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Datasheet for the decision of 4 April 2025

Case Number: T 1153/23 - 3.3.07

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Language of the proceedings: EN

Title of invention:

STABLE COMPOSITIONS COMPRISING HEPARINOID, ACUTE-ACTING ANESTHETIC, AND BUFFER

Applicant:

Urigen Pharmaceuticals, Inc.

Headword:

Stable Heparinoid Lidocaine Compositions / URIGEN

Relevant legal provisions:

EPC Art. 56, 54(2), 123(2)

Keyword:

Novelty - (no)
Inventive step - (no)
Amendments - added subject-matter (yes)

Decisions cited:
T 0713/01

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Case Number: T 1153/23 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 4 April 2025

Appellant: (Applicant)	Urigen Pharmaceuticals, Inc. 675 US Route 1 Suite 206B North Brunswick, New Jersey 08902 (US)
Representative:	Körfer, Thomas Mitscherlich PartmbB Patent- und Rechtsanwälte Karlstraße 7 80333 München (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 4 January 2023 refusing European patent application No. 14785471.5 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairwoman	Y. Podbielski
Members:	E. Duval
	J. Molina de Alba

Summary of Facts and Submissions

I. The appeal was filed by the appellant (applicant) against the decision of the examining division to refuse the European patent application.

II. The decision was based on a main request and auxiliary requests 1-4 filed on 13 July 2020, on auxiliary requests 5-7 filed on 28 October 2022, and on auxiliary request 8 filed during oral proceedings on 29 November 2022.

Claims 1, 7 and 13 of the main request read as follows:

"1. A method for preparing a composition useful for treatment of a lower urinary tract disease or condition comprising a heparinoid, lidocaine, and a buffer, the method comprising the steps of:
(a) providing a heparinoid, either as a solid or as an aqueous liquid, in a quantity of 10,000 units to 250,000 units per unit dose or, alternatively, from 50 mg to 1250 mg per unit dose;
(b) buffering the heparinoid to a pH value of greater than 6.8 to 8.3 with a buffer compatible with both the heparinoid and lidocaine that is to be added subsequently;
(c) adding lidocaine, either as a solid or as an aqueous liquid, in a quantity of from 50 mg to 1000 mg per unit dose, to the buffered heparinoid from step (b) to form a solution including heparinoid, lidocaine, and buffer; and
(d) rebuffering the solution of step (c) to a pH value of greater than 6.8 to 8.3 to form a stable solution, wherein the stability of the heparinoid and the acute-

acting anesthetic is at least 90% after one year, up to 18 months."

"7. A method for preparing a composition useful for treatment of a lower urinary tract disease or condition comprising a heparinoid, lidocaine, and a buffer, the method comprising the steps of:
(a) mixing the heparinoid and the lidocaine to produce a liquid form in which the heparinoid and the lidocaine are slightly more concentrated than in the final product;
(b) adding the buffer to produce a pH of 7.0 in the solution of (a); and
(c) raising the pH to a value in the range of from 7.1 to 8.3 using sodium hydroxide and adding water as required to achieve the final desired concentrations of the heparinoid and the lidocaine, wherein the stability of the heparinoid and the lidocaine is at least 90% after one year, up to 18 months."

"13. A stable composition produced by the method of claim 1 or 7 wherein the stability of the heparinoid and the lidocaine is at least 90% after one year, up to 18 months."

In auxiliary requests 1-8, the following amendments were introduced:

Each of auxiliary requests 1-4 comprised a claim (respectively, claims 12, 5, 12 and 5) corresponding to claim 13 of the main request and directed to a composition defined in terms of the process for its preparation and by a stability of at least 90% after one year, up to 18 months.

Furthermore, claim 5 of auxiliary request 1 and claim 1 of auxiliary request 2 corresponded to claim 1 of the main request where the pH in the rebuffering step (d) was limited to 7.2 to 7.6. Claim 5 of auxiliary request 3 and claim 1 of auxiliary request 4 corresponded to claim 1 of the main request where the amount of heparinoid was amended to 100-250,000 units or 0.5-1250 mg per unit dose, the amount of lidocaine to 5-1000 mg per unit dose, and the rebuffering step (d) was carried out "if required" and to a pH value of 7.5.

In auxiliary requests 5-8, the claim directed to a stable composition *per se* (corresponding to claim 13 of the main request) was deleted. Claim 6 of auxiliary request 5, and claim 1 of auxiliary request 6 were both identical to claim 7 of the main request. Claim 1 of auxiliary request 7 differed from claim 7 of the main request in that the heparinoid was limited to heparin, and claim 1 of auxiliary request 8 further specified the pH in step (c) to be 7.5.

III. The examining division decided that:

(a) The subject-matter of the main request and auxiliary requests 1-4 lacked novelty over the composition comprising heparin, lidocaine and a buffer (solution 2) shown in D1 (WO 2012/094515 A1).

(b) Auxiliary request 5 met the criteria of novelty.

However, regarding inventive step, starting from solution 2 of D1, the problem to be solved was the provision of an alternative method for preparing compositions comprising heparin, lidocaine and a

buffer for use in the treatment of a lower urinary tract disease. The claimed solution was obvious.

(c) None of auxiliary requests 6-8 met the requirements of inventive step either.

IV. In the appeal proceedings, the appellant upheld the same main request and auxiliary requests 1-8 as underlying the appealed decision.

V. The Board issued a summons to oral proceedings, and set out its preliminary opinion in a communication under Article 15(1) RPBA.

VI. By letter dated 21 March 2025, the appellant withdrew their request for oral proceedings. The Board cancelled the oral proceedings.

VII. The appellant requests that the decision under appeal be set aside and that a patent be granted on the basis of the main request or, in the alternative, on the basis of one of auxiliary requests 1-8 as underlying the appealed decision.

VIII. The appellant's arguments may be summarised as follows:

(a) Article 123(2) EPC

Claim 1 of the main request was based on paragraph [0041] of the application as filed as regards the ranges 10,000-250,000 units or 50-1250 mg for the amount of heparinoid, and on paragraph [0045] for the range 50-1000 mg for the amount of lidocaine.

(b) Novelty

The subject-matter of claim 13 was novel over D1, because D1 did not show a composition with a stability of the heparinoid and the lidocaine of at least 90% after one year, up to 18 months, and because D1 was silent on a method according to any of present claims 1 and 7. The product-by-process claim 13 was characterized by its method of preparation and its resulting significant improvement of stability.

(c) Inventive step

The claimed processes differed from the teaching of D1 (solution 2) by the specific sequences of addition specified in claims 1 and 7 and by the stability of at least 90% after one year, up to 18 months. The technical problem was the provision of an increased stability and avoidance of precipitation of lidocaine such that a stable solution containing lidocaine and heparin could be generated suitable for storage prior to administration to a patient. The claimed solutions were not suggested by the prior art.

Regarding the auxiliary requests, D1 was silent on the step of buffering to a pH value of 7.2 to 7.6, or of adapting the pH first to 7.0 and then raising it to 7.5, which lead to the best stability.

Reasons for the Decision

1. Main request

1.1 Article 123(2) EPC

1.1.1 Claim 1 of the main request differs from the combination of claims 38 and 50 as filed as follows (amendments emphasised by the Board):
- the quantity of heparinoid in step (a) is "~~about 100~~ 10,000 units to ~~about~~ 250,000 units per unit dose or, alternatively, from ~~about 0.5~~ 50 mg to ~~about~~ 1250 mg per unit dose"; and
- the quantity of the acute-acting anesthetic lidocaine in step (c) is "from ~~about 5~~ 50 mg to ~~about~~ 1000 mg per unit dose".

1.1.2 The appellant indicates paragraph [0041] as basis for the amended amounts of heparinoid. However, this paragraph only discloses the amounts 10,000 units and 50 mg among several alternative intermediate quantities, and only in respect of heparin (and not more generally any heparinoid). As indicated at the end of the same paragraph, determining suitable quantities of heparinoids other than heparin would require a calculation based on the molecular weight of the heparinoid to be used. The values given in this paragraph for heparin can accordingly not be generalised as such to any heparinoid. This generalisation in claim 1 of the main request thus introduces added subject-matter.

1.1.3 In addition, paragraph [0045] discloses the amount of 50 mg also as one of many alternative intermediate quantities of lidocaine, and in the context of lidocaine amounts of at most 400 mg. The subject-matter of claim 1 of the main request thus results from the combination of a range (50-1000 mg) created by selecting one quantity of lidocaine as the lower limit, with a range (either 10,000-250,000 units or 50-1250 mg) which also involves a selection from the various

heparin(oid) amounts. In the absence of a pointer to this combination of selections, the amendment introduces added subject-matter.

The criteria of Article 123(2) EPC are thus not met.

1.2 Novelty - product-by-process claim

1.2.1 Claim 13 of the main request relates to:
- a stable composition
- produced by the method of claim 1 or 7,
- wherein the stability of the heparinoid and the lidocaine is at least 90% after one year, up to 18 months.

1.2.2 The composition of claim 13 is thus firstly defined in terms of the process for its manufacture, i.e. by the method of claim 1 or 7. Claim 13 is nonetheless directed to the composition *per se*. Claims for products defined in terms of a process of manufacture are allowable only if the products as such fulfil the requirements for patentability, i.e. *inter alia* that they are new and inventive. A product is not rendered novel merely by the fact that it is produced by means of a new process. Furthermore, in proceedings before the examining division, the burden of proof for an allegedly distinguishing "product-by-process" feature lies with the applicant (see T 713/01, point 2.5.8 of the reasons, and Case Law of the Boards of Appeal of the European Patent Office, 10th edition ("CLB"), III.G.5.1.2 a)).

D1 discloses (see page 25, solution 2) a stable composition produced by a method comprising dissolving heparin (50,000 units) and lidocaine (200 mg) in water

and then adding sodium bicarbonate, yielding a final pH of 7.4.

Even if the particular sequence of steps of the processes of claims 1 and 7 are not shown in D1, there is no evidence that the claimed processes impart to the resulting products any property differentiating them from those of the prior art.

1.2.3 The only property on which the appellant relies is the claimed stability of the heparinoid and lidocaine of "at least 90% after one year, up to 18 months", which is specified in claim 13.

It is however not shown either that the product of D1, solution 2, fails to achieve this property. Considering that D1 describes the resulting solutions as stable for three months or more with no precipitation (see paragraph [0031]), and that similar process features are employed in D1 and in the application to avoid precipitation and decomposition of lidocaine (i.e. the presence of the heparinoid when buffering lidocaine, see paragraph [0031] of the application and [0030] of D1), the silence of D1 as to the particular parameter of stability after one year cannot be equated with a proof that this claimed parameter is not fulfilled in D1.

On the contrary, as noted by the examining division, the process of D1 (solution 2) is very similar to the process of example 1 of the application, which is stated to lead to a stability over 95% after both 12 and 18 months. Both processes use the same amounts of heparin and lidocaine, the same buffer (sodium bicarbonate), and lead to the same volume (15 mL) with essentially the same pH (7.4 vs 7.5). This similarity

of the process of D1 with a process which the application states to lead to the claimed stability supports the view that the stability parameter is implicitly met in D1.

Under these circumstances, the onus of proof remains with the applicant to show a distinction with D1. No benefit of the doubt can be accorded. The appellant chose to use this unusual parameter to define the claimed composition, but did not provide evidence that this parameter feature as such represents a difference over D1.

1.2.4 Accordingly, the subject-matter of claim 13 of the main request lacks novelty.

1.3 Inventive step - claims 1 and 7

1.3.1 The closest prior art D1 discloses a process for preparing a stable composition comprising dissolving heparin (50,000 units) and lidocaine (200 mg) in water and then adding sodium bicarbonate, yielding a final pH of 7.4 (see page 25, solution 2).

1.3.2 The process of claim 1 differs by step (b) of buffering the heparinoid to a pH value of greater than 6.8 to 8.3.

The appellant contends that the stability of the heparinoid and lidocaine of at least 90% after one year, up to 18 months, constitutes a technical difference to D1. The Board does not share this view. For the reasons given above (see 1.2.3), the silence of D1 as to this precise parameter cannot be regarded as evidence that this parameter is not met by solution 2.

1.3.3 The appellant further argues that, by controlling the pH of the heparinoid solution to 6.8-8.3 prior to adding the lidocaine, the method of claim 1 allows to achieve a superior stability of at least 90% for one year, up to 18 months. There is however no evidence supporting this assertion in the application, considering that it does not contain any example of the claimed processes. In particular, the process of paragraph [0078] (example 1) does not comprise the step of claim 1 of buffering the heparinoid before adding lidocaine, nor the steps of claim 7 of buffering to pH 7.0 followed by raising the pH using sodium hydroxide.

1.3.4 Lastly, the appellant submits that the fact that solution 2 in D1 requires a sterile filtration step is a clear pointer that a precipitation is expected or already occurred in D1 for solution 2. The Board does not consider this sterile filtration to be indicative of any stability issue. Such a filtration step is also considered in the application, and the stability period is anyway defined to start after the preparation of the final vial (see paragraph [0068] of the application).

1.3.5 The appellant defines the technical problem as the provision of an increased stability and avoidance of precipitation of lidocaine such that a stable solution containing lidocaine and heparin can be generated suitable for storage prior to administration to a patient.

However, no evidence or comparison was adduced to show that the claimed process achieves any improvement over the process of D1. In fact, the product resulting from the claimed process is not shown to differ from that of D1, for the reasons set out above (see 1.2). There is also no evidence that the pH adjustment would be

relevant to immediate versus long term stabilization of lidocaine.

Accordingly, the objective technical problem may be seen in the provision of an alternative method for preparing compositions comprising heparin, lidocaine and a buffer for use in the treatment of a lower urinary tract disease.

The Board shares the conclusion of the examining division that the solution proposed in claim 1 does not involve an inventive step. D1 suggests in one embodiment to buffer the heparinoid before the addition of lidocaine (see paragraph [0055]). In the absence of an associated technical effect, the skilled person would consider this measure in order to solve the problem of providing an alternative.

1.3.6 As to claim 7, starting from D1 (solution 2), the differentiating features are
- step (b) of adding the buffer to produce a pH of 7.0 in the heparinoid+lidocaine solution of (a), and
- the fact that, in step (c) of raising the pH to a value in the range of from 7.1 to 8.3, sodium hydroxide is used. In D1, the adjustment to pH 7.4 is done using sodium bicarbonate.
The vague feature that the solution of step (a) is "slightly" more concentrated than the final product merely represents a consequence of the additions in steps (b) and (c).

In the case of claim 7 also, no evidence of any improvement over the process of D1 was adduced. The objective technical problem is to provide an alternative method for preparing compositions

comprising heparin, lidocaine and a buffer for use in the treatment of a lower urinary tract disease.

The Board shares the examining division's view that the claimed solution is obvious in light of paragraphs [0057]-[0058] of D1, which suggest the addition of a buffer to the heparinoid + lidocaine solution and the subsequent pH adjustment. The particular pH values defined in claim 1 for each of steps (b) and (c), and the use of sodium hydroxide, are also not associated with any particular effect and remain within the ambit of what the skilled person would select based on the disclosure of D1.

1.3.7 Accordingly, the subject-matter of the main request does not involve an inventive step.

2. Auxiliary requests

2.1 Each of auxiliary requests 1-4 comprises a claim (respectively, claims 12, 5, 12 and 5) directed at a composition defined in terms of the process for its preparation and by a stability of at least 90% after one year, up to 18 months. For the same reasons as for claim 13 of the main request (see 1.2 above), none of auxiliary requests 1-4 meet the criteria of novelty.

2.2 In addition, in auxiliary requests 1 and 2, step (a) of claim 1, the same intermediate quantities (10,000 units and 50 mg) are extracted from their disclosure in the context of heparin in paragraph [0041] and generalised without basis to all heparinoids (see 1.1.2 above). Auxiliary requests 1 and 2 thus infringe Article 123(2) EPC.

2.3 None of the amendments introduced in auxiliary requests 1-8 overcome the objection of inventive step either.

In claim 1 of auxiliary request 1, the addition of sodium hydroxide or potassium hydroxide is optional ("possible addition") and has no impact on the assessment of inventive step.

There is furthermore no evidence for the appellant's allegation, or statement on page 12 (paragraph [0031]) of the application, that a pH of 7.2 to 7.6 (as specified in auxiliary requests 1 and 2), or even of 7.5 (as required in auxiliary requests 3, 4 and 8), leads to the best lidocaine stability. The Board recalls that alleged advantages to which the appellant merely refers, without offering sufficient evidence to support the comparison with the closest prior art, cannot be taken into consideration in determining the problem underlying the invention and therefore in assessing inventive step.

The amendments to the ranges defining the amount of heparinoid and lidocaine (100-250,000 units or 0.5-1250 mg heparinoid and 5-1000 mg lidocaine per unit dose, see claim 5 of auxiliary request 3 and claim 1 of auxiliary request 4), and the limitation of the heparinoid to heparin (see claim 1 of auxiliary request 7), do not define any additional differentiating feature over D1. Lastly, claim 6 of auxiliary request 5, and claim 1 of auxiliary request 6 are both identical to claim 7 of the main request (see 1.3.6 above). The same conclusion as for the main request therefore applies.

Accordingly, none of auxiliary requests 1-8 meet the criteria of inventive step.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

A. Vottner Y. Podbielski

Decision electronically authenticated