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## Committee of Experts on the Transport of Dangerous Goods and on the Globally Harmonized System of Classification and Labelling of Chemicals

### Forty-sixth session

Geneva, 3-5 July 2024

Item 2 (j) of the provisional agenda

### Work on the Globally Harmonized System of Classification and Labelling of Chemicals: Other matters

## Proposed revision of the term “radioisotopic” in chapter 3.4

Transmitted by the experts from the United Kingdom and the Netherlands\*

### I. Discussion

1. During the non-animal testing methods (NATM) informal working group discussions to revise chapter 3.4 to include criteria and guidance on mixtures classified as skin sensitizers, a potential inconsistency was identified within the chapter in relation to the use of the terms “radioactive”, “non-radioactive” and “radioisotopic”.
2. The Netherlands and United Kingdom project leads for the NATM group undertook to consider the issue and identified where these terms were used in the Globally Harmonized System of Classification and Labelling of chemicals (GHS, tenth revised edition) as detailed in paragraphs 3 to 5 below.
3. The term “radioisotopic” is currently used once in the GHS:  
3.4.2.2.3.1: “...radioisotopic local lymph node assay (LLNA).”
4. The term “radioactive” is currently used five times in the GHS:  
3.4.5.3.3.2: “...radioactive assay...”  
3.4.5.3.3.2 and 3.4.5.3.3.5: “...radioactive LLNA...”  
A9.5.2.3.9.3 and table A11.2.2: “...radioactive material...”
5. The term “non-radioactive” is currently used three times in the GHS:  
3.4.2.2.3.1: “...non-radioactive modifications to the LLNA...;”  
3.4.5.3.3.2: “...non-radioactive assay...”  
3.4.5.3.3.5: “...non-radioactive LLNA...”
6. The term “radiolabelled” is used several times in A9.5.2.3.9 and the appendices to annex 9.

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\* A/78/6 (Sect. 20), table 20.5.

7. The term “radioisotopic” is not used in OECD Test Guideline 429 (Skin sensitization: Local Lymph Node Assay). The term radioactive is used several times but not when referencing the method or assay. OECD test guidelines 442A and 442B describe themselves as non-radioactive modifications to the LLNA and describe OECD Test Guideline 429 as the radioactive LLNA. However, the term radioisotopic and radiolabelled are also used when describing technical details.

8. The authors of this document considered that it would be appropriate to propose the replacement of the term “radioisotopic” with “radioactive” in 3.4.2.2.3.1 on the basis that the terms are interchangeable and it would ensure more consistent use of this terminology in the GHS. This is also considered consistent with the use of the terms radioactive and non-radioactive to describe the different modifications of the LLNA in the OECD test guidelines. However, as this paragraph relates to classification of skin sensitizers based on standard animal data the authors considered that such a proposal was outside the scope of the work of the NATM informal working group.

9. Consequently, the authors of this document make this proposal independent of the NATM, though have consulted with the group on this matter, who have expressed support for the proposal.

10. The proposed amended paragraph (deleted text in strikethrough and new text in bold underlined) would read:

“3.4.2.2.3.1 A substance is classified as a skin sensitizer if there are positive results from an appropriate animal test. For Category 1, when an adjuvant type test method for skin sensitization is used, a response of at least 30 % of the animals is considered as positive. For a non-adjuvant Guinea pig test method a response of at least 15 % of the animals is considered positive. For Category 1, a stimulation index of three or more is considered a positive response in the ~~radioisotopic~~ **radioactive** local lymph node assay (LLNA). For the non-radioactive modifications to the LLNA, a stimulation index of 1.8 or more in the LLNA: DA, 1.6 or more in the LLNA: BrdU-ELISA, and 2.7 or more in the LLNA: BrdU-FCM are considered positive. Test methods for skin sensitization are described in OECD Guideline 406 (the Guinea Pig Maximisation test and the Buehler guinea pig test) and guidelines 429/442A/442B (Local Lymph Node Assays). Other methods may be used provided that they are well-validated and scientific justification is given. The Mouse Ear Swelling Test (MEST), appears to be a reliable screening test to detect moderate to strong sensitizers, and can be used as a first stage in the assessment of skin sensitization potential.”

## II. Proposal

11. Replace “radioisotopic” with “radioactive” in the fourth sentence of paragraph 3.4.2.2.3.1.

## III. Action requested

12. The Sub-Committee is invited to agree the proposal as outlined in section II of this document.

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