

15 Carcinogenic Effects – Subclass 6.7

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15.1 General considerations

15.1.1 Carcinogenicity overview

See section 9.6 in [chapter 9](#) for definitions of the key terms used in this chapter.

The purpose of carcinogenicity studies is to observe test animals for the development of neoplastic lesions during or after prolonged and repeated exposure to various doses of a test substance. Exposure should occur by an appropriate route and encompass a major portion of the animal's life span. Carcinogenesis is considered a multi-stage phenomenon with direct and indirect effect on the genome leading to the development of cancerous cells. The predominant theory is that 'initiating' events, which directly mutate DNA, are needed to cause cells to become cancerous. This process can be accelerated by promotional factors that increase cell division or decrease the effectiveness of repair mechanisms. The entire phenomenon usually takes considerable time for all the necessary events to occur and the effects to manifest. Chemical carcinogens can have initiating and/or promoting properties.

Chronic studies also observe test animals after prolonged and repeated exposure for a major portion of their life span, but determine effects that require a long latent period or are cumulative to become manifested. These studies generate data to identify the majority of chronic effects and to determine dose–response relationships for general toxicity, including neurological, physiological, and biochemical effects and exposure-related, morphological effects. The endpoints identified in chronic studies are considered as specific target organ effects (see [chapter 17](#)).

Some studies are designed to detect both carcinogenic and chronic effect endpoints.

15.1.2 Weight of evidence

The best quality data should be used as the fundamental basis for classification. Preferably, classification should be based on primary data sources. It is essential that test conditions be clearly and completely articulated.

Data from internationally harmonised test methods are preferred for classification under this subclass. Data should preferably be derived using Organisation for Economic Co-operation and Development Test Guidelines or equivalent, according to the principles of Good Laboratory Practice. When such data are not available, classification should be based on the best available data using a weight-of-evidence approach.

See section 1.3 in [chapter 1](#) for information about assessing data quality. See [Appendix 15A](#) for a detailed list of acceptable test methods for carcinogenicity.

15.2 Carcinogenicity threshold and classification criteria

15.2.1 Carcinogenicity threshold criteria

Schedule 4 to the Hazardous Substances (Minimum Degrees of Hazard) Regulations 2001 states:

2 Minimum degrees of hazard

- (1) A substance with toxic properties is not hazardous for the purposes of the Act unless—
...
 - (p) reliable information for the substance indicates to an expert that exposure to the substance causes the development of cancer or an increase in the incidence of benign or malignant tumours in an organ or an organism.

15.2.2 Carcinogenicity classification criteria

Schedule 4 to the Hazardous Substances (Classification) Regulations 2001 identifies two classification categories for substances that are carcinogenic (subclass 6.7).

- *Category 6.7A – substances that are known or presumed human carcinogens*
 - (a) A substance for which data indicate sufficient evidence in humans of a causal relationship between exposure to the substance and the development of cancer in humans.
 - (b) A substance for which data indicate sufficient evidence in animals of a causal relationship between exposure to the substance and an increased incidence of tumours.
 - (c) A substance for which data indicate:
 - (i) limited evidence in humans of a positive correlation between exposure to the substance and the development of human cancer; and
 - (ii) limited evidence in animals that exposure to the substance may lead to an increased incidence of tumours.
- *Category 6.7B – substances that are suspected human carcinogens:*

A substance for which data indicate limited evidence in humans or limited evidence in animals that exposure to the substance may lead to the development of cancer or an increased incidence of tumours, where the strength and weight of the evidence indicate to an expert that the evidence is not sufficient to classify the substance in hazard classification 6.7A.

The classification criteria above are based on the Globally Harmonised System for Classification and Labelling of Chemicals (GHS) (United Nations, 2007). See [Appendix 15B](#) for a comparison of the HSNO Act criteria with those of the GHS. See

[Appendix 15C](#) for comparisons with the EU and other jurisdictions' criteria for carcinogenicity.

'Evidence' in carcinogenicity studies involves the enumeration of tumours in human and animal studies and determination of their level of statistical significance. Sufficient human evidence demonstrates causality between human exposure and the development of cancer, whereas sufficient evidence in animals shows a causal relationship between the agent and an increased incidence of tumours. Limited evidence in humans is demonstrated by a positive association between exposure and cancer, but a causal relationship cannot be stated. Limited evidence in animals is provided when data suggest a carcinogenic effect, but are less than sufficient. See also the definitions in section 9.6 in [chapter 9](#).

Assignment to either category 6.7A or 6.7B depends on the strength of the evidence and the weight of evidence obtained from human and/or animal studies.

Classify as category 6.7A (known human carcinogen), if evidence from human data showing a causal relationship between human exposure and the development of cancer in which chance, bias, and confounding could be ruled out with reasonable confidence. The existence of a causal relationship would be any of:

- an increased incidence of one or more cancer types in an exposed population in comparison with a non-exposed population;
- evidence of dose–time–response relationships; that is, an increased cancer incidence associated with higher exposure levels or with increasing exposure duration;
- an association between exposure and increased risk observed in more than one study;
- a demonstration of a decline in risk after reduction of exposure; and
- the specificity of any association, defined as an increased occurrence of cancer at one target organ or of one morphological type.

Classify as category 6.7A (presumed human carcinogen), if:

- evidence from animal data establishes a causal relationship between the substance and an increased incidence of malignant neoplasms or an appropriate combination of benign and malignant neoplasms, in two or more species of animal or in two or more independent studies in one species carried out at different times or in different laboratories or under different protocols; or
- a single study in one animal species establishes that malignant neoplasms occur to an unusual degree with regard to incidence, site, type of tumour, or age at onset.

Evidence of mutagenic activity *in vivo* may indicate that a substance has a potential for carcinogenic effects.

Classify as category 6.7B (suspected human carcinogen), if:

- evidence obtained from human data shows a positive association between exposure to the substance and cancer, but chance, bias, or confounding could not be ruled out with reasonable confidence;
- evidence obtained from animal data suggests a carcinogenic effect, but the evidence is not sufficiently convincing to place the substance in category 6.7A; for example:
 - the evidence of carcinogenicity is restricted to a single experiment;
 - carcinogenic effects occur only at very high dose levels exceeding the maximal tolerated dose (which is characterised by toxic effects that, although not yet reducing lifespan, go along with physical changes such as about a 10% retardation in weight gain);
 - the appearance of tumours, especially at high dose levels, only in particular organs of certain species known to be susceptible to a high spontaneous tumour formation; and
 - the appearance of tumours only at the site of application in very sensitive test systems (for example, intraperitoneal or subcutaneous application of certain locally active compounds), if the particular target is relevant to humans;
- questions are unresolved regarding the adequacy of the design, conduct, or interpretation of the study; for example:
 - the existence of a secondary mechanism of action with the implication of a practical threshold above a certain dose level (for example, hormonal effects on target organs or on mechanisms of physiological regulation or chronic stimulation of cell proliferation); and
 - the existence of a species-specific mechanism of tumour formation (for example, by specific metabolic pathways) irrelevant for humans;
- the substance increases the incidence only of benign neoplasms or lesions of uncertain neoplastic potential, or of certain neoplasms that may occur spontaneously in high incidences in certain strains; or
- there is a lack of genotoxicity in short-term tests *in vivo* and *in vitro*.

Do not assign a classification for carcinogenicity, if the:

- mechanism(s) of experimental tumour formation is/are clearly identified, with good evidence that such mechanism(s) cannot be extrapolated to humans for each tumour;
- only available tumour data are liver tumours in certain sensitive strains of mice (for example, B6C3F1 mice), without any other supplementary evidence; or
- only available tumour data are neoplasms at sites and in strains where they are well known to occur spontaneously with a high incidence.

15.3 Additional considerations for carcinogenicity classification

Some of the criteria discussed in section [15.2](#) are complex and require expert judgement and a weight-of-evidence assessment as set out below.

Beyond the determination of the strength of evidence for carcinogenicity, other factors should be considered that influence the overall likelihood that an agent may pose a carcinogenic hazard in humans. The full list of factors that influence this determination is lengthy, but the most important ones are considered here.

The factors can increase or decrease the level of concern for human carcinogenicity. The relative emphasis accorded to each factor depends on the amount and coherence of evidence bearing on each. Generally there is a requirement for more complete information to decrease, rather than increase, the level of concern. Additional considerations should be used in evaluating the tumour findings and the other factors in a case-by-case manner.

Important factors that may be taken into consideration when assessing the overall level of concern include:

- tumour type and background incidence (see section [15.3.5](#));
- multi-site responses;
- the progression of lesions to malignancy; and
- reduced tumour latency.

Additional factors that may increase or decrease the level of concern include:

- whether responses are in a single sex or both sexes (see section [15.3.3](#));
- whether responses are in a single or several species (see section [15.3.2](#));
- whether there is structural similarity with a chemical for which there is good evidence of carcinogenicity;
- the routes of exposure (certain chemicals can cause carcinogenicity through a specific route of exposure; for example, crystalline silica is a known human carcinogen when inhaled as a fine respirable dust);
- a comparison of absorption, distribution, metabolism, and excretion between test animals and humans;
- the possibility of a confounding effect of excessive toxicity at test doses (see section [15.3.4](#)); and
- the mode of action and its relevance for humans, such as mutagenicity, cytotoxicity with growth stimulation, mitogenesis, and immunosuppression (see section [15.3.6](#)).

15.3.1 Mode of action

Mode of action in and of itself, or a consideration of comparative metabolism, should be evaluated on a case-by-case basis, and is part of an analytic evaluative approach. Any mode of action must be looked at closely in animal experiments, taking into consideration comparative toxicokinetics and toxicodynamics between the animal test

species and humans to determine the relevance of the results to humans. This may lead to the possibility of discounting very specific effects of certain types of chemical. Life stage-dependent effects on cellular differentiation may also lead to qualitative differences between animals and humans. Only if a mode of action of tumour development is conclusively determined not to be operative in humans, may the carcinogenic evidence for that tumour be discounted. However, a weight-of-evidence evaluation for a substance calls for any other tumorigenic activity to be evaluated as well.

15.3.2 Response in multiple animal experiments

Positive responses in several species add to the weight of evidence that a chemical is a carcinogen. Taking into account the factors listed in section [15.3](#), chemicals with positive outcomes in two or more species would provisionally be classified 6.7A, until the human relevance of animal results is assessed. It should be noted, however, that positive results for one species in at least two independent studies, or a single positive study showing unusually strong evidence of malignancy, may also lead to a 6.7A classification. Consideration should also be given to evidence of mutagenic activity *in vivo*.

15.3.3 Responses in one sex or both sexes

Any case of sex-specific tumours should be evaluated in light of the total tumorigenic response to the substance observed at other sites (multi-site responses or incidence above background) in determining the carcinogenic potential of the substance.

If tumours are seen only in one sex of one animal species, the mode of action should be carefully evaluated to see if the response is consistent with the postulated mode of action. Effects seen in only one sex in a test species may be less convincing than effects seen in both sexes, unless there is a clear patho-physiological difference consistent with the mode of action to explain the single-sex response.

15.3.4 Confounding effects of excessive toxicity or localised effects

Tumours occurring only at excessive doses associated with severe toxicity generally have doubtful potential for carcinogenicity in humans. In addition, tumours occurring only at sites of contact and/or only at excessive doses need to be carefully evaluated for human relevance for carcinogenic hazard. For example, forestomach tumours in rats, following administration by gavage of an irritating or corrosive, non-mutagenic chemical may be of questionable relevance. However, such determinations must be evaluated carefully in justifying the carcinogenic potential for humans; any occurrence of other tumours at distant sites must also be considered.

15.3.5 Tumour type, reduced tumour latency

Unusual tumour types or tumours occurring with reduced latency may add to the weight of evidence for the carcinogenic potential of a substance, even if the tumours are not statistically significant.

Toxicokinetic behaviour is normally assumed to be similar in animals and humans, at least from a qualitative perspective. On the other hand, certain tumour types in animals

may be associated with toxicokinetics or toxicodynamics that are unique to the animal species tested and may not be predictive of carcinogenicity in humans. Very few such examples have been agreed internationally. However, one example is the lack of human relevance of kidney tumours in male rats associated with compounds causing α 2 μ -globulin nephropathy (Capen et al, 1999). Even when a particular tumour type may be discounted, expert judgement must be used in assessing the total tumour profile in any animal experiment.

15.3.6 Mutagenicity

It is recognised that genetic events are central in the overall process of cancer development. Therefore, evidence of mutagenic activity *in vivo* may indicate that a chemical has a potential for carcinogenic effects.

15.3.7 Other considerations

The following additional considerations apply to classification of chemicals into either category 6.7A or 6.7B. A chemical that has not been tested for carcinogenicity may in certain instances be classified in 6.7A or 6.7B based on tumour data from a structural analogue together with substantial support from consideration of other important factors such as formation of common significant metabolites, for example, for benzidine congener dyes.

The classification should also take into consideration whether the chemical is absorbed by a given route(s), or whether there are only local tumours at the site of administration for the tested route(s), and adequate testing by other major route(s) show a lack of carcinogenicity.

It is important that whatever is known of the physico-chemical, toxicokinetic and toxicodynamic properties of the substances, as well as any available relevant information on chemical analogues, that is, the structure activity relationship, is taken into consideration when undertaking classification.

15.4 Classification of mixtures

15.4.1 Classification of mixtures when data are available for the complete mixture

The classification of mixtures is based on the available test data of the individual ingredients of the mixture using cut-off values or concentration limits for those ingredients. 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 (for example, statistical analysis and test sensitivity) of carcinogenicity test systems.

15.4.2 Classification of mixtures when data are not available for the complete mixture: bridging principles

When the mixture itself has not been tested to determine its carcinogenic hazard, but there are sufficient data on the individual ingredients and similar tested mixtures to adequately characterise the hazards of the mixture, these data will be used in accordance with the following agreed bridging rules. This ensures the classification process uses the available data to the greatest extent possible in characterising the hazards of the mixture without needing additional testing in animals.

(a) Dilution

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

(b) Batching

The carcinogenic 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 manufacturer, unless there is reason to believe there is significant variation in composition such that the carcinogenic potential of the batch has changed. If the latter occurs, a new classification is necessary.

(c) Substantially similar mixtures

Given:

- (i) two mixtures: (A + B) and (C + B);
- (ii) the concentration of carcinogenic ingredient B is the same in both mixtures;
- (iii) the concentration of ingredient A in mixture (A + B) equals that of ingredient C in mixture (C + B); and
- (iv) data on toxicity for ingredients A and C are available and substantially equivalent; that is, they are in the same hazard category and are not expected to affect the carcinogenicity of ingredient B; then

if mixture (A + B) has already been classified by testing, mixture (C + B) can be assigned the same category.

(d) Aerosols

A hazard classification may be assigned for carcinogenicity for aerosol products. The classification should also take into account the propellant in the aerosol.

15.4.3 Classification of mixtures when data are available for all or some ingredients of the mixture

The mixture will be classified as a carcinogen when at least one ingredient has been classified as a 6.7A or 6.7B carcinogen and is present at or above the appropriate cut-off value or concentration limit as shown in [Table 15.1](#) for 6.7A and 6.7B respectively.

Table 15.1: Cut-off values or concentration limits of ingredients

Ingredient classified as category	Cut-off values or concentration limits triggering classification of a mixture as category	
	6.7A	6.7B
6.7A carcinogen	≥ 0.1%	–
6.7B carcinogen	–	≥ 0.1%

Note: The hazard cut-off values or concentration limits in the table apply to solids and liquids (by weight) as well as gases (by volume).

The generic hazard cut-off values or concentration limits do not apply if it can be shown that the substance causes a carcinogenic hazard that will be evident below the generic hazard cut-off values or concentration limits.

References

Capen, CC, Dybing, E, Rice, JM, Wilbourn, JD (eds.) 1999. *Species Differences in Thyroid, Kidney and Urinary Bladder Carcinogenesis*, Scientific Publication 147. International Agency for Research on Cancer.

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Appendix 15A: Acceptable test methods for carcinogenicity

15A.1 Introduction

Most of the guidelines mentioned in this appendix are found in compilations from the organisation issuing them. The guidelines listed below are not exclusive. If data have been generated using other valid international guidelines, then the results from those tests may also be applicable.

The main references to international guidelines referred to in this appendix are as follows.

- European Commission (EC) guidelines:
European Commission 1996. *Classification, Packaging and Labelling of Dangerous Substances in the European Union. Part 2 – Testing Methods*. <http://ecb.jrc.it/testing-methods> Retrieved 14 August 2007.
- Organisation for Economic Co-operation and Development (OECD) guidelines:
OECD 1993. *OECD Guidelines for the Testing of Chemicals*. Organisation for Economic Co-operation and Development, Paris, with regular updates. http://www.oecd.org/document/40/0,3343,en_2649_34377_37051368_1_1_1_1,00.html Retrieved 14 August 2007.
- United States Environmental Protection Agency (USEPA) Office of Prevention, Pesticides and Toxic Substances (OPPTS) guidelines:
USEPA 2007. *Harmonized Test Guidelines*. United States Environmental Protection Agency. <http://www.epa.gov/opptsfrs/home/guidelin.htm> Retrieved 14 August 2007.

15A.2 Carcinogenicity test guidelines

The guidelines in [Table 15A.1](#) are primarily relevant to substances that are, or solely contain, chemical substances. However, the Hazardous Substances and New Organisms Act 1996 also covers biopesticides that include micro-organisms. More specialised test methods may be required to adequately characterise the potential effects of biopesticides in mammals.

For testing microbial biopesticides, see the USEPA website for specific tests.

- USEPA 2007. *OPPTS Harmonized Test Guidelines: Series 885 Microbial Pesticide Test Guidelines – Final Guidelines*. Office of Prevention, Pesticides and Toxic Substances, United States Environmental Protection Agency. http://www.epa.gov/opptsfrs/publications/OPPTS_Harmonized/885_Microbial_Pesticide_Test_Guidelines/Series Retrieved 14 August 2007.

See also [Table 15A.1](#).

Table 15A.1: Carcinogenicity test guidelines for chemicals

Test protocols	Test guideline		
	OECD	EC	USEPA OPPTS
Carcinogenicity	451	EC B.32 Carcinogenicity test	870.4200
Combined chronic toxicity and carcinogenicity	453	EC B.33 Combined chronic toxicity/carcinogenicity test	870.4300

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Appendix 15B: Comparison of Globally Harmonized System of Classification and Labelling of Chemicals and HSNO Act carcinogenicity hazard classification

[Table 15B.1](#) displays the carcinogenicity categories from the Globally Harmonized System of Classification and Labelling of Chemicals (United Nations, 2007) and the Hazardous Substances and New Organisms Act 1996 (HSNO Act) equivalent.

Table 15B.1: Comparison of Globally Harmonized System of Classification and Labelling of Chemicals and HSNO Act carcinogenicity hazard classification

GHS carcinogenicity classification	HSNO Act equivalent category*
<p>Category 1: Known or presumed human carcinogens</p> <p>The placing of a chemical in category 1 is done on the basis of epidemiological and/or animal data. An individual chemical may be further distinguished.</p> <ul style="list-style-type: none"> • <i>Category 1A:</i> Known to have carcinogenic potential for humans; the placing of a chemical is largely based on human evidence. • <i>Category 1B:</i> Presumed to have carcinogenic potential for humans; the placing of a chemical is largely based on animal evidence. <p>Based on the strength of evidence together with additional considerations, such evidence may be derived from human studies that establish a causal relationship between human exposure to a chemical and the development of cancer (known human carcinogen).</p> <p>Alternatively, evidence may be derived from animal experiments for which there is sufficient evidence to demonstrate animal carcinogenicity (presumed human carcinogen).</p> <p>In addition, on a case-by-case basis, scientific judgement may warrant a decision of presumed human carcinogenicity derived from studies showing limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals.[†]</p> <p><i>Classification:</i> Category 1 (A and B) carcinogen.</p>	6.7A
<p>Category 2: Suspected human carcinogens</p> <p>The placing of a chemical in category 2 is done on the basis of evidence obtained from human and/or animal studies, but which is not sufficiently convincing to place the chemical in category 1. Based on the strength of evidence together with additional considerations, such evidence may be from limited evidence of carcinogenicity in human studies or from limited evidence of carcinogenicity in animal studies.</p> <p><i>Classification:</i> Category 2 carcinogen</p>	6.7B

Notes

- * The GHS (United Nations, 2007) proposes a distinction between known (class 1A) and presumed (class 1B) human carcinogens. The HSNO Act classification system groups these two subclasses under the same category (6.7A).
- † The GHS (United Nations, 2007) wording differs from that in the regulations made under the HSNO Act in that it assigns classification in this category on a case-by-case basis where expert judgement considers there is limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals. The wording in the HSNO Act regulations separates these two data sources. The GHS wording, based on expert judgement of these two data sources together, will result in a category 6.7A classification. If they occur separately, then the classification is category 6.7B.

References

United Nations 2007. *The Globally Harmonized System of Classification and Labelling of Chemicals (GHS)*, 2nd revised edition. United Nations, Geneva.

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Appendix 15C: Comparison of European Union carcinogenicity risk phrases with HSNO Act carcinogenicity classifications

The European Union (EC, 1967) risk phrases are converted into the equivalent Hazardous Substances and New Organisms Act 1996 (HSNO Act) classification in [Table 15C.1](#). Note that some cut-off values are not totally aligned with the HSNO Act classification categories. This is noted in the table, and for classification purposes a precautionary approach is advocated such that the higher hazard category is assigned.

Table 15C.1: Comparison of European Union acute toxicity risk phrases with HSNO Act carcinogenicity classifications

European Union risk phrases	HSNO Act equivalent category
Carcinogens	
Substances are determined to be hazardous due to carcinogenic effects if they fall into one of the following categories:	
<ul style="list-style-type: none"> Category 1: Substances known to be carcinogenic to humans. 	6.7A
<ul style="list-style-type: none"> Category 2: Substances that should be regarded as if they are carcinogenic to humans. 	6.7A
<ul style="list-style-type: none"> Category 3: Substances that cause concern for humans owing to possible carcinogenic effects but in respect of which the available information is not adequate for making a satisfactory assessment. 	6.7B
<hr/>	
<i>Category 1</i>	6.7A
Substances are determined to be hazardous and classified as Toxic (T) and assigned risk phrase R45 or R49 in accordance with the criteria given below.	
<i>R45 May cause cancer</i>	
<i>R49 May cause cancer by inhalation</i>	
A substance is included in category 1, if there is sufficient evidence to establish a causal association between human exposure and the development of cancer on the basis of epidemiological data.	
<hr/>	
<i>Category 2</i>	6.7A
Substances are determined to be hazardous and classified as Toxic (T) and assigned risk phrase R45 or R49 in accordance with the criteria given below.	
<i>R45 May cause cancer</i>	
<i>R49 May cause cancer by inhalation</i>	
A substance is included in category 2, if there is sufficient evidence, on the basis of appropriate long-term animal studies or other relevant information, to provide a strong presumption that human exposure to that substance may result in cancer developing.	
<hr/>	
<i>Category 3</i>	6.7B
Substances are determined to be hazardous and classified as Harmful (Xn) and assigned risk phrase R40 in accordance with the criteria given below.	
<i>R40 possible risk of irreversible effects</i>	
A substance is included in category 3 if there is some evidence from appropriate animal studies that human exposure can result in the development of cancer, but this evidence is insufficient to place the substance in category 2.	
Category 3 comprises two subcategories.	
<ul style="list-style-type: none"> Substances that are well investigated, but for which the evidence of a tumour-inducing effect is insufficient for classification in category 2. Additional experiments would not be expected to yield further relevant information with respect to classification. Substances that are insufficiently investigated. The available data are inadequate, but they raise concern for humans. This classification is provisional; further experiments are necessary before a final decision can be made. 	

Source: EC (1967).

References

- EC 1967. General classification and labelling requirements for dangerous substances and preparations. *Council Directive 67/548/EEC of 27 June 1967 on the Approximation of Laws, Regulations and Administrative Provisions Relating to the Classification, Packaging and Labelling of Dangerous Substances*. European Commission, Annex VI.
http://ec.europa.eu/environment/dansub/consolidated_en.htm.

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Appendix 15D: Comparison of HSNO Act classifications with other carcinogenicity classifications

[Table 15D.1](#) compares Hazardous Substances and New Organisms Act 1996 (HSNO Act) classifications with other carcinogenicity classifications.

Table 15D.1: HSNO Act classifications compared with other carcinogenicity classifications

HSNO Act category	USEPA	IARC	NTP	OSHA	EU risk phrase
6.7A	(Group A) Human carcinogen	(Group 1) Carcinogenic to humans	Human carcinogen	Category I	R45 R49
	(Group B1, B2) Probable human carcinogen	(Group 2A) Probably carcinogenic to humans	Reasonably anticipated to be a carcinogen	Category II	R45 R49
6.7B	(Group C) Possible human carcinogen	(Group 2B) Possibly carcinogenic to humans			R40
No	(Group D) Not classifiable as to human carcinogenicity	(Group 3) Not classifiable as to human carcinogenicity			
	(Group E) Evidence of non-carcinogenicity for humans	(Group 4) Probably not carcinogenic to humans			

Notes

- EU = European Union; IARC = International Agency for Research on Cancer; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; USEPA = United States Environmental Protection Agency.
- This table is only a guideline, so should not be used to overrule a classification based on the best available human or animal data.