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Datasheet for the decision of 24 June 2025

Case Number: T 0827/23 - 3.3.07

Application Number: 17727907.2

Publication Number: 3468568

IPC: A61K35/19, A61M1/00, A61P25/00, A61P25/28, A61P17/00, A61P29/00

Language of the proceedings: EN

Title of invention:
HUMAN PLATELET LYSATE DERIVED EXTRACELLULAR VESICLES FOR USE IN MEDICINE

Patent Proprietor:
Lysatpharma GmbH

Opponent:
Universität Duisburg-Essen

Headword:
Human platelet lysate derived extracellular vesicles / LYSATPHARMA

Relevant legal provisions:
RPBA 2020 Art. 12(1)(a), 12(2), 12(6) sentence 1
EPC Art. 56

Keyword:
Basis of proceedings - Admittance of requests (yes)
Admittance of late-filed evidence - not admitted in first-instance proceedings - (no)
Inventive step - main request and auxiliary requests (no)

Decisions cited:
G 0002/21

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Case Number: T 0827/23 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 24 June 2025

Appellant: (Patent Proprietor)	Lysatpharma GmbH Klosterlausnitzer Str. 81 07607 Eisenberg (DE)
Representative:	DTS Patent- und Rechtsanwälte PartmbB Brienner Straße 1 80333 München (DE)
Respondent: (Opponent)	Universität Duisburg-Essen Universitätsstrasse 2 45141 Essen (DE)
Representative:	Seyer & Nobbe Patentanwälte PartmbB Mülheimer Straße 210 47057 Duisburg (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 16 March 2023 revoking European patent No. 3468568 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman	A. Usuelli
Members:	J. Lécaillon
	L. Basterreix

Summary of Facts and Submissions

I. European patent 3 468 568 (hereinafter "the patent") was granted on the basis of 14 claims and related to a pharmaceutical preparation comprising a fraction that is enriched for *human* platelet lysate derived extracellular vesicles for use in medicine, in particular in the treatment and/or prevention of specific diseases.

II. An opposition was filed against the patent on the grounds that its subject-matter lacked novelty and inventive step and it was not sufficiently disclosed.

III. The opposition division took the decision to revoke the patent.

IV. The decision of the opposition division, posted on 16 March 2023, cited *inter alia* the following documents:

D5: European Cells & Materials Vol. 28, 2014, pages 137-151
D7: WO 2014/013029 A1
D9: WO 2012/020307 A2
D17: Cardiovascular research, 67 , 2005, pages 30-38
D19: Current Neurovascular Research, 2012, 9, pages 185-192
D29: Systemic immunosuppressive efficacy of enriched human platelet-derived extracellular vesicle fractions (hPLEV-F) in a mouse model
D30: Impact on TNF-alpha signalling pathway of *in vitro* qualified immunomodulatory hPLEV-F
Annex 1: Bundesgesundheitsbl. 2015, 58:1126-1128

V. The opposition division decided in particular as follows:

(a) The product for use in medicine of granted claim 1 was not novel.

(b) Auxiliary requests 1, 1A to 1D, 2, 2A, 3, 4, 4A, 5 to 7 and 8 did not meet the requirements of Articles 54, 84 and/or 123(2) EPC and auxiliary requests 4B, 4C and 6A were not admitted into the proceedings.

(c) Auxiliary requests 9 and 10 were admitted into the proceedings and met the requirements of Articles 123(2), 123(3), 83 and 54 EPC. These requests did however not comply with Article 56 EPC starting from D9 as closest prior art in combination with common general knowledge.

VI. The patent proprietor (appellant) lodged an appeal against the above decision of the opposition division. With their statement setting out the grounds of appeal the appellant defended their case on the basis of auxiliary request 9 as the main request, and on the basis of auxiliary request 10, both filed during the opposition proceedings on 14 November 2022 and resubmitted with the statement setting out the grounds of appeal.

VII. With their submission of 22 December 2023 the appellant filed further auxiliary requests 11 and 12.

VIII. The content of the claims upon which the present decision is based can be illustrated as follows:

Claim 1 of auxiliary request 9 read as follows:

"1. Pharmaceutical preparation comprising a fraction that is enriched for *human* platelet lysate derived extracellular vesicles for use in the prevention and/or treatment of inflammatory driven diseases, immune/ autoimmune diseases, transplant rejections, or Graft-versus-Host Disease, wherein the *human* platelet lysate originates from pooled donor-donated platelets."

Claim 1 of auxiliary request 10 corresponded to claim 1 of auxiliary request 9 wherein the feature "of at least 15 donors" was added at the end of the claim to further specify the pooled donor-donated platelets.

Claims 1 of auxiliary requests 11 and 12 corresponded to claims 1 of auxiliary requests 9 and 10 respectively wherein the feature "inflammatory driven disease" had been deleted from the list of diseases.

IX. The following items of evidence were filed by the parties during the appeal proceedings:

(a) Document filed by the appellant with their statement setting out the grounds of appeal:

D32: letter of the appellant dated 21 January 2020 submitted during the examination proceedings

(b) Documents filed by the respondent on 30 April 2024:

D33: Karen English, Immunology and Cell Biology (2013) 91, 19-26
D34: Olivieri *et al.*, The ScientificWorldJOURNAL, (2011) 11, 1908-1931

D35: Adzemovic et al., PLOS ONE, February 2013, Vol. 8, Issue 2, e56586
D36: Wikipedia entry "Autoimmunerkrankung"

X. Oral proceedings were held before the Board on 24 June 2025.

XI. The appellant requested that the decision under appeal be set aside and the patent be maintained based on auxiliary request 9 (new main request), or that the patent be maintained on the basis of one of auxiliary requests 10 to 12, wherein auxiliary requests 9 and 10 were filed during the opposition proceedings on 14 November 2022 and resubmitted with the statement setting out the grounds of appeal and auxiliary requests 11 and 12 were newly filed during the appeal proceedings on 22 December 2023.

XII. The respondent requested that the appeal be dismissed, *i.e.* that the patent be revoked.

They further requested that auxiliary requests 9 to 12 not be admitted into the appeal proceedings.

XIII. The arguments of the appellant, as far as relevant for the present decision, can be summarised as follows:

(a) Auxiliary requests 9 and 10 were filed during the opposition proceedings within the time limit according to Rule 116 EPC and were admitted into the proceedings by the opposition division. They therefore formed part of the appeal proceedings. Furthermore they were filed in direct reaction to objections on file and did not represent a modification of the appellant's case.

(b) Auxiliary request 9 met the requirement of Article 56 EPC.

D9 relied upon by the opposition division did not represent a promising starting point for the assessment of inventive step. It related to a different technical field namely the medical use of microvesicles from pancreas-derived pathfinder cells (PDPC) instead of *human* platelet lysate derived extracellular vesicles (hPLEV) as in the present request. D17 or D19 represented the closest prior art instead.

Nevertheless, the disclosure of D9 regarding other vesicles than PDPC was very general and D9 disclosed neither (i) the specific combination of hPLEV and the claimed diseases nor (ii) the pooling of donor-donated platelets.

The patent and the experimental data provided in D29, D30 and D32 substantiated that extracellular vesicles from *human* platelet lysate (hPL) had noticeable anti-inflammatory and immunosuppressive efficacy. Furthermore a reduced variability and hence more reliable efficacy were obtained from the pooling of donor-donated platelets.

The objective technical problem therefore resided in the discovery of a medical use of a pharmaceutical preparation encompassing hPLEV with reliable efficacy.

D9 did not provide any suggestion to use hPLEV originating from pooled samples in order to treat the specific claimed diseases. Moreover, D5 did not provide any indication that hPLEV from pooled

samples would be advantageous. Finally, the skilled person would not have combined the teachings of D17 or D19 with the one of D9 since these documents related to the treatment of different diseases. The skilled person would rather have consulted D7 relating to the treatment of inflammatory conditions, transplant rejections and Graft-versus-Host Disease and teaching the use of mesenchymal stem cells.

(c) Auxiliary request 10 fulfilled the requirement of Article 56 EPC. The additional distinguishing feature, namely the minimum number of 15 donors, provided the possibility of production on an industrial scale without issues regarding reliable efficacy or compatibility. This was supported by Annex 1 filed during the second oral proceedings in the opposition proceedings. The number of donors used in the prior art was limited to maximum 4 donors and there was no indication that a higher number of donors could be used.

(d) Auxiliary requests 11 and 12 complied with Article 56 EPC in view of the further restriction of the list of claimed diseases.

XIV. The arguments of the respondent, as far as relevant for the present decision, can be summarised as follows:

(a) Auxiliary requests 9 and 10 were to be rejected because they were late filed, not convergent with the previous auxiliary requests and were *prima facie* not patentable. The decision of the opposition division to admit these auxiliary requests was wrong and should be reviewed.

(b) Auxiliary request 9 did not meet the requirement of Article 56 EPC.

D9 could be considered to represent the closest prior art, since it disclosed microvesicles from various sources, including from thrombocytes, for use in the treatment of a variety of inflammatory driven diseases (see *e.g.* claims 1 to 7 and 15 and paragraphs [0073]).

The claimed subject-matter differed from D9 only in that the *human* platelet lysate originated from pooled donor-donated platelets.

Neither the patent nor the post-published experimental data D29, D30 and D32 substantiated any technical effect compared to the closest prior art D9. Furthermore, even if it was considered that pooling of samples would reduce variability, the degree of variability was not in direct relation with the degree of efficacy, so that no improvement in terms of reliability of treatment efficacy could be acknowledged.

The objective technical problem could therefore only be formulated as the provision of an alternative preparation.

The pooling of samples had already been used in the art (see *e.g.* D5) and could therefore not render the claimed solution inventive. Furthermore, effects on inflammation and immunomodulation had already been suggested for hPLEV in D17 or D19. Finally, the level of disclosure in terms of experimental data regarding the efficacy of hPLEV on the claimed diseases of the patent was not

higher than the one of D9, so that it did not provide any technical contribution over D9.

(c) Auxiliary request 10 did not fulfil the requirement of Article 56 EPC. The technical effects allegedly linked to the additional distinguishing feature of at least 15 donors were not substantiated by any experimental data. Moreover, there was no indication in the prior art that the number of donors had to be limited to 4 donors. In the absence of any particular effect the additional feature could not involve any inventive step.

(d) Auxiliary requests 11 and 12 did not comply with Article 56 EPC. The remaining diseases were also inflammation driven and generally disclosed in D9, so that the performed limitation did not overcome the issue of lack of inventive step.

Reasons for the Decision

1. Admittance of auxiliary requests 9 and 10

1.1 The respondent requested that auxiliary requests 9 and 10 not be admitted into the appeal proceedings because:
- they were late-filed during the opposition proceedings as they were filed on the last day of the time limit according to Rule 116 EPC before the second oral proceedings in opposition proceedings,
- they were not convergent with the previous auxiliary requests discussed in opposition, and
- they were not *prima facie* allowable.

1.2 The Board observes that auxiliary requests 9 and 10 were admitted in the opposition proceedings and form part of the decision under appeal.

1.3 Hence, according to Articles 12(1)(a) and 12(2) RPBA, these requests form part of the appeal proceedings. Moreover, there is no indication that the opposition division exercised its discretion on the basis of the wrong criteria or in an unreasonable manner.

Auxiliary request 9 (main request)

2. Inventive step

2.1 Closest prior art

2.1.1 The parties disagreed concerning the choice of the closest prior art document. Against the decision of the opposition division, the appellant considered that D17 or D19 represented better starting points than D9. The respondent developed their problem solution approach starting from D9.

2.1.2 On the one hand, as underlined in the impugned decision, D9 explicitly discloses the use of microvesicles in the treatment of *inter alia* inflammation and inflammation driven diseases as well as autoimmune diseases, diseases associated with graft rejection and graft versus host disease (see paragraph [0120] to [0122] and [124] to [0125]).

2.1.3 On the other hand, D17 and D19 do not directly and unambiguously disclose the treatment of such diseases. D17 reports a study of the effect of platelet-derived microparticles (PMP) on angiogenesis and stimulation of post-ischemic revascularization (see title and abstract). D19 describes a study of the effect of PMP on angiogenesis and neurogenesis after cerebral ischemia in rats (see title and abstract). As argued by

the appellant themselves in the context of novelty, these therapeutic applications do not directly and unambiguously correspond to the presently claimed specific diseases.

2.1.4 It follows that D9 relates to the same purpose as the claimed subject-matter while the medical indications of D17 and D19 are more remote.

2.1.5 The appellant argued that D9 would mainly relate to microvesicles from pancreas-derived pathfinder cells and only randomly mention microvesicles from other sources such as human platelet lysate whereas D17 and D19 concern the therapeutic use of human platelet lysate derived vesicles. As a result D9 would not represent the most promising starting point.

2.1.6 According to established case law, the criteria of being directed to the same purpose or effect as the claimed invention is central when determining the closest prior art (see Case Law of the Boards of Appeal, 11th Edition, 2025, I. D. 3.4). As detailed above, D9 fulfils this criteria. Furthermore, even if some preferred embodiments and the examples of D9 focus on microvesicles from pancreas-derived pathfinder cells (PDPC), D9 still considers microvesicles of other cell types including derived from human platelet (see paragraphs [0073] and [0041]).

2.1.7 The Board therefore considers that D9 represents an appropriate choice as starting point for the assessment of inventive step.

2.2 Distinguishing features

2.2.1 It was undisputed that the subject-matter of claim 1 of auxiliary request 9 differs from D9 in that the human platelet lysate originates from pooled donor - donated platelets (no disclosure of pooling in D9).

2.2.2 Furthermore, as argued by the appellant, D9 relates to microvesicles originating form a large variety of cells (see claim 15 and paragraph [0073]) as well as to a variety of therapeutic applications (see claims 2 to 11). D9 does therefore not disclose the specific combination of *human* platelet derived extracellular vesicles (hPLEV) with the treatment of the presently claimed diseases. In this context, the interdependency of claims 5 and 15 mentioned by the respondent does not provide any specific disclosure of this combination.

2.3 Associated technical effects

2.3.1 According to the appellant, hPLEVs would have noticeable anti-inflammatory and immunosuppressive activity as substantiated in the patent and D29, D30 and D32.

2.3.2 The Board observes that anti-inflammatory and immunosuppressive effects have been described in the original application (see page 16 line 11 to page 17 line 8, page 36 lines 9 to 17, page 37 lines 22 to 24 and page 38 lines 14 to 20) but no experimental data were provided. In this context, the passage on page 38 lines 14 to 22 of the original application mentioning ELISpot assays does not provide any details regarding the allegedly performed assays (*e.g.* exact cell and exosome type, measurement method). Contrary to the opinion of the appellant, this passage does not provide

experimental evidence of immunomodulatory effects for the claimed vesicles.

Anti-inflammatory and immunosuppressive effects have hence been experimentally substantiated only with the post-published data provided in D29, D30 and D32 (see D29, Figure 2, D30, Figures 1 and 2 and D32, figures 2A-2C, 3A-3C and 4). The Board observes that the respondent did not contest that these data could be taken into account in line with G 2/21.

2.3.3 However, as argued by the respondent, no particular effect over the microvesicles of the closest prior art D9 has been substantiated. The data provided in D29, Figure 2, D30, Figures 1 and 2 and D32, figures 2A-2C, 3A-3C and 4 do not provide any comparison with the administration of other vesicles. During the oral proceedings, the appellant relied on an alleged surprising improved effect compared to the known immunosupressive agent prednisolon and referred to Figure 5 of D32. The synergetic immunosuppressive effect with prednisolon reported in Figure 5 of D32 cannot however substantiate any surprising effect compared to the specific microvesicles (PDPC) exemplified in D9.

2.3.4 The appellant further argued that the pooling of platelets would reduce variability and hence provide more reliable efficacy as substantiated by D29.

2.3.5 The Board observes that none of the experimental data on file is suitable to substantiate this effect. In particular, while the samples of 10 donors were pooled in D29, no comparison with the absence of pooling was performed. Nevertheless, the Board concurs with the impugned decision that reduced variability due to

pooling of samples appears to be usually recognised based on common general knowledge. However, as underlined by the respondent, a direct and necessary correlation between reduced variability and more reliable efficacy has not been substantiated.

2.4 Objective technical problem

Accordingly, starting from D9, the objective technical problem resides in the provision of a microvesicles preparation having reduced variability for use in the treatment of inflammatory diseases, autoimmune diseases, diseases associated with graft rejection and graft versus host disease.

2.5 Obviousness of the claimed solution

2.5.1 The Board observes that, in the absence of any particular effect, the choice of hPLEVs for use in the present treatments amongst the various equally disclosed options described in D9 represents an arbitrary choice, which does not require any inventive skills.

2.5.2 In this context, the appellant brought forward that hPLEVs and the present diseases would be disclosed in unrelated passages of D9, so that D9 would not provide any hint regarding immunosuppressive activity of microvesicles from whole blood described therein. Autoimmune and inflammatory diseases would only be mentioned in the specific context of PDPC and not for any of the described vesicles (see *e.g.* paragraph [0126]).

This argument is not convincing. The disclosure of the treated diseases in paragraphs [0120] to [0122] and

[0124] to [0125] of D9 is general and refers to "methods and compositions of the present invention". The skilled person would therefore understand that, according to D9, any of the described vesicles can be used in said treatments.

2.5.3 The appellant further contended that D9 would not provide any data for the presently claimed vesicles (hPLEV). The disclosure of D9 would be very broad and the examples limited to PDPC.

The Board reiterates that the patent does not provide any experimental data either and that the post-published data only show some efficacy without providing any comparison with the vesicles used in the examples of D9 (PDPC). It follows that no technical contribution over D9 has been substantiated.

2.5.4 Furthermore, as argued by the respondent, potential effects on inflammation and immunomodulation have been suggested for hPLEV in the prior art (see *e.g.* D17, page 31, 2nd full paragraph, antepenultimate sentence and D19, page 190, second paragraph). Hence, if at all required, the skilled person would have been reassured in the choice of hPLEV for the claimed treatments.

The appellant disagreed and considered that the skilled person would not take D17 or D19 into consideration because they related to different diseases, namely angiogenesis (D17) and ischemia (D19). Furthermore, the passage of D19 referred to by the respondent (*i.e.* page 190, second paragraph) would be hypothetical. The appellant considered that the skilled person considering alternative vesicles described in D9 would have been prompted to use mesenchymal stem cells instead, since theses cells are disclosed in D7 as

useful in the treatment of inflammatory conditions (title), transplant rejections and Graft-versus-Host Disease (page 7, 3rd paragraph, last sentence).

This argument is not convincing.

The skilled person would have been directed to hPLEV already from D9. Since D17 and D19 relate to the use of such vesicles, the skilled person would have indeed consulted the documents and would have found the indication of a potential use in the present indications. The fact that D17 and D19 do relate to the treatment of different conditions and hence do not provide data on the presently claimed indications, does not mean that the skilled person would have ignored the further information provided therein, including the mention of a potential use against inflammation and in immunomodulation.

Concerning the reference to D7, this document merely discloses another one of the equally disclosed alternatives in D9. The Board considers that D7 does however neither undermine the disclosure of the presently chosen alternative nor teach away therefrom. Both alternatives are equally obvious.

2.5.5 Finally, the pooling of samples is not interrelated with the choice of hPLEV for the specific claimed diseases and can be assessed separately. This feature is not linked to any particular effect beyond the reduction of variability, which is considered to be established from common general knowledge. Furthermore the pooling of specifically hPLEV has already been routinely done in the prior art as substantiated by D5 (see page 138, left column, 2nd full paragraph). This

feature would therefore have appeared obvious to the skilled person.

2.6 Conclusion

Accordingly, the subject-matter of claim 1 of auxiliary request 9 does not comply with the requirement of Article 56 EPC.

Auxiliary requests 10

3. Inventive step

3.1 The subject-matter of claim 1 of auxiliary request 10 differs from the one of claim 1 of auxiliary request 9 in that a minimal number of donors (at least 15) was specified.

3.2 Admittance of Annex 1

3.2.1 During the oral proceedings the appellant provided for the first time in the appeal proceedings specific arguments regarding alleged unexpected effects of a pooling of samples of at least 15 donors based on the "Annex 1" submitted during the second oral proceedings in the opposition proceedings and annexed to the minutes of this second oral proceedings.

3.2.2 The Board observes that this document was not admitted into the opposition proceedings as being late filed and not relevant for the discussion (see minutes of the second oral proceedings, page 5 and impugned decision, paragraph 45.). The opposition division used its discretion not to admit this document by applying the correct criteria of *prima facie* relevance. Furthermore, this document was not referred to in the appeal

proceedings before and no reasons for any late-admittance were provided. This document does therefore not form part of the appeal proceedings according to Articles 12(1), 12(2) and 12(6), 1st sentence RPBA.

3.3 Inventive step over D9

3.3.1 During the oral proceedings, the appellant argued that the use of at least 15 donors for the pooling of samples would provide particular effects, namely the possibility of production on an industrial scale without issues regarding reliable efficacy or compatibility. According to the appellant, these effects were not expected from the prior art, which discloses a lower number of donors.

3.3.2 As argued by the respondent, these alleged effects were not substantiated by any experimental data. There are in particular no data on file providing a comparison between the pooling of a lower number of donors (such a in D5, see page 138, left column, 2nd full paragraph) and a higher number of donors (15 or more as in present claim 1) and the experimental data provided by the appellant involve only 10 donors (see D29).

3.3.3 Furthermore, increasing the number of donors to increase the volume of vesicles in order to ensure production on an industrial scale represents an obvious measure for the skilled person.

3.3.4 Finally, the appellant did not provide any evidence in support of the alleged prejudice in the art against the use of more than 4 donors when pooling buffy coats (as in D5).

3.3.5 The additional distinguishing feature introduced in claim 1 of auxiliary request 10 is therefore arbitrary and cannot render the claimed subject-matter inventive. It follows that the same reasoning as detailed for auxiliary request 9 apply *mutatis mutandis*.

3.3.6 As a result, the subject-matter of claim 1 of auxiliary request 10 does not comply with the requirement of Article 56 EPC.

Auxiliary requests 11 and 12

4. Inventive step

4.1 Claims 1 of auxiliary requests 11 and 12 differ from claims 1 of auxiliary requests 9 and 10 respectively in that the feature "inflammatory driven disease" was deleted from the list of diseases.

4.2 The Board observes that the remaining diseases are still disclosed in D9 (see paragraphs [0122], [0124] and [0125]), so that no further distinguishing feature in addition to those identified in the case of auxiliary requests 9 and 10 has been introduced. It follows that the same reasoning as detailed for auxiliary requests 9 and 10 apply *mutatis mutandis*.

4.3 Therefore, the subject-matter of claims 1 of auxiliary requests 11 to 12 does not comply with the requirement of Article 56 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated