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Datasheet for the decision of 16 January 2025

Case Number: T 1701/22 - 3.3.04

Application Number: 13737808.9

Publication Number: 2866825

IPC: A61K38/26, A61P3/04

Language of the proceedings: EN

Title of invention:
Use of long-acting GLP-1 peptides

Patent Proprietor:
Novo Nordisk A/S

Opponents:
Teva Pharmaceutical Industries Ltd
Generics [UK] Limited
Galenicum Health S.L.U.

Headword:
Obesity treatment with semaglutide/NOVO NORDISK

Relevant legal provisions:
EPC Art. 56

Keyword:
Selection of the closest prior art
Inventive step - (no)

Decisions cited:
T 2759/17, T 0787/17, T 1409/06

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Beschwerdekammern

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Case Number: T 1701/22 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 16 January 2025

Appellant: (Patent Proprietor)	Novo Nordisk A/S Novo Allé 2880 Bagsværd (DK)
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Respondent: (Opponent 3)	Galenicum Health S.L.U. CL Sant Gabriel n°50 08950 Esplugues de Llobregat (ES)
Representative:	Galenicum Health S.L.U. CL Sant Gabriel n°50 08950 Esplugues de Llobregat (ES)

Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted on 10 May 2022 revoking European patent No. 2866825 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairwoman M. Pregetter
Members: O. Lechner
A. Bacchin

Summary of Facts and Submissions

I. The patent proprietor (appellant) filed an appeal against the opposition division's decision to revoke European patent No. 2 866 825.

II. The patent is based on European patent application No. 13 737 808.9, which was filed as an international patent application and published as WO 2014/005858 ("application as filed").

III. In its decision, the opposition division held that the sets of claims in accordance with the then-main request (as granted) did not add subject-matter within the meaning of Article 100(c) EPC, was sufficiently disclosed within the meaning of Article 100(b) EPC, but did not involve an inventive step within the meaning of Articles 100(a) and 56 EPC. Auxiliary requests 1 and 2 were also found to lack an inventive step under Article 56 EPC.

IV. With its statement of grounds of appeal, the appellant provided arguments as to why the subject-matter of the set of claims in accordance with the then-main request and of auxiliary requests 1 and 2 (as filed by letter dated 28 January 2022) involved an inventive step.

V. Opponents 1 to 3 (respondents 1 to 3) replied to the statement of grounds of appeal.

VI. The appellant submitted, by letter dated 22 September 2023, sets of claims in accordance with a main request (identical to the set of claims in accordance with auxiliary request 2 as filed by letter dated 28 January 2022) and a new auxiliary request 1.

These two claim requests replaced the previous claim sets on file.

VII. Respondent 1 replied to said letter.

By letter dated 9 July 2024, respondent 3 announced that it would not be attending the oral proceedings scheduled for 16 January 2025.

VIII. In reaction to the board's preliminary opinion under Article 15(1) RPBA, respondent 1 submitted further arguments.

IX. The oral proceedings before the board took place on 16 January 2025. The appellant and respondents 1 and 2 were represented. Respondent 3, as announced in writing, did not attend the oral proceedings.

At the end of the proceedings, the Chairwoman announced the board's decision.

X. Claim 1 reads as follows:

(a) Main request

"1. A composition comprising the GLP-1 agonist semaglutide and one or more pharmaceutically acceptable excipients for use in the prevention or treatment of obesity, wherein said use comprises administration of said GLP-1 agonist in an amount of at least 0.7 mg per week; and said composition is in the form of an aqueous formulation with pH between 3 and 10."

(b) Auxiliary request 1

"1. A composition consisting of the GLP-1 agonist semaglutide and one or more pharmaceutically acceptable excipients for use in the prevention or treatment of obesity, wherein said use comprises administration of said GLP-1 agonist in an amount of at least 0.7 mg per week; and said composition is in the form of an aqueous formulation with pH between 3 and 10."

XI. Reference is made to the following documents

D1 WO 2012/080471 Al

D2 History of Changes for Study: NCT00696657, version 8, 22 September 2022

D3 Madsbad S. et al., Diabetes Obes. Metab. (2011), 13(5):394-407

D4 Torekov S. et al., Obes. Rev. (2011), 12(8):593-601

D10 WO 2011/138421 Al

D11 WO 2006/097537 A2

D15a Astrup A. et al., The Lancet (2009), 374:1606-16

D15b Astrup A. et al., Int. J. Obes. (2012), 36(6): 843-54

D19 Broadhead J. and Gibson M., Chapter 9, Parenteral Dosage Forms, in Gibson M. (ed.), "Pharmaceutical Preformulation and Formulation: A Practical Guide from Candidate Drug Selection to Commercial Dosage Form", Second Edition (2009), CRC Press [Volume 199 of Drugs and the Pharmaceutical Sciences], pages 325 to 347

D25 Gallagher J. (11 February 2021) https://www.bbc.com/news/health-56011979 - 7 pages

D27 Wilding J. et al., N. Engl. J. Med. (2021), 384(11):1-13

D28 Samuelson K. (11 February 2021) https://news.feinberg.northwestern.edu/2021/02/11/new-anti-obesity-medication-almost-twice-as-effective-as-most-currently-approved-weight-loss-drugs/- 3 pages

D29 Bhansali A. et al., J. Assoc. Physicians India (2010), 58 (SPEC. ISSUE):10-14

D30 Hribal M. and Sesti G., Clin. Invest. (2011), 1(2): 327-43

D31 Steinert R. et al., Am. J. Clin. Nutr. (2010), 92(4):810-7

D32 Valentino M. et al., Expert Rev. Endocrinol. Metab. (2010), 5(5):765-83

XII. The appellant's arguments may be summarised as follows.

(a) Main request

Inventive step - Article 56 EPC

Closest prior art and starting point for assessing inventive step

Document D10 was the closest prior art and contained multiple teachings that each had to be assessed, in line with T 2759/17, as candidates for the closest prior art — i.e. whether, from the skilled person's

perspective, they represent the most promising springboard for developing a therapy for obesity.

The skilled person would have considered the example in D10, which demonstrates effective weight reduction in an obesity animal model with exenatide, as the most promising springboard. In contrast, other passages in D10, particularly claims 8 and 17, were speculative about using other GLP-1 receptor agonists for obesity and would not have been seen as a realistic starting point, especially for semaglutide, with no prior art showing its efficacy for obesity. To start the inventive-step assessment from claim 8 would thus be based on hindsight.

Difference, its technical effect, and objective technical problem

The key difference from D10 was that claim 1 requires semaglutide at a dosage of at least 0.7 mg/week in the claimed formulation. D10 taught that exenatide had to be given in combination with a DPP-4 inhibitor to avoid severe side effects.

Documents D4 and D25 highlight that bariatric surgery was the only successful treatment for severe obesity at the relevant time, and neither document mentions semaglutide.

The patent was the first to demonstrate safe and effective weight reduction with semaglutide in obese subjects (Example 1, Figure 5), showing it to be statistically superior to liraglutide in weight loss. Given prior art suggesting that liraglutide, exenatide (documents D3, D4 and D29) and albiglutide (document D3) were each similarly effective for weight reduction,

the skilled person would reasonably expect semaglutide to outperform these agents, including exenatide.

The objective technical problem was the provision of an improved, highly effective, and safe therapy for the treatment or prevention of obesity.

The solution was provided by claim 1, which required semaglutide as a single agent.

Obviousness

The appellant based its obviousness line of argument on the objective technical problem as defined by the board during the oral proceedings, i.e. how to put the treatment of obesity as defined in claim 8 of document D10 into practice.

The skilled person would not have arrived at the claimed solution in an obvious manner starting from document D10 because there had been nothing in the prior art to suggest that the use of at least 0.7 mg per week of semaglutide, as claimed, would provide a safe and more efficacious therapy for the treatment or prevention of obesity (paragraph [0087] of the patent in suit).

Document D10 taught against using a GLP-1 receptor agonist alone for obesity, as exenatide caused severe side effects and required a DPP-4 inhibitor for weight loss maintenance. In contrast, the patent in paragraph [0087] showed effective weight loss with semaglutide at doses ≥0.8 mg, without safety concerns.

None of the cited documents highlighted semaglutide as particularly advantageous, so the skilled person would

have had no clear motivation to select it over other known GLP-1 receptor agonists like exenatide or liraglutide for obesity treatment. Even if considering the GLP-1 receptor agonists in claim 2 of document D10, the skilled person would have favoured approved GLP-1 receptor agonists with established clinical use and known safety profiles, such as exenatide, exenatide LAR (long-acting release) or liraglutide (documents D3, D4, D15a, D15b, D29 or D31), but would have stopped at taspoglutide due to its severe side effects, and not considered the other GLP-1 receptor agonists listed thereafter.

Even if semaglutide were considered an alternative to liraglutide or exenatide, the skilled person would not reasonably have expected that 0.7 mg per week, as claimed, would provide an improved therapy for obesity treatment or prevention. Document D10 (page 43, line 13), cited by the respondents as providing a suitable dosage for semaglutide, does not specify its use for obesity but rather for type 2 diabetes (T2D), based on the clinical study in document D2. A cautious skilled person would likely have opted for the lower end of the dosage range, which Figure 5 of the patent shows to have no effect on weight reduction. Furthermore, D10 (page 43, line 21 ff) also suggests alternative administration routes to subcutaneous injection.

Additionally, the skilled person had no indication to provide semaglutide in an aqueous formulation with pH 3 to 10. Document D19, a book chapter on parenteral formulations, suggests non-aqueous formulations for parenteral administration (page 334) and discloses in Table 1 on page 327 a list of 14 buffers for parenteral formulations, most of which have pH-range endpoints outside the claimed pH 3 to 10.

Even years after the filing of the present patent, semaglutide has been described as a "*game changer*" in the treatment of obesity (D25, D27 or D28). An expert in the field remarked, "*I have spent the last 20 years doing obesity research; up until now we've not had an effective treatment for obesity apart from bariatric surgery*" (document D25, page 2, penultimate paragraph).

The two short statements on a clinical trial of semaglutide in T2D patients in documents D29 and D30 would not have provided any incentive to the skilled person to use semaglutide. These documents explicitly state that semaglutide is being developed for the treatment of T2D, with no data showing its effect on body weight in overweight or obese patients.

Document D4 suggested that future obesity treatments would likely involve combination therapies with multiple hormones, such as GLP-1, PYY and/or oxyntomodulin, for a superior appetite-suppressing profile and greater weight loss than single-agent trials. Based on these insights, the skilled person would have focused on combining agents to maximise efficacy rather than exploring individual GLP-1 receptor agonists like semaglutide.

(b) Auxiliary request 1

Inventive step - Article 56 EPC

Auxiliary request 1 was identical to the main request except wherein claim 1 of auxiliary request 1 is simply a combination of claims 1 and 2 of the main request. Claim 1 of auxiliary request 1 uses the "consisting of" language, which distinguishes the invention even

further from the cited prior art, such as the combination of a GLP-1 receptor agonist and the DPP-4 inhibitor linagliptin.

XIII. The respondents' arguments may be summarised as follows.

(a) Main request

Inventive step - Article 56 EPC

Closest prior art

Document D10 represented the closest prior art and claims 7, 8 or 17 a feasible starting point for assessing inventive step.

Difference, its technical effect, and objective technical problem

The only distinguishing feature was the formulation of the composition as an aqueous formulation having a pH between 3 and 10. This feature had no apparent technical effect.

The objective technical problem was the provision of an alternative composition of semaglutide for the treatment or prevention of obesity.

However, when considering that semaglutide had to be selected, and taking into account the objective technical problem as defined by the board — namely how to put the treatment of obesity as defined in claim 8 of document D10 into practice - the following was applicable.

Obviousness

Selecting any GLP-1 receptor agonist listed in claim 2 of document D10 would have been an obvious choice to solve the objective technical problem. Document D10 already taught that semaglutide was suitable for treating obesity and suggested a highest dose of 1.6 mg/week. Moreover, the weight reducing effect of different GLP-1 receptor agonists and also of semaglutide had already been described in the common general knowledge, such as documents D3, D4 or D29 to D32. Suitable dosage ranges for each of the specific GLP-1 receptor agonists listed were already provided on page 43 of document D10. The prior art also disclosed suitable parenteral formulations and their pH, as evidenced by documents D1, D11 and D19.

The skilled person, applying routine experimentation, would have had a reasonable expectation, if not certainty, that semaglutide could provide an alternative treatment for obesity to exenatide, and would have arrived at the subject-matter of claim 1 without inventive skill.

(b) Auxiliary request 1

Inventive step - Article 56 EPC

Claim 1 of auxiliary request 1 lacked an inventive step for the same reasons as given for claim 1 of the main request.

XIV. The parties' requests were as follows:

(a) The appellant (patent proprietor) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the set of claims in accordance with the main request or, alternatively, on the basis of the set of claims of auxiliary request 1, both as filed by letter dated 22 September 2023.

(b) Respondents 1 to 3 (opponents 1, 2 and 3) requested that the appeal be dismissed.
Respondent 1 also requested that auxiliary request 1 not be admitted into the proceedings.
Respondent 2 requested that the objections under Article 100(c) EPC against claims 2 to 15 be considered, as they were never withdrawn during opposition proceedings and thus did not constitute an amendment to its appeal case, subject to the provisions of Article 12(4) and (6) RPBA.

Reasons for the Decision

1. Respondent 3 did not attend the oral proceedings. It had notified the board of its non-attendance in writing. Respondent 3 was treated as relying on its written case, in line with Rule 115(2) EPC and Article 15(3) RPBA.

Main request

Inventive step - Article 56 EPC

Closest prior art and starting point

2. It was common ground that document D10 could be a suitable choice for the closest prior art. However, a key point of dispute was the choice of the starting

point within document D10 for assessing inventive step. The appellant argued that the example in document D10 was the correct starting point, while the respondents considered claim 8 to be the appropriate point of departure.

3. Document D10 relates to methods for treating and/or preventing metabolic diseases, especially type 2 diabetes mellitus (T2D), obesity and/or conditions related thereto (e.g. diabetic complications), comprising the combined administration of a GLP-1 receptor agonist (e.g. exogenous GLP-1 or a GLP-1 analogue) and a certain DPP-4 inhibitor (page 1, paragraph 1).

Claim 8 defines a combination comprising a GLP-1 receptor agonist and the DPP-4 inhibitor linagliptin, as defined in any of claims 1 to 5, for use in the treatment of T2D, obesity or both, said treatment comprising the steps i) administering an effective amount of the GLP-1 receptor agonist to the patient, e.g. for inducing body weight loss and/or body fat loss, and ii) administering an effective amount of the DPP-4 inhibitor to the patient, e.g. for maintaining the reduced body weight and/or body fat, wherein the DPP-4 inhibitor treatment ii) is subsequent to the GLP-1 receptor agonist treatment i).

Claim 2 provides exenatide, exenatide LAR, liraglutide, taspoglutide, semaglutide, albiglutide, lixisenatide and dulaglutide as GLP-1 receptor agonists to be used. Document D10 clearly teaches the use of each one, as its description on page 43 provides a dosing scheme for each.

The example in document D10 (page 51, paragraph 1 ff) evaluates the effects of repeated subcutaneous (s.c.) administration of a GLP-1 receptor agonist, such as e.g. exenatide (30 µg/kg/day), with an osmotic minipump for 10 or 28 days and exenatide (30 µg/kg/day s.c.) for 10 days followed by vehicle or the DPP-4 inhibitor BI 1356 (3 mg/kg; linagliptin) given perorally (p.o.), on body weight in dietary-induced obese (DIO) female Wistar rats - an animal model of obesity. The results show that exenatide, the only GLP-1 receptor agonist tested despite the use of "e.g." in the introductory part of the example, leads to significant weight loss during the first 11 days. When the treatment is discontinued, the animals gain weight again. However, the animals treated further with linagliptin stabilised their body weight at the new weight level and were significantly lighter than the vehicle-treated control animals (Figures 1, 3 and 4).
Document D10 does not provide experimental data with semaglutide as GLP-1 receptor agonist.

4. The board recalls that, under Article 56 EPC, an invention involves an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art. This state of the art includes any prior disclosure, within the meaning of Article 54(2) EPC, without ranking or distinction. Any such prior disclosure may be used as the starting point for assessing inventive step, and also as supplementary prior art in alternative scenarios with different starting points. It is established case law of the boards of appeal, based on the wording of Article 56 EPC, that if inventive step is to be acknowledged the claimed subject-matter must be inventive starting from any starting point in the prior art. If inventive step is to be denied, the choice of

starting point needs no specific justification (see T 787/17, Reasons 5.1 and also Case Law of the Boards of Appeal of the European Patent Office, 10th edn., 2022, I.D.3.1).

5. The selection of a starting point serves the purpose of assessing inventive step and is performed by the body deciding on inventive step, which makes its selection from the cited prior art disclosures that are eligible under Article 56 EPC. Depending on the circumstances of the individual case, either only one starting point or several alternative starting points will have to be considered.

5.1 The practice of selecting, in cases where this is appropriate, one among several potential starting points on the basis of its greater similarity to the claimed subject-matter and its intended purpose (the so-called closest prior art) serves efficiency by permitting a combined assessment.

The test is to establish if the claimed subject-matter would have been non-obvious even when starting from such a particularly "promising" starting point. Thus, in a situation where inventive step is ultimately to be acknowledged, carrying out a detailed assessment of inventive step according to the problem-solution approach with the closest prior art as the starting point may avoid having to perform an equally detailed assessment for numerous alternative starting points that are comparatively more remote as well.

The consideration in such a case is that since an inventive step can be acknowledged in a scenario starting from the closest prior art, it can also be acknowledged, for at least the same reasons, starting

from the more remote alternative starting points, without the need for a detailed analysis in each of these cases.

Obviously, this shortcut only works in cases where it can be confirmed that the same reasons for acknowledging an inventive step are indeed also applicable to the scenarios based on the alternative starting points. The reasoning addressing the alternative scenarios must at least set out why this criterion is met.

Nonetheless, comparative remoteness does not prohibit the consideration of any prior disclosure as a starting point in a detailed step-by-step assessment according to the problem-solution approach. If a chosen starting point is "too remote" from the claimed subject-matter in terms of structural features and purpose, the problem-solution approach will simply not result in a finding of obviousness.

5.2 In view of its purpose as described above, the concept of the "closest prior art" — and particularly the choice of the "starting point" within that closest prior art — is not relevant in a situation where an inventive step cannot ultimately be acknowledged. If the assessment of inventive step from a given starting point results in a finding of obviousness, this starting point is evidently close enough to the claimed invention to lead to a conclusion that decides the question of inventive step.

5.3 Since, in the case at hand, the assessment with claim 8 of document D10 as the starting point resulted in a finding of obviousness (as set out below), it is not relevant whether another piece of prior art or another

starting point within document D10 might be even closer to the claimed subject-matter.

Despite this conclusion, the appellant's arguments on the choice of the starting point are briefly addressed in the following.

6. The appellant argued that document D10 contains multiple teachings which each had to be assessed in line with T 2759/17 as candidates for the starting point for assessing inventive step – i.e. whether, from the perspective of the skilled person, they represent the most promising springboard for the provision of a therapy for obesity.

7. The appellant's line of argument follows the "second approach" described in decision T 2759/17 (Reasons 5.3.2 and 5.4), according to which the skilled person is involved in the assessment of inventive step already when the closest prior art disclosure is being selected, and the most promising springboard towards the invention is determined as the technical teaching from which the skilled person would realistically have started. Following this approach, it is possible to reject an inventive-step attack on the ground that the skilled person would not realistically have selected the specific disclosure relied upon in the attack as a starting point.

8. The appellant, following this approach for selecting the closest prior art as explained in T 2759/17, argued that the exenatide example of D10 should be taken as the closest prior art, whereas the skilled reader would not realistically select the specific disclosure of claim 8, except with the benefit of hindsight.

9. In the case at hand, the example in document D10 provides experimental evidence for an anti-obesity effect for exenatide in a rat obesity model, demonstrating the potential for weight reduction with a GLP-1 receptor agonist, and thus provides proof of concept.

While this example is useful, independent claim 8 reflects what a skilled reader would understand from document D10 as a whole. As such, claim 8 is considered a feasible starting point for assessing inventive step in the context of obesity, as it directly relates, *inter alia*, to the treatment of obesity by inducing weight and fat loss, which is consistent with the teaching of document D10 as a whole. Claim 8 integrates the proof of concept from the example in document D10 and the common general knowledge on the weight reducing effect of GLP-1 receptor agonists (documents D3, D4, D29 or D30; see point 15. below). Hence a skilled reader would not have disregarded the specific disclosure of claim 8 but would have rather realistically selected it as a starting point, so that there is no reason to reject this inventive step attack.

10. The board thus finds that, in the present case, the selection of claim 8 as the starting point would be consistent with either of the approaches described in points 4. and 7. above, as it represents a realistic and justifiable starting point under either approach. Consequently, there is no need for further discussion of the appellant's point of view.

11. In summary, claim 8 provides the use of a GLP-1 receptor agonist, which according to claim 2 may be selected from a list including, *inter alia*,

semaglutide, for treating T2D, obesity or both, with the effect of inducing body weight loss and/or body fat loss.

Difference, its technical effect, and objective technical problem

12. The subject-matter of claim 1 differs from the disclosure in claim 8 of document D10 by
- the selection of a specific GLP-1 receptor agonist, i.e. semaglutide;
- the dosage regimen of at least 0.7 mg per week; and
- the formulation in the form of an aqueous formulation with a pH between 3 and 10.

The administration of an effective amount of a DPP-4 inhibitor to the patient is not considered a difference since it occurs subsequent to treatment with the GLP-1 receptor agonist. Such a sequential treatment setting is not excluded by the subject-matter of claim 1.

Therefore three aspects must be considered: the effect of semaglutide, the impact of the dosage regimen, and the influence of the formulation.

12.1 Effect of semaglutide

The skilled reader would have considered all the GLP-1 receptor agonists listed in claim 2 of document D10 as potential actives with body weight reducing activity. It was common general knowledge that all the GLP-1 receptor agonists listed in claim 2 of document D10 have body weight reducing activity (e.g. documents D3, D4, D29 or D30, as discussed in point 15. below). Consequently, the skilled reader would have viewed the actives listed in claim 2 as alternatives.

The data in the patent in suit show that treating subjects with T2D (who had an average BMI of just over 30 kg/m², meaning that a portion were obese) with at least 0.8 mg semaglutide once weekly in an unspecified formulation resulted in a safe, statistically significant greater reduction in body weight compared with treatment with liraglutide (Figure 5). Semaglutide and liraglutide are thus both administered according to the dosage regimens taught in document D10, which is 0.5 to 2 mg daily for liraglutide and 0.1 to 1.6 mg once weekly for semaglutide. These findings indicate a potential benefit of semaglutide for weight reduction in obese (T2D) individuals over liraglutide.

The patent in suit compares the weight reducing effect of semaglutide with only one of the alternative GLP-1 receptor agonists listed in claim 2 of document D10, namely liraglutide. It may be acknowledged, as argued by the appellant, that based on observations in the prior art (see document D3, page 395, right-hand column, paragraph 2 and page 401, right-hand column, paragraph 2; document D4, page 597, left-hand column, end of penultimate paragraph) the skilled reader would expect exenatide and albiglutide to have a similar effect on body weight reduction to liraglutide, but potentially be inferior to semaglutide. The patent does not provide comparative data on weight reduction for the other GLP-1 receptor agonists listed in claim 2 of document D10, such as exenatide LAR, lixisenatide or dulaglutide.

Further, reports of safety concerns leading to the discontinuation of taspoglutide's development (see e.g. D3, page 401, right-hand column, paragraph 1, or D4, paragraph bridging pages 597 and 598) would have led the person skilled in the art merely to refrain from

using taspoglutide as an active. Excluding a single active from a list does not imply that the skilled reader would have completely disregarded the other GLP-1 receptor agonists listed in claim 2 of document D10.

12.2 *Impact of the dosage regimen*

The claimed dosage regimen is consistent with the range proposed in the closest prior art document D10, with no apparent difference in effect, as the claimed dose of at least 0.7 mg/week overlaps to a great extent with the dose range proposed in document D10, i.e. the upper half of the 0.1 to 1.6 mg/week, *inter alia* for the treatment of obesity. In line with the dose-dependent effects reported in the common general knowledge for the whole class of GLP-1 receptor agonists (e.g. document D4, page 596, left-hand column, third paragraph), Figure 5 of the patent in suit shows a dose-dependent effect of semaglutide. Thus the claimed range of at least 0.7 mg/week is arguably not associated with a surprising effect.

12.3 Influence of the formulation

No surprising effect is apparent for the claimed formulation in an aqueous solution with pH between 3 and 10.

13. Thus the overall technical effect is the treatment of obesity with the efficacy and safety inherent to semaglutide.

The objective technical problem is considered to be how to put the treatment of obesity as defined in claim 8 of document D10 into practice.

The claimed solution is the use of semaglutide in an amount of at least 0.7 mg per week in the form of an aqueous formulation with pH between 3 and 10.

Obviousness

14. According to established case law, it is not necessary for the success of an envisaged solution to a technical problem to be predictable with certainty. In order to render a solution obvious, it is sufficient to establish that the skilled person would have followed the teaching of the prior art with a reasonable expectation of success.

Treatment of obesity

15. The weight reducing effects of GLP-1 receptor agonists in general and also of semaglutide were well established, as evidenced by review articles D3, D4, D29 and D30.

Documents D3 and D4 discuss the efficacy and safety of GLP-1 receptor agonists, including exenatide, taspoglutide, albiglutide and liraglutide, with D3 noting no clinically significant differences in weight control among these agents (D3, abstract; page 402, right-hand column, last sentence of penultimate paragraph). Figure 1 of D3 also discloses semaglutide as a subcutaneously administered GLP-1 receptor agonist. D4 reports that GLP-1 significantly enhances satiety and reduces food intake in both normal and obese subjects, including those with T2D, with exenatide twice a day (BID) and liraglutide 1.8 mg daily showing similar effects on weight loss in T2D patients (D4, pages 596 to 598).

Documents D29 and D30 highlight semaglutide, a once-weekly human GLP-1 analogue, for its ability to lower blood glucose and reduce body weight (D29, page 13, right-hand column, 3rd paragraph; D30, page 340, right-hand column, first full paragraph), with D30 also providing an overview for other GLP-1 agonists, including long-acting exenatide, liraglutide, albiglutide, taspoglutide and lixisenatide.

16. With reference to document D4 (abstract and page 598, middle of left-hand column), the appellant also argued that prior to the present invention there was no truly successful drug-based treatment for obesity, and that even other GLP-1 receptor agonists had been described as resulting only in a "*moderate average weight loss*" in obese patients.
The appellant referred to the therapeutic success of semaglutide, highlighted in recent post-published documents D25 (pages 1 to 2), D27 (page 12, last paragraph) and D28 (page 1), describing it as a "*game changer*" in obesity treatment, as a further indication of the presence of an inventive step over the prior art.

17. However, it was common general knowledge that GLP-1 receptor agonists, including semaglutide, are successful in reducing body weight, and their use in the treatment of obesity was therefore seriously considered (document D3, abstract; D29, page 13, right-hand column, paragraphs 3 and 4; D30, abstract and page 340, first full paragraph). Document D10, which specifically claims treatment of obesity by inducing body weight and/or fat loss, further supports this expectation, demonstrating body-weight reduction in an animal model of obesity.

18. Thus, based on the common general knowledge and the data in document D10, the skilled person had a reasonable expectation of achieving weight loss and being able to treat or prevent obesity using any of the GLP-1 receptor agonists listed in claim 2 of the closest prior art, including semaglutide. They would therefore have used semaglutide without applying any inventive skill.

19. In that context it is not relevant that semaglutide shows an improved effect compared with liraglutide (and probably also exenatide and albiglutide), since document D10 already teaches the use of any of the GLP-1 receptor agonists listed in claim 2, including semaglutide.

20. Consequently, the skilled person would have arrived at the use of semaglutide for treating or preventing obesity in an obvious manner, based on the teachings of the prior art and the well-established weight reducing properties of GLP-1 receptor agonists.

Other GLP-1 receptor agonists would be preferred over semaglutide

21. The appellant argued that the skilled person had no motivation to select semaglutide when faced with the objective technical problem. Not all GLP-1 receptor agonists exhibited the same activity, and the skilled person would have favoured approved GLP-1 receptor agonists with established clinical use and known safety profiles, such as exenatide or liraglutide (documents D3, D4, D15a, D15b, D29 or D31). The skilled person would have refrained from testing GLP-1 receptor agonists like semaglutide, for which no data were available regarding its use in the treatment of

obesity, and concentrated on further-developed GLP-1 receptor agonists such as liraglutide or exenatide.

22. However, it was known in the field, as disclosed in the prior art (document D32, page 7, end of third paragraph) and also review articles (document D29, page 13, right-hand column, paragraph 3; D30, page 340, right-hand column, paragraph 2), that semaglutide had been successfully tested in a clinical trial showing a body weight reducing effect (document D29, page 13, right-hand column, paragraph 3; D30, page 340, right-hand column, paragraph 2). Therefore, in the course of putting into practice the subject-matter of claim 8 of document D10, the skilled person would also have tested semaglutide.

23. The later description of semaglutide as a "*game changer*" (documents D25, D27 or D28) confirms the teaching of document D10 and is in line with what was already known in the field from the prior art at the relevant date of the patent, which had demonstrated its weight reducing effects in clinical trials.

24. Thus, despite the appellant's arguments, the skilled person would have been motivated to include semaglutide among the GLP-1 receptor agonists to be tested in the context of document D10, given the available prior art evidence of its body weight reducing effects and its advancement in clinical development.

Safety concerns when using GLP-1 receptor agonists (other than taspoglutide)

25. In another line of argument, the appellant also pointed out that document D10 described that treatment with exenatide led to skin alterations that resulted in a

higher mortality in the treated animals (euthanisation due to severe reactions: document D10, page 53, paragraph 2). This finding, according to the appellant, taught away from using a GLP-1 analogue like exenatide for obesity treatment on its own, as it highlighted the unacceptable safety risks involved, which was contrary to the safe and effective use of semaglutide, as demonstrated in the patent in suit.

26. Focusing solely on document D10, the board agrees with the respondents that the skilled person would have recognised that the survival data in document D10 (Figure 2) are inconclusive. These data show that exenatide (s.c.) alone (group F) results in significantly lower survival (45%) compared with exenatide (s.c.) + vehicle (p.o.; group B, 67%) or even vehicle (p.o.) alone (group A, 65%), but there is no explanation for these differences or indication of statistical significance. Since the data in Figure 2 concern survival rather than weight loss, they cannot be used to draw conclusions on the efficacy of exenatide for weight loss.

27. Moreover, as evidenced by documents D3 (page 395, left-hand column, last paragraph), D4 (page 596, chapter "Exenatide"), D29 (abstract; page 12, chapter "GLP-1 receptor agonist") or D30 (page 328, left-hand column, chapter "Exenatide"), and also acknowledged by the appellant, exenatide was an approved medicament for use in humans, with dose-dependent nausea, vomiting and diarrhoea as reported most common adverse events (document D30, page 331, right-hand column, last paragraph).

28. Given the common general knowledge regarding the side effects of exenatide in human patients, the skilled

person would not have been discouraged from using it or other GLP-1 receptor agonists (for which no safety issues have been reported) to treat patients. More importantly, the skilled person would not have questioned the proof of concept, as provided in the example of document D10, that a GLP-1 receptor agonist is suitable for treating obesity, as both the treatment's effect on weight loss and its safety are supported by other prior art disclosures including review articles.

29. Accordingly, the skilled person would not have been dissuaded by the survival data in document D10 or the known side effects of exenatide from pursuing the use of GLP-1 receptor agonists, including semaglutide, for the treatment of obesity, as the overall prior art supported both their efficacy and acceptable safety profile.

Semaglutide dosage

30. Based on the dosage indications provided on page 43, line 13 of document D10 for semaglutide (0.1 to 1.6 mg per week subcutaneously), the skilled person would have been aware of a suitable dosage range and, through routine testing, would have established the optimal dosage regimen for the induction of efficient weight reduction when selecting semaglutide as the GLP-1 receptor agonist (see e.g. T 1409/06, Reasons 3.2.1).

Contrary to the appellant's assertion, there is no indication that the dosage indications provided for semaglutide in the patent are derived from the clinical study for the treatment of T2D described in document D2.

Even if this were the case, it would not prevent the skilled person from using this dosage regimen for the treatment of obesity and, in particular, from focusing on the use of higher doses.

31. Thus the skilled person would have arrived at a suitable dosage of semaglutide for treating obesity through routine optimisation based on the disclosure in document D10.

Aqueous formulation with a pH between 3 and 10

32. Notwithstanding the fact that no surprising technical effect was shown for the claimed formulation, suitable formulations for semaglutide, such as an aqueous formulation with a pH between 3 and 10, were known to the skilled person, as evidenced by documents D1 (Example 1) and D11 (Example 4 on page 47 and pharmaceutical formulation on page 63, lines 10 to 15).

Moreover, as stated in paragraph [0067] of the patent, it was known in the art how to prepare formulations of pharmaceutical compositions comprising a GLP-1 receptor agonist.

Consistent with this, document D10 discloses (page 39, lines 23 to 26) that injectable formulations of the GLP-1 receptor agonists may be prepared according to known formulation techniques, e.g. using suitable liquid carriers, which usually comprise sterile water and optionally further additives.

33. The appellant further argued that, based on Table 1 of document D19, the skilled person would not have automatically selected a pH range of 3 to 10. Table 1

lists 14 different buffers approved for parenteral products, covering a broader pH range of 2.0 to 10.8.

However, document D19 itself, in Chapter 9, "Parenteral Dosage Forms", specifically states under the heading "*pH and Tonicity Requirements*" (starting on page 326) that parenteral solutions should have a pH close to physiological levels unless stability or solubility concerns arise. While pH values between 2 and 12 are tolerated, extremes are discouraged. In practice, most licensed parenteral products have a pH between 3 and 9, as values above 9 may cause necrosis, and values below 3 may lead to pain and phlebitis.

34. As argued by the appellant, document D10 mentions on page 43, paragraph 2 different potential routes of administration for GLP-1 receptor agonists. However, the same page explicitly discloses that semaglutide is to be administered subcutaneously (page 43, line 13). Additionally, lines 1 and 25 to 26 confirm that subcutaneous administration is the preferred route for GLP-1 receptor agonists.

35. Consequently, the skilled person would have arrived at the claimed aqueous formulation with a pH between 3 and 10 for subcutaneous administration of semaglutide using routine formulation knowledge and standard practices disclosed in the prior art.

Conclusion on inventive step

36. In conclusion, based on the disclosure in document D10 and the skilled person's common general knowledge as disclosed in document D29 or D30, the skilled person would have arrived at the claimed invention in an obvious way.

Auxiliary request 1

Admittance - Article 13(1) RPBA

37. In view of the board's findings regarding inventive step of auxiliary request 1 (see point 39. below), the board finds it unnecessary to provide reasons for the admittance of this claim request.

Inventive step - Article 56 EPC

38. Claim 1 of auxiliary request 1 differs from claim 1 of the main request only in that it is directed to "A composition consisting of the GLP-1 agonist semaglutide[...]" instead of "A composition comprising the GLP-1 agonist semaglutide[...]" (underlining by the board).

39. The board considers that the same conclusion on inventive step as provided for claim 1 of the main request (see points 15. to 36. above) applies to the subject-matter of claim 1 of auxiliary request 1, since the limitation to a composition consisting of only semaglutide pertains to its formulation and does not affect the administration of further formulations, such as a DPP-4 inhibitor. It must be re-emphasised that, in claim 8 of document D10, the GLP-1 receptor agonist formulation is administered in a separate composition from the DPP-4 inhibitor, which is used subsequently to stabilise the weight reduction achieved by the semaglutide treatment. Consequently, the inventive-step assessment starting from claim 8 of document D10 does not change.

Thus the subject-matter of claim 1 of auxiliary request 1 lacks an inventive step for the same reasons as provided for the subject-matter of claim 1 of the main request (see points 15. to 36. above).

40. Given that claim 1 lacks an inventive step, it was not necessary to decide on respondent 2's request to consider the objections under Article 100(c) EPC against claims 2 to 15.

Order

For these reasons it is decided that:

- The appeal is dismissed.

The Registrar: The Chairwoman:

I. Aperribay M. Pregetter

Decision electronically authenticated