7 September 2011
EMA/358709/2011
Committee for Medicinal Products for Human Use (CHMP)

Overview of comments on 'Draft guideline on core summary of product characteristics and package leaflet for radiopharmaceuticals' (EMA/CHMP/167834/2011)

Interested parties (organisations or individuals) that commented on the draft document as released for consultation.

Stakeholder no.	Name of organisation or individual
1	Bfarm
2	GE Healthcare
3	SNRPH (Syndicat National des Radiopharmaciens)
4	European Association of Nuclear Medicine, Vienna

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
1	Guidance and standard statements, already included in QRD templates and SmPC guideline and not specific for radiopharmaceuticals, should not be included, especially as there is a reference to these documents in the introduction. SmPC and package leaflet should be revised in line with the revised QRD template.	Comment taken into consideration
2	When compared with the QRD templates available for the MRP/DCP and centralised procedures, some sections of the SmPC are not completely aligned (see sections 2, 4.2 4.3, 4.4, 4.6, 4.7, 4.8, 6.4). Alignment would be helpful to avoid misinterpretation.	Template has been aligned with version 8 of the QRD template

2. Specific comments on text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
SmPC Section 1 '[*Please insert the strength at the date and time of calibration]'*	2	Comment: 1) 'Strengh' is a typographical error. 2) Clarity is required on the 'date and time of calibration' versus reference date and time. The activity may be calibrated on one day but the strength on the label may reference some days thereafter. 3) May be helpful to add examples for how the strength should be quantified e.g., for radioactive capsules (xxMBq/capsule), for injections (xxMBq/mL or xxMBq per single dose injection or xxMBq per vial contents), for cold kits (mg ligand per vial), for generators (xxMBq parent or xxMBq elutable daughter)? Proposed change (if any):	1)taken into consideration 2) Comment not implemented as it is clear the way it is currently written in the core SmPC 3) Not implemented. Refer to the NRG document on the name for radiopharmaceuticals
SmPC Section 1	1	Comment:" Strengh" has a typographical error. Proposed change (if any): "Strength".	Taken into consideration
Page 6 §1	4	Comment: We believe that INN names would be more appropriate than the (invented) name Proposed change (if any): name (INN), strength pharmaceutical form}	Comment not implemented. This is in line with the current QRD template v8.0.
SmPC Section 2 *'[For radiolabelled radiopharmaceuticals, the physical half-life of the*	2	Comment: Consider adding guidance as to whether the emissions should be listed in order of their abundance or their energies, and for particulates (e.g., betas, should the mean or maximum energy be stated)?	There is not an accepted way of describing the abundance and energies. Comment not implemented.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
radionuclide should be stated with a summary of the energies of the principal particle and photon emissions…..]'		Proposed change (if any):	
SmPC Section 2	1	Comment: The text has been amended. Proposed change (if any): <Excipient(s) with known effect:> <For ~~a~~ the full list of excipients, see section 6.1. >	Taken into consideration
SmPC Section 4.1	1	Comment: The text has been amended. Proposed change (if any): *[The text should be as short and precise as possible.]* *[If indications are diagnostic:]* <This medicinal product is for diagnostic use only. > *[For kits for radiopharmaceutical preparation:]* <After radiolabelling with *[e.g. sodium pertechnetate (^{99m}Tc) solution]*, *[the solution obtained]* is indicated in <adults> <neonates> <infants> <children> <adolescents> <aged {x to y}> <years> <months> for …>	There is no reason to differentiate between neonates, infants and adolescents. Comment not implemented.
Page 6 §2	4	Comment: activity at date and time of calibration should be added. Description of the primary and protective shielded secondary container in order to estimate the dose rate for radioprotection should be described.	Activity and date and time of calibration is in section 2, according to the SmPC guideline. New sentence on the primary and protective

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		Proposed change (if any): For radiolabelled radiopharmaceuticals, the physical half-life of the radionuclide should be stated with a summary of the energies of the principal particle and photon emissions. Activity at date and time of calibration and a description of primary and secondary container should be included	shielded secondary container in order to estimate the dose rate for radioprotection is added in section 6.5.
Page 6 §2	4	Comment: For radiopharmaceutical kits the amount of stannous choride (reducing agent) must be stated	The wording "excipients with known effect" is already included. The point is already covered.
SmPC Section 4.2 'Renal impairment/Hepatic impairment'	2	Comment: The heading 'Renal impairment/Hepatic Impairment' should be optional. This heading is not included in the MRP/DCP QRD template and is an optional heading for the draft CP QRD template. Proposed change (if any):	From SmPC guideline "renal and hepatic impairement" is not optional.
SmPC Section 4.2 <Paediatric population> *'[When the minimum recommended activity in the EANM dosage card for Paediatrics is different than the baseline activity,*	2	Comment: Reference to 'baseline activity' in this statement implies that the EANM dosage card (2007/8 modified version) should be used for any dosage recommendations included under the paediatric population sub-heading. The baseline activity is a nominal dose administered to a 3kg subject for calculation purposes and was instigated as a construct to avoid quoting a reference dose for adults. 3kg is less than the body weight of the average newborn and in all but 5 of the 39 procedures listed in the EANM card the baseline activity is less than the minimum recommended activity for diagnostically useful information. We therefore do not support using this. Note also that under the 'adult' sub-heading in Section 4.2 there is inclusion of an activity range which invalidates the concept of the precise 'baseline activity' and the dosage card multiplication factors.	Comment not implemented as there is no scientific justification for the deletion.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
it should be stated here]'		Proposed change (if any): Delete the statement *[When the minimum recommended activity in the EANM dosage card for Paediatrics is different than the baseline activity, it should be stated here].*	
Page 7 4.2 Method of administration	3	Comment: radiolabelling cannot be considered as simple "reconstitution". Reconstitution should be used only for addition of a simple diluant (e.g. kit of sodium pyrophosphate reconstituted with sodium chloride 0.9%) Proposed change (if any): the medicinal product should be <reconstituted> <prepared> before administration to the patient	Not implemented as <reconstitution> is considered the correct wording.
SmPC Section 4.2 Method of Administration	1	Comment: The text has been amended. Proposed change (if any): *[Product specific, it should be ~~specified here and in the labelling~~ if multidose or for single use only.] ~~This information of multisode/single use is also to be included in the labelling~~.* *[For kits for radiopharmaceutical preparation:]* <This medicinal product should be reconstituted before administration to the patient.> <For instructions on <reconstitution> <dilution> of the medicinal product before administration, see section <6.6> <and> <12>.> <For patient preparation, see section 4.4.>	Comment not implemented as this is per the QRD template.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		[For a diagnostic radiopharmaceutical intended for imaging or for a therapeutic radiopharmaceutical allowing imaging biodistribution] <Image acquisition>	
Page 7 §4.2 Method of administration Section6.6 of the SPC	4	Comment: The leaflet should contain only a general statement on the administration procedure without details that may become obsolete. For example the statement that a shielded syringe should be used for the administration prevents the use of injectors now being commercialized Proposed change (if any): Add: Administration procedures should be carried out in a way to minimize risk of contamination of the medicinal product and irradiation of the operators .	Implemented. This is a minimum required Ment that appropriate shielding is required for the syringe and/or injector. Adequate shielding is described in 6.6.
Page 7 §4.2 Method of administration	4	Comment: art. 23 - Directive 2001/83 states After an authorization has been issued, the authorization holder must, in respect of the methods of manufacture and control provided for in Article 8(3)(d) and (h), take account of scientific and technical progress and introduce any changes that may be required to enable the medicinal product to be manufactured and checked by means of generally accepted scientific methods. These changes shall be subject to the approval of the competent authority of the Member State concerned.	Not implemented as the sentence is beyond the remit of the SPC.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		Proposed change (if any): Add: Scientific and technical progresses including evidences related to new indications and individual posology should also be taken into account by the authorization holder to enable the medicinal product to be used in clinical practice in relation to such scientific and technical progresses.	
Page 7 § 4.2.	4	Comment: EANM has given specific guidance for paediatric applications (EANM dosage card), to be found at www.EANM.org: https://www.eanm.org/scientific_info/dosagecard/dosagecard.php?navId=548 , respective reference should be made Proposed change (if any): Reference could be made to relevant data proposed by bodies specialised in radiation protection and/or Nuclear Medicine, e.g.: https://www.eanm.org/scientific_info/dosagecard/dosagecard.php?navId=548]	The dosage card is included. However the reference should not be included in the SPC.
Page 7 §4.2 Method of administration And page 14 §12	4	Comment: radiolabelling of a radiopharmaceutical kit (e.g. by adding 99mTc-generator eluate cannot be considered as simple “reconstitution”. Reconstitution should be used only for addition of a simple diluent (e.g. addition of sodium chloride 0.9%) Proposed change (if any): replace in the context of radiopharmaceutical kits: “reconstitution” by “reconstitution/preparation”	Implemented. “Extemporary Preparation” was included in the sentence.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
Page 7 §4.2 Method of administration	4	Image acquisition is rather complicated to add. There are so many imaging protocols, depended on clinical needs, camera characteristics, national clinical guidelines, that for a single radiopharmaceutical these are impossible to list here. Suggest to leave this out.	Not implemented. This sentence is very important for the physician. It is general guidance only and should be updated when necessary.
Page 7 § 4.3.	4	Comment: Pregnancy is usually a contraindication and should be mentioned Proposed change (if any):	Not implemented. This should be a case-by-case evaluation.
SmPC Section 4.4 Specific Warnings	1	Comment: Excipient warnings are product specific and have to be included on a case-by-case basis in line with the Guideline on excipients. Examples should not be included in the core SmPC. The following paragraph should be deleted Proposed change (if any):	Not implemented. The examples are derived from the excipient guideline. These sentences are optional.
SmPC Section 4.4 Specific warnings '<According to the time of conditioning injection for the patient, the content of sodium may in some cases be greater than 1 mmol. This should be taken	21	Comment: Re-word to give more clarity as suggested below. Proposed change (if any): <According to the ~~time of conditioning~~ preparation of the injection for the patient, the content of sodium may in some cases be greater than 1 mmol. This should be taken into account in patient on low sodium diet.>	Implemented. Wording was revised.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
into account in patient on low sodium diet.>'			
SmPC Section 4.5 Interaction with other medicinal products and other forms of interaction	1	Comment: The text has been amended. Proposed change (if any): *[Interactions should be presented as brief as possible perhaps with a table of interactions. Only generic names of interacting substances should be used. Only true drug interactions should be included i.e. those which may produce inaccuracies in diagnostic accuracy or interfere with therapeutic efficacy.]* *[The following statement may be used where appropriate:]* <No ~~drug-drug~~ interactions have been described to date.> <No interaction studies have been performed.>	Not implemented. This is a standard sentence.
SmPC Section 4.6 Pregnancy *'[If contraindicated:]* The use of {active substance} is contraindicated in pregnancy women due to {reason} (see section 4.3)'	2	Comment: 1) Delete 'women' in this statement as suggested below. 2) It would improve clarity to include this guidance statement under section 4.3 also and cross refer to section 4.6. Proposed change (if any): *[If contraindicated:]* The use of {active substance} is contraindicated in pregnancy ~~women~~ due to {reason} (see section 4.3)	"Pregnancy" was amended to "pregnant" Cross section in 4.3 is not implemented as this should be on a case-by-case.
SmPC Section 4.6 Pregnancy	1	Comment: The following text has been amended. Proposed change (if any): *[If contraindicated:]* The use of	See above.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		{active substance} is contraindicated in ~~pregnancy~~ pregnant women due to {reason} (see section 4.3)	
SmPC Section 4.6 Breast-Feeding	1	Comment: Proposed change (if any): As the following statement doesn't refer to breast-feeding only, it should be moved to section 4.4.<Close contact with infants should be restricted during> <this period> <[*or specifying such period*]>.	
SmPC Section 4.8 Undesirable Effects	1	Comment: The following text has been amended. Proposed change (if any): ~~The following table presents how the frequencies are reflected in this section:~~ ~~*[Use MedDRA system organ classes (SOCs). The frequency of individual adverse reactions should be stated where possible. The order of presentation should be first adverse reactions like e.g. anaphylaxis (which should be listed with all observed symptoms in the SOC Immune System Disorders/ subheading anaphylactic reactions) then adverse reactions due to radiation exposure as follows a statement about the risk of radiation exposure].*~~ ~~*[Tabulated list of adverse reactions]*~~ ~~Very common (≥1/10)~~ ~~Common (≥1/100 to <1/10)~~ ~~Uncommon (≥1/1,000 to <1/100)~~ ~~Rare (≥1/10,000 to <1/1,000)~~ ~~Very rare (<1/10,000)~~	implemented

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		~~Not known (cannot be estimated from the available data)~~ *[For therapeutic ~~agents~~ medicinal products:]* The radiation dose resulting from therapeutic exposure may result in higher incidence of cancer and mutations *[specify if known]*. In all cases it is necessary to ensure that the risks of the radiation are less than from the disease itself. <The effective dose is […] mSv when the maximal recommended activity of […] MBq is administered.>	
SmPC Section 4.9 Overdose 'It might be helpful to estimate the effective dose that was applied.'	2	Comment: It is unclear how an estimate of the effective dose might be helpful. The statement is ambiguous as it appears to imply that the extent of the forced diuresis should be dependent on how high or low is the estimated effective dose. Proposed change (if any): Delete statement 'It might be helpful to estimate the effective dose that was applied.'	Not implemented. It is considered that the effective dose should be estimated in case of an overdose.
SmPC Section 5.3 Preclinical safety data 'Toxicological studies with [mice/rats] have demonstrated that with a single [IV injection] of [..] and [..] mg/kg no deaths were observed. Toxicity	2	Comment: This text is not aligned with the current EC Guideline on Summary of Product Characteristics (September 2009). The text describes the results of negative toxicological findings and the effects of the pharmacology of the drug at doses in considerable excess of those encountered in clinical use. The current EU Guideline on Summary of Product Characteristics with respect to non-clinical safety data suggests that if the results of the non-clinical studies do not add to the information needed by the prescriber, then the results (either positive or negative) need not be repeated in the SmPC. Additionally it states that the findings of the non-clinical testing should be described in brief with qualitative statements. Proposed change (if any):	Not implemented. It is an obligation to have toxicology studies described in the SPC and provide the results of those studies.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
with repeated administration of [..] mg,/kg/day over [..] days in ... [rats] ... was not observed.'			
Page 11 § 5.3.	4	Comment: Many radiopharmaceuticals fulfil the requirements of microdosing whereby no chronic, repeated toxicity, mutagenicity, genotoxicity and carcinogenicity is required, Proposed change (if any): reference should be made to the microdosing concept here	Not implemented.
Page 12 §6.6 General warnings	3	Comment: shelf life can extend to several hours, so the term of “extemporary” should be avoided Proposed change (if any): for instructions on <reconstitution> <dilution> <preparation> of the medicinal product (...)	Not implemented. Extemporary is preparation just before administration to patient, therefore there is no relation with the shelf-life.
SmPC Section 6.6	1	Comment: The first part of the “General warning”, not referring to preparation, should be moved to section 4.4. In line with the Guideline on SmPC only information necessary for the pharmacist or other health personnel to prepare the product for administration to the patient should be included here. Instructions on handling of the product by the doctor, other health personnel, or patient should be included, as well as general information concerning	Not implemented. These are instructions related to handling therefore the warnings should be included in section 6.6 and not 4.4. The proposed paragraph is already included in the SPC.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		the administration of the product (whether administered by the patient or the health personnel) in section 4.2. Proposed change (if any): ~~General warnings~~ ~~Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the competent official organisation.~~ ~~Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.~~ *[For kits for radiopharmaceutical preparation:]* Contents of the ~~<vial>~~ <container> are intended only for use in the preparation of […] and are not to be administered directly to the patient without first undergoing the preparative procedure. *<Precautions to be taken before handling or administration of the medicinal product>* *[Any special precautions related to the manipulation or administration of the product by healthcare professionals (including pregnant healthcare professionals) should be mentioned here, with a cross-reference to section 12.]* Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality	

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		requirements. Appropriate aseptic precautions should be taken	
Page 13 §6.6 Only for kits for radiopharmaceutical preparation	3	Comment: see above Proposed change (if any): the content of the kit before <reconstitution> <preparation> is not radioactive	Implemented.
SmPC Section 9	1	Comment: The text has been amended as follows. Proposed change (if any):<br~~<{DD/MM/YYYY}> <{DD month YYYY}>~~ <Date of first authorisation: {DD month YYYY}> <Date of latest renewal: {DD month YYYY}>	Implemented
SmPC Section 10	1	Comment: The text has been amended as follows: Proposed change (if any): ~~{MM/YYYY}~~ <{MM/YYYY}> <{DD/MM/YYYY}> <{DD month YYYY}>	Implemented
Page 13/14 § 11	4	Full details of dosimetry is not very well defined. What is meant with full details?	Not implemented. Full details describes best the intended description.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		Next, is this overlap with §4.8? Proposed change: adequate details of dosimetry.....	There is some overlap with section 4.8. but this is justified with the fact that the effective dose is in relation of the low probability of the expected effects.
Page 15 §12 Method of preparation	3	Comment: radiopharmaceuticals can be administred by non parenteral route (e.g. oral) Proposed change (if any): information on the appearance of the <reconstituted> <prepared> solution should appear here	Not implemented as for oral solutions, appearance of the solutions are not described.
SmPC Section 12	1	Comment: The text has been amended as follows: Proposed change (if any): [*For ready-to-use radiopharmaceuticals:]* *[Instructions on the dilution of the ready-to-use radiopharmaceutical before administration could be given here (e. g. with sodium chloride 9 mg/ml (0.9%) solution for injection). Information on the appearance of the diluted parenteral solution should appear here.]* *[Additional requirements for diluents, etc. should appear here.]* */Special instructions relating to the disposal of containers and unused contents should be included.]* <Any unused medicinal product or waste material should be disposed of in accordance with local requirements.>	0.9%:not implemented as this is not recommended by the Eur Pharmacopeia. The sentence is in 6.6. As the sentence is not about disposal it does not belong in this section. – comment not implemented.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
Page 14 § 12	4	Comment: It should be clarified that the extemporaneous preparation of radiopharmaceuticals is not part of the marketing authorization. The term extemporaneous preparation should also be cleary defined in a comment EANM has released specific guidelines for the extemporaneous preparation of radiopharmaceuticals (see www.eanm.org, guidelines: https://www.eanm.org/scientific_info/guidelines/gl_radioph_cgrpp.pdf Proposed change (if any): Add: [Instructions on reconstitution/extemporary preparation of the medicinal product before administration should be included here. Give clear indication that the extemporaneous preparation step is not part of the marketing authorization, guidelines on Good Radiopharmacy Practice can be found e.g. at https://www.eanm.org/scientific_info/guidelines/gl_radioph_cgrpp.pdf	Not implemented. It is not considered appropriate to include weblinks in the SPC. It is important to note that extemporary preparation in this context means just before administration to patients.
Page 15 § 12	4	Comment: The statement: [Section 12 is also designated to describe the extemporaneous preparation of radiopharmaceuticals which requires several steps.] is unclear. See also above	See comment above.
Page 15 § 12 Quality Control	4	Comment: The statement “..... the way to check the rate of radionuclide labelling in case of doubt or when it is performed periodically or systematically.” Is unclear	Not implemented. The rate of radionuclide labelling and radiochemical purity are very different statements/concepts. The aim here is to be more general.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		Proposed change (if any): "..... the way to check the radiochemical purity."	
	2	Comment: Text has been amended as follows: **1. What X is and what it is used for** <This medicine is a radiopharmaceutical product for diagnostic use only.> <This medicine is a radiopharmaceutical product for therapy only.> X is used for <indication understandable to the patient> The use of X does involve exposure to <small> amounts of radioactivity. Your doctor and the Nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the radiopharmaceutical overcomes the risk due to radiation.	Implemented.
Package Leaflet Section 2		Comment: Text has been amended as follows: **2. What you need to know before X is used** **X must not be used** if you are allergic to {active substance(s)} or any of the other ingredients of this medicine (listed in section 6).> [include reference to residues, if applicable.] **Warnings and precautions** Comment Pregnancy and breastfeeding should only be included here, if they are mentioned in section 4.4 SmPC. Therefore the standard statement should not be included.	Implemented

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		Before administration of X you should: - <drink plenty of water before the start of the examination in order to urinate as often as possible during the first hours after the study. > - <avoid all important physical activity> - <be fasting for at least 4 hours> - ... **Children <and teenagers>** Please talk to your Nuclear medicine doctor <if you are under 18 years old> **Other medicines and X** <Tell your <doctor> <nuclear medicine doctor|> <or> <pharmacist> if you are <taking> <using>, have recently <taken> <used> or might <take> <use> any other medicines.> <since they may interfere with the interpretation of the images>: - [*product specific*] **X with <food> <and><,> <drink> <and> <alcohol>** **Pregnancy <and><,> breast-feeding <and fertility>** <If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your <doctor> <nuclear medicine doctor> <or> <pharmacist> for advice before you are given this medicine.> If you are pregnant [*product specific]*	

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		The Nuclear medicine doctor will only administer this product during pregnancy if a benefit is expected which would outweigh the risks. If you are breast-feeding [*product specific*] Please ask your Nuclear medicine doctor when you can resume breast-feeding . **Driving and using machines** <It is considered unlikely that X will affect your ability to drive or to use machines or <product specific> **X contains {name the excipient(s)}**	
Package Leaflet Section 3 '.....MBq (Mega Becqueral, the united used to express radioactivity).'	2	Comment: Change suggested below to correct term and typographical error. Proposed change (if any): '.....MBq (~~Mega Becqueral~~ Megabecquerel, the unit~~ed~~ used to express radioactivity).'	Implemented.
	2	Comment: Text has been amended as follows: **3. How to use X** There are strict laws on the use, handling and disposal of radiopharmaceutical products. {(Invented) name} will only be	Implemented. According to the QRD template, the product is to be administered by the health care professional. Thus, the wording How X is used.... best reflects this aspect.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		used in special controlled areas. This product will only be handled and given to you by people who are trained and qualified to use it safely. These persons will take special care for the safe use of this product and will keep you informed of their actions. The Nuclear medicine doctor supervising the procedure will decide on the quantity of X to be used in your case. It will be the smallest quantity necessary to get <the desired information> <the desired effect>. The quantity to be administered usually recommended for an adult ranges from <product specific> to <product specific> MBq (Mega Becquerel, the united used to express radioactivity). **<Use in children** <and teenagers>>**</br>** In children and teenagers, the quantity to be administered will be adapted to the child's body mass. **Administration of X and conduct of the procedure** X is administered <route of administration>. <One injection is sufficient to conduct the test that your doctor needs.> <After injection, you will be offered a drink and asked to urinate immediately preceding the test.> The Nuclear medicine doctor will inform you if you need to take any special precautions after receiving this medicine. Contact your Nuclear medicine doctor if you have any questions. Comment The warning to avoid close contact to young children should be moved under the subheading "**Warnings and**	Not implemented as the sentence referring to children and pregnant women is included in the section 3 after administration of X….

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		precautions". **After administration of X, you should:** - <avoid any close contact with young children for the {xx} hours following the injection> - <urinate frequently in order to eliminate the product from your body> - ... **Duration of the procedure** Your Nuclear medicine doctor will inform you about the usual duration of the procedure. **If you have been given more X than you should** An overdose is almost impossible < because you will only receive a single dose of X precisely controlled by the Nuclear medicine doctor supervising the procedure.> However, in the case of an overdose, you will receive the appropriate treatment. <product specific> Should you have any further question on the use of X, please ask the Nuclear medicine doctor who supervises the procedure.	
Package Leaflet Section 4	2	Comment: Text has been amended as follows: **Possible side effects** Like all medicines, this medicine can cause side effects, although not everybody gets them. *[for diagnostic radiopharmaceuticals only]* This radiopharmaceutical will deliver <low> amounts of ionising radiation with very low risk of cancer and hereditary abnormalities.	Comment was implemented.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		If you get any side effects talk to your <doctor> <or> <nuclear medicine doctor> <,> <pharmacist> <or nurse>. This includes any possible side effects not listed in this leaflet.	
Package Leaflet Section 5 Entire section	2	Comment: Presume that this section is added to be in line with the QRD templates but seems unnecessary information for the patient to have to consider. Proposed change (if any):	Not implemented. This information is derived from the legislation and must be included in the PL.
		Comment: Text has been amended as follows: **How to store X** You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials. The information is intended for the specialist only. X must not be used after the expiry date which is stated on the <label> <carton> <bottle> <...> <after {abbreviation used for expiry date}.> <The expiry date refers to the last day of that month.> <X must not be used if it is noticed {description of the visible signs of deterioration}.>	Please refer to previous comment. QRD implemented.
Package Leaflet Section 6		Comment: Text has been amended as follows: **Contents of the pack and other information**	Implemented.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		What X contains - The active substance(s) is (are)… - The other ingredient(s) <(excipient(s))>is (are)... **What X looks like and contents of the pack** *[Product specific]* <Pack sizes> *[Product specific]* **Marketing Authorisation Holder and Manufacturer** {Name and address} <{tel}> <{fax}> <{e-mail}> <For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:> …. **This leaflet was last revised on {MM/YYYY} {month YYYY}** <This medicine has been given “conditional approval”. This means that there is more evidence to come about this medicine. The European Medicines Agency will review new information on the medicine every year and this leaflet will be updated as necessary.>	

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		<This medicine has been authorised under “Exceptional Circumstances”. This means that <because of the rarity of this disease> <for scientific reasons> <for ethical reasons> it has been impossible to get complete information on this medicine. The European Medicines Agency will review any new information on the medicine every year and this leaflet will be updated as necessary.> **<Other sources of information>** Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu <There are also links to other websites about rare diseases and treatments.> <This leaflet is available in all EU/EEA languages on the European Medicines Agency website.> <---------- <The following information is intended for medical or healthcare professionals only:>	

Please add more rows if needed.