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**Datasheet for the decision of 24 January 2024**

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| **Case Number:** | T 1259/22 - 3.3.04 |
| **Application Number:** | 10184509.7 |
| **Publication Number:** | 2371361 |
| **IPC:** | A61K31/33, A61K31/555, A61K38/19, A61P43/00, A61K31/496, A61K31/55, A61K31/551, A61K31/395, A61K31/4427, A61K35/28, A61K35/12, C12N5/0789 |
| **Language of the proceedings:** | EN |

**Title of invention:**
Methods to mobilize progenitor/stem cells

**Patent Proprietor:**
Genzyme Corporation

**Opponents:**
Generics [UK] Limited (trading as Mylan)
Teva Pharmaceutical Industries Ltd.
Accord Healthcare Ltd
Sandoz AG
Zentiva, k.s.
STADA Arzneimittel AG
betapharm Arzneimittel GmbH

**Headword:**
Plerixafor to mobilise progenitor/stem cells/GENZYME

**Relevant legal provisions:**
EPC Art. 76(1), 54(5)

**Keyword:**
Divisional application - added subject-matter (yes)
Claim construction - Article 54(5) EPC applicable (no)
Novelty - novelty of claimed substance (no)

**Decisions cited:**
G 0001/07, G 0002/08, T 0434/15, T 0081/84, T 0826/06, T 1758/15, T 0558/20, T 2003/08

Europäisches Patentamt
European Patent Office
Office européen des brevets

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**Case Number: T 1259/22 - 3.3.04**

# D E C I S I O N
# of Technical Board of Appeal 3.3.04
# of 24 January 2024

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|---|---|
| **Appellant:** (Patent Proprietor) | Genzyme Corporation<br>450 Water Street<br>Cambridge, MA 02141 (US) |
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| **Appellant:** (Opponent 2) | Teva Pharmaceutical Industries Ltd.<br>124 Dvora HaNevi'a St.<br>6944020 Tel Aviv (IL) |
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| **Party as of right:**<br>(Opponent 4) | Sandoz AG<br>Lichtstrasse 35<br>4056 Basel (CH) |
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| **Representative:** | Hoppe, Daniel<br>Preu Bohling & Partner<br>Neuer Wall 72<br>20354 Hamburg (DE) |
| **Decision under appeal:** | **Interlocutory decision of the Opposition Division of the European Patent Office posted on 24 May 2022 concerning maintenance of the European Patent No. 2371361 in amended form** |

**Composition of the Board:**

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| **Chair** | M. Pregetter |
| **Members:** | S. Albrecht |
| | M. Blasi |
| | B. Rutz |
| | L. Bühler |

## Summary of Facts and Submissions

I. European patent 2 371 361 ("patent") was granted on European patent application 10 184 509.7 ("application"). This application is a divisional application of the earlier European patent application 02 750 370.5 which had been filed as an international application under the PCT published as WO 03/011277 (document D76 in these proceedings).

II. The patent was opposed by seven opponents. The grounds for opposition were Article 100(a) EPC for exclusion from patentability under Article 53(a) and (c) EPC, lack of novelty and lack of inventive step, and Article 100(b) and (c) EPC.

III. The documents filed during the opposition proceedings included:

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| D1 | EP 1 016 413 A1 |
| D13 | WO 00/45814 A1 |
| D17 | JM Croop et al., "Large-scale mobilization and isolation of $CD34^+$ cells from normal donors", Bone Marrow Transplantation 26, 2000, pages 1271 to 1279 |
| D48 | Excerpts from a textbook entitled "Novel Developments in Stem Cell Mobilization - Focus on CXCR4", ed. S. Fruehauf, W. J. Zeller and G. Calandra, Springer, 2012, pages 3, 4, 7, 8, 11, 12, 103, 104, 115, 201, 206, 209, 210, 221, 222 |
| D55 | Copy of decision T 434/15 of 25 June 2019 relating to the earlier European patent application 02 750 370.5 |

D76 WO 03/011277 A2

D78 Excerpt from a textbook entitled "Novel Developments in Stem Cell Mobilization - Focus on CXCR4", ed. S. Fruehauf, W. J. Zeller and G. Calandra, Springer, 2012, pages 97 to 99

IV. In the course of the opposition proceedings, the patent proprietor submitted 14 sets of claims filed as auxiliary requests 1 to 14. The sets of claims of auxiliary requests 1 to 10 were filed on 19 February 2021, and those of auxiliary requests 11 to 14 on 7 December 2021.

V. The opposition division decided that the patent, as amended in the form of auxiliary request 6, and the invention to which it related met the requirements of the EPC. The decision was based on the patent as granted as the main request and on sets of claims of auxiliary requests 1 to 6.

The opposition division concluded, *inter alia*, that

(a) claims 1, 3, 4 and 12 of the main request comprised added subject-matter (Articles 76(1) and 123(2) EPC),

(b) claim 6 of the main request fulfilled the requirements of Articles 76(1) and 123(2) EPC,

(c) the sets of claims in each of auxiliary requests 1 to 5 comprised added subject-matter (Articles 76(1) and 123(2) EPC) and

(d) claim 1 of auxiliary request 6 was a purpose-limited product claim under Article 54(5) EPC.

VI. Claim 1 of the main request reads as follows:

"1. A compound which is 1,1'-[1,4-phenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane or a pharmaceutically acceptable salt or metal complex thereof, for use in a method comprising:
(a) administering said compound to a subject, to mobilize progenitor and/or stem cells in said subject; and
(b) harvesting said progenitor and/or stem cells."

Claim 2 of the main request differs from claim 1 in that it further stipulates that the progenitor and/or stem cells to be mobilised are CD34+ cells and that these are to be harvested via apheresis.

Claim 3 of the main request is a dependent claim of claims 1 and 2, and further specifies that the harvested cells are suitable for use in cell transplantation.

Claim 6 of the main request is dependent, *inter alia*, on claim 3 and further specifies that the harvested cells are suitable for treating a haematopoietic deficit from chemotherapy or radiation therapy.

Claims 1 to 3 of auxiliary request 2 are identical to claims 1 to 3 of the main request, respectively.

Claim 5 of auxiliary request 2 is dependent, *inter alia*, on claim 3, and further specifies that the harvested cells are suitable for treating a

haematopoietic deficit from chemotherapy or radiation therapy.

The subject-matter of claim 1 of each of auxiliary requests 3 and 5 is identical to the subject-matter of claim 3 of the main request when dependent on claim 1.

Claim 1 of auxiliary request 4 differs from claim 1 of the main request in that the following passage has been added to the end of step b):

", and using them in cell transplantation" (termed "step c)" in the following)

Claim 1 of auxiliary request 6 is identical to claim 1 of auxiliary request 4.

The subject-matter of claim 1 of each of auxiliary requests 7 and 9 is identical to the subject-matter of claim 3 of the main request when dependent on claim 2.

Claim 1 of each of auxiliary requests 8 and 10 differs from claim 1 of auxiliary request 4 by limiting the progenitor and/or stem cells to be mobilised to CD34+ cells and by specifying that these are harvested via apheresis.

Claim 1 of auxiliary request 11 differs from claim 1 of auxiliary request 3 in that the passage "or a pharmaceutically acceptable salt or metal complex thereof," has been deleted and in that the following feature has been added at the end of the claim: ", and wherein said method comprises administering G-CSF to said subject".

Claim 1 of auxiliary request 12 comprises the same amendments as claim 1 of auxiliary request 11, and is otherwise identical to claim 1 of auxiliary request 4.

The same amendments as in claim 1 of auxiliary request 11 have been made to claim 1 of auxiliary request 13 which is otherwise identical to claim 1 of auxiliary request 9.

The same amendments as in claim 1 of auxiliary request 12 have been made to claim 1 of auxiliary request 14 which is otherwise identical to claim 1 of auxiliary request 10.

VII. The compound recited in claim 1 of the main request is also known by its international non-proprietary name "plerixafor". In the following, the compound from claim 1, including pharmaceutically acceptable salts and metal complexes thereof, are referred to as "plerixafor".

VIII. The patent proprietor and opponents 1, 2, 4, 5 and 6 lodged each an appeal against the opposition division's decision.

IX. With its statement of grounds of appeal, the patent proprietor resubmitted the sets of claims of auxiliary requests 1 to 14, filed before the opposition division (see point IV. above), and filed four further sets of claims as auxiliary requests 15, 16, 17 and 18, respectively.

Claim 1 of auxiliary request 15 and claim 1 of auxiliary request 16 are identical to claim 1 of auxiliary request 11 and claim 1 of auxiliary request 12, respectively, except that the feature ", and

wherein said method comprises administering G-CSF to said subject" has been replaced by the wording "wherein said subject has been treated with G-CSF".

Claim 1 of auxiliary request 17 differs from claim 1 of auxiliary request 15 by limiting the progenitor and/or stem cells to be mobilised to CD34+ cells and by specifying that these are harvested via apheresis.

The same amendments as in claim 1 of auxiliary request 17 have been made to claim 1 of auxiliary request 18 which is otherwise identical to claim 1 of auxiliary request 16.

X. By letter dated 11 May 2023, the patent proprietor filed three further sets of claims as auxiliary requests 19, 20 and 21.

Claim 1 of auxiliary request 19 is identical to claim 1 of auxiliary request 4 (see point VI. above).

Claim 1 of each of auxiliary requests 20 and 21 differs from claim 1 of auxiliary request 19 in that the following passages have been added to the end of the claim, respectively.

", wherein said method comprises administering G-CSF to said subject"

", wherein said subject has been treated with G-CSF"

XI. By letter dated 6 September 2023, opponent 4 withdrew its appeal.

Consequently, the patent proprietor ("appellant-patent proprietor") and opponents 1, 2, 5 and 6 are appellants

in these proceedings ("appellant-opponents"), while opponents 3, 4 and 7 are parties as of right and respondents to the appellant-patent proprietor's appeal ("respondent-opponents").

XII. In a communication pursuant to Article 15(1) RPBA ("board's communication"), the board drew the parties' attention to the points to be discussed during the oral proceedings, which had been scheduled in view of corresponding requests of the parties, and raised the question whether claim 1 of auxiliary request 19 was to be interpreted as a purpose-limited product claim under Article 54(5) EPC.

XIII. Subsequently, appellant-opponents 2, 5 and 6 and all three respondent-opponents informed the board that they would not be attending the oral proceedings.

XIV. By letter dated 16 January 2024, the appellant-patent proprietor filed two further sets of claims as auxiliary requests 5a and 15a, respectively.

Claim 1 of each of auxiliary requests 5a and 15a is identical to claim 1 of each of auxiliary requests 5 and 15, respectively.

The text of all claim requests is available in the electronic file which can be inspected online via the European patent register.

XV. Oral proceedings took place before the board on 24 January 2024 in the presence of the appellant-patent proprietor and appellant-opponent 1. In the course of these proceedings, the appellant-patent proprietor withdrew the main request and auxiliary request 1. At

the end of the oral proceedings, the chair announced the board's decision.

XVI. The appellant-patent proprietor's submissions, where relevant to this decision, can be summarised as follows.

*Auxiliary requests 2 to 18 - amendments (Article 76(1) EPC)*

*(a) Auxiliary request 2 - claim 3 (see point VI. above)*

The claimed feature "wherein the harvested cells are suitable for use in cell transplantation" had the same technical meaning as the wording "harvesting of progenitor cells and/or stem cell [sic] for subsequent stem cell transplantation" used in the last sentence of paragraph [0045] of the earlier application as filed (i.e. document D76). This interpretation was in line with the commonly understood meaning of the word "for" as "suitable for".

Contrary to appellant-opponent 1's contention, the aforementioned last sentence of paragraph [0045] did not disclose transplantation as an essential step that had to occur after harvesting. The term "subsequent" used in this sentence solely expressed the order of the steps, i.e. harvesting before transplantation. This exact same order was expressed by the claimed feature "wherein the harvested cells are suitable for use in cell transplantation".

*(b) Auxiliary request 2 - claim 5 (see point VI. above)*

As evidenced by paragraph [0012] of document D76, it was commonly known that haematopoietic deficits from

chemotherapy or radiation therapy constituted the clinical indication of harvested progenitor and/or stem cells ("PSCs"). Consequently, the skilled person would have read the reference to these deficits in paragraph [0045] of document D76 in conjunction with progenitor and/or stem cell ("PSC") harvesting and transplantation.

*(c) Auxiliary requests 3 to 18*

These requests did not add subject-matter for the same reasons as given for claims 3 and 5 of auxiliary request 2.

*Auxiliary requests 19 to 21 - claim construction and novelty (Article 54(5) EPC)*

*(a) Claim 1 of auxiliary request 19*

The opposition division was correct in considering the method recited in claim 1 as a whole, rather than each of the three method steps a) to c) in isolation. As set out in the opposition division's decision, this method was excluded from patentability under Article 53(c) EPC. Hence, claim 1 of auxiliary request 19 was to be read as a purpose-limited product claim under Article 54(5) EPC.

This claim did not read any differently, if method steps a) to c) were considered separately, because each of these steps was excluded from patentability under Article 53(c) EPC.

Step a) was a therapeutic step. In this step, plerixafor increased the number of circulating blood cells, which led to an inherent physiological effect in

all subjects, for example in regenerating myocardium, enhancing wound healing, restoring organ tissue, improving the ability to fight infection, and increasing oxygen transport. Moreover, administering plerixafor prior to harvesting reduced the number of harvest procedures required and thereby reduced the severe side effects caused by harvesting. These effects were therapeutic effects experienced by all subjects.

Step b) was a surgical step. The prior administration of plerixafor was essential to this step in that it ensured that sufficient PSCs were present in the peripheral blood for harvesting. Moreover, the PSC population achieved with plerixafor was clinically superior to that obtained with G-CSF. Therefore, similarly to the case dealt with in decision T 826/06, there was a causal link between the administration of the claimed compound and the later surgical step b). As a matter of fact, steps a) and b) taken as a whole could also be considered as a single surgical step.

Step c) had surgical character, and additionally represented an excluded method of therapy under Article 53(c) EPC, at least in the event of an autologous transplantation. As explicitly stated in claim 1, the PSCs transplanted in step c) were exactly the same cells that had been mobilised by plerixafor in step a) and harvested in step b). Hence, claim 1 expressed a clear causal link between step c) and the preceding steps a) and b). The fact that claim 1 did not indicate any limitation concerning the timing of the individual steps was of no concern. As was apparent from decision T 826/06, the case law of the boards of appeal required a causal link rather than a timing link between the individual method steps.

Since none of the prior-art documents on file disclosed the medical use recited in claim 1, the subject-matter of this claim was novel.

*(b) Claim 1 of each of auxiliary requests 20 and 21*

The considerations set out in respect of claim 1 of auxiliary request 19 equally applied to claim 1 of each of these two auxiliary requests.

XVII. The submissions by the appellant-opponents and respondent-opponent 4, where relevant to this decision, can be summarised as follows.

*Auxiliary requests 2 to 18 - amendments (Article 76(1) EPC)*

The last sentence of paragraph [0045] of document D76 did not constitute an appropriate basis for the subject-matter of claims 3 and 5 of auxiliary request 2. This sentence disclosed the PSC harvesting step exclusively in conjunction with a subsequent transplantation step. By contrast, claim 3 of auxiliary request 2 did not specify such a transplantation step.

With respect to claim 5 of auxiliary request 2, paragraph [0045] of document D76 disclosed the treatment set out in this claim (i.e. treatment of haematopoietic deficits from chemotherapy or radiation therapy) in the context of a therapeutic use, rather than in the context of a transplantation.

Auxiliary requests 3 to 18 added subject-matter for the same reasons as auxiliary request 2.

*Auxiliary requests 19 to 21 - claim 1 - claim construction and novelty (Article 54(5) EPC)*

*(a) Claim 1 of auxiliary request 19*

In determining whether a claim directed to a compound for use in a multi-step method should be read as a purpose-limited product claim under Article 54(5) EPC, the individual steps of the method needed to be considered separately to determine whether a causal link existed between the compound being claimed and those steps of the method which were excluded from patent protection under Article 53(c) EPC.

In the case at issue, there was no such causal link.

*Step a)*

This step included PSC mobilisation in healthy stem-cell donors who did not receive any therapeutic benefit from the treatment with plerixafor. Step a) thus defined methods which were not all excluded under Article 53(c) EPC. The therapeutic effects invoked by the appellant-patent proprietor did not occur because the PSCs mobilised in step a) were immediately removed from the donor afterwards.

*Step b)*

As set out in decision T 434/15 (point 4.3 of the Reasons), step b) was principally performed via apheresis and therefore was a surgical method excluded under Article 53(c) EPC; however, in contrast to the case underlying decision T 826/06, step b) did not involve the use of plerixafor or contain any other specific feature that would have allowed it to tie in

with plerixafor used in step a). The harvesting of PSCs in step b) remained the same regardless of how these cells were mobilised. Consequently, step b) was not causally linked to plerixafor.

*Step c)*

Step c) was a therapeutic method not involving the use of plerixafor. Furthermore, step c) was sequentially disconnected from step b) and both steps could be carried out in completely different patients. Hence, step c) was not causally linked to plerixafor either.

It followed from the above that claim 1 could not be read as a purpose-limited product claim under Article 54(5) EPC. Instead, it defined a compound (plerixafor) suitable for use in the multi-step method recited in this claim. This compound was already disclosed in the prior art, e.g. in document D13. Hence, the subject-matter of claim 1 lacked novelty.

*(b) Claim 1 of each of auxiliary requests 20 and 21*

The considerations set out in respect of claim 1 of auxiliary request 19 equally applied to claim 1 of each of these two auxiliary requests.

XVIII. The parties' final requests were as follows.

The appellant-patent proprietor requested that the decision under appeal be set aside and that the patent be maintained in amended form on the basis of one of auxiliary requests 2 to 5, 5a, 6 to 15, 15a and 16 to 21.

Appellant-opponents 1, 2, 5 and 6 requested that the decision under appeal be set aside and that the patent be revoked.

Respondent-opponent 4 withdrew its appeal and did not submit any new requests.

Respondent-opponents 3 and 7 did not file any requests or make any submissions on substance in the appeal proceedings.

## Reasons for the Decision

1. The appeals are admissible.

2. Procedural issues

*Absence of appellant-opponents 2, 5, and 6, and respondent-opponents 3, 4, and 7 from the oral proceedings*

2.1 Appellant-opponents 2, 5, and 6, and respondent-opponents 3, 4, and 7, although duly summoned, did not attend the oral proceedings, as they had announced in their letters dated 15 January 2024, 8 January 2024 (appellant-opponents 5 and 6), 16 January 2024, 10 January 2024 and 16 January 2024, respectively. In accordance with Rule 115(2) EPC and Article 15(3) RPBA, the board continued the proceedings in the absence of these parties who were treated as relying on their written case (if any). By absenting themselves from the oral proceedings the absent parties waived their opportunity to make any further submissions on the relevant issues of the case. Hence, the board was in a position to announce a decision at the conclusion of the oral proceedings, as provided for in Article 15(6) RPBA.

*Admittance of auxiliary requests 5a and 15 to 21 into the proceedings*

2.2 The board decided to admit these auxiliary requests into the proceedings.

2.3 In view of the outcome of the appeal proceedings, detailed reasoning on the admittance of these requests is not necessary.

3. Substantive issues

*Auxiliary request 2 - claim 3 - amendments (Article 76(1) EPC)*

3.1 Contrary to the appellant-patent proprietor's view, the last sentence of paragraph [0045] of document D76 does not directly and unambiguously disclose the claimed subject-matter. The reasons are as follows.

3.1.1 This sentence states, *inter alia*, that "[t]he method of the invention thus targets a broad spectrum of conditions ... where harvesting of progenitor cells and/or stem cell [sic] for subsequent stem cell transplantation would be beneficial". According to paragraph [0002] of document D76, the invention referred to in this sentence is in the field of therapeutics and medicinal chemistry and concerns methods for mobilising progenitor stem cells (PSCs) in subjects by administering certain polyamines (e.g. plerixafor).

3.1.2 This has not been contested by the appellant-patent proprietor. Hence, the harvesting step disclosed in the last sentence of paragraph [0045] of document D76 is

carried out for the purpose of subsequent stem cell transplantation in a clinical setting.

3.1.3 As alluded to in point 2.4 of the board's communication, this purpose forms a technically limiting feature of the progenitor and/or stem cell harvesting step, i.e. this harvesting step must be performed in a manner that the PSC harvest as a whole is suitable for a subsequent clinical use in stem cell transplantation. This implies not only that the PSCs in the harvest are suitable for subsequent stem cell transplantation, but also that these are collected in sufficient numbers to achieve a clinically relevant cell engraftment dose (see paragraph A.26 of the appellant-patent proprietor's statement setting out the grounds of appeal; document D1, paragraph [0008]).

3.1.4 By contrast, claim 3 only requires that the harvested PSCs are suitable for the stated purpose.

3.2 The subject-matter of claim 3 is therefore an impermissible generalisation of the disclosure in paragraph [0045] of document D76, contrary to the requirements of Article 76(1) EPC.

*Auxiliary request 2 - claim 5 - amendments (Article 76(1) EPC)*

3.3 Contrary to the appellant-patent proprietor's contention, the subject-matter of this claim (see point VI. above) does not have a basis in paragraph [0045] of document D76. The reasons are as follows.

3.3.1 The first four sentences of paragraph [0045] give examples of a variety of medical conditions that may be ameliorated or otherwise benefited by "the method of the invention", i.e. the mobilisation of PSCs in

subjects by administering certain polyamines (see paragraph [0002] of document D76). Among the cited conditions are haematopoietic deficits from chemotherapy or radiation therapy (see first sentence of paragraph [0045]).

3.3.2 Following on from these disclosures, the fifth sentence of paragraph [0045] states:

"*The method of the invention thus targets a broad spectrum of conditions for which elevation of progenitor cells and/or stem cells in a subject would be beneficial or, where harvesting of progenitor cells and/or stem cell [sic] for subsequent stem cell transplantation would be beneficial*".

3.3.3 The use of the word "or" in this passage makes it clear that the method of the invention has two distinct applications, i.e.

(a) in a first embodiment, it elevates a subject's PSCs *in vivo* and, by virtue of this effect, directly treats a disorder with which this same subject is afflicted;

(b) in a second, separate embodiment, it is used in PSC transplantation settings, i.e. it elevates PSCs in a subject followed by the harvesting of these PSCs for subsequent stem cell transplantation in the same subject (autologous transplantation) or a different subject (allogenic transplantation).

3.3.4 None of the first four sentences of paragraph [0045] discloses any harvesting and/or transplantation step. Paragraph [0045], last sentence, second half, in turn,

does not further specify the conditions to be treated with the stem cell transplants.

3.3.5 In light of these facts, the skilled person would understand the medical conditions disclosed in the first four sentences of paragraph [0045], including haematopoietic deficits from chemotherapy and radiation therapy, to be examples of disorders in accordance with the first embodiment only (see point 3.3.3 above).

3.4 Relying on paragraph [0012] of document D76, the appellant-patent proprietor submitted that it was common general knowledge that PSCs were harvested to treat haematopoietic deficits from chemotherapy or radiation therapy. Consequently, the skilled person would immediately understand the disclosure "conditions ..., where harvesting of progenitor cells and/or stem cell [sic] for subsequent stem cell transplantation would be beneficial" in paragraph [0045] of document D76 to mean haematopoietic deficits from chemotherapy or radiation therapy.

3.5 This argument is not convincing. As explained in points 3.3.3 to 3.3.5 above, document D76 does not directly and unambiguously disclose haematopoietic deficits from chemotherapy or radiation in the context of PSC harvesting and subsequent stem cell transplantation.

3.6 As a consequence, the appellant-patent proprietor's argument amounts to inferring technical information which does not belong to the content of document D76 itself from common general knowledge. The so-called "gold standard" established in the case law provides as limits within which amendments can be made what a skilled person would derive directly and unambiguously, using common general knowledge, and seen objectively

and relative to the date of filing, from the whole of the documents as filed. The use of common general knowledge referred to in the "gold standard" is, however, not meant to extend the teaching of the application as filed, but only to aid the skilled person in understanding that teaching.

*Auxiliary requests 3, 5, 5a, 7, 9, 11, 13, 15, 15a and 17 - added subject-matter (Article 76(1) EPC)*

3.7 Like the subject-matter of claim 3 of auxiliary request 2, the subject-matter of claim 1 of each of auxiliary requests 3, 5, 5a, 7, 9, 11, 13, 15, 15a and 17 requires the harvested progenitor and/or stem cells to be suitable for use in cell transplantation.

3.8 The appellant-patent proprietor did not present any arguments beyond those already submitted with respect to claim 3 of auxiliary request 2.

3.9 As a consequence, each of these auxiliary requests fails to meet the requirements of Article 76(1) EPC for the same reasons as claim 3 of auxiliary request 2.

*Auxiliary requests 4, 6, 8, 10, 12, 14, 16 and 18 - added subject-matter (Article 76(1) EPC)*

3.10 Like the subject-matter of claim 5 of auxiliary request 2, the subject-matter of claim 4 of each of auxiliary requests 4, 6, 12 and 16 and that of claim 3 of each of auxiliary requests 8, 10, 14 and 18 stipulates that the harvested progenitor and/or stem cells are suitable for treating a haematopoietic deficit from chemotherapy or radiation therapy.

3.11 In the absence of any arguments from the appellant-patent proprietor beyond those already presented with respect to claim 5 of auxiliary request 2, each of auxiliary requests 4, 6, 8, 10, 12, 14, 16 and 18 fails to meet the requirements of Article 76(1) EPC for the same reasons as claim 5 of auxiliary request 2.

*Auxiliary request 19 - claim construction and novelty (Article 54(5) EPC)*

3.12 Claim 1 of auxiliary request 19 is directed to plerixafor for use in a method comprising:

a) administering plerixafor to a subject, to mobilise progenitor and/or stem cells in said subject,

b) harvesting said progenitor and/or stem cells, and

c) using them in cell transplantation.

3.13 The parties were in dispute as to whether claim 1 of auxiliary request 19 constitutes a purpose-limited product claim in accordance with Article 54(5) EPC.

3.14 Article 54(5) EPC establishes that a substance or composition referred to in Article 54(4) EPC for any specific use in a method referred to in Article 53(c) EPC shall be considered to be new, provided that such use is not comprised in the state of the art (second medical use).

3.15 Hence, Article 54(5) EPC is to be read and understood together with the provisions of Articles 54(4) and 53(c) EPC.

3.15.1 Under Article 54(4) EPC, a substance or composition, comprised in the state of the art, for use in a method referred to in Article 53(c) EPC shall be considered to be new, provided that its use for any such method is not comprised in the state of the art (first medical use).

3.15.2 Under Article 53(c), first sentence, EPC methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body are excluded from patentability. As stated in decision G 1/07 (OJ EPO 2011, 134, points 3.3.10 and 3.2.3.2 of the Reasons, respectively), the exception clause of Article 53(c) EPC includes, amongst other things,

(a) methods for treatment of the human or animal body by surgery not pursuing a therapeutic purpose,

(b) multi-step methods encompassing a therapeutic or a surgical step.

3.16 The provisions of Article 54(4) and (5) EPC were also the object of decision G 2/08 (OJ EPO 2010, 456). In point 5.10.9 of the Reasons, the Enlarged Board of Appeal stated:

"*By virtue of a legal fiction Article 54(4) and (5) EPC acknowledges the notional novelty of substances or compositions even when they are as such already comprised in the state of the art, provided they are claimed for a new use in a method which Article 53(c) EPC excludes as such from patent protection.*

*In such cases the notional novelty and following it the non-obviousness, if any, is not derived from the substance or composition as such but from the purpose the claimed substance or composition is related to, namely from its intended therapeutic use.*

*Such use can be either a new indication stricto sensu (in the sense of a disease not yet treated by the claimed substance or composition), or one or more steps pertaining by their nature to a therapeutic method which may not be claimed as such*.".

3.17 The aforementioned considerations set out in decision G 2/08 thus apply also to claims which do not define the intended medical use of the claimed compound in terms of a treatment of a subject's condition requiring therapeutic and/or surgical intervention, but by way of several individual method steps carried out on a human or animal body.

3.18 Accordingly, it is relevant whether the method steps of such a multi-step method pertain "by their nature" to a method for treatment by therapy or surgery making use of the claimed compound. If so, this therapeutic or surgical method constitutes the medical use possibly conferring novelty and inventive step to the claimed compound.

3.19 Hence, for such a claim to be considered as a purpose-limited product claim under Article 54(5) EPC, it is not sufficient that

(a) the multi-step method as a whole is excluded from patent protection in accordance with Article 53(c) EPC by virtue of only part of the

method steps pertaining to a treatment of a human or animal body by therapy or surgery,

(b) the individual steps of the multi-step method are causally linked to one another, and/or

(c) the use of the claimed substance or composition in one method step facilitates one or more subsequent method steps.

3.20 In addition, the claimed substance or composition must have a treatment-related link to a medical step of the multi-step method in that the claimed substance or composition as such must exert a technical effect pertaining to a therapeutic or surgical step in the human or animal in which the at least one medical step is carried out, i.e. the claimed substance or composition must have activity in relation to therapy or surgery in this medical step.

3.21 As a consequence, each step of the multi-step method has to be considered separately to determine whether this one step is a medical step and, if so, whether the claimed compound has activity in relation to surgery or therapy in this step.

3.22 Turning to the current case, it was common ground that the subject-matter of claim 1 of auxiliary request 19 encompasses a substance (plerixafor) for use in a multi-step method characterised by the following steps ("multi-step method of claim 1"):

a) administering plerixafor to a healthy stem-cell donor, to mobilise progenitor and/or stem cells in this donor ("step i)"),

b) harvesting said progenitor and/or stem cells via apheresis ("step ii)"), and

c) using these cells in allogenic PSC transplantation ("step iii)").

3.23 The above-mentioned embodiment of claim 1 formed the basis for the board's considerations set out in the following.

*Each step of the multi-step method of claim 1 to be considered separately*

3.24 Each step of the multi-step method of claim 1 has to be considered separately to determine whether one step of this method (or more) is a medical step and, if so, whether plerixafor has activity in relation to surgery or therapy in this step (see points 3.14 to 3.21 above).

3.25 To support its argument that the multi-step method of claim 1 must be considered as a whole, the appellant-patent proprietor referred to decisions T 558/20, T 2003/08 and T 826/06.

3.26 However, the circumstances of the cases underlying these decisions are not comparable to those of the case at issue. In decisions T 558/20 and T 2003/08, the claims at issue related to multi-step methods defined not only in terms of their individual method steps but also in terms of an overall therapeutic purpose in terms of a treatment of a subject's condition requiring therapeutic and/or surgical intervention, i.e. the treatment of a patient suffering from a degenerative bone disease in decision T 558/20 (see point 3.2 of the Reasons) and the treatment of a patient suffering from

dilated cardiomyopathy in decision T 2003/08 (see wording of claim 1 of auxiliary request 2 in point III of the decision). Likewise, in decision T 826/06, the overall method recited in claim 1 of auxiliary request 5 was defined as a surgical procedure for cataract extraction comprising performance of a capsulorhexis (see point XVIII of the decision). As a consequence, the boards' findings in these decisions are not applicable to the case at issue.

*Assessment of the presence of a treatment-related link between the claimed compound (plerixafor) and the medical steps of the multi-step method of claim 1*

3.27 In terms of the individual method steps, the points of dispute were the following.

(a) Does step i) define a method for treatment by therapy?

(b) Is there a treatment-related link between plerixafor and step ii), i.e. does plerixafor have activity in relation to surgery or therapy in step ii)?

(c) Is there a treatment-related link between plerixafor and step iii), i.e. does plerixafor have activity in relation to surgery or therapy in step iii)?

*With regard to point (a) - step i) does not define a method for treatment by therapy*

3.28 Step i) defines a method for treatment of a healthy stem-cell donor with plerixafor. The technical effect of this treatment is the mobilisation of the donor's

PSCs, i.e. the movement of the PSCs from the donor's bone marrow to the donor's peripheral blood.

3.29 The appellant-patent proprietor contended that this mobilisation gave rise to the following therapeutically beneficial effects in healthy stem-cell donors.

(i) Enhanced wound healing (see paragraph [0018] of the patent)
(ii) Restoring organ tissue (see paragraph [0018] of the patent)
(iii) Regeneration of myocardium (see paragraph [0037] of the patent)
(iv) Increase in the level of circulating blood cells, giving rise to an improved ability to fight infection and increased oxygen transport

3.30 It is established case law that a prophylactic treatment, aimed at maintaining health by preventing ill effects that would otherwise arise, amounts to a method for treatment by therapy as referred to in Article 53(c) EPC (see also Case Law of the Boards of Appeal, 10th edition 2022, referred to in the following as "Case Law", I.B.4.5.1.b)).

3.31 However, as submitted by the appellant-patent proprietor itself at the oral proceedings, the mobilised PSCs are harvested only a few hours after plerixafor is administered to the donor (see Table 4 of the patent), when most of the PSCs will have moved from the bone marrow to the peripheral blood. This means that the PSCs mobilised in step i) remain within the donor's body for less than two days before being harvested and are not returned to it afterwards.

3.32 Against this background, the board does not find it credible that the PSC donor treated in step i) will benefit from any of the effects listed in point 3.29 above.

3.33 In a further line of argument, the appellant-patent proprietor contended that the process of harvesting PSCs may involve a number of separate apheresis sessions in order to collect sufficient cells, each process causing unpleasant side effects for the donor and being associated with the risk of serious complications. Administering plerixafor in advance of cell collection would reduce the number of apheresis procedures needed to collect the required number of PSCs, and thereby reduce these side effects and complications. The use of plerixafor also entirely avoided the need for collection of cells from the bone marrow, which was associated with serious side effects.

3.34 This argument cannot succeed either for the reasons indicated here below (see points 3.39, 3.40, and 3.42 to 3.45).

3.35 The board therefore concludes that step i) of claim 1 does not define a method for treatment by therapy.

*With regard to point (b) - no treatment-related link between plerixafor and step ii) / plerixafor does not have any activity in relation to surgery or therapy in step ii)*

3.36 In step ii) of the multi-step method of claim 1, the PSCs mobilised in step i) are harvested via apheresis. Apheresis is a method in which blood is removed from a person, passed through an apparatus for separating and collecting a particular constituent of the blood (in the current case, PSCs), and retransfused without the

collected constituent (see decision T 434/15, Reasons 4.2.3). For the steps of removing and returning blood, cannulas are inserted into the person's veins.

3.37 The technical effect of step ii) is the removal of the PSCs mobilised in step i) from the donor's peripheral blood. Undisputedly, this effect pertains to a surgical step.

3.38 The appellant-patent proprietor submitted that plerixafor was active in the surgical method defined in step ii) by causing a physiological effect (mobilisation of PSCs into the donor's peripheral blood) which facilitated this method. Hence, a causal link as required in decision T 826/06 had to be acknowledged.

3.39 As is apparent from documents D1 (see paragraph [0008]) and D17 (see page 1276, right-hand column, fifth sentence), plerixafor-induced PSC mobilisation is an essential step of the claimed multi-step method in that it leads to a clinically relevant yield of PSCs in the donor's peripheral blood, which PSCs can then be harvested in step ii). As a consequence, the number of apheresis sessions needed to achieve a number of cells sufficiently high for an engraftment are reduced, thereby reducing unpleasant side-effects and complications caused by these sessions.

3.40 However, this reduction in side effects and complications is independent of the surgical step ii), i.e. the removal of the PSCs mobilised in step i) from the donor's peripheral blood, which is done by the apheresis procedure alone (see point 3.36 above). The appellant-patent proprietor has not demonstrated that plerixafor improves or otherwise impacts this removal,

i.e. the step of carrying out the apheresis (the method of surgery under consideration) as such.

3.41 By contrast, in the earlier decision T 826/06, the factual circumstances were different. In this decision, the claimed substance (dye) selectively stained the outer surface of the anterior lens capsule (of the eye), thereby providing a clear distinction between the portion of the anterior lens capsule to be removed and the underlying lenticular material, which distinction facilitated the controlled opening of the anterior lens capsule (see point 5.2.1 of the Reasons). Hence, the claimed dye not only facilitated the surgical method for cataract extraction, but also played an active part in it, i.e. it was an active principle in the context of the surgical method under consideration (see also decision T 1758/15 referencing decision T 826/06 in point 7.2.6 of the Reasons). In contrast, in the current case plerixafor mobilises the product (PSC population) that is to be collected in a subsequent surgical step (apheresis), but it does not affect the surgical procedure itself, regardless of whether steps i) and ii) are considered as two separate steps or as one single surgical step.

3.42 In a further line of argument, the appellant-patent proprietor contended that the aforementioned reduction in side effects and complications due to a reduced number of apheresis sessions represented a method for treatment by therapy in the context of Article 53(c) EPC. In support of its argument, the appellant-patent proprietor referred to decision T 81/84, in which the competent board held that the term "therapy" should not be construed narrowly (see also Case Law, I.B.4.5.1 a)). The appellant-patent proprietor also pointed to the fact that plerixafor

allowed for PSC harvesting from peripheral blood which was much less harmful to the donor than harvesting from bone marrow.

3.43 However, it remains that the purpose of therapy is invariably to counteract a human's or animal's pathological condition, or to prevent pathology in the first place (see also Case Law, I.B.4.5.1 c)).

3.44 As submitted by several appellant-opponents, the apheresis procedure defined in step ii) is carried out on healthy PSC donors who are not in need of this or any other type of PSC harvesting procedure to restore their health, nor do they require such a procedure to prevent a pathological condition that would otherwise arise.

3.45 The board therefore concludes that plerixafor does not exhibit any activity in relation to surgery or therapy in step ii), i.e. there is no treatment-related link between plerixafor and step ii).

*With regard to point (c) - no treatment-related link between plerixafor and step iii) / plerixafor does not have any activity in relation to surgery or therapy in step iii)*

3.46 Step iii) includes the transplantation of the PSCs harvested in step ii) into a subject other than the donor of these PSCs (allogeneic PSC transplantation).

3.47 It is common ground that this step has surgical character. The appellant-patent proprietor did not invoke any activity of plerixafor in relation to surgery in this step.

3.48 As submitted by several appellant-opponents, step iii) gives rise to a therapeutic effect in the recipient of the PSC transplant ("recipient"). Step iii) thus additionally defines a method for treatment by therapy. This was not disputed by the appellant-patent proprietor.

3.49 However, the therapeutic effect in step iii) results from the donor's PSCs collected in step ii), not from plerixafor. It is accepted that plerixafor is essential for these PSCs. Plerixafor not only achieves a clinically relevant number of these PSCs in the bloodstream (see point 3.39 above), but also appears to mobilise the right type of PSCs to enable effective haematological reconstitution (see documents D48, page 4, fifth line from the bottom, and D78, Figure 6.7); however, plerixafor does not form part of the PSCs collected in step ii) and hence does not act as a therapeutic agent in step iii).

3.50 Furthermore, there is no treatment-related link between plerixafor and the therapeutic effect achieved in step iii) via plerixafor's PSC mobilisation activity in step i). As submitted by appellant-opponent 1, these two technical effects occur in distinct, non-overlapping groups of subjects, i.e. healthy PSC donors versus patients in need of a PSC transplant. Moreover, step iii) is not necessarily closely associated with the preceding steps i) and ii) in terms of time. Claim 1 does not specify a particular period of time that may or must elapse between these three steps (see also point 2.15.7 of the board's communication). Whilst a close association in terms of time can nonetheless be recognised for steps i) and ii) (see point 3.31 above), the same does not hold true for steps ii) and iii). Also, the description of the patent

does not specify any time period in which step iii) must follow step ii), nor is such a close association in terms of time implicit from the technical context of claim 1. In contrast, in the case underlying decision T 826/06, the surgical step was carried out when the staining (by the dye) took place.

3.51 In view of the preceding considerations, the board concludes that plerixafor does not have any activity in relation to surgery or therapy in step iii), i.e. there is no treatment-related link between plerixafor and step iii).

*Overall conclusion on claim construction*

3.52 The board concludes that the multi-step method of claim 1 comprises two medical steps, i.e. steps ii) and iii); however, the claimed compound (plerixafor) does not have any activity in relation to surgery or therapy in either of these two steps.

3.53 As a consequence, claim 1 is not a purpose-limited product claim under Article 54(5) EPC. Instead, claim 1 is to be understood as being directed to a compound (plerixafor) suitable for use in the multi-step method of claim 1.

*Lack of novelty over document D13*

3.54 It is uncontested that plerixafor is comprised in the state of the art. By way of example, reference is made to claim 8 of document D13, which discloses plerixafor for use in the treatment of subjects who would benefit from their white blood cell count being raised.

3.55 Document D13 thus discloses plerixafor in a form which is suitable for the claimed use. This was not disputed by the appellant-patent proprietor.

3.56 The subject-matter of claim 1 thus lacks novelty over document D13 (Article 54 EPC).

*Auxiliary requests 20 and 21 - claim construction and novelty (Article 54(5) EPC)*

3.57 The appellant-patent proprietor did not submit any additional arguments on claim construction and novelty beyond those put forward for claim 1 of auxiliary request 19.

3.58 The subject-matters of claim 1 of each of auxiliary requests 20 and 21 differ from the subject-matter of claim 1 of auxiliary request 19 only in that they further specify that

(a) the method also comprises administering G-CSF to the subject (claim 1 of auxiliary request 20),

(b) the subject has been treated with G-CSF (claim 1 of auxiliary request 21).

3.59 Hence, the reasoning set out in points 3.14 to 3.53 above with regard to claim 1 of auxiliary request 19 still applies. The board therefore concludes that claim 1 of each of auxiliary requests 20 and 21 is to be construed in the same manner as claim 1 of auxiliary request 19.

3.60 As a consequence, the subject-matter of claim 1 of each of auxiliary requests 20 and 21 lacks novelty over document D13 for the same reasons as set out for

claim 1 of auxiliary request 19 (see points 3.54 to 3.56 above).

## Order

## For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chair:

I. Aperribay M. Pregetter

Decision electronically authenticated