 October, 1994 (OECD Monograph Series on Testing and Assessment No. 17, 1998). For classification purposes, the known induction of ~~genetically based~~genetically based inheritable effects in the offspring is addressed elsewhere, since in the present classification system it is considered more appropriate to address such effects under the separate end-point of germ-cell mutagenicity.

2. In this classification system, reproductive toxicity is subdivided under two main headings:

a) Adverse effects on reproductive ability or capacity

Any effect of chemicals that would interfere with reproductive ability or capacity. This may include, but not be limited to, alterations to the female and male reproductive system, adverse effects on onset of puberty, gamete production and transport, reproductive cycle normality, sexual behaviour, fertility, parturition, premature reproductive senescence, or modifications in other functions that are dependent on the integrity of the reproductive systems. Adverse effects on or via lactation can also be included in reproductive toxicity, but for classification purposes, such effects are treated separately (see paragraph 183). This is because it is desirable to be able to classify chemicals specifically for adverse effect on lactation so that a specific hazard warning about this effect can be provided for lactating mothers.

b) Adverse effects on development of the offspring

Taken in its widest sense, developmental toxicity includes any effect which interferes with normal development of the conceptus, either before or after birth, and resulting from exposure of either parent prior to conception, or exposure of the developing offspring during prenatal development, or postnatally, to the time of sexual maturation. However, it is considered that classification under the heading of developmental toxicity is primarily intended to provide hazard warning for pregnant women and men and women of reproductive capacity. Therefore, for pragmatic purposes of classification, developmental toxicity essentially means adverse effects induced during pregnancy, or as a result of parental exposure. These effects can be manifested at any point in the life span of the organism. The major manifestations of developmental toxicity include (1) death of the developing organism, (2) structural abnormality, (3) altered growth, and (4) functional deficiency.

CONSIDERATIONS

3. The purpose of the harmonised system for the classification of chemicals which may cause an adverse effect on reproduction in humans is to provide a common ground which could be used internationally for the classification of reproductive toxicants.

4. The system is hazard based, classifying chemicals on the basis of intrinsic ability to produce an adverse effect on reproductive function or capacity, and/or on development of the offspring. The

present system involves consideration of any substance-related adverse effect on reproduction seen in humans, or observed in appropriate tests conducted in experimental animals.

5. The Explanatory Notes (paragraphs 16-30) provide essential guidance and should be regarded as an integral part of the Classification System.

CLASSIFICATION CRITERIA FOR ~~MIXTURES~~SUBSTANCES

Weight of Evidence

6. Classification as a reproductive toxicant is made on the basis of an assessment of the total weight of evidence. This means that all available information that bears on the determination of reproductive toxicity is considered together. Included are such information as epidemiological studies and case reports in humans and specific reproduction studies along with sub-chronic, chronic and special study results in animals that provide relevant information regarding toxicity to reproductive and related endocrine organs. Evaluation of substances chemically related to the material under study may also be included, particularly when information on the material is scarce. The weight given to the available evidence will be influenced by factors such as the quality of the studies, consistency of results, nature and severity of effects, level of statistical significance for intergroup differences, number of endpoints affected, relevance of route of administration to humans and freedom from bias. Both positive and negative results are assembled together into a weight of evidence determination. However, a single, positive study performed according to good scientific principles and with statistically or biologically significant positive results may justify classification (see also paragraph 8).

7. Toxicokinetic studies in animals and humans, site of action and mechanism or mode of action study results may provide relevant information, which could reduce or increase concerns about the hazard to human health. If it can be conclusively demonstrated that the clearly identified mechanism or mode of action has no relevance for humans or when the toxicokinetic differences are so marked that it is certain that the hazardous property will not be expressed in humans then a substance which produces an adverse effect on reproduction in experimental animals should not be classified.

8. In some reproductive toxicity studies in experimental animals the only effects recorded may be considered of low or minimal toxicological significance and classification may not necessarily be the outcome. These include for example small changes in semen parameters or in the incidence of spontaneous defects in the foetus, small changes in the proportions of common foetal variants such as are observed in skeletal examinations, or in foetal weights, or small differences in postnatal developmental assessments.

9. Data from animal studies ideally should provide clear evidence of specific reproductive toxicity in the absence of other, systemic, toxic effects. However, if developmental toxicity occurs together with other toxic effects in the dam, the potential influence of the generalised adverse effects should be assessed to the extent possible. The preferred approach is to consider adverse effects in the embryo/foetus first, and then evaluate maternal toxicity, along with any other factors which are likely to have influenced these effects, as part of the weight of evidence. In general, developmental effects that are observed at maternal toxic doses should not be automatically discounted. Discounting developmental effects that are observed at maternal toxic doses can only be done on a case-by-case basis when a causal relationship is established or refuted.

10. If appropriate information is available it is important to try to determine whether developmental toxicity is due to a specific maternally mediated mechanism or to a non-specific secondary mechanism, like maternal stress and the disruption of homeostasis. Generally, the presence of maternal toxicity should not be used to negate findings of embryo/foetal effects, unless it can be

clearly demonstrated that the effects are secondary non-specific effects. This is especially the case when the effects in the offspring are significant, e.g. irreversible effects such as structural malformations. In some situations it is reasonable to assume that reproductive toxicity is due to a secondary consequence of maternal toxicity and discount the effects, for example if the chemical is so toxic that dams fail to thrive and there is severe inanition; they are incapable of nursing pups; or they are prostrate or dying.

Hazard Categories

11. For the purpose of classification for reproductive toxicity, chemical substances are allocated to one of two classes. Effects on reproductive ability or capacity, and on development, are considered as separate issues.

CATEGORY 1:

KNOWN OR PRESUMED HUMAN REPRODUCTIVE OR DEVELOPMENTAL TOXICANT

This Category includes substances which are known to have produced an adverse effect on reproductive ability or capacity or on development in humans or for which there ~~is evidence~~is evidence from animal studies, possibly supplemented with ~~other information~~other information, to provide a strong presumption that the substance has the capacity to interfere with reproduction in humans. For regulatory purposes, a substance can be further distinguished on the basis of whether the evidence for classification is primarily from human data (Category 1A) or from animal data (Category 1B).

CATEGORY 1A~~: KNOWN~~: KNOWN to have produced an adverse effect on reproductive ability or capacity or on development in humans. The placing of the substance in this category is largely based on evidence from humans.

CATEGORY 1B~~: PRESUMED~~: PRESUMED to produce an adverse effect on reproductive ability or capacity or on development in humans. The placing of the substance in this category is largely based on evidence from experimental animals. Data from animal studies should provide clear evidence of specific reproductive toxicity in the absence of other toxic effects, or if occurring together with other toxic effects the adverse effect on reproduction is considered not to be a secondary non-specific consequence of other toxic effects. However, when there is mechanistic information that raises doubt about the relevance of the effect for humans, classification in Category 2 may be more appropriate.

CATEGORY 2:

SUSPECTED HUMAN REPRODUCTIVE OR DEVELOPMENTAL TOXICANT

This Category includes substances for which there is some evidence from humans or experimental animals, - possibly supplemented with other information - of an adverse effect on reproductive ability or capacity, or on development, in the absence of other toxic effects, or if occurring together with other toxic effects the adverse effect on reproduction is considered not to be a secondary non-specific consequence of the other toxic effects, and where the evidence is not sufficiently convincing to place the substance in Category 1. For instance, deficiencies in the study may make the quality of evidence less convincing, and in view of this Category 2 could be the more appropriate classification.

EFFECTS ON OR VIA LACTATION

Effects on or via lactation are allocated to a separate single category. It is appreciated that for many substances there is no information on the potential to cause adverse effects on the offspring via lactation. However, for substances which are absorbed by women and have been shown to interfere with lactation or which may be present (including metabolites) in breast milk in amounts sufficient to cause concern for the health of a breastfed child, should be classified to indicate this property hazardous to breastfed babies. This classification can be assigned on the basis of:

(a~~) absorption~~) absorption, metabolism, distribution and excretion studies that would indicate the likelihood the substance would be present in potentially toxic levels in breast milk; and/or

(b~~) results~~) results of one or two generation studies in animals which provide clear evidence of adverse effect in the offspring due to transfer in the milk or adverse effect on the quality of the milk; and/or

(c~~) human~~) human evidence indicating a hazard to babies during the lactation period.

Basis of Classification

12. Classification is made on the basis of the appropriate criteria, outlined above, and an assessment of the total weight of evidence. Classification as a reproductive or developmental toxicant is intended to be used for chemicals which have an intrinsic, specific property to produce an adverse effect on reproduction or development and chemicals should not be so classified if such an effect is produced solely as a non-specific secondary consequence of other toxic effects.

13. In the evaluation of toxic effects on the developing offspring, it is important to consider the possible influence of maternal toxicity.

14. For human evidence to provide the primary basis for a Category 1A classification there must be reliable evidence of adverse effect on reproduction in humans. Evidence used for classification should ideally be from well conducted epidemiological studies which include the use of appropriate controls, balanced assessment, and due consideration of bias or confounding factors. Less rigorous data from studies in humans should be supplemented with adequate data from studies in experimental animals and classification in Category 1B should be considered.

15. Data already generated for classifying chemicals under existing systems should be acceptable when reviewing these chemicals with regard to classification under the harmonised system. Further testing should not normally be necessary.

Explanatory Notes

Maternal toxicity

16. Development of the offspring throughout gestation and during the early post-~~natal stages~~natal stages can be influenced by toxic effects in the mother either through non-specific mechanisms related to stress and the disruption of maternal homeostasis, or by specific maternally-mediated mechanisms. So, in the interpretation of the developmental outcome to decide classification for developmental effects it is important to consider the possible influence of maternal toxicity. This is a complex issue because of uncertainties surrounding the relationship between maternal toxicity and developmental outcome. Expert judgement and a weight of evidence approach, using all available studies, should be used to determine the degree of influence that should be attributed to maternal toxicity when interpreting the criteria for classification for developmental effects. The adverse effects in the embryo/foetus should be first considered, and then maternal toxicity, along with any other

factors which are likely to have influenced these effects, as weight of evidence, to help reach a conclusion about classification.

17. Based on pragmatic observation, it is believed, that maternal toxicity may, depending on severity, influence development via non-specific secondary mechanisms, producing effects such as depressed foetal weight, retarded ossification, and possibly resorptions and certain malformations in some strains of certain species. However, the limited number of studies which have investigated the relationship between developmental effects and general maternal toxicity have failed to demonstrate a consistent, reproducible relationship across species. Developmental effects which occur even in the presence of maternal toxicity are considered to be evidence of developmental toxicity, unless it can be unequivocally demonstrated on a case by case basis that the developmental effects are secondary to maternal toxicity. Moreover, classification should be considered where there is significant toxic effect in the offspring, e.g. irreversible effects such as structural malformations, embryo/foetal lethality, significant post-natal functional deficiencies.

18. Classification should not automatically be discounted for chemicals that produce developmental toxicity only in association with maternal toxicity, even if a specific maternally-mediated mechanism has been demonstrated. In such a case, classification in Category 2 may be considered more appropriate than Category 1. However, when a chemical is so toxic that maternal death or severe inanition results, or the dams are prostrate and incapable of nursing the pups, it may be reasonable to assume that developmental toxicity is produced solely as a secondary consequence of maternal toxicity and discount the developmental effects. Classification may not necessarily be the outcome in the case of minor developmental changes e.g. small reduction in foetal/pup body weight, retardation of ossification when seen in association with maternal toxicity.

19. Some of the end points used to assess maternal toxicity are provided below. Data on these end points, if available, needs to be evaluated in light of their statistical or biological significance and dose response relationship.

Maternal Mortality: An increased incidence of mortality among the treated dams over the controls should be considered evidence of maternal toxicity if the increase occurs in a dose-related manner and can be attributed to the systemic toxicity of the test material. Maternal mortality greater than 10% is considered excessive and the data for that dose level should not normally be considered for further evaluation.

Mating Index (no. animals with seminal plugs or sperm/no. mated x 100)[1]

Fertility Index (no. animals with implants/no. of matings x 100)[1]

Gestation Length (if allowed to deliver)

Body Weight and Body Weight Change: Consideration of the maternal body weight change and/or adjusted (corrected) maternal body weight should be included in the evaluation of maternal toxicity whenever such data are available. The calculation of ~~a~~an adjusted (corrected) mean maternal body weight change, which is the difference between the initial and terminal body weight minus the gravid uterine weight (or alternatively, the sum of the weights of the foetuses), may indicate whether the effect is maternal or intrauterine. In rabbits, the body weight gain may not be useful indicators of maternal toxicity because of normal fluctuations in body weight during pregnancy.

Food and Water Consumption (if relevant)~~: The~~: The observation of a significant decrease in the average food or water consumption in treated dams compared to the control group may be useful in evaluating maternal toxicity, particularly when the test material is administered in the diet or drinking water. Changes in food or water consumption should be evaluated in conjunction with maternal body weights when determining if the effects

1 . It is recognised that this index can also be affected by the male.

noted are reflective of maternal toxicity or more simply, unpalatability of the test material in feed or water.

Clinical evaluations (including clinical signs, markers, haematology and clinical chemistry studies)~~: The~~: The observation of increased incidence of significant clinical signs of toxicity in treated dams relative to the control group may be useful in evaluating maternal toxicity. If this is to be used as the basis for the assessment of maternal toxicity, the types, incidence, degree and duration of clinical signs should be reported in the study. Examples of frank clinical signs of maternal intoxication include: coma, prostration, hyperactivity, loss of righting reflex, ataxia, or laboured breathing.

Post-mortem data~~: Increased~~: Increased incidence and/or severity of post-mortem findings may be indicative of maternal toxicity. This can include gross or microscopic pathological findings or organ weight data, e.g., absolute organ weight, organ-to-body weight ratio, or organ-to-brain weight ratio. When supported by findings of adverse histopathological effects in the affected organ(s), the observation of a significant change in the average weight of suspected target organ(s) of treated dams, compared to those in the control group, may be considered evidence of maternal toxicity.

Potency and cut-off doses

20. In the present scheme, the relative potency of a chemical to produce a toxic effect on reproduction is not included in the criteria for reaching a conclusion regarding classification. Nevertheless, during the development of this scheme it was suggested that cut-off dose levels should be included, in order to provide some means of assessing and categorising the potency of chemicals for the ability to produce an adverse effect on reproduction. This concept has not been readily accepted by all member countries because of concerns that any specified cut-off level may be exceeded by human exposure levels in certain situations, e.g. inhalation of volatile solvents, the level may be inadequate in cases where humans are more sensitive than the animal model, and because of disagreements about whether or not potency is a component of hazard.

21. There has been interest in this concept to further consider it as a future development of the classification scheme.

Limit dose

22. Member countries appear to be in agreement about the concept of a limit dose, above which the production of an adverse effect may be considered to be outside the criteria which lead to classification. However, there is disagreement between members regarding the inclusion within the criteria of a specified dose as a limit dose. Some Test Guidelines specify a limit dose, other Test Guidelines qualify the limit dose with a statement that higher doses may be necessary if anticipated human exposure is sufficiently high that an adequate margin of exposure would not be achieved. Also, due to species differences in toxicokinetics, establishing a specific limit dose may not be adequate for situations where humans are more sensitive than the animal model.

23. In principle, adverse effects on reproduction seen only at very high dose levels in animal studies (for example doses that induce prostration, severe inappetence, excessive mortality) would not normally lead to classification, unless other information is available, e.g. toxicokinetics information indicating that humans may be more susceptible than animals, to suggest that classification is appropriate. Please also refer to the section on Maternal Toxicity for further guidance in this area.

24. However, specification of the actual 'limit dose' will depend upon the test method that has been employed to provide the test results, e.g. in the OECD Test Guideline for repeated dose toxicity studies by the oral route, an upper dose of 1000 mg/kg unless expected human response indicates the need for a higher dose level, has been recommended as a limit dose.

Animal and experimental data

25. A number of internationally accepted test methods are available; these include methods for developmental toxicity testing (e.g., OECD Test Guideline 414, ICH Guideline S5A, 1993), methods for peri- and post-natal toxicity testing (e.g. ICH S5B, 1995) and methods for one or two-generation toxicity testing (e.g. OECD Test Guidelines 415, 416).

26. Results obtained from Screening Tests (e.g. OECD Guidelines 421 - Reproduction/Developmental Toxicity Screening Test, and 422 - Combined Repeated Dose Toxicity Study with Reproduction/Development Toxicity Screening Test) can also be used to justify classification, although it is recognised that the quality of this evidence is less reliable than that obtained full studies.

27. Adverse effects or changes, seen in short- or long-term repeated dose toxicity studies, which are judged likely to impair reproductive ability or capacity and which occur in the absence of significant generalised toxicity, may be used as a basis for classification, e.g. histopathological changes in the gonads.

28. Evidence from in vitro assays, or non-mammalian tests, and from analogous substances using structure-activity relationship (SAR), can contribute to the procedure for classification. In all cases of this nature, expert judgement must be used to assess the adequacy of the data. Inadequate data should not be used as a primary support for classification.

29. It is preferable that animal studies are conducted using appropriate routes of administration which relate to the potential route of human exposure. However, in practice, reproductive toxicity studies are commonly conducted using the oral route, and such studies will normally be suitable for evaluating the hazardous properties of the substance with respect to reproductive toxicity. However, if it can be conclusively demonstrated that the clearly identified mechanism or mode of action has no relevance for humans or when the toxicokinetic differences are so marked that it is certain that the hazardous property will not be expressed in humans then a substance which produces an adverse effect on reproduction in experimental animals should not be classified.

30. Studies involving routes of administration such as intravenous or intraperitoneal injection, which may result in exposure of the reproductive organs to unrealistically high levels of the test substance, or elicit local damage to the reproductive organs, e.g. by irritation, must be interpreted with extreme caution and on their own would not normally be the basis for classification.

CLASSIFICATION CRITERIA FOR MIXTURES

Classification of Mixtures ~~When Data~~When Data are Available for the Complete Mixture.

31. Classification of mixtures will be based on the available test data of the individual constituents of the mixture using cut-off values/concentration limits for the components of the mixture. The classification may be modified on a case-by case basis based on the available test data for the mixture as a whole. In such cases, the test results for the mixture as a whole must be shown to be conclusive taking into account dose and other factors such as duration, observations and analysis (e.g., statistical analysis, test sensitivity) of reproduction test systems. Adequate documentation supporting the classification should be retained and made available for review upon request.

Classification of Mixtures When Data are not Available for the Complete Mixture.

Bridging Principles

32. Where the mixture itself has not been tested to determine its reproductive toxicity, but there are sufficient data on the individual ingredients and similar tested mixtures to adequately characterise the hazards of the mixture, this data will be used in accordance with the following agreed bridging rules. This ensures that the classification process uses the available data to the greatest extent possible in characterising the hazards of the mixture without the necessity for additional testing in animals.

Dilution

33. If a mixture is diluted with a diluent which is not expected to affect the reproductive toxicity of other ingredients, then the new mixture may be classified as equivalent to the original mixture.

Batching

34. The reproductive toxicity potential of one production batch of a complex mixture can be assumed to be substantially equivalent to that of another production batch of the same commercial product produced by and under the control of the same manufacture unless there is reason to believe there is significant variation in composition such that the reproductive toxicity potential of the batch has changed. If the latter occurs, a new classification is necessary.

Substantially similar mixtures

35. Given the following:

a). Two mixtures: i.) A + B
ii.) C + B

b). The concentration ~~of Ingredient~~of Ingredient B, toxic to reproduction, is the same in both mixtures.

c). The concentration of ingredient A in mixture i equals that of ingredient C in mixture ii.

d). Data on toxicity for A and C are available and substantially equivalent, i.e. they are not expected to affect the reproductive toxicity of B.

If mixture (i) is already classified by testing, mixture (ii) can be assigned the same category

Classification of Mixtures When Data are Available for All Components or Only for Some Components of the Mixture.

36. The mixture will be classified as a reproductive toxin when at least one ingredient has been classified as a Category 1 or Category 2 reproductive toxicant and is present at or above the appropriate cut-off value/concentration limit as mentioned in Table 1 below for Category 1 and 2 respectively.

Table 1 : Cut-off values/concentration limits of ingredients of a mixture classified as reproductive toxicants that would trigger classification of the mixture.[1]

Ingredient **Classified as:**	**Cut-off/concentration limits triggering classification of a mixture as:**	
	Category 1 reproductive toxicant	**Category 2 reproductive toxicant**
Category 1 reproductive toxicant	≥ 0.1 % (note 1) ---------- ≥ 0.3 % (note 2)	
Category 2 reproductive toxicant		≥ 0.1 % (note 3)
		≥ 3.0 % (note 4)

Note 1: If a Category 1 reproductive toxicant is present in the mixture as an ingredient at a concentration between 0.1% and 0.3%, every regulatory authority would require information on the MSDS for a product. However, a label warning would be optional. Some authorities will choose to label when the ingredient is present in the mixture between 0.1% and 0.3%, whereas others would normally not require a label in this case.

Note 2: If a Category 1 reproductive toxicant reproductive toxicant is present in the mixture as an ingredient at a concentration of $\geq$ 0.3%, both an MSDS and a label would generally be expected.

Note 3: If a Category 2 reproductive toxicant is present in the mixture as an ingredient at a concentration between 0.1% and 3.0%, every regulatory authority would require information on the MSDS for a product. However, a label warning would be optional. Some authorities will choose to label when the ingredient is present in the mixture between 0.1% and 3.0%, whereas others would normally not require a label in this case.

Note 4: If a Category 2 reproductive toxicant is present in the mixture as an ingredient at a concentration of $\geq$ 3.0%, both an MSDS and a label would generally be expected.

[1] This compromise classification scheme involves consideration of differences in hazard communication practices in existing systems. Although it is recognised that this may result in a lack of harmonisation for some mixtures, the OECD Expert Group is recommending to the ILO Hazard Communication Work Group that this compromise be accepted as a way to move the process forward. It is expected that the number of affected mixtures will be small; the differences will be limited to label warnings; and the situation will evolve over time to a more harmonised approach. All of these hazard communication recommendations are subject to review by the ILO Work Group, and may be affected by that group's determinations regarding the possibility of using risk considerations in labelling in the consumer sector.

HAZARD COMMUNICATION

Allocation of Label Elements

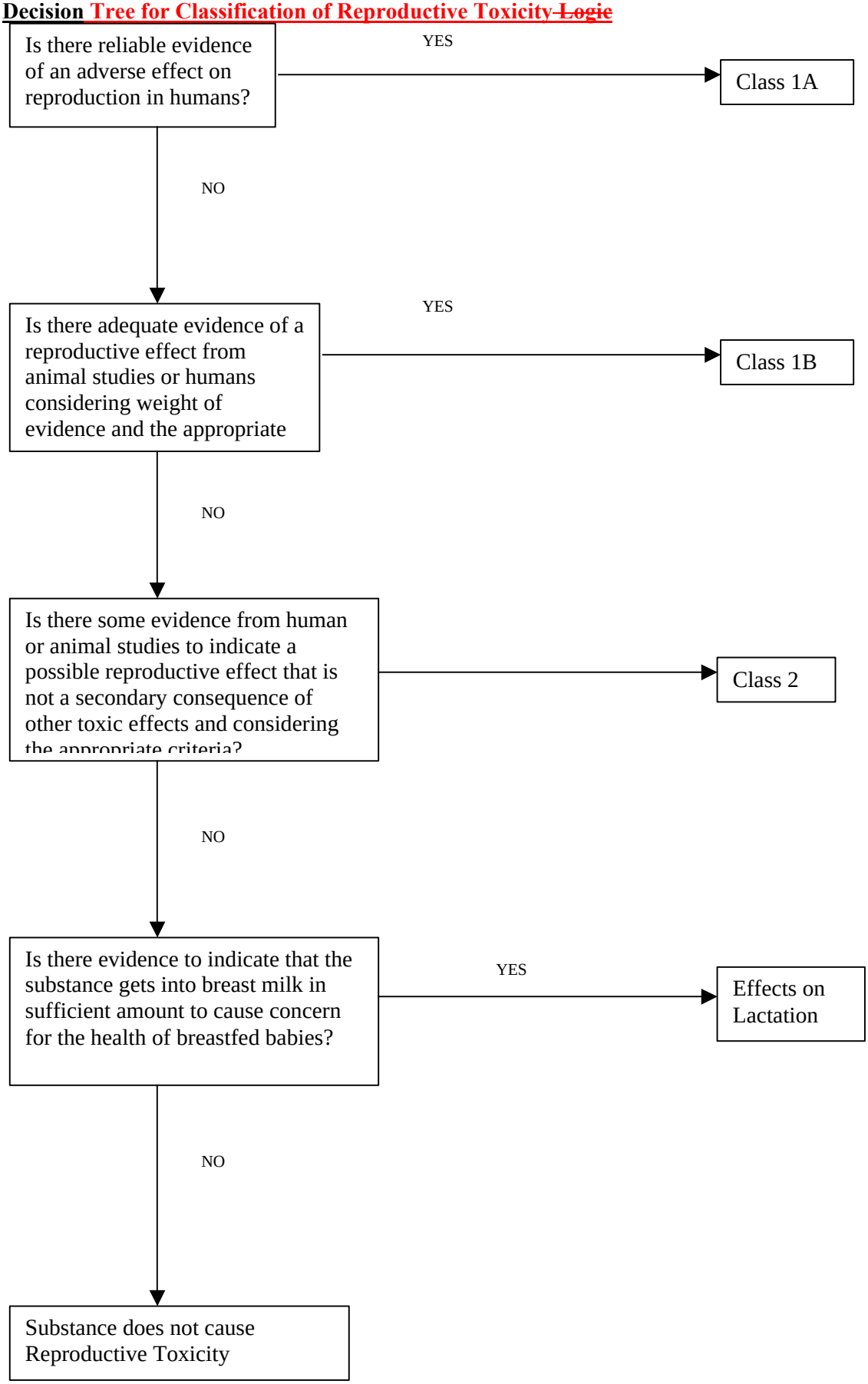
37. General and specific considerations concerning labelling requirements are provided in Chapter 4. Annex 5 contains examples of precautionary statements and pictograms which can be used where allowed by the competent authority. Additional reference sources providing advice on the use of precautionary information is also included.

Table 2: Label elements for Reproductive Toxicity

	Category 1A	**Category 1B**	**Category 2**	**Additional Category**
Symbol	New health hazard symbol	New health hazard symbol	New health hazard symbol	~~Effects on or via lactation~~
Signal Word	Danger	Danger	Warning	?
Hazard Statement	May damage fertility or the unborn child (state specific effect if known or route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)	May damage fertility or the unborn child (state specific effect if known or route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)	Suspected of damaging fertility or the unborn child (state specific effect if known or route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)	May cause harm to breast-fed children.

DECISION LOGIC AND GUIDANCE

Decision Tree for Classification of Reproductive Toxicity ~~Logic~~



Guidance

What Guidance extra do we need here since there is specifc guidance in the criteria?

~~SUMMARY TABLE~~Classification and Labelling Summary

Class	**Criteria**	**Hazard Communication Elements**	
Class 1A	Known human reproductive or developmental toxicant Mixtures ≥0.3 %	*Signal Word*	New heath hazard symbol
		Symbol	Danger
		Hazard Statement	May damage fertility or the unborn child (state specific effect if known or route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)
	Mixtures ≥0.1 % (Note 1)	*MSDS*	Hazard statement above
Class 1B	Presumed human reproductive or developmental toxicant Mixtures ≥0.3 %	*Signal Word*	New heath hazard symbol
		Symbol	Danger
		Hazard Statement	May damage fertility or the unborn child (state specific effect if known or route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)
	Mixtures ≥0.1 % (Note 1)	*MSDS*	Hazard statement above
Class 2	Suspected human reproductive or developmental toxicant Mixtures ≥3.0 %	*Signal Word*	New heath hazard symbol
		Symbol	Warning
		Hazard Statement	Suspected of damaging fertility or the unborn child (state specific effect if known or route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)
Additional Category	Effects on or via lactation	*Signal Word*	?
		Symbol	?
		Hazard Statement	May cause harm to breast-fed children.

Note 1: f a Category 1 reproductive toxicant is present in the mixture as an ingredient at a concentration between 0.1% and 0.3%, every regulatory authority would require information on the MSDS for a product. However, a label warning would be optional. Some authorities will choose to label when the ingredient is present in the mixture between 0.1% and 0.3%, whereas others would

EXAMPLES