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Datasheet for the decision of 25 February 2025

Case Number: T 0066/23 - 3.3.02

Application Number: 16712997.2

Publication Number: 3268337

IPC: C07B59/00, C07C251/24, A61B5/00, C07F5/00, A61K51/04, A61K51/08, A61P35/00, C01G15/00

Language of the proceedings: EN

Title of invention:
METHODS AND KITS FOR PREPARING RADIONUCLIDE COMPLEXES

Patent Proprietor:
Theragnostics Limited

Opponent:
Dehmel & Bettenhausen Patentanwälte PartmbB

Headword:
THERAGNOSTICS / RADIONUCLIDE COMPLEXES

Relevant legal provisions:
EPC R. 103(1)(a)
EPC Art. 123(2), 123(3), 84, 56, 111(1)
RPBA 2020 Art. 12(2), 13(1), 13(2)

Keyword:
Substantial procedural violation (no) - Reimbursement of appeal fee - (no)
Amendments - extension of the protection conferred (no) - added subject-matter (no)
Clarity (yes)
Inventive step - (no)
Request filed at the oral proceedings - exceptional circumstances (yes) - admitted (yes)
Remittal to the opposition division (yes)

Decisions cited:

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

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Case Number: T 0066/23 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 25 February 2025

Appellant: (Patent Proprietor)	Theragnostics Limited c/o Ignition Law Moray House, First Floor 23-31 Great Titchfield Street London W1W 7PA (GB)
Representative:	Aera A/S Niels Hemmingsens Gade 10, 5th Floor 1153 Copenhagen K (DK)
Appellant: (Opponent)	Dehmel & Bettenhausen Patentanwälte PartmbB Herzogspitalstr. 11 80331 München (DE)
Representative:	De Clercq & Partners Edgard Gevaertdreef 10a 9830 Sint-Martens-Latem (BE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 11 November 2022 concerning maintenance of the European Patent No. 3268337 in amended form.**

Composition of the Board:

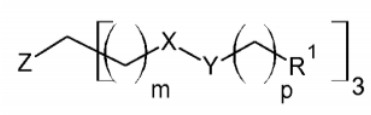
Chairman	M. O. Müller
Members:	M. Maremonti
	R. Romandini

Summary of Facts and Submissions

I. The appeals by the opponent and the patent proprietor lie from the opposition division's interlocutory decision, according to which European patent No. 3 268 337 ("the patent") as amended in the form of auxiliary request 9 filed during the oral proceedings, and the invention to which it relates, meet the requirements of the EPC.

II. Claim 1 of auxiliary request 9, found allowable by the opposition division, reads as follows:

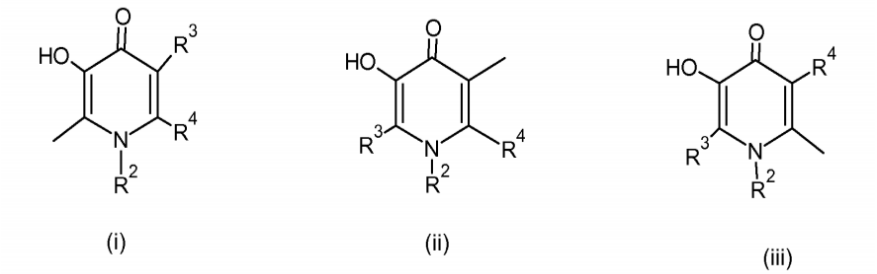
"*1. A method for preparing a complex comprising a radioisotope of gallium for use in radiotherapy or in a medical imaging procedure, said method comprising adding a gallium radioisotope solution obtained directly from a gallium radionuclide generator to a composition comprising a pharmaceutically acceptable buffer and optionally also a pharmaceutically acceptable basic reagent, in amounts sufficient to increase the pH to a level in the range of 3 to 8, wherein the composition further comprises a chelator that is able to chelate radioactive gallium within said pH range and at moderate temperature, said chelator being optionally linked to a biological targeting agent, wherein said chelator is a compound of formula (I)*



(I)

or a salt thereof; wherein one of X and Y is C=O and the other is NR; wherein each m and p are independently selected from 0 to 6; wherein R^1 is a chelating group

capable of chelating a radionuclide and is selected from:



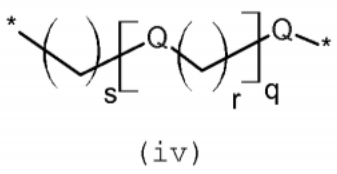
wherein R, R^2, R^3 and R^4 are independently hydrogen or an optionally substituted C_{1-7} alkyl group; and where Z is hydrogen or a group of formula -B'-H, -B'-A, or a group -B'-A-T, where*

T is a targeting group capable of binding to a target of interest in a subject;

A is a reactive group allowing coupling to the group T,

A is a reacted reactive group A;*

B' is a linker group for linking the chelating group to a reactive group A, and is represented by the formula:



wherein each Q is independently selected from a group consisting of $-NR^5-$, $-C(O)NR^5-$, $-C(O)O$, $-NR^5C(O)NR^5-$, $-NR^5C(S)NR^5-$ and -0-, each R^5 is independently hydrogen or an optionally substituted C_{1-7} alkyl group, each q and s are independently selected from 0 to 6 and each r is independently selected from 1 to 6,

wherein said chelator, buffer, and basic agent are in lyophilized or freeze-dried form."

III. The opposition was based on the grounds under Article 100(a) to (c) EPC. Reference was made, *inter alia*, to the following documents:

D2: WO 2012/063028 A1

D12: WO 03/059397 A2

D17: Eder, M. *et al.*, "*^{68}Ga-Complex Lipophilicity and the Targeting Property of a Urea-Based PSMA Inhibitor for PET Imaging*", Bioconjugate Chemistry, 2012, 23, pages 688-97

IV. By letter dated 12 August 2022, the patent proprietor filed sets of claims according to a main request and auxiliary requests 1, 2a, 2b, 3a, 3b, 4, 5a, 5b, 6a, 6b, 7a, 7b and 8. During the oral proceedings, it additionally filed a set of claims according to auxiliary request 9. The appealed decision is based on these requests. The opposition division came, *inter alia*, to the following conclusions.

- The subject-matter of claim 1 of the main request and all the auxiliary requests 1, 2a, 2b, 3a, 3b, 5a, 5b, 6a, 6b, 7a and 7b did not comply with the requirements of Article 123(2) and (3) EPC.
- The subject-matter of the claims of auxiliary request 9 involved an inventive step in view of D12 taken as the closest prior art.

V. In its appeal submissions, the patent proprietor alleged that the opposition division had committed a substantial procedural violation justifying the immediate remittal of the case for further prosecution. Moreover, while not defending the main request and auxiliary request 1 underlying the appealed decision, the patent proprietor contested the opposition division's reasoning as regards auxiliary requests 2a, 2b, 3a, 3b, 6a, 6b, 7a and 7b. It argued, *inter alia*,

that the subject-matter of these requests did not extend the protection conferred by the claims as granted and did not extend beyond the content of the application as filed. Additionally, the patent proprietor contested the admissibility of the opponent's appeal. It further submitted that the subject-matter of auxiliary request 9, which was found allowable by the opposition division, involved an inventive step. The patent proprietor corroborated its arguments by filing the following new items of evidence (labelled D24 to D27 and D31 by the patent proprietor; new numbering introduced by the board):

A24: Wikipedia, the free encyclopedia, "*Chelation*", found at https://web.archive.org/web/20150212015013/http://en.wikipedia.org:80/wiki/Chelation

A25: Ogawa and Saji, International Journal of Molecular Imaging, Volume 2011, pages 1 to 7

A26: Schuhmacher *et al.*, Nucl. Med. Biol., Volume 19(8), 1992, pages 809 to 824 in Int. J. Radiat. Appl. Instrum. Part B

A27: Eder *et al.*, Eur. J. Nucl. Med. Mol. Imaging, 2008, 35, pages 1878 to 1886

A31: Imberti *at al.*, Dalton Transactions, 2019, 48, pages 4299 to 4313

VI. In its appeal submissions, the opponent argued, *inter alia*, that the subject-matter of auxiliary requests 2a, 2b, 3a, 3b, 6a, 6b, 7a and 7b extended the protection conferred by the claims as granted and/or extended beyond the content of the application as filed. Moreover, the opponent raised objections to clarity, novelty and inventive step in respect of these requests. The opponent further submitted that the

subject-matter of auxiliary request 9, which was found allowable by the opposition division, lacked an inventive step. It also contested the admittance of documents A26 and A27, *inter alia*. The opponent corroborated its arguments by filing the following new items of evidence (labelled D28 to D30 by the opponent; new numbering introduced by the board):

A28: Velikyan, Theranostics, Vol. 4, Issue I, 2014, pages 47 to 80

A29: Hammerstein *et al.*, Angewandte Chemie International Edition, 49, 2010, pages 5085 to 5090

A30: Tagliaferro and Martell, Inorganica Chimica Acta, Volume 85, 1984, pages 9 to 15

As regards the issues dealt with in the present decision, the opponent relied only on A29 and A30. Therefore, document A28 was not relevant for the present decision and will not be referred to in the following.

VII. The parties were summoned to oral proceedings as per their requests. In preparation for the oral proceedings, the board issued a communication under Article 15(1) RPBA. In this communication, the board expressed the preliminary opinion, *inter alia*, that no substantial procedural violation had been committed by the opposition division justifying immediate remittal of the case. Moreover, the board provisionally held the opponent's appeal admissible and considered the subject-matter of claim 1 of auxiliary request 9, which was found allowable by the opposition division, to lack an inventive step. The board further observed that this inventive-step objection applied to the subject-matter

of claim 1 of all the higher-ranking requests 2a, 2b, 3a, 3b, 6a, 6b, 7a and 7b.

VIII. By letter dated 24 January 2025, the patent proprietor replied to the board's communication and filed sets of claims according to auxiliary requests 11 and 12.

IX. Oral proceedings before the board were held by videoconference on 25 February 2025 in the presence of both parties. During the oral proceedings, the patent proprietor filed a new set of claims according to auxiliary request 2c.

X. Final requests relevant to the decision

The patent proprietor requested that the appealed decision be set aside and that the case be remitted to the opposition division for further prosecution on the basis of auxiliary request 2a, or, alternatively, on the basis of auxiliary request 2b underlying the appealed decision. The patent proprietor further requested the reimbursement of the appeal fee under Rule 103(1)(a) EPC. Additionally, the patent proprietor requested that the appealed decision be set aside and that the patent be maintained in amended form on the basis of the claims of one of auxiliary requests 2a or 2b underlying the appealed decision. Alternatively, it requested that the case be remitted to the opposition division for further prosecution on the basis of the claims of auxiliary request 2c filed during the oral proceedings before the board. The patent proprietor also requested that documents A24 to A27 be admitted.

The opponent requested that the patent proprietor's request to remit the case to the opposition division due to a substantial procedural violation be rejected. It further requested that auxiliary requests 2a and 2b be held not to be allowable by the board. The opponent further requested that auxiliary request 2c filed

during the oral proceedings before the board not be admitted. Alternatively, the opponent requested that the case be remitted to the opposition division for further prosecution on the basis of the claims of auxiliary request 2c. The opponent also requested that A24 to A27 not be admitted.

XI. As regards the parties' submissions that are relevant to the decision, reference is made to them in the reasons for the decision below.

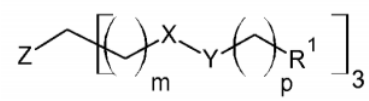
Reasons for the Decision

Violation of the right to be heard - Article 113(1) EPC - request to remit the case to the opposition division for further prosecution on the basis of auxiliary request 2a or 2b - Article 11 RPBA - reimbursement of the appeal fee - Rule 103(1)(a) EPC

1. Auxiliary request 2a filed by the patent proprietor by letter dated 12 August 2022 and underlying the appealed decision is the highest-ranking request on appeal. Claim 1 of this request reads as follows, the amendments to claim 1 as granted having been highlighted by the board:

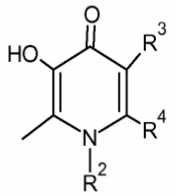
"*1. A method for preparing a complex comprising a radioisotope of gallium for use in radiotherapy or in a medical imaging procedure, said method comprising adding a gallium radioisotope solution obtained directly from a gallium radionuclide generator to a composition comprising a pharmaceutically acceptable buffer and optionally also a pharmaceutically acceptable basic reagent, in amounts sufficient to increase the pH to a level in the range of 3 to 8, wherein the composition further comprises a chelator that is able to chelate radioactive gallium within said*

pH range and at moderate temperature, said chelator being optionally linked to a biological targeting agent, wherein said chelator is ~~selected from desferrioxamine-B (DFO), bis(2-hydroxybenzyl)ethylenediaminediacetic acid (HBED), 1,4,7-triazacyclononane macrocycle substituted with phosphonic groups at the amines (NOTP), or~~ a compound of formula (I)

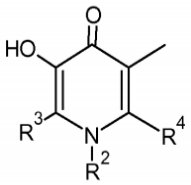


(I)

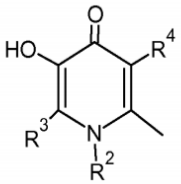
or a salt thereof; wherein one of X and Y is C=O and the other is NR; wherein each m and p are independently selected from 0 to 6; wherein R^1 is a chelating group capable of chelating a radionuclide and is selected from:



(i)



(ii)



(iii)

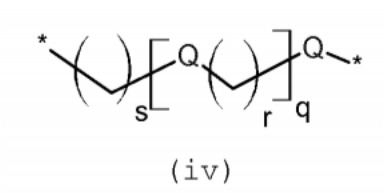
wherein R, R^2, R^3 and R^4 are independently hydrogen or an optionally substituted C_{1-7} alkyl group; and where Z is hydrogen or a group of formula -B'-H, -B'-A, or a group -B'-A-T, where*

T is a targeting group capable of binding to a target of interest in a subject;

A is a reactive group allowing coupling to the group T,

A is a reacted reactive group A;*

B' is a linker group for linking the chelating group to a reactive group A, and is represented by the formula:



(iv)

wherein each Q is independently selected from a group consisting of -NR^5-, -$C(O)NR^5$-, -$C(O)O$, -$NR^5C(O)NR^5$-, -$NR^5C(S)NR^5$- and -O-, each R^5 is independently hydrogen or an optionally substituted C_{1-7} alkyl group, each q and s are independently selected from 0 to 6 and each r is independently selected from 1 to 6, ***or wherein said chelator is linked to said biological targeting agent and is DKFZ-PSMA-11, and***

wherein said chelator, buffer, and basic agent are in lyophilized or freeze-dried form,

with the proviso that said method does not comprise (a) eluting a 68Ge/68Ga generator by fractionation with about 1.8 ml HCl 0.1N directly into a reaction vial containing 10 µg DKFZ-PSMA-11 in lyophilized form and 800-1800 mg sodium formate in lyophilized form, and (b) mixing and incubating the reaction vial at room temperature for about 5 minutes."

As regards auxiliary request 2b underlying the appealed decision, claim 1 of this request differs from claim 1 of auxiliary request 2a only in that the disclaimer was amended.

2. As set out above, the opposition division considered auxiliary requests 2a and 2b not to comply with the requirements of Article 123(3) EPC, *inter alia*.

2.1 The patent proprietor argued that the opposition division had raised its objection under Article 123(3) EPC leading to this conclusion for the first time at

the oral proceedings. The objection was based on an assumption amounting to nothing more than speculation without a genuine attempt to establish the relevant facts. The patent proprietor had not had an adequate opportunity to respond to this objection, especially since no time was available to file documents such as A24 to A27. The opposition division should have adjourned the oral proceedings to establish the relevant facts. The patent proprietor's right to be heard had thus been violated, and therefore the remittal to the opposition division under Article 11 RPBA and the reimbursement of the appeal fee were justified.

2.2 According to Article 11 RPBA, the board will not remit a case to the opposition division for further prosecution, unless special reasons present themselves for doing so. Fundamental deficiencies which are apparent in the proceedings before the opposition division constitute such special reasons.

2.2.1 In the case in hand, claim 1 of auxiliary requests 2a and 2b (point 1 above) had been amended in comparison with claim 1 as granted, by inserting the following feature, *inter alia*:

"*or wherein said chelator is linked to said biological targeting agent and is DKFZ-PSMA-11*"

The opposition division (appealed decision, point 3.4.1.3 on pages 12 to 14 and point 4.2 on pages 18 and 19) held that this alternative of the chelator being linked to a biological targeting agent and specifically being DKFZ-PSMA-11 was not covered by the claims as granted. In fact, the chelator in the compound DKFZ-PSMA-11 was HBED-CC. This was a different chelator from the HBED mentioned in claim 1 as granted. The opposition division concluded that including the above-

mentioned alternative in claim 1 of auxiliary requests 2a and 2b therefore led to an infringement of Article 123(3) EPC.

2.2.2 It is undisputed that this objection was raised by the opposition division at the oral proceedings for the first time; however, the opposition division (*loc. cit.*) provided detailed reasoning as to why the requirements of Article 123(3) EPC were not met. Moreover, the opposition division gave the patent proprietor the option of responding to this objection (minutes of the oral proceedings, page 3, points 4.1 to 4.6) and the patent proprietor indeed filed auxiliary request 9 in direct response to this (minutes of the oral proceedings, page 3, point 5.2). The patent proprietor did not request that the oral proceedings be postponed.

2.2.3 Even assuming that the opposition division had committed a procedural violation by not postponing the oral proceedings of its own motion, this violation was not substantial. In fact, auxiliary requests 2a and 2b were found by the opposition division to also infringe Article 123(2) EPC, and therefore if the patent proprietor wanted to pursue these requests, an appeal had to be filed anyway.

2.2.4 The patent proprietor responded to the opposition division's objection under Article 123(3) EPC by filing A24 to A27 with the statement of grounds of appeal. Therefore, the patent proprietor had sufficient time to respond to the opposition division's objection under Article 123(3) EPC, and therefore remittal was not justified.

2.3 For these reasons, the board decided not to remit the case for further prosecution on the basis of the claims of auxiliary request 2a or 2b. Moreover, since no

substantial procedural violation had been committed by the opposition division, the patent proprietor's request to reimburse the appeal fee under Rule 103(1)(a) EPC was rejected.

Auxiliary request 2a - claim 1 - extension of the protection conferred by the claims as granted - Article 123(3) EPC

3. In comparison with claim 1 as granted, in claim 1 of auxiliary request 2a (point 1 above), several alternatives for the chelator have been deleted, notably the alternative in which the chelator is bis(2-hydroxybenzyl)ethylenediaminediacetic acid (HBED). Moreover, the alternative of the chelator being linked to a biological targeting agent and specifically being DKFZ-PSMA-11 has been added.

3.1 In fact, DKFZ-PSMA-11 is not a chelator, but a compound formed by the chelator N,N'-bis [2-hydroxy-5-(carboxyethyl)benzyl] ethylenediamine-N,N'-diacetic acid (HBED-CC) and the prostate-specific membrane antigen PSMA-11, i.e. a cancer-specific marker; see, in this respect, paragraph [0043] of the patent referring to document D17; see also the abstract of D17.

3.2 The opponent argued that the chelator in the molecule DKFZ-PSMA-11 was HBED-CC, which was not included in the chelators listed in claim 1 as granted. The latter mentioned only HBED and not its derivatives. When derivatives had to be included, this was specified in claim 1 as granted, for example with reference to 1,4,7-triazacyclononane macrocycle chelators (NOTP). The opponent submitted that even if the carboxylic -CC substituents did not take part in the gallium chelation, these substituents still affected the value of the equilibrium dissociation constant (Kd), as they changed the electron density in the whole molecule and at the chelating moieties. A different Kd value implied

a different chelator. Document A29 confirmed the complexity of the chelating reaction. Document A30 showed that SHBED, i.e. a sulfoxy analogue to HBED-CC, had a different Kd value from HBED. The possibility of using HBED-CC as a chelator was not covered by the claims as granted, thus leading to an extension of the protection conferred.

3.3 The board disagrees.

3.3.1 It is acknowledged that claim 1 as granted does not include HBED-CC, but only HBED, in the list of the possible chelators. It was also not disputed by the patent proprietor that HBED and HBED-CC possibly have a different Kd value; however, claim 1 as granted comprises the alternative of the chelator, HBED, *inter alia*, being linked to a biological targeting agent. As pointed out by the patent proprietor and not disputed by the opponent at the oral proceedings, in order to be linked to a biological targeting agent, HBED must necessarily be modified, i.e. functionalised, by including groups capable of effecting this link. In fact, in the absence of any structural modification, the HBED molecule, once gallium ions have been chelated, gives rise to a saturated complex with no substituents being available to effect a link with a biological targeting agent.

3.3.2 Therefore, when reciting the alternative of HBED linked to a biological targeting agent, claim 1 as granted implicitly covers all the structural modifications to the HBED molecule to introduce functional groups capable of effecting the link to a biological targeting agent.

3.3.3 The feature of claim 1 of auxiliary request 2a expressing that the "*chelator is linked to said*

biological targeting agent and is DKFZ-PSMA-11" has two limiting effects:

- it restricts the structural modifications to the HBED molecule in claim 1 as granted to the inclusion of the carboxylic -CC groups in the HBED molecule, and
- it specifies that HBED is linked to PSMA-11 as the biological targeting agent by virtue of this modification.

3.4 The board thus concludes that the protection conferred by claim 1 of auxiliary request 2a has been restricted in comparison with the protection conferred by claim 1 as granted. Therefore, the requirements of Article 123(3) EPC are met.

3.5 In arriving at this conclusion, the board did not take documents A24 to A27 filed by the patent proprietor into account, the admittance of which had been disputed by the opponent. Therefore, a decision by the board on the admittance of these documents was not needed.

Auxiliary request 2a - claim 1 - added subject-matter - Article 123(2) EPC

4. The opponent argued that the feature of claim 1 of auxiliary request 2a expressing that the "*chelator is linked to said biological targeting agent and is DKFZ-PSMA-11*" infringed Article 123(2) EPC. It submitted that HBED-CC as a chelator was not disclosed in the application as filed, which only mentioned HBED; see page 6, lines 1 to 3 of the application as filed. DKFZ-PSMA-11 was disclosed in the application as filed only as an example of a biological targeting moiety T in formula (I) (see page 11, line 29 to page 12, line 16), but not as an option to be used in the claimed method. Indeed, the application as filed, e.g. in example 4,

disclosed PSMA as a targeting moiety T only in the context of chelators according to formula (I) and not in combination with HBED as a chelator, let alone with HBED-CC. By changing the scope of protection to the actual DKFZ-PSMA-11 molecule as such, i.e. uncoupled from moiety T in formula (I), an intermediate generalisation was made, which is unallowable under Article 123(2) EPC.

5. These arguments are not convincing.

5.1 It is acknowledged that the application as filed, from page 10, line 22 to page 12, line 12, discloses that the chelator of formula (I) (point 1 above) is linked, or has the capability of becoming linked, to a targeting moiety T, and that the latter can be a ligand that targets a cancer-specific marker; however, the following paragraph on page 12, lines 13 to 16 of the application as filed discloses that, in a particular embodiment, "[s]*uch ligands include DKFZ-PSMA-11*". As set out above, it was common ground that DKFZ-PSMA-11 is not a ligand but a molecule containing the chelator HBED-CC linked to the targeting agent PSMA-11. Therefore, when mentioning DKFZ-PSMA-11, the application as filed does not disclose a ligand linked to a chelator of formula (I) but directly and unambiguously discloses that an embodiment of the chelator linked to a biological targeting agent is the chelator HBED-CC linked to the targeting agent PSMA-11, as included in claim 1 of auxiliary request 2a.

5.2 As discussed during the oral proceedings before the board and not disputed by the opponent, claims 1 and 18 as filed disclose all the method features required by claim 1 of auxiliary request 2a, except for the specification of the chelator that is linked to a biological targeting agent. Claim 1 of auxiliary request 2a additionally specifies that the chelator

linked to a biological targeting agent is DKFZ-PSMA-11. At the oral proceedings, the opponent argued that the inclusion of this feature in the claimed method required a triple selection, namely the selections of the chelator HBED-CC, the targeting agent PSMA, this specifically being PSMA-11; however, as set out above, the application as filed directly and unambiguously discloses on page 12, lines 13 to 16 that, in an embodiment of the invention, the chelator linked to a biological targeting agent is DKFZ-PSMA-11. Therefore, only the single selection within the application as filed of this specific embodiment is needed to arrive at the alternative in claim 1 of auxiliary request 2a objected to by the opponent.

5.3 For these reasons, the board concludes that the inclusion of the feature expressing that the "*chelator is linked to said biological targeting agent and is DKFZ-PSMA-11*" in claim 1 of auxiliary request 2a complies with the requirements of Article 123(2) EPC.

6. The opponent also objected to the inclusion of the disclaimer in claim 1 of auxiliary request 2a (point 1 above), submitting that this inclusion infringed Article 123(2) EPC. In this respect, the opponent referred to decision G 1/03 of the Enlarged Board of Appeal (OJ EPO 2004, 413).

This objection was not discussed at the oral proceedings before the board. Therefore, the board has not reached a conclusion with respect to the inclusion of the disclaimer in claim 1 of auxiliary request 2a.

Auxiliary request 2a - claim 1 - clarity under Article 84 EPC

7. The opponent argued that the feature of claim 1 of auxiliary request 2a expressing that "*said chelator is linked to said biological targeting agent and is DKFZ-*

PSMA-11" lacked clarity. It submitted that two interpretations of this feature were possible, namely:

- the biological targeting agent is DKFZ-PSMA-11, which would be unclear since DKFZ-PSMA-11 already comprises a chelator, i.e. HBED-CC linked to the PSMA ligand, or
- DKFZ-PSMA-11 is the chelator, meaning that HBED-CC in the molecule is the chelator and PSMA is the biological targeting agent, which would be in contradiction with the application as filed only discussing HBED chelators and not HBED-CC chelators.

7.1 This objection is not convincing. As set out above, it was common ground that DKFZ-PSMA-11 represents a molecule containing the chelator HBED-CC linked to the targeting agent PSMA-11. Therefore, it would have been immediately clear to the skilled person that DKFZ-PSMA-11 as mentioned in the feature objected to is not the biological targeting agent, but the combination of the chelator HBED-CC with the targeting agent PSMA-11. As mentioned above, DKFZ-PSMA-11 is disclosed on page 12 of the description, and therefore a contradiction between claim 1 of auxiliary request 2a and the description does not arise.

7.2 The board thus concludes that the feature of claim 1 of auxiliary request 2a expressing that "*said chelator is linked to said biological targeting agent and is DKFZ-PSMA-11*" does not introduce any lack of clarity under Article 84 EPC.

Auxiliary request 2a - claim 1 - inventive step under Article 56 EPC

8. Closest prior art

8.1 In accordance with the appealed decision (page 22, point 6), both parties indicated document D12 as the closest prior art. In view of the disclosure in D12, the board has no reason to take another stance.

8.2 In fact, D12 concerns methods for labelling targeting agents, particularly with Ga68. In particular, D12 discloses (page 8, second paragraph to page 11, and claims 9 to 18) a method for eluting, with an acidic solution, a Ge68/Ga68 generator, wherein Ga68 is eluted with HCl such that the entire available yield of Ga68 is passed directly into a vial containing a solution or a lyophilised preparation of the chelate-targeting agent conjugate that is to be labelled, without further purification procedures. The chelate-targeting agent conjugate can be compounded into kits, formulated and stabilised, thus being ready to use. According to D12, the chelators are macrocyclic derivatives such as 1,4,7-triazacyclononane-N,N',N"-triacetic acid ("NOTA") or l,4,7,10-tetraazacyclododecane-N,N’,N'',N'''-tetraacetic acid ("DOTA"). Moreover, a neutralising buffer is used in the vial to increase the pH to 5 to 8. D12 also indicates (claim 34) that the components of the vial can be lyophilised.

9. Distinguishing feature

It was common ground that the subject-matter of claim 1 of auxiliary request 2a differs from the above disclosure in D12 on account of the chelator used in the method, which, according to claim 1 (point 1 above), can be a compound of formula (I) or a salt of it. As stated above, in D12 NOTA and DOTA are disclosed

as possible chelators, these two chelators being different from those defined in claim 1.

10. Objective technical problem

10.1 The patent proprietor referred to the results reported in example 3 (paragraphs [0094] and [0095]) and figure 1 of the patent (identical to example 3 (page 25) and figure 1 of the application as filed). In line with the appealed decision (pages 23 and 24, points 6.2 and 6.3), it submitted that figure 1 showed an improvement in terms of labelling efficiency at lower concentrations of chelator as achieved with chelator CP256 (THP-Ac) according to formula (I) of claim 1 of auxiliary request 2a over the use of DOTA and NOTA (chelators from D12). This result was not limited to the tested compound CP256. Indeed, the post-published document A31 reported (table 1, page 4303) an even higher labelling efficiency when methyl, as the R^2 substituent, was replaced with hydrogen in the chelator of formula (I).

10.2 Therefore, the patent proprietor formulated the objective technical problem as that of providing an improved method for preparing a radiolabelling complex with gallium having higher labelling efficiency.

10.3 The board accepts this formulation of the objective technical problem as proposed by the patent proprietor.

11. Obviousness of the claimed solution

11.1 As a solution to the above-mentioned objective technical problem, claim 1 of auxiliary request 2a proposes, *inter alia*, using chelators of formula (I) or salts of it.

11.2 In line with the appealed decision (page 24, first paragraph), the patent proprietor argued that neither D12 nor any other prior-art document suggested this

claimed solution. In its communication under Article 15(1) RPBA, the board had referred to document D2, especially to its example 3, stating that this example rendered the claimed solution obvious; however, the patent proprietor pointed to the different operating conditions used in D12 on the one hand and in example 3 of D2 on the other hand. D12 disclosed a method in which the Ga68 generator was eluted under extremely acidic conditions directly into a vial containing the chelator, i.e. without intermediate purification procedures. This meant that the eluate in D12 contained several impurities which could potentially affect the labelling efficiency. In D12, it was found that NOTA and DOTA chelators were able to efficiently bind Ga68 even under these harsh conditions. On the contrary, in example 3 of D2 (page 43), a purified and buffered Ga solution was used to compare the labelling efficiencies of CP256 (a compound of formula (I) of the claimed method) and DOTA. The use of purified and buffered Ga solutions was further disclosed in example 7 of D2 (pages 53 to 55). In view of the different operating conditions, the skilled person would not have reasonably expected that the improved labelling efficiency reported in example 3 of D2 to be associated with CP256 would have been maintained under the harsh conditions used in D12.

11.3 The board disagrees.

11.3.1 Document D2 discloses (page 2, line 17 to page 4, line 32) the use of chelators of formula (I) as defined in claim 1 of auxiliary request 2a in lieu of DOTA in methods for molecular imaging. In particular, example 3 (page 43) of D2 discloses the comparison in terms of labelling efficiency with Ga67 between the use of a compound of formula (I) (CP256, i.e. the same compound as used in example 3 of the application as filed) and

the use of DOTA as the chelator. The results of example 3 are shown in figure 1 of D2 and demonstrate a higher labelling efficiency at low concentrations obtained with CP256 at room temperature in comparison with the use of DOTA at an elevated temperature.

11.3.2 It is acknowledged that example 3 of D2 was carried out under different operating conditions in comparison with the method taught in D12, namely with a purified and buffered Ga solution; however, the patent proprietor did not provide any technical considerations explaining why the skilled person would have assumed that the improved labelling efficiency obtained in example 3 of D2 with a chelator of formula (I) of claim 1 of auxiliary request 2a over DOTA would not also be maintained under the operating conditions taught by D12. The mere argument that the skilled person would not have expected this improvement to be maintained is not corroborated by any technical explanation and thus amounts to mere speculation.

11.3.3 Therefore, it must be assumed that the skilled person aiming to solve the above-mentioned objective technical problem would have been prompted by the results of example 3 of D2 to replace the DOTA chelator used in D12 with a chelator of formula (I), thus arriving at the subject-matter of claim 1 of auxiliary request 2a in an obvious way.

11.4 For these reasons, the board concludes that the subject-matter of claim 1 of auxiliary request 2a does not involve an inventive step (Article 56 EPC). Hence, auxiliary request 2a is not allowable.

Auxiliary request 2b - claim 1 - inventive step under Article 56 EPC

12. Claim 1 of auxiliary request 2b differs from claim 1 of auxiliary request 2a (point 1 above) only in that the disclaimer was amended. This amendment does not affect the alternative in claim 1 of auxiliary request 2a in which the chelator is a compound of formula (I). This alternative is contained in claim 1 of auxiliary request 2b in unamended form.

12.1 It follows that the conclusion of lack of inventive step of the subject-matter of claim 1 of auxiliary request 2a applies, *mutatis mutandis*, to claim 1 of auxiliary request 2b. This conclusion was not disputed by the patent proprietor at the oral proceedings.

12.2 Therefore, the subject-matter of claim 1 of auxiliary request 2b does not involve an inventive step (Article 56 EPC). Hence, auxiliary request 2b is not allowable.

Auxiliary request 2c filed during the oral proceedings before the board - admittance into the proceedings - Article 13(1) and (2) RPBA

13. During the oral proceedings before the board, after having heard the board's conclusion on auxiliary requests 2a and 2b, the patent proprietor filed the set of claims according to auxiliary request 2c. Claim 1 of this request reads as follows:

"*1. A method for preparing a complex comprising a radioisotope of gallium for use in radiotherapy or in a medical imaging procedure, said method comprising adding a gallium radioisotope solution obtained directly from a gallium radionuclide generator to a composition comprising a pharmaceutically acceptable buffer and optionally also a pharmaceutically acceptable basic reagent, in amounts sufficient to*

increase the pH to a level in the range of 3 to 8, wherein the composition further comprises a chelator that is able to chelate radioactive gallium within said pH range and at moderate temperature, said chelator being linked to a biological targeting agent, wherein said chelator is linked to said biological targeting agent and is DKFZ-PSMA-11, and

wherein said chelator, buffer, and basic agent are in lyophilized or freeze-dried form,

with the proviso that said method does not comprise (a) eluting a 68Ge/68Ga generator by fractionation with about 1.8 ml HCl 0.1N directly into a reaction vial containing 10 µg DKFZ-PSMA-11 in lyophilized form and 800-1800 mg sodium formate in lyophilized form, and (b) mixing and incubating the reaction vial at room temperature for about 5 minutes."

Therefore, in comparison with claim 1 of auxiliary request 2a, the alternative according to which the chelator is a compound of formula (I) was deleted.

13.1 The opponent requested that auxiliary request 2c not be admitted into the proceedings. It referred to the Case Law of the Boards of Appeal and argued that it was established case law that a late-filed request may be admitted only if it was *prima facie* allowable and/or amounted to a response to an unforeseeable development in the proceedings. Neither of these conditions applied to auxiliary request 2c. Claim 1 of this request was not *prima facie* allowable in view of the presence of the disclaimer, to which clarity and added-matter objections had been raised. Additionally, the feature of claim 1 of auxiliary request 2c stating "*said chelator being linked to a biological targeting agent, wherein said chelator is linked to said biological targeting agent*" lacked clarity since it repeated the

same clause twice. Furthermore, the filing of auxiliary request 2c was not a response to an unforeseeable development in the proceedings; an inventive-step objection to the alternative in claim 1 of auxiliary request 2a, which has now been deleted, had been raised by both the opponent and the board. It was thus clearly foreseeable by the patent proprietor that this alternative could have been found to be unallowable. Indeed, in its letter dated 24 January 2025, the patent proprietor had envisaged the possibility of filing a request in which this alternative had been deleted, but chose not to file it. Therefore, auxiliary request 2c was not to have been admitted.

13.2 Under Article 13(1) RPBA, an amendment to a party's appeal case filed after the grounds of appeal or reply may be admitted only at the discretion of the board. The board exercises its discretion in view of, *inter alia*, the suitability of the amendment for resolving issues raised by another party or by the board. Moreover, under Article 13(2) RPBA, an amendment filed after notification of a communication under Article 15(1) RPBA will, in principle, not be taken into account unless there are exceptional circumstances, which have been justified with cogent reasons by the party concerned.

13.2.1 As explained above, the patent proprietor had already been confronted with an objection under Article 123(3) EPC raised by the opposition division at the oral proceedings for the first time. More importantly, the patent proprietor was confronted with a new inventive-step objection raised by the board in its communication issued under Article 15(1) RPBA against auxiliary request 9, which was found allowable by the opposition division (point II above). In fact, for the first time in this communication, the board noted that when

starting from D12 as the closest prior art, example 3 of D2 rendered the method claimed in auxiliary request 9 obvious. While the opponent had raised an objection in view of D12 as the closest prior art against auxiliary request 9, it had not pointed to example 3 of D2. Moreover, in its communication the board had additionally noted that the same objection applied, *mutatis mutandis*, to the higher-ranking requests, to auxiliary request 2a, *inter alia*. An inventive-step objection starting from D12 as the closest prior art had not been raised by the opponent to auxiliary request 2a.

13.2.2 The board holds that this course of the proceedings represents an exceptional circumstance justifying the filing of auxiliary request 2c as a direct response to the new objection raised by the board to auxiliary request 2a. It is acknowledged that the patent proprietor did not file auxiliary request 2c with its letter dated 24 January 2025 submitted in response to the board's communication; however, in this letter (see the last two paragraphs), the patent proprietor had announced the filing of such a request precisely for the case which occurred during the oral proceedings before the board, namely in which the board had concluded a lack of inventive step on the basis of the above-mentioned new objection, while at the same time concluding that auxiliary request 2a complied with Article 123(2) and (3) EPC and Article 84 EPC.

13.2.3 Furthermore, it is immediately evident that by deleting the alternative according to which the chelator is a compound of formula (I) from claim 1, auxiliary request 2c overcomes the board's objection of lack of inventive step of claim 1 of auxiliary request 2a reported above.

13.3 In view of these considerations, the board decided to admit auxiliary request 2c into the proceedings, pursuant to Article 13(1) and (2) RPBA.

Auxiliary request 2c - remittal to the opposition division - Article 111(1) EPC

14. Both parties requested that the case be remitted to the opposition division for further prosecution should the board admit auxiliary request 2c into the proceedings.

14.1 Pursuant to Article 111(1) EPC, in the event that the appealed decision has to be set aside, the board has discretion over whether or not to exercise the powers within the competence of the opposition division or to remit the case to the opposition division for further prosecution.

14.2 The board notes that the appealed decision deals, *inter alia*, with the issues of compliance with Article 123(3) EPC and inventive step; the opposition division concluded, *inter alia*, that auxiliary request 2a infringed Article 123(3) EPC while the alternative in the claimed method according to which the chelator is a compound of formula (I) involved an inventive step (auxiliary request 9, point II above).

14.3 For the reasons set out above, both of the opposition division's conclusions have been reversed, and therefore the appealed decision has to be set aside.

14.4 Both parties requested remittal, which remains at the discretion of the board (Article 111(1) EPC). In this case, the board decided to remit the case to the opposition division since essential questions regarding the patentability of the subject-matter of claim 1 of auxiliary request 2c, particularly the allowability of the disclaimer under Articles 84 and 123(2) EPC, as well as the novelty and inventive step of the claimed

method, have not yet been examined and decided upon by the opposition division. Deciding on these issues for the first time in appeal proceedings would not be in line with the primary object of these proceedings, which, according to Article 12(2) RPBA, is the judicial review of the appealed decision.

Order

For these reasons it is decided that:

1. The decision under appeal is set side.

2. The case is remitted to the opposition division for further prosecution on the basis of the claims of auxiliary request 2c filed during the oral proceedings before the board.

The Registrar: The Chairman:

U. Bultmann M. O. Müller

Decision electronically authenticated