

INSTRUCTIONS TO AUTHORS

The Nordic Expert Group for Criteria documentation
of Health Risks from Chemicals
(NEG)

<http://www.nordicexpertgroup.org>

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Instructions to authors

Introduction

A NEG criteria document is a risk assessment report. The document aims at establishing dose-effect and dose-response relationships, and at defining a critical effect and its NO(A)EL and LO(A)EL based on the scientific literature. The data are presented in such a way that they can serve as a scientific basis for setting occupational exposure limits.

To facilitate international use the NEG documents are written in English. However, a short summary in a Danish/Norwegian/Swedish is added, reflecting the origin of the author.

Procedure

The elaboration of a NEG criteria document proceeds in several consecutive steps:

1. Author writes first draft
2. Draft is reviewed by NEG and discussed with author
3. The draft, or more likely a revised version, is accepted for publication.
4. The author's fee is paid.
5. The NEG secretariat and the author finalise the document.
6. The author prepares a short summary draft in a more popular style
7. The author delivers copies of the cited literature to the NEG secretariat.
8. The document is published in *Arbete och Hälsa*
9. The short popular summary is published on www.nordicexpertgroup.org together with a link to a downloadable version of the document.

The author is responsible for the content and quality of the document. If desired, the secretariat can assist in the search and retrieval of literature. The draft document is carefully reviewed and discussed in depth at one or several NEG meetings. The author is expected to participate during these meetings. A draft document that is thoroughly prepared according to the instructions will increase the efficacy and speed of the review process.

Literature search

Databases to be searched include Medline, TOXNET, NIOSHTIC and HSELINE. Information from other sources regarded as reliable and relevant is also used (see below).

Cited literature

The document should as far as possible make use of peer-reviewed scientific publications. This means that e.g. industry reports and conference abstracts should not be cited. The following exceptions are accepted:

1. Handbooks (e.g. Patty's Industrial Hygiene and Toxicology), encyclopaedias, text books and other sources regarded to be of good quality may be used for secondary information, i.e. substance identification, properties, occurrence, exposure data, etc (chapters 2-5, see below)
2. Scientific reviews, criteria documents, and risk assessments reports (from e.g. WHO, NIOSH and the Dutch Expert Committee on Occupational Standards) regarded to be of good quality may replace original papers, since this reduces the amount of duplicate work, the length of the text, and the number of references. However, original references must always be given to studies critical for the final evaluation and conclusion.

In some cases the critical studies have not been published in peer-reviewed journals. The inclusion of such "unpublished" studies is a case-by-case decision, taken after careful discussions in the NEG. In such a case, it should be clearly stated that the referred study has not undergone peer-review prior to publication.

Units and abbreviations

Units should be consistently used throughout the document. NEG recommends the use of ppm (mg/m^3) for air levels, else e.g. mg/kg , $\mu\text{g}/\text{l}$ or μM . Other sub-units may be more practical in some instances, use common sense. For metal compounds give doses, air and tissue levels for the metal, not the compound. Avoid ppm for water and food intake.

Abbreviations should be introduced the first time they appear in the text and should thereafter be used consistently throughout the document. Avoid excessive use of abbreviations. If an expression is used only a few times it may be better not to introduce an abbreviation.

The NEG review process

The review by the NEG primarily focuses on the clarity and logic of the presentation, i.e. that the information is given:

- in the proper chapter according to the document format
- in a logical order, in a way that is reasonably easy to understand
- adequately and concisely, i.e. with the necessary information but no unnecessary details or repetitions
- with proper referencing.

The NEG also checks that the evaluations and conclusions in chapters 12-14 are derived from the basic information given in the previous chapters. Questions relating to the interpretation of the cited papers often arise during the discussions, or the author may hesitate on how to interpret a study. The author shall therefore bring the referenced papers to the NEG meeting.

Following acceptance by the NEG, the NEG secretariat in collaboration with the author finalises the draft document according to the specifications given by the scientific serial Arbete och Hälsa.

Document format

The table of contents of the NEG documents is very similar to e.g. the content lists of the European documents. The different chapters of the document normally have the following heading. Chapters and headings may need to be added or deleted for particular purposes, e.g. interactions.

1. Introduction
2. Substance identification
3. Physical and chemical properties
4. Occurrence, production and use
5. Measurements and analysis of workplace exposure
6. Occupational exposure data
7. Toxicokinetics
 - 7.1 Uptake
 - 7.2 Distribution
 - 7.3 Biotransformation
 - 7.4 Excretion
8. Biological monitoring
9. Mechanism of toxicity
10. Effects in animals and in vitro studies
 - 10.1 Irritation and sensitisation
 - 10.2 Effects of single exposure
 - 10.3 Effects of short-term exposure (up to 90 days)
 - 10.4 Mutagenicity and genotoxicity
 - 10.5 Effects of long-term exposure and carcinogenicity
 - 10.6 Reproductive and developmental studies
 - 10.7 Other studies
11. Observations in man
 - 11.1 Irritation and sensitisation
 - 11.2 Effects of single and short-term exposure
 - 11.3 Effects of long-term exposure
 - 11.4 Genotoxic effects
 - 11.5 Carcinogenic effects
 - 11.6 Reproductive and developmental effects
12. Dose-effect and dose-response relationships
 - 12.1 Single/short-term exposures
 - 12.2 Long-term exposures
13. Previous evaluations by national and international bodies
14. Evaluation of human health risks
 - 14.1 Assessment of health risks
 - 14.2 Groups at extra risk
 - 14.3 Scientific basis for an occupational exposure limit
15. Research needs

16. Summary
 17. Summary in Danish/Norwegian/Swedish
 18. References
 19. Data bases used in the search for literature
- Appendix with occupational exposure limits (when applicable)

The author is advised to check several recent NEG criteria documents to get a feeling for how to arrange his/her own document.

1. Introduction

The reasons for writing the document are presented.

2. Substance identification

CAS-number(s), the chemical formula, molecular weight, common synonyms, etc are given, if available.

3. Physical and chemical properties

Most of the data are given in a tabular form. The properties generally include melting point, boiling point, density, vapour pressure (at room temperature), saturation concentration, vapour density, specific gravity, solubility in water and other (organic) solvents, and the octanol/water partition coefficient. In this chapter the aggregation state(s), the form and colour of the substance is also given, as are the odour and the conversion factors between ppm and mg/m³ (at 20°C and 101.3 kPa).

4. Occurrence, production and use

An overview of the circumstances in which the substance occurs in the workplace is presented. When available, quantitative or semi-quantitative data on occurrence, production and use in the Nordic countries are given. Information on the use of chemical compounds in Denmark, Finland, Norway, and Sweden is available on <http://www.spin2000.net/spin.html>.

Occurrence in the “background” environment is usually shortly commented e.g. occurrence in foodstuffs and/or cigarette smoke.

5. Measurements and analysis of workplace exposure

Methods available for sampling and analysing of the substance in the workplace are described. The detection limits should be given for each method. Also, methods for analysing the substance (or metabolites) in biological media are presented. This information will help when considering the possibilities of conducting biological monitoring.

6. Occupational exposure data

Exposure levels and the quality of measured data are presented. If good exposure data are only presented in reports and not published in a scientific journal they may be used in this chapter in order to gain an idea of the exposure levels that are common in the workplace.

7. Toxicokinetics

This chapter describes how the body handles the chemical. Absorption rates (different routes) should, if possible, be presented quantitatively. The distribution/retention part should present the transport of the substance, or metabolites, to organs/tissues, binding to blood constituents, passage through the blood-brain and blood-placenta barrier. The mechanisms of biotransformation and the metabolites formed should, if possible, be presented both qualitatively and quantitatively. The excretion through exhaled air, urine, bile/faeces or other routes should be covered. The function of time is important. The elimination half-times in blood and other tissues as well as in urine and for other excretion pathways should be given.

8. Biological monitoring

The chapter should discuss, with respect to toxicokinetics, the possibilities and usefulness of assessing the internal load, such as the concentration in organs, tissues or other biological media. *Note: Analytical methods for measurements in biological media should be in chapter 5.*

9. Mechanism of toxicity

The mode of action of the substance on a biochemical, molecular and/or cellular level should be described. Mere descriptions of toxic effects should be avoided.

10. Effects in animal and in vitro studies and

11. Observations in man

These chapters are the most important sections in the criteria document as they provide the key health information on which the critical effect (i.e. the effect occurring at the lowest level) is based.

When reviewing separate studies the effect end points and the quality characteristics must be described in sufficient detail. An interpretation of the data should be provided. Especially for critical studies it is important to describe the aim and design of the study, methods used, number of exposed subjects or animals, control groups, exposure conditions including data about continuous or intermittent exposure, dermal or mixed exposure. It is particularly noteworthy to make a remark when there are obvious shortcomings in study reports.

Contradictory data should be commented. If such data are important for the conclusions of the document the credibility of conflicting data should be discussed. Excessive use of numbers in the text should be avoided. Numerical data are preferably presented in tables.

Note: Short summaries at the end of longer sections are recommended for chapters 7-11.

12. Dose-effect and dose-response relationships

Based on the data given so far in the document chapter 12 is preferably presented in a tabular form. Such tables should be introduced and briefly summarised at the beginning of the chapter. It may be advisable to separate the tabular data by route of administration and species. If possible, NO(A)ELs and/or LO(A)ELs should be presented here. The effects from single or short-term exposure should be differentiated from those from long-term exposure.

13. Previous evaluation by national and international bodies

This chapter cites previous overall evaluations of the substance(s) performed by e.g. ACGIH, DECOS, HSE, IARC, IPCS, NEG, and NIOSH.

14. Evaluation of human health risks

In 14.1, the data presented should be thoroughly evaluated. Major effects should be summarised, and at what levels and in what kind of studies (animal, human, single, short-term or long-term) they occur. The potential for dermal uptake should be indicated.

In 14.2 groups of workers at extra risk due to their susceptibility or sensitivity should be identified.

In 14.3, a critical effect and the NO(A)EL and LO(A)EL should be established that could form the scientific basis for an occupational exposure limit. It should also be pointed out on what kind of study the critical effect is based, and whether there are data indicating the need for a short-term exposure limit (STEL).

Notes:

- No new studies should be reported in chapters 12-17.
- Unnecessary repetitions should be avoided when evaluating studies in chapters 12 and 14 since the studies have already been described in the preceding chapters.
- Effect levels should **not** be discussed in relation to existing occupational exposure limits.
- **No** numerical proposals for occupational exposure limits should be made.

15. Research needs

The chapter should summarise important gaps in knowledge that are expected to have an impact on the scientific basis for an occupational exposure limit.

16 Summary and

17. Summary in Danish/Norwegian/Swedish

The summary is written in English and Danish/Norwegian/Swedish, respectively, according to the publication format of *Arbete och Hälsa*. A maximum of one printed page and approximately 10 key words per summary is allowed.

18. References

The references should contain information of the sources used in such a way that anyone interested can obtain a copy from a library. References to “personal communication” and unpublished material should for that reason be avoided. The formats of the most common references are

a. journal articles:

Axelsson NO, Sundell L. Mining, lung cancer and smoking. *Scand J Work Environ Health* 1978;4:42-52.

b. book chapters:

Birmingham DJ. Occupational dermatoses. In: Clayton GD, Clayton FE, eds. *Patty's industrial hygiene and toxicology Vol.1*. 3rd ed. New York: John Wiley, 1978:203-235.

The format of the reference list is further described in the “Instructions to authors” in *Arbete och Hälsa*.

19. Data bases used in the search for literature

A list of data bases used should be given together with the date of the last search.

Appendix

An appendix with occupational exposure limits (when applicable) is provided by the secretariat.