# Submission of comments on Concept paper on the revision of the Guideline on Radiopharmaceuticals

Fields marked with * are mandatory.

* Name of organisation or individual

European Association of Nuclear Medicine

* Country of organisation or individual

Austria

* Email

euaffairs@eanm.org

If you respond on behalf of an organization, please allocate yourself a name abbreviation to be used as "Stakeholder name" in the comment tables below. If you comment as an individual, please ignore this field and use your full name as your "Stakeholder name".

EANM

Please click here to be redirected to the guideline text. The public consultation is launched on 21 July 2023 until 31 October 2023.

Those participating in the public consultation are asked to please submit comments via the EU Survey tool, by using the specific table for each section. Please note that login is not required to fill in the survey.

Before submission, a draft of the comments can be saved in the EU Survey tool. Once submitted, comments can be edited (by 31 October 2023) by clicking on "Edit contribution" in the link https://ec.europa.eu/eusurvey/ and entering your ID contribution that can be found on the pdf copy of your submission sent via email.

You are invited to provide your organisation or name, country and email address below for the purpose of this public consultation (for further information, please see EMA's Data Protection Statement below).

**EMA Privacy Statement**

All personal data provided within this survey questionnaire will be processed in accordance with Regulation (EU) 2018/1725 on the protection of individuals regarding the processing of personal data by the Union institutions and bodies on the free movement of such data.

This data protection statement provides details on how the Agency, in its capacity as data controller, will process the information that you have given in your questionnaire.

Internally, an 'Internal Controller' has been appointed to ensure the lawful conduct of this processing operation. The contact details of the Internal Controller are the following: Datacontroller.HumanMedicines@ema.europa.eu

Collection of data

EMA will collect all the personal data in this questionnaire, such as your name, organisation, your view on the topics subject to the survey, country of residence and your contact details. Please do not reveal any other personal data in the free text fields. EMA does not directly intend to collect personal data but to use the aggregated data for the purpose of this survey.

For the collection of data in this survey, EMA relies on the EU Survey external system. For more information on how EU Survey processes personal data, please see: https://ec.europa.eu/eusurvey/home/privacystatement

The EU Survey external system uses:

- Session "cookies" to ensure communication between the client and the server. Therefore, user's browser must be configured to accept "cookies". The cookies disappear once the session has been terminated.
- Local storage to save copies of the inputs of a participant to a survey to have a backup if the server is not available during submission or the user's computer is switched off accidentally or any other cause.
- The local storage contains the IDs of the questions and the draft answers.
- IP of every connection is saved for security reasons for every server request.
- Once a participant has submitted one's answers successfully to the server or has successfully saved a draft on the server, the data is removed from the local storage.

Your consent to the processing of your data

When you submit this questionnaire, you consent that EMA will process your personal data provided in the questionnaire as explained in this data protection statement. You may also withdraw your consent later at any time. However, this will not affect the lawfulness of any data processing carried out before your consent is withdrawn.

Start of data processing

EMA will start processing your personal data as soon as the questionnaire response is received.

Purpose of data processing

The purpose of the present data processing activity is to collect the views of stakeholders and/or concerned individuals in relation to the subject-matter of the survey. Your personal data may be used to contact you in relation to the feedback you have provided in response to the survey. No further processing of your

personal data for any other purposes outside the scope of this specific context is envisaged.

Location of data storage

All data is stored within a secure data centre at the EMA premises which is password protected and only available to EMA staff members.

Publication of data

The following data collected in this questionnaire will be published on the EMA website at the time of issuing the final guideline subject to this survey:

- organisation name (the entity on behalf you respond to this survey)
- or your name (only if you do not respond to the survey on behalf of an organisation)
- your view/comments on the topics concerned

Country information and your email address will not be published.

Retention period

If you complete and submit this survey, your personal data will be kept until the results have been completely analysed and utilised. Your personal data will be deleted by EMA at the latest 5 years after the questionnaire response was submitted. The file of the data as published will remain stored for archiving purposes beyond the maximum 5 years-retention time of the submitted questionnaire responses.

Your rights

You have the right to access and receive a copy of your personal data processed, as well as to request rectification or completion of these data. You may also request erasure of the data or restriction of the processing in accordance with the provisions of Regulation (EU) 2018/1725. You can exercise your rights by sending an e-mail to Datacontroller.HumanMedicines@ema.europa.eu.

Complaints

If you have any complaints or concerns about the processing of your personal data, you can contact EMA's Data Protection Officer at dataprotection@ema.europa.eu.

You may also lodge a complaint with the European Data Protection Supervisor: edps@edps.europa.eu.

* Please confirm that you have read and understood the Data Protection Statement above and that you consent to the processing of your personal data.

- (●) Yes
- ( ) No

* Please confirm that you consent to possibly be contacted by EMA in relation to your survey responses to support the finalisation of the document subject this EU Survey.

- (●) Yes
- ( ) No

* Please confirm that you consent to the publication of your organisation name, your name (only if you do not respond to the EU Survey on behalf of an organisation) and your survey responses on the EMA website at the time of issuing the final guideline subject to this survey.

- (●) Yes
- ( ) No

Should you not want to give consent to publish, please send your objections to Datacontroller. HumanMedicines@ema.europa.eu.

Please be aware that the sender of the comments is responsible to not disclose any personal data of third parties in the comments.

When you have filled in the EU Survey, please use the submission button at the end of the form to submit the comments to the European Medicines Agency.

For additional information, please consult EMA's privacy statement.

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**1. General comments on the Concept paper on the revision of the Guideline on Radiopharmaceuticals**

| | Stakeholder name<br>*(to be repeated in all rows)* | General comment |
|---|---|---|
| 1 | EANM | The EANM very much welcomes the revision, especially in view of the tremendous developments in the field of radiopharmaceuticals and especially with theranostics.<br><br>Based on the outcomes of the EANM/EMA meeting in March 2023, the EANM sees the below as main reasons for the review of the current guideline:<br>- New types of preparation of radiopharmaceuticals aside from kit-based compounding have gained importance (esp. in-house): kit-based compounding vs. complex preparation.<br>- EMA guideline addressing primarily marketing authorization applications.<br>- Constraints for (equivalent of) strength: fixed activity concentration at defined timepoint.<br>- Therapeutic radiopharmaceuticals gaining more importance need specific consideration.<br><br>According to the EANM, the revised guideline needs to address the following:<br>- Clear differentiation between requirements for early phase clinical trials and in-house preparations vs. marketing authorization requirements (mainly reduced GMP requirements and documentation)<br>- Clarification that the API is the radioactive compound.<br>- Quality requirements according to Ph Eur Monograph 2902 Precursors for radiopharmaceutical preparations<br>- Differentiation based on type of preparation (risk based), with potentially reduced requirements for production and especially documentation requirements.<br>- Adaptation of other parts of the guideline (e.g. no fixed activity concentration for short physical half-lives,...) |

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| 2 | EANM | The EANM is aware that the 'Radiopharmaceuticals based on Monoclonal Antibodies´ Guideline is being revised in parallel. However, we believe that having two separate guidelines is not needed anymore as the use of specific monoclonal antibodies only for radiopharmaceutical applications is outdated while other protein and peptide based constructs gain importance that do not need a separate guideline. We strongly advise to merge the two guidelines into one for reasons of clarity and applicability. |
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## 2. Specific comments on text

### 2.1. Introduction

| | Line number(s) of the relevant text<br>*(e.g. 20-23)* | Stakeholder name<br>*(to be repeated in all rows)* | Comment and rationale | Proposed guidance text |
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**2.2 Problem statement**

| | Line number(s) of the relevant text<br>*(e.g. 20-23)* | Stakeholder name<br>*(to be repeated in all rows)* | Comment and rationale | Proposed guidance text |
|---|---|---|---|---|
| 1 | 33 | EANM | Even though the concept of radionuclide precursors being handled in the same way as medicinal products within Directive 2001 /83, we believe that this concept should be modified and that radionuclides should be seen as starting materials in the process of radiopharmaceutical preparation, with appropriate considerations in terms of the required quality framework. | Delete “radionuclide precursor” |
| 2 | 35-45 | EANM | EANM welcomes the necessity of updating the current guideline on radiopharmaceuticals and the recognition of recent changes of Ph. Eur. Texts on radiopharmaceuticals. | |

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| 3 | 46-49 | EANM | The current timing of the revision does not consider the current revision of the EU Pharmaceutical Legislation. In order to keep both frameworks aligned, it is of utmost importance that the changes that are currently being brought to the Pharmaceutical Legislation, mainly with regards to definitions, are considered within the revised guideline.<br><br>In reply to the revised Pharmaceutical Directive, main stakeholders on radiopharmaceuticals have proposed revision of definitions and other topics related to radiopharmaceuticals. In particular it has been suggested to revise the current definitions and especially the current legal meaning of “radionuclide precursor”, meaning that it will not be treated as a medicinal product as such. The definition of radionuclide precursor with its requirement for marketing authorization is a factor slowing down innovation in the field. This should also be reflected in the guideline. | The ongoing revision of the EU pharmaceutical legislation should be kept in mind, keeping texts and definitions of other relevant legal and regulatory framework should be envisaged. |

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| 4 | 50-51 | EANM | While the guideline has never been intended for in-house preparations, this guideline is the only reference being used by authorities to judge submissions that clinicians/researchers are doing.<br>Without any specific in-house production guideline, the normal way that regulators are looking at the in-house production is that they take into account what they have, and this is this guideline on radiopharmaceuticals intended for marketing authorization applicants. Then the requirements that are made for the marketing authorisation applications are transferred without consideration of specific requirements, to the in-house production.<br>Similar to in house products the guideline also is not intended for radiopharmaceutical investigational Medicinal Products. | The ongoing revision of the EU pharmaceutical legislation should be kept in mind, keeping texts and definitions of other relevant legal and regulatory framework should be envisaged.<br><br>In this respect, EANM sees the need for:<br>- A clear exclusion, stating that in-house productions are not in the scope of this guideline and referring, for example, to the European pharmacopoeia<br>a dedicated guideline for in-house production, or at least include sub-chapter to the existing guideline.<br>- A clear statement that the guideline is not applicable to investigational Medicinal products |
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**2.3 Discussion (on the problem statement)**

| | Description of the element of the figure | Stakeholder name<br>*(to be repeated in all rows)* | Comment and rationale | Proposed guidance text / element of the figure |
|---|---|---|---|---|
| 1 | 57-62 | EANM | As mentioned above, the ongoing revision of the EU pharmaceutical legislation should be kept in mind, e.g. definitions of medicinal products. | |
| 2 | 66-68 | EANM | Regarding definitions consider International consensus Nomenclature guidelines (e.g.: PMID: 30989249) and also align with Pharm Eur definitions. | |
| 3 | 73 | EANM | Consider alignment with GMP in Annex 3 and clearly differentiate IMP requirements (also for chemical precursors) from radiopharmaceuticals for marketing authorization application. | |
| 4 | 82-83 | EANM | Statement on the applicability and use of the different texts of the Ph.Eur. specific for radiopharmaceuticals is welcomed, e.g. Ph. Eur. General Monographs 0125 and 2902 and all specific monographs on radiopharmaceutical preparations. A specific clarification that Ph Eur 2902 should be the basis for quality requirements of chemical precursors used for radiopharmaceutical preparations including kits is highly recommended. | |

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| 5 | 92-96 | EANM | Also ensure traceability of measurements to international metrology standards. | |
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**2.4 Recommendation**

| | Line number(s) of the relevant text<br>*(e.g. 20-23)* | Stakeholder name<br>*(to be repeated in all rows)* | Comment and rationale | Proposed guidance text |
|---|---|---|---|---|
| 1 | 98-104 | EANM | As stated above, aim to clarify differences in requirements for in-house radiopharmaceuticals and IMPs. | |
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**2.5 Proposed timetable**

| | Line number(s) of the relevant text<br>*(e.g. 20-23)* | Stakeholder name<br>*(to be repeated in all rows)* | Comment and rationale | Proposed guidance text |
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**2.6 Resource requirements for preparation**

| | Line number(s) of the relevant text (e.g. 20-23) | Stakeholder name (to be repeated in all rows) | Comment and rationale | Proposed guidance text |
|---|---|---|---|---|
| 1 | | EANM | Please consider involving experts in in-house preparation of radiopharmaceuticals through the EANM network. | |
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**2.7 Impact assessment (anticipated)**

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**2.8 Interested parties**

| | Line number(s) of the relevant text (e.g. 20-23) | Stakeholder name (to be repeated in all rows) | Comment and rationale | Proposed guidance text |
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**2.9 References to literature, guidelines, etc.**

| | Line number(s) of the relevant text (e.g. 20-23) | Stakeholder name (to be repeated in all rows) | Comment and rationale | Proposed guidance text |
|---|---|---|---|---|
| 1 | | EANM | Please consider the following reference: https://link.springer.com/article/10.1007/s00259-022-05694-z | |
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**Other comments**

| | Line number(s) of the relevant text (e.g. 20-23) | Stakeholder name (to be repeated in all rows) | Comment and rationale | Proposed guidance text |
|---|---|---|---|---|
| 1 | | EANM | It should be clearly stated that in case of continuous production (e.g. for most PET radiopharmaceuticals prepared by cyclotron produced radionuclides), it may not be applicable to provide information in several 2.S paragraphs (e.g. control of drug substance, specifications, container /closure, stability, etc.) | |
| 2 | | EANM | In relation to 3.2.P.1, which states "Only one radioactive concentration (volumic activity in Bq/mL) may be included in the application of radiopharmaceuticals presented as solutions. However, diagnostic and therapeutic products should be in separate applications": this may not be applicable for several therapeutic new Radiopharmaceuticals. | |
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Thank you for your contribution.


## Contact

Contact Form