

# Changes in the Classification of Carcinogenic Chemicals in the Work Area

## MAK Value Documentation, supplement – Translation of the German version from 2021

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## Abstract

According to the criteria of the MAK Commission, carcinogenic substances for which a MAK or BAT value can be derived are classified in Carcinogen Category 4 or 5 if their mechanism of action is known and their contribution to the cancer risk for humans is considered to be nonexistent or very low if the MAK or BAT value is observed. To date, substances that in general fulfill these criteria but for which there are not enough data available to derive a MAK or BAT value have been assigned to Category 3 A to indicate this gap in the dataset. Since the introduction of Carcinogen Category 3 A in 2000, however, the substances classified in this category have frequently been misinterpreted in practice as only “suspected of being carcinogenic”. Therefore, Category 3 A has been removed from the classification system and the substances have been reassigned to Carcinogen Category 1 or 2 and given the annotation “Prerequisite for Category 4 (or 5) in principle fulfilled, but insufficient data available for the establishment of a MAK or BAT value” in the List of MAK and BAT Values. Category 3 B for substances suspected of being carcinogenic has been renamed Category 3.

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## Changes in Carcinogen Category 3

New criteria for the classification of carcinogenic substances in the work area were adopted by the Commission in 1998 (Greim 1999); further definitions were elaborated by the supplements published in 2000 and 2006 (Greim 2000, 2006, available in German only). According to these criteria, carcinogenic substances in the work area are assigned to Carcinogen Categories 4 or 5 if these substances do not or only marginally contribute to the cancer risk for humans if exposure remains within the limits established by the MAK or BAT values.

However, this means that substances may only be classified in Categories 4 or 5 if the derivation of a MAK or BAT value is possible. In the past, if this was not possible, the substances were classified in Category 3A to draw attention to the lack of data and to encourage the generation of relevant data.

Since Category 3A was introduced in 2000, however, these criteria have often been misinterpreted in practice with respect to the carcinogenic effects induced by the substances classified in this category. These substances have a carcinogenic potential, but their mechanism of action suggests the existence of a “no adverse effect level” (NAEL), or dose or concentration at which the substance does not induce adverse effects. However, the available data do not allow the derivation of a MAK value. Category 3A has been discontinued to avoid these substances being interpreted merely as “suspected carcinogens”. The substances previously classified in this category have been re-evaluated and assigned to one of the other carcinogen categories or removed from the carcinogen categories on the basis of new findings relating to the relevance of specific types of tumours or other adverse effects. Examples of substances that were re-classified or taken out of Carcinogen Category 3A are “Dichloroacetic acid and its salts” (Hartwig and MAK Commission 2021) and “Nitrilotriacetic acid and its sodium salts” (Hartwig and MAK Commission 2022 b), which have been re-classified in Carcinogen Category 4, or “Cresol (all isomers)” (Hartwig and MAK Commission 2022 a), which is no longer considered a carcinogenic substance.

In future, carcinogenic substances of Categories 1 or 2 for which the existence of a NAEL for carcinogenic effects may be assumed on the basis of their mechanism of action, but for which a MAK value cannot be derived for lack of sufficient data, will be listed in Section II and III of the List of MAK and BAT Values with the annotation “*Prerequisite for Category 4 (or 5) in principle fulfilled, but insufficient data available for the establishment of a MAK or BAT value*”.

Substances suspected of inducing carcinogenic effects, but for which no definite conclusions about a possible carcinogenic potential can be drawn because of an overall lack of data, shall remain in the former Category 3B for suspected carcinogens. This category has now been renamed Category 3:

### Category 3:

**Substances that give cause for concern because there is evidence of carcinogenicity or a potential for inducing carcinogenic effects, but no definite conclusions can be drawn for lack of sufficient information. This is a provisional classification.**

**After reviewing all of the available data, the evidence suggests a carcinogenic effect. However, the evidence is not strong enough to classify the substance in a different category. A final assessment can only be made after further studies have been performed. A MAK or BAT value may be derived if the substance or its metabolites do not cause genotoxic effects or the genotoxic effects are not the primary effects.**

## Notes

### Competing interests

The established rules and measures of the Commission to avoid conflicts of interest ([www.dfg.de/mak/conflicts\\_interest](http://www.dfg.de/mak/conflicts_interest)) ensure that the content and conclusions of the publication are strictly science-based.

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