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**Datasheet for the decision  
of 2 June 2016**

**Case Number:** T 1777/12 - 3.3.04

**Application Number:** 01991093.4

**Publication Number:** 1349563

**IPC:** A61K38/22, A61P3/04, A61P3/06,  
A61P3/12, A61P9/00

**Language of the proceedings:** EN

**Title of invention:**  
Peptide PYY[3-36] for treatment of metabolic disorders

**Patent Proprietor:**  
Amylin Pharmaceuticals, Inc.

**Opponents:**  
Glaxo Group Limited  
Novo Nordisk A/S (opposition withdrawn)

**Headword:**  
Metabolic disorders/AMYLIN PHARMACEUTICALS

**Relevant legal provisions:**  
EPC Art. 54, 56, 83, 84, 123(2), 123(3)  
EPC R. 115(2)  
RPBA Art. 15(3)

**Keyword:**

Main request - requirements of the EPC met (yes)

**Decisions cited:**

T 0238/88, T 1063/06, T 1642/06, T 1523/07

**Catchword:**



**Beschwerdekammern**  
**Boards of Appeal**  
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Case Number: T 1777/12 - 3.3.04

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.04**  
**of 2 June 2016**

**Appellant :** Glaxo Group Limited  
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**Decision under appeal:** Interlocutory decision of the Opposition  
Division of the European Patent Office posted on  
21 June 2012 concerning maintenance of the  
European Patent No. 1349563 in amended form.

**Composition of the Board:**

**Chairwoman**            G. Alt  
**Members:**            M. Montrone  
                             L. Bühler

## **Summary of Facts and Submissions**

- I. Appeals were lodged by opponent 01 (appellant I) and opponent 02 (appellant II) against the interlocutory decision of the opposition division maintaining European patent No. 1 349 563, titled "*Peptide PYY[3-36] for treatment of metabolic disorders*".
- II. The patent was opposed under Article 100(a) EPC on the grounds of lack of novelty and inventive step and under Articles 100(b) and 100(c) EPC.
- III. The impugned decision deals with a main request and an auxiliary request 1aa, the latter submitted during the oral proceedings. The opposition division held that the subject-matter of claims 5 and 6 of the main request extended beyond the content of the application as filed, whereas auxiliary request 1aa met the requirements of the EPC.
- IV. Appellants I and II both submitted with their statements of grounds of appeal arguments as to why the subject-matter of claims 1 to 11 of auxiliary request 1aa underlying the impugned decision lacked novelty and an inventive step and was not disclosed in the patent in a manner sufficiently clear and complete for it to be carried out by the skilled person.
- V. With its reply to the appellant's statements of grounds of appeal the patent proprietor (hereinafter the "respondent") submitted a main request - identical to auxiliary request 1aa underlying the impugned decision - and eleven auxiliary requests.

Claims 1, 4, 8, and 10 of the main request read:

"1. Use of a PYY agonist in the manufacture of a medicament for treating a metabolic disorder in an obese or overweight subject in need of said treating, wherein said treating comprises reducing weight or reducing weight gain, wherein the PYY agonist is to be administered peripherally to said subject in an amount therapeutically effective to reduce weight or reduce weight gain, wherein the PYY agonist is the peptide PYY[3-36] and wherein the metabolic disorder is selected from the group consisting of: obesity, diabetes mellitus, insulin resistance, insulin resistance syndrome (also known as Syndrome X), dyslipidemia, and cardiovascular disease.

4. Use according to any one of the preceding claims wherein the amount of PYY agonist is from about 1 µg to about 5 mg per day in single or divided doses.

8. Use according to any one of the preceding claims wherein the subject is a human.

10. A PYY agonist for use in treating a metabolic condition in an obese or overweight subject in need of said treating, wherein said treating comprises reducing weight or reducing weight gain, wherein the PYY agonist is to be administered peripherally to said subject in an amount therapeutically effective to reduce weight or reduce weight gain, wherein the PYY agonist is the peptide PYY [3-36] and wherein the metabolic disorder is selected from the group consisting of: obesity, diabetes mellitus, insulin resistance, insulin resistance syndrome (also known as Syndrome X), dyslipidemia, and cardiovascular disease."

VI. By letter dated 29 May 2013 appellant II withdrew its opposition to the grant of the patent. It therefore ceased to be a party to the proceedings and appellant I became the only remaining appellant in these proceedings and will be hereinafter referred to as the "appellant".

VII. The appellant announced by letter dated 18 February 2016 that it would not be attending the oral proceedings.

VIII. The following documents are cited in this decision:

D1: WO 00/47219

D2: Zukowska-Grojec, DN&P, 10, 1997, p. 587-595

D3: Bischoff and Michel, TiPS, 20, 1999, p. 104-106

D4: Grandt *et al.*, Biochem. Biophys. Research Comm., 186, 1992, p. 1299-1306

D6: Morley, Neuropsychobiology, 21, 1989, p. 22-30

D7: Morley and Flood, Life Sciences, 41, 1987, p. 2157-2165

D10: WO 01/76631

D16: Chen *et al.*, Neurogastroenterol. Mot., 9, 1997, p. 109-116

D17: Yoshinaga *et al.*, Am. J. Physiol., 263, 1992, p. G695-G701

D18: Grandt *et al.*, *Regulatory Peptides*, 51, 1994,  
p. 151-159

D21: Rogers and Hermann, *Biomedical Reviews*, 8, 1997,  
p. 55-69

- IX. Oral proceedings before the board were held on 2 June 2016. The duly summoned appellant was not present, as announced. At the end of the oral proceedings the chairwoman announced the board's decision.
- X. The appellant's arguments submitted in writing may be summarised as follows:

*Main request*

*Sufficiency of disclosure (Article 83 EPC)*

The patent disclosed that PYY[3-36] reduced weight gain. That made it suitable for treating obesity (example 6), but, not the other disorders referred to in claims 1 and 10, which had a complex etiology that was not simply caused by excess weight. The other effects disclosed for PYY in the patent likewise did not establish a functional relationship between them and the claimed therapeutic applications, except for obesity. Accordingly, the use of PYY[3-36] was not suitable for all the therapeutic applications referred to in claims 1 and 10, contrary to the case law and in breach of the requirements of Article 83 EPC (see decision T 1642/06).

Furthermore, claims 1, 4, 8 and 10 encompassed non-working embodiments.



The use of PYY[3-36] in the claimed therapeutic applications to reduce weight gain in obese or overweight patients was an embodiment of claims 1 and 10. However, merely slowing weight gain down had no therapeutic effect in any of the claimed therapeutic applications, since the weight of the patients continued to increase.

Moreover, the patent disclosed in example 6 that a minimum dose of 300 µg/kg/day of PYY[3-36] was required to achieve a reduction in weight gain. However, claims 1 and 10 did not define an effective dose of PYY[3-36], while claim 4 specified a dose range which encompassed doses below the minimum effective dose. Moreover, claim 8 was directed to the therapy of human patients and it was doubtful whether even the minimum effective dose of PYY[3-36] as disclosed in example 6 achieved a therapeutic effect.

Lastly, the ambit of the claimed invention was not commensurate with the actual technical contribution of the patent to the art, since the patent only disclosed the suitability of PYY[3-36] in the therapy of obesity (see decision T 1063/06).

*Novelty (Article 54 EPC)*

The subject-matter of claims 1 and 10 lacked novelty with regard to the explicit and implicit disclosure of document D1 and the implicit disclosure of document D10 taking into account the common general knowledge of the skilled person as established by the disclosure of documents D2 to D4, D16 to D18 and D21. The latter documents disclosed that PYY[3-36] was the major endogenous form of PYY *in vivo* and therefore mediated its biological actions.

*Inventive step (Article 56 EPC)*

Depending on the therapeutic applications referred to in claims 1 and 10, the disclosure of documents D1, D3, D6, D7 or D10 represented the closest prior art.

Document D1 disclosed the use of PYY therapeutics in the therapy of metabolic disorders characterised by an aberrant glucose metabolism, including *inter alia* obesity and diabetic complications. The subject-matter of claims 1 and 10 differed therefrom by using PYY[3-36]. There was no advantageous technical effect associated with this difference. Thus, the technical problem to be solved was the provision of a specific or alternative PYY agent in the therapy of the claimed metabolic disorders. The use of PYY[3-36] as a specific or alternative agent to PYY was obvious in view of the teaching of document D1 combined with that of any of documents D2 to D4, D16 to D18 and D21. All of these documents disclosed that PYY[3-36] was the key active fragment of PYY which mediated the physiological functions of PYY *in vivo*. Moreover, PYY[3-36] had a longer half-life than PYY.

Document D3 disclosed that peripherally administered PYY[3-36] lowered blood glucose. However, no therapeutic use of the compound was disclosed. The subject-matter of claims 1 and 10 differed therefrom by referring to specific disorders, such as *inter alia* diabetes. The technical problem to be solved was the provision of a therapeutic agent for the therapy of the claimed metabolic diseases. The use of PYY[3-36] in the therapy of diabetes was obvious in the light of the teaching of document D3 alone. Moreover, in view of the teaching of document D3 combined with that of document D1, the use of PYY[3-36] in the therapy of all the

other disorders referred to in claims 1 and 10 was likewise obvious.

Document D6 reviewed the development of drugs for the therapy of appetite disorders, including obesity. By referring to document D7, it disclosed that the peripheral administration of full-length PYY caused weight loss, without affecting food intake (document D6, page 23, column 1, page 24, column 1, third paragraph, document D7, abstract and Figures 5A and B). Disclosed agents which appeared to have the most potential in the management of obesity included *inter alia* PYY agonists (document D6, page 26, column 2, last paragraph and Table 2). The claimed invention differed therefrom by using PYY[3-36] as an alternative to PYY. The use of PYY[3-36] as an alternative agent to PYY in the therapy of obesity was however obvious in view of the teaching of documents D2 to D4, D16 to D18 and D21 (see document D1 above).

Document D10 disclosed the use of PYY and functional analogs thereof in the therapy of obesity by inducing satiety which reduced appetite and desire for food. The claimed invention differed therefrom by using PYY[3-36] as an alternative to PYY. The technical problem to be solved was the provision of a specific PYY analog in the therapy of metabolic disorders. The use of PYY[3-36] as a solution to this problem was obvious in the light of the teaching of documents D2 to D4, D16 to D18 and D21 (see document D1 above).

XI. The respondent's arguments may be summarised as follows:

*Main request*

*Sufficiency of disclosure (Article 83 EPC)*

Claims 1 and 10 were directed to the peripheral administration of a therapeutically effective dose of PYY[3-36] to obese or overweight patients in the claimed therapeutic applications - all of which were commonly known to be associated with obesity or overweight (patent, paragraph [0010]). The patent further disclosed experimental evidence that PYY[3-36] inhibited food intake (example 1) and gastric emptying in normal mice (example 2), reduced weight or weight gain in obese mice (examples 6 and 7) and improved glycaemic control in obese diabetic mice (example 8). Accordingly, the patent disclosed that PYY[3-36] was effective in reducing weight or weight gain in obese mice, which demonstrated concomitantly its suitability in all of the claimed therapeutic applications, since the risk of developing these disorders was significantly lower, if weight or weight gain was reduced.

Moreover, the teaching disclosed in the patent enabled the skilled person to optimise the dose of PYY[3-36] in the claimed therapeutic applications for individual patients.

*Novelty (Article 54 EPC)*

The disclosure of documents D1 and D10 did not anticipate the subject-matter of claims 1 and 10 either explicitly or implicitly taking into account the common

general knowledge of the skilled person as established in documents D2 to D4, D16 to D18 and D21.

*Inventive step (Article 56 EPC)*

Document D7 represented the closest prior art for the subject-matter of claims 1 and 10, since it disclosed that the peripheral administration of PYY caused weight reduction, *i.e.* was directed to the same purpose as the claimed invention. The subject-matter of claims 1 and 10 differed therefrom in that PYY[3-36] was used as the therapeutic agent. The technical effect associated with this difference was a stronger reduction of food uptake compared to PYY (example 1 of the patent). Thus, the technical problem to be solved was the provision of an agent for use in an improved therapy of the disorders referred to in claims 1 and 10. The use of PYY[3-36] was not an obvious solution to this problem since none of prior art documents D2 to D4, D16 to D18 and D21 suggested that the parenteral administration of this agent to obese subjects caused weight reduction. Nor was that to be expected, since PYY and PYY[3-36] bound to different receptors and thereby mediated distinct physiological functions *in vivo*.

- XII. The appellant requested in writing that the decision under appeal be set aside and that European patent No. 1 349 563 be revoked.

The respondent requested that the appeal be dismissed (main request), or, alternatively, that the decision under appeal be set aside and that the patent be maintained on the basis of one of auxiliary requests 1 to 11, all filed with the reply to the statement of grounds of appeal.

## **Reasons for the Decision**

1. As announced, the duly summoned appellant was not present at the oral proceedings, which therefore took place in its absence in accordance with Rule 115(2) EPC and Article 15(3) RPBA.

### *Introduction to the invention*

2. The invention concerns the use of the peptide hormone Peptide YY [3-36] (PYY[3-36]), a derivative of PYY, in the therapy of metabolic disorders in obese or overweight subjects. The numbers in square brackets indicate that the peptide lacks two of the 36 amino acids of full-length PYY at its N-terminal end.
3. PYY[3-36] is a natural proteolytic fragment of PYY which is released from the intestine following a meal. Both hormones are ligands of several receptor subtypes all belonging to the pancreatic polypeptide (PP) receptor family (see paragraphs [0002], [0004] and [0006] of the patent).

### *Main request*

*Clarity and support (Article 84 EPC), amendments (Article 123(2) EPC), extension of protection (Article 123(3) EPC)*

4. The appellant did not raise objections under Articles 84, 123(2) and (3) EPC, and also the board too has none.
5. Accordingly, the main request meets the requirements of Articles 84, 123(2) and (3) EPC.

*Sufficiency of disclosure (Article 83 EPC)*

6. Claims 1 and 10 are medical use claims. It is the established case law of the boards of appeal that for such claims to fulfil the requirements of Article 83 EPC the patent has to disclose the product's suitability to be manufactured for the therapeutic applications claimed. Clinical trials are not required to establish suitability. It may suffice that *in vitro* or *in vivo* data directly and unambiguously reflect the therapeutic effect on which the claimed therapeutic application relies or, alternatively, that there is an established relationship between the physiological activities of the compound under consideration and the disease in question (see Case Law of the Boards of Appeal, 8th edition 2016 (hereinafter "CLBA"), section II.C.6.2).
  
7. In the present case, the therapeutic applications according to claims 1 and 10 are metabolic disorders in obese or overweight subjects selected from the group consisting of obesity, diabetes mellitus, insulin resistance, insulin resistance syndrome, dyslipidemia, and cardiovascular disease. According to these claims, the mechanism of action underlying the therapeutic effect of PYY[3-36] is the reduction of weight or weight gain.
  
8. It was common ground between the parties that the patent disclosed that PYY[3-36] achieved a reduction of weight or weight gain in obese mice when administered at certain concentrations, *i.e.* at 300 and 1000 µg/kg/day, over a certain time period (see example 6). Therefore, the experimental evidence disclosed in the patent establishes the suitability of PYY[3-36] in the therapy of obesity in obese or overweight subjects.

9. Obesity is only one of several therapeutic applications claimed (see point 7 above). The question is thus whether or not the patent discloses further evidence that PYY[3-36] is a suitable therapeutic agent for all of them.
  
10. The patent discloses that "*Obesity and its associated disorders are common and very serious public health problems in the United States and throughout the world. Upper body obesity is the strongest risk factor known for type 2 diabetes mellitus, and is a strong risk factor for cardiovascular disease [...] insulin resistance [...], insulin resistance syndrome, or Syndrome X" (see paragraph [0010], emphasis added).*
  
11. Accordingly, the patent reports that obesity and therefore also overweight are established risk factors in all of the disorders according to claims 1 and 10, *i.e.* the probability of developing these disorders is higher in obese and overweight subjects than in subjects with normal body weight. In other words, all the diseases referred to in claims 1 and 10 are associated with obesity or overweight. Therefore, the board considers that agents which have a beneficial effect in obesity therapy by reducing weight or weight gain concomitantly have a beneficial effect for all obesity- or overweight-associated disorders, since the risk of developing these disorders is likewise reduced. As a result of the therapy, patients may either not develop the disorders or their onset may be postponed. Alternatively, the disorders may be less severe than in non-treated obese or overweight subjects.
  
12. The appellant argued that the etiology underlying the claimed obesity-associated therapeutic applications was complex and not solely caused by overweight. However,



as set out in point 11 above, obesity or overweight are established risk factors in these disorders, thereby contributing to the etiology of all of them. Also, obese or overweight patients affected by any of these disorders benefit from a weight or weight gain reducing effect mediated by PYY[3-36], even if obesity is not their sole disease-causing factor. Therefore, the reduction of weight or weight gain in obese mice mediated by PYY[3-36], as disclosed in example 6 of the patent, is a beneficial effect which can in fact be relied on for the therapeutic applications claimed (see e.g. decision T 1642/06, point 2.2 of the Reasons).

13. The appellant further submitted that the use of PYY[3-36] in reducing weight gain in obese or overweight patients in the claimed therapeutic applications was an embodiment of claims 1 and 10. However, the slowing down in weight gain did not have a beneficial effect in all the claimed therapeutic applications, since despite the therapy the patients continued to gain weight, albeit at a slower rate than previously.
14. The board does not agree. Slowing weight gain down in obese or overweight patients - compared to such patients untreated for obesity - is already in itself a beneficial therapeutic effect in the therapy of obesity, and in addition for the reasons set out above (see point 11), reduces the risk of these patients developing any of the obesity-associated disorders referred to in claims 1 and 10. Moreover, slower weight gain might also postpone the need to administer further disease-specific therapeutic agents, such as insulin in case of diabetes mellitus.

15. Accordingly, the board concludes that the disclosure in the patent demonstrates the suitability of PYY[3-36] for achieving a beneficial effect in all of the claimed therapeutic applications by reducing weight or weight gain.
  
16. In a second line of argument relating to insufficiency of disclosure, the appellant submitted that the subject-matter of claims 1 and 10 encompassed non-working embodiments since the feature "*the PYY agonist is to be administered peripherally to said subject in an amount therapeutically effective to reduce weight or reduce weight gain*" was not defined by a specific dose of PYY[3-36], although the patent reported in example 6 that the minimum effective therapeutic dose of PYY[3-36] was 300 µg/kg/day. The same objection applied to embodiments falling within the range of "*about 1 µg to about 5 mg*" referred to in claim 4 and to the therapy of human patients according to claim 8, for whom even the administration of 300 µg/kg/day PYY[3-36] was "*likely too low*".
  
17. However, claims 1 and 10 explicitly require that the PYY[3-36] used is parenterally administered in an "*amount therapeutically effective to reduce weight or weight gain*". Thus, any amount of PYY[3-36] not fulfilling this functional requirement is excluded from the claims.
  
18. Furthermore, the patent informs the skilled person that effective doses of PYY[3-36] are, for example, "*about 1 µg to about 5 mg per day in single or divided doses or at about 0.01 µg/kg to about 500 µg/kg per dose, more preferably about 0.05 µg/kg to about 250 µg/kg, most preferably below about 50 µg/kg*" (see paragraph [0024], or the similar disclosure in paragraph [0043]).

Paragraph [0043] further discloses that "*The exact dose to be administered is readily determined by one of skill in the art and is dependent upon the potency of the particular compound, as well as upon the age, weight and condition of the individual.*"

19. The skilled person would derive from the passages of the patent indicated in point 18 above that effective doses of PYY[3-36] are available but that the exact dose has to be determined individually, depending *inter alia* on the age, weight and condition of the patient. Therefore, although example 6 of the patent reports a minimum effective dose of 300 µg/kg/day of PYY[3-36] to reduce weight or weight gain in obese mice, it is evident to the skilled person that this is not the minimum effective dose of PYY[3-36] in the therapy of all obese or overweight patients falling within the ambit of claims 1 and 10.
  
20. With regard to claim 4, the board notes that some doses of PYY[3-36] in the range of "*about 1 µg to about 5 mg*" may indeed encompass non-working embodiments when administered to obese mice, in view of example 6 of the patent. However, the appellant has submitted no evidence that doses of PYY[3-36] below 300 µg/kg/day fail to reduce weight or weight gain in patients other than obese mice falling within the subject-matter of claim 4. The same applies to the alleged failed efficacy of 300 µg/kg/day of PYY[3-36] in the therapy of human patients according to claim 8. In contrast, in the paragraphs indicated in point 18 above the patent discloses sufficient information on the relevant criteria to identify appropriate alternative dosages of PYY[3-36] without undue burden.

21. Therefore, in view of the considerations in points 17 to 20 above, the board concludes that the subject-matter of claims 1, 8 and 10 does not encompass non-working embodiments, and the fact that claim 4 may embrace some non-working embodiments is not detrimental to sufficiency of disclosure (see e.g. decision T 238/88, OJ EPO 1992, 709, point 4.1 of the Reasons).
22. Lastly, the appellant argued that the protection conferred by the claims of the patent as granted was not commensurate with the patent's actual contribution to the art and that the patent therefore did not disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art (decision T 1063/06, published in OJ 2009, 516).
23. The board notes that the legal principle of fair patent protection cited by the appellant is not applied *per se* for assessing whether or not the requirements of Article 83 EPC are fulfilled. Rather such protection is achieved by a proper application of all of the requirements of the EPC. Moreover, since the board has concluded above that the patent demonstrates that PYY[3-36] is suitable for use in the therapeutic applications referred to in claims 1 and 10 (see point 15 above) and that the subject-matter of claims 1, 4, 8 and 10 does not contain non-working embodiments, at least not to an extent detrimental to compliance with Article 83 EPC (see point 21 above), this argument too must fail.
24. Accordingly, the board concludes - from the evidence on file - that the the main request meets the requirements of Article 83 EPC.

*Novelty (Article 54 EPC)*

25. Novelty of the subject-matter of claims 1 and 10 was challenged by the appellant with regard to the explicit and implicit disclosure of document D1 and the implicit disclosure of document D10 at their publication dates taking into account the skilled person's common general knowledge as established in documents D2 to D4, D16 to D18 and D21. It was uncontested by the parties that the latter documents were indeed publicly available at the publication date of documents D1 and D10.
  
26. It is a generally accepted principle that, for an invention to lack novelty, all the claim's features must be directly and unambiguously derivable from the prior art document as a whole, either explicitly or implicitly, taking account also of the skilled person's common general knowledge at the publication date of the cited documents. In this context "implicit disclosure" means a disclosure which any person skilled in the art would objectively consider as necessarily implied in the explicit content (see CLBA, I.C.4 and I.C.4.3; decision T 1523/07, point 2.4 of the Reasons).
  
27. Document D1 discloses *inter alia* parenterally administered PYY therapeutics, for example PYY agonists, for use in treating a disease associated with altered glucose metabolism selected *inter alia* from insulin resistance, obesity, or a Type II diabetes mellitus (see claims 23, 28, 29, page 5, lines 20 to 25, page 6, lines 16 to 30, page 7, lines 9 to 11, page 34, lines 10 to 12, 17 and 18). A PYY agonist is defined in this document as an agent "(e.g. which mimics or enhances) PYY activity" or "having the effect of inducing the activity of PYY" (see page 5, lines 20 to 23 and page 7, lines 9 and 10). Its agonistic action

is - like that of a PYY antagonist which inhibits PYY's activity - mediated by PP receptor binding (see e.g. page 7, lines 22 to 24). Document D1 does not disclose a weight reducing activity mediated by PYY.

28. The passage in document D1 on which the appellant particularly relies for its novelty objection is on page 12, starting at line 15, and reads: *"Agonists of the PYY receptors may also be identified using the instant invention. PYY belongs to the family of peptides termed the "PP family", other members of which include NPY and PP. Several PP-family receptor subtypes have been cloned. These all contain several transmembrane domains and belong to the G-protein coupled superfamily of receptors. The PP receptor family includes Y1-R, Y2-R, Y3-R, Y4-R, Y5-R and Y6-R, each receptor differing in binding properties and tissue distribution and sequence identity [...]. Y1, Y2, Y5 and Y6, for example, bind to PYY and NPY3-36 and PYY[3-36] C-terminal fragments. [...]. Naturally occurring endogenous agonists of the PYY receptors have been described (e.g., PYY1-36 and NPY1-36)"* (emphasis added).
29. The board notes that this passage discloses that PYY[3-36] binds to several members of the PP receptor family, but, not that it is a PYY agonist. The only explicitly reported agonists are "PYY1-36" and Neuropeptide Y 1-36 ("NPY1-36"), neither of which are identical to PYY[3-36], since the numbers 1-36 indicate that both peptides have a length of 36 amino acids, as opposed to to the 34 amino acids of PYY[3-36] (see point 2 above). Hence, the board concludes that document D1 does not explicitly disclose that PYY[3-36] is a PYY agonist.

30. Document D10 discloses that PYY or functional analogs thereof increase a feeling of satiety in the therapy of obesity (see e.g. page 15, lines 29 to 31 and page 22, lines 3 to 5). Examples of reported functional PYY analogs in document D10 are PYY (22-36), BIM43004, BIM-43073D and BIM-43004C (see page 4, lines 22 to 28 and page 28, lines 14 to 17). A weight reducing activity mediated by PYY is not disclosed in document D10. Moreover, it was common ground between the parties that document D10 does not explicitly disclose PYY[3-36] and its function as a PYY agonist.
31. It therefore needs to be assessed whether or not PYY[3-36]'s function as a PYY agonist is implicitly disclosed in documents D1 or D10, taking account of the skilled person's common general knowledge as established by the disclosure of documents D2 to D4, D16 to D18 and D21.
32. With regard to the definition provided in document D1 for a PYY agonist (see point 28 above), the question is whether or not the skilled person would derive from the PP receptor binding of PYY[3-36] disclosed in document D1 that this necessarily indicates that PYY[3-36] mimics, enhances or induces the same biological functions as PYY or that the functional analog of PYY as disclosed in document D10 necessarily implies PYY[3-36].
33. Document D1 discloses that the binding of agents to PP receptors either induces agonistic or antagonistic effects with regard to PYY (see point 27 above). The document is silent as regards any effects mediated by PYY[3-36] except for disclosing its binding to specific receptors of the PP receptor family (see point 28 above). Accordingly, the mere disclosure in

document D1 of the binding of PYY[3-36] to PP receptors does not necessarily imply to the skilled person that PYY[3-36] is a PYY agonist because its receptor binding may mediate agonistic or antagonistic effects *vis-à-vis* PYY.

34. Documents D2 to D4 disclose that PYY[3-36] - unlike PYY - binds to the Y2 but not to the Y1 receptor or, if so, then only with a very low potency (see documents D2, page 589, column 1, third paragraph; D3, page 104, column 2, second paragraph; D4, summary on page 1299). In this context, document D4 reports that the "*activation of Y1 and Y2 receptors results in different biological actions*" (see page 1304, second paragraph, emphasis added), which means that PYY[3-36] and PYY by binding to either Y1 or Y2 receptors do not induce the same physiological functions. This is also suggested in document D17 which states that "*endogenous PYY-(3-36) may act as a physiological antagonist of PYY-(1-36)*" (see page G699, column 2, fourth paragraph; emphasis added). Moreover, documents D16, D18 and D21 consistently refer to PYY[3-36] as a "Y2 agonist" and not as a PYY agonist which further suggests that the biological functions of PYY[3-36] and PYY (which binds to Y1) are different (see documents D16, page 114, column 1, fourth paragraph; D18, page 157, column 2, fifth paragraph; D21, page 64, column 2, second paragraph).
35. Accordingly, the skilled person reading documents D1 and D10 at their publication dates and taking into account the common general knowledge as established in documents D2 to D4, D16 to D18 and D21 would not have derived from the disclosed binding of PYY[3-36] to PP receptors in document D1 that this necessarily implied the induction of the same biological functions as those



mediated by PYY, or that the "functional analog" of PYY reported in document D10 necessarily implied PYY[3-36].

36. Furthermore, in view of the disclosure in particular of documents D4 and D17 as outlined in point 34 above, the board is not convinced by the appellant's argument that the reported identification of PYY[3-36] as the major endogenous form of PYY *in vivo* necessarily implies that it mediates the same biological functions as PYY and thereby acts as a PYY agonist, since an antagonistic action of PYY[3-36] is also explicitly suggested.
37. The board therefore concludes that PYY[3-36] as a PYY agonist and its effect in reducing weight or weight gain are not disclosed in documents D1 and D10. The subject-matter of claims 1 and 10 is therefore novel. The same applies to the subject-matter of claims 2 to 9 and 11 dependent thereon. The main request therefore meets the requirements of Article 54 EPC.

*Inventive step (Article 56 EPC)*

*Closest prior art*

38. For assessing whether or not a claimed invention meets the requirements of Article 56 EPC, the boards of appeal apply the "problem and solution" approach. This requires as a first step the identification of the closest prior art, which is generally a prior art document disclosing subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention and having the most technical features in common, *i.e.* requiring a minimum of modifications (see CLBA, I.D.3.1).

39. The appellant considered the disclosure of documents D1, D3, D6, D7 or D10 to be the closest prior art for the subject-matter of claims 1 and 10, whereas the respondent took the view that it was document D7.
40. The disclosure of documents D1 and D10 has already been summarised in points 27, 28 and 30 above.
41. Document D3 reports that PYY[3-36] mimics the activity of Neuropeptide Y (NPY) in lowering blood glucose levels, which is not accompanied by plasma insulin alterations, thereby implying that the effect is due to enhanced glucose utilisation or reduced gluconeogenesis (see page 106, column 1, lines 7 to 11). Document D3 does not disclose either a therapeutic application of PYY[3-36] or its weight reducing effect.
42. Document D6 is a review article in the field of drug development for the therapy of eating disorders including obesity (see abstract, page 23, column 1, second paragraph to page 24, column 1, third paragraph). The document discloses by reference to document D7 that PYY has been shown to produce weight loss upon peripheral administration without altering food intake, and suggests using *inter alia* PYY agonists as potential anti-obesity drugs (see page 24, column 1, second paragraph referring to "[15]", *i.e.* document D7, see page 28, column 2 of document D6, and page 27, column 2, last paragraph and Table 2 on page 28). Further agents disclosed for the therapy of obesity are "Tetrahydrolipistatin", "ABRL 26830A", "Fluoxetine" or "Fenfluramine" (see Table 2).
43. Document D7 discloses *in vivo* studies in mice of normal weight comparing the effect on weight loss of chronic peripherally administered anorexigenic drugs, *i.e.* of

agents which induce a loss of appetite or aversion to food. The document reports that numerous anorectic agents have been investigated as possible anti-obesity agents (see page 2157, first and second paragraphs). Furthermore, it discloses that PYY causes a significant weight loss compared to untreated control mice, without altering their food intake. In other words, after administration of PYY mice lose weight without eating less (see page 2163, figure 5 and second paragraph bridging to page 2164).

44. In the board's view, with the exception of document D3 which is concerned with the lowering of blood sugar without actually disclosing a therapeutic application for PYY[3-36], all the above-mentioned documents relate to the same purpose as that underlying the claimed invention, *i.e.* the use of PYY or agonists thereof in the therapy of metabolic disorders, for example obesity.
  
45. However, only documents D6 and D7 disclose that PYY induces a weight reduction as the relevant mechanism of action in the therapy of obesity. While document D7 discloses experimental data showing this effect of PYY (see point 43 above), document D6 refers only to document D7 in this respect (see point 42 above). Thus document D7 shares more of the technical features with the claimed invention than document D6 and thus represents the closest prior art in accordance with the criteria established by the case law (see point 38 above).

*Technical problem and solution*

46. The subject-matter of claims 1 and 10 differs from the closest prior art in that PYY[3-36] is administered

instead of PYY, and lacks two amino acids at its N-terminal end (see point 2 above). Moreover, the patient group according to claims 1 and 10 is obese or overweight whereas the mice treated in document D7 have a normal weight (see point 43 above).

47. The respondent argued that the effect of PYY[3-36] in reducing the amount of food intake was superior to that of PYY in view of the data disclosed in Figure 1 and paragraph [0051] of the patent.
48. Paragraph [0051] reads: "*As seen in Figure 1, PYY administered peripherally (intraperitoneal injection) at doses of 10, 100 and 500 µg/kg significantly reduced food intake measured over 60 min in overnight-fasted female NIH/SW mice. These doses of PYY[3-36] had approximately equal efficacy. [...] The rank order of potency was: PYY[3-36] ≥ PYY >> NPY = NPY[3-36] = PP = Ac-PYY[22-36]. The rank order of potency, and in particular the lack of effect of NPY, does not reflect the pharmacology of any of the known cloned receptors*" (emphasis added).
49. The patent thus explicitly reports that the therapeutic efficacy of PYY[3-36] is "approximately equal" to PYY. Moreover, although the rank order places PYY[3-36] ahead of PYY, the disclosed relationship between the two agents reads "≥", i.e. greater or equal. Hence, in the board's opinion, the skilled person would not conclude, from the disclosure in Figure 1 and paragraph [0051] of the patent, that there is a significant difference in the efficacy of PYY[3-36] and PYY in reducing the amount of food intake. Nor does, the patent report that this difference is significant, despite such an explicit statement being made in the context of the reduction of food intake by PYY (see

point 48 above). Further comparative experimental data disclosing advantageous properties of PYY[3-36] *vis-à-vis* PYY are not disclosed in the patent and were also not put forward by the respondent.

50. Accordingly, the technical problem to be solved is formulated as the provision of alternative agents of PYY for use in the claimed therapeutic applications.

51. The board is satisfied that the solution provided by the subject-matter of claims 1 and 10 solves this technical problem.

#### *Obviousness*

52. It remains to be assessed whether or not the skilled person, starting from the use of PYY in the therapy of obesity as disclosed in document D7 and faced with the technical problem defined above, would modify the teaching of document D7 either in view of this document alone or in combination with another teaching in the prior art to arrive at the claimed subject-matter in an obvious manner.

53. The board notes that document D7 suggests several alternative anorexic drugs for PYY in reducing weight (see page 2157, first paragraph), but is silent with regard to PYY[3-36] and its potential in causing weight reduction or slowing-down weight gain.

54. Accordingly, the board concludes that the subject-matter of claims 1 and 10 is not obvious in the light of the teaching of document D7 alone.

55. Further alternative PYY agonists in the therapy of metabolic disorders are disclosed in documents D1, D6

and D10 (see points 28, 30 and 42 above). However, none of these documents point to PYY[3-36] and its potential in reducing weight or weight gain.

56. Moreover, for the reasons set out above (see points 34 and 41), the teaching of documents D2 to D4, D16 to D18 and D21 likewise provides no hint that PYY[3-36] reduces weight or weight gain in obese or overweight patients. On the contrary, due to the reported binding of PYY[3-36] and PYY to different PP receptors, the skilled person would derive from the teaching of these documents that the two agents may cause different, even opposing physiological reactions *in vivo* (see e.g. document D4, page 1304, second paragraph and document D17, page G699, column 2, fourth paragraph).
57. In the light of the teaching in documents D1 to D4, D6, D10, D16 to D18 and D21 the skilled person had no motivation to replace PYY with PYY[3-36] as an alternative agent in any of the therapeutic applications referred to in claims 1 and 10. Therefore the board concludes that the subject-matter of claims 1 and 10 cannot be considered obvious in the light of the teaching of document D7 combined with that of documents D1 to D4, D6, D10, D16 to D18 and D21 either. The same applies to the subject-matter of claims 2 to 9 and 11, which is dependent thereon.
58. Consequently, the main request meets the requirements of Article 56 EPC.

**Order**

**For these reasons it is decided that:**

The appeal is dismissed

The Registrar:

The Chairwoman:



P. Cremona

G. Alt

Decision electronically authenticated