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Nanotechnologies — Considerations for radioisotope labelling methods of nanomaterials for performance evaluation

National foreword

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Technical Report

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Nanotechnologies — Considerations for radioisotope labelling methods of nanomaterials for performance evaluation

*Nanotechnologies — Considérations relatives aux méthodes de
marquage radio-isotopique des nanomatériaux pour l'évaluation
des performances*

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Foreword

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This document was prepared by Technical Committee ISO/TC 229, *Nanotechnologies*.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

Prior to the clinical trials of nanomaterials intended for use in human medicine, their *in vivo* behaviour has been evaluated in animal experiments. Several quantitative methods for assessing the biodistribution of nanomaterials have been developed. Among these methods, the biodistribution of radioisotope-labelled nanomaterials provides quantitative information on their distribution throughout the entire body.

The use of radioisotope-labelled nanomaterials for biodistribution studies is a well-established method for understanding the pharmacokinetics or toxicokinetics of nanomaterials *in vivo*. These methods assume that the distribution pattern of nanomaterials and radioisotope-labelled nanomaterials will be similar or nearly identical *in vivo*.

Radioisotope labelling of nanomaterials can be accomplished using a wide variety of radionuclides and associated labelling methods. However, for nanomaterials used for medicinal purposes, there are only a few matching pairs of nanomaterial and radioisotope labelling method that ensure the *in vivo* integrity of the radioisotope-labelled nanomaterial. Failure to identify and apply matching pairs of nanomaterial and radioisotope labelling method in studies preceding the clinical trial phase can lead to experimental data on biodistribution in which the nanomaterial and radio-label separate during the experiment. This in turn can result in a large number of nanomaterials or nano-drugs failing in the clinical trial phase.

Nanotechnologies — Considerations for radioisotope labelling methods of nanomaterials for performance evaluation

1 Scope

This document provides:

- a) a review of radioisotope labelling methods that can be used for nanomaterials;
- b) the advantages and disadvantages of each radioisotope labelling method;
- c) information on the selection of a matched pair of nanomaterial and radioisotope labelling method to ensure the in vivo integrity of radioisotope-labelled nanomaterials^[1] or the stability of their performance.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 80004-1, *Nanotechnologies — Vocabulary — Part 1: Core vocabulary*

ISO/TS 80004-8, *Nanotechnologies — Vocabulary — Part 8: Nanomanufacturing processes*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 80004-1, ISO/TS 80004-8 and the following apply.

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

- ISO Online browsing platform: available at <https://www.iso.org/obp>
- IEC Electropedia: available at <https://www.electropedia.org/>

3.1

nanoscale

length range approximately from 1 nm to 100 nm

[SOURCE: ISO 80004-1:2023, 3.1.1]

3.2

nanomaterial

material with any external dimension in the *nanoscale* (3.1) or having internal structure or surface structure in the nanoscale

[SOURCE: ISO 80004-1:2023, 3.1.4, modified — Notes have been removed.]

3.3**nanoparticle**

nano-object with all external dimensions in the *nanoscale* (3.1)

Note 1 to entry: If the dimensions differ significantly (typically by more than three times), terms such as nanofibre or nanoplate are preferred to the term nanoparticle.

[SOURCE: ISO/TS 80004-1:2023, 3.3.4]

3.4**radioisotope**

unstable isotope of an element that decays or disintegrates spontaneously, emitting ionizing radiation that can be alpha particles, beta particles and/or gamma rays

Note 1 to entry: Approximately 5 000 natural and artificial radioisotopes have been identified.

[SOURCE: ISO 19461-1:2018, 3.9, modified — "that can be alpha particles, beta particles and/or gamma rays" has been added to the definition.]

3.5**biodistribution**

technique used to monitor the movement and distribution of specific radiolabelled *nanomaterials* (3.2) within an experimental animal or human subject

3.6**chelating agent**

substance having a molecular structure embodying several electron-donor groups which render it capable of combining with metallic ions by chelation

[SOURCE: ISO 862:1984, 81]

3.7**specific activity**

total radioactivity of the sample divided by its mass

Note 1 to entry: Specific activity is expressed in Bq/g.

[SOURCE: ISO 3925:2014, 3.4, modified — In the term, "activity" has been changed to "radioactivity"; Note 1 to entry has been added.]

4 Abbreviated terms

BFC	bifunctional chelating agent
NP	nanoparticle
TATE	1,4,8,11- tetraazacyclotetradecane-1,4,8,11-tetraacetic acid
CB-TE2A	4,11-bis(carboxymethyl)-1,4,8,11-tetraazabicyclo[6.6.2]hexadecane
NOTA	1,4,7-triazacyclononane-1,4,7-triacetic acid
DOTA	1,4,7,10-tetraazacyclododecane- 1,4,7,10-tetraaceticacid
DFO	desferrioxamine
PET	positron emission tomography
SPECT	single photon emission computed tomography