Datasheet for the decision
of 6 October 2010

Case Number: T 0163/08 - 3.3.04
Application Number: 00926404.5
Publication Number: 1173197
IPC: A61K 38/26
Language of the proceedings: EN

Title of invention:
Metabolic intervention with GLP-1 to improve the function of ischemic and reperfused tissue

Patentee:
AMYLIN PHARMACEUTICALS, INC.

Opponent:
Novo Nordisk A/S

Headword:
GLP-1 to improve reperfusion/AMYLIN PHARMACEUTICALS, INC.

Relevant legal provisions:
EPC Art. 54, 56, 83, 114(2), 123(2)

Relevant legal provisions (EPC 1973):
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Keyword:
"Admission of late-filed documents (yes)"
"Added subject-matter (no)"
"Sufficiency of disclosure (yes)"
"Novelty (yes)"
"Inventive step (yes)"

Decisions cited:
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Catchword:
-
Case Number: T 0163/08 - 3.3.04

DECISION
of the Technical Board of Appeal 3.3.04
of 6 October 2010

Appellant: AMYLIN PHARMACEUTICALS, INC.
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Decision under appeal: Decision of the Opposition Division of the European Patent Office posted 29 November 2007 revoking European patent No. 1173197 pursuant to Article 102(1) EPC.

Composition of the Board:
Chairman: C. Rennie-Smith
Members: R. Gramaglia
G. Alt
Summary of Facts and Submissions

I. European Patent No. EP-B-1173197, based on application No. 00926404.5 (published as WO 00/66138) and having the title "Metabolic intervention with GLP-1 to improve the function of ischemic and reperfused tissue" has been granted with 11 claims.

II. Against the aforementioned patent an opposition was filed by the respondent requesting revocation of the patent in its entirety on the grounds of Article 100(a) EPC in conjunction with Articles 54 and 56 EPC, Article 100(b) EPC in conjunction with Article 83 EPC and Article 100(c) EPC in conjunction with Article 123(2) EPC.

III. The opposition division came to the conclusion that the claims of the main request filed with the appellant's letter dated 15 June 2006 did not satisfy the requirements of Article 83 EPC, and revoked the patent.

IV. Claim 1 of this request read as follows:

"1. Use of a composition which includes GLP-1, or a biologically active analogue thereof, and a pharmaceutically acceptable carrier, for the manufacture of a medicament for treating individuals in need of amelioration of organ tissue injury caused by reperfusion of blood flow following a period of ischemia, said treatment does not include the co-administration of glucose."

Dependent claims 2 to 11 related to specific embodiments of the use according to claim 1.
The following documents are cited in the present decision:

D1  WO-A-00/16797;

D3  WO-A-98/08531;

D4  Voll C.L. et al. Stroke, Vol. 20, pages 646-651 (1989);

D5  EP-A-0 708 179;

D6  Diaz R. et al., Circulation, Vol. 98, pages 2227-2234 (1998);

D12  Bose A.K. et al., Diabetes, Vol. 54, pages 146-151 (2005);

D14  Dokken B.B. et al., Diabetes, Vol. 56, Supplement 1, Abstract [0058-OR], (2007);

D11  Nikolaidis L.A. et al., Journal of Pharmacology and Experimental Therapeutics, Vol. 312, No. 1, pages 303-308 (2005);

D18  Nikolaidis L.A. et al., Circulation, Vol. 109, pages 962-965 (2004);

D19  Kavianipour M. et al., Peptides, Vol. 24, pages 569-578 (2003);

D20  Declaration of Prof. David Erlinge dated 6 September 2010;
VI. The submissions by the appellant (patentee), insofar as they are relevant to the present decision, can be summarized as follows:

Admissibility of documents D20 to D25 into the proceedings

− These documents should not be admitted into the proceedings as having been filed too late and as being irrelevant.

Article 123(2) EPC

− There was a direct and unambiguous disclosure of the wording "said treatment does not include the co-administration of glucose" in claim 1 in the passage

D21 Kristensen J. et al., BMC Cardiovascular Disorders, Vol. 9, No. 31, pages 1/8 to 8/8 (2009);

D22 Nauck M.A. et al., Diabetologia, Vol. 36, pages 741-744 (1993);

D23 Summary of Product Characteristics for the GLP-1 molecule Victoza/Liraglutide, pages 1/29, 2/29 and 10/29;

D24 Edwards C.M.B. et al., Experimental Physiology, Vol. 82, pages 709-716 (1997);

on page 8, line 31 to page 9, line 2 and on page 9, lines 15-16 of the published WO application as filed.

Article 83 EPC

- The claimed medical use was based on experimental evidence that GLP-1, when administered to healthy humans, reduced the free fatty acid (FFAs) levels to less than 10% of the control values.

- Since the patent in suit already provided by itself a clear experimental teaching that GLP-1 or a biologically active analogue thereof was useful in ameliorating tissue injury caused by reperfusion of blood flow following ischemia, no need arose even to consider post-published documents D11, D12, D14 and D18.

- Post-published document D12 did not demonstrate that the claimed subject matter was not enabled in the case where no DPPIV inhibitor was co-administered.

- Post-published documents D21 to D25 did not show that the claimed subject matter was not enabled.

Article 54 EPC

- The claimed medical use was novel over the disclosure in document D1 or document D3.
Article 56 EPC

- None of documents D3, D4 and D22 related to ameliorating injury caused by reperfusion following a period of ischemia.

- Document D6 failed to suggest the use of anything other than GIK (glucose-insulin-potassium). The skilled person would not be motivated to modify the methods described in document D6 by substituting GIK with GLP-1 and eliminating the administration of glucose.

- Document D5 related to a completely different problem, namely that of increasing the in vivo half-life of GLP-1 when used for the treatment of Type II diabetics via stimulation of insulin secretion, which problem was of little relevance to the clinical situation described in document D6.

- Documents D3 and D22 had no bearing on reperfusion injury.

- The technical information referred to in the patent on page 4, lines 2-13 that reperfusion-induced myocardial stunning and reperfusion ventricular arrhythmias were due to high plasma FFAs did not belong to the prior art.

- Even assuming that document D4 taught an amelioration of reperfusion injury, the skilled person was not motivated to replace glucose and insulin with GLP-1 and eliminate the administration of glucose.
VII. The submissions by the respondent (opponent), insofar as they are relevant to the present decision, can be summarized as follows:

Admissibility of documents D20 to D25 into the proceedings

- These documents had to be admitted into the proceedings because they put the sufficiency of disclosure into question.

Article 123(2) EPC

- The sentence "said treatment does not include the co-administration of glucose" in claim 1 contravened Article 123(2) EPC.

Article 83 EPC

- The patent failed to provide any disclosure going beyond speculation.

- Post-published documents D11, D12, D14 and D18 could not be used to show that GLP-1 could achieve the claimed therapeutic effect.

- Post-published document D21 showed that Liraglutide (a GLP-1 analogue) failed to ameliorate tissue injury caused by reperfusion.

- Post-published document D22 showed that the administration of GLP-1 to patients suffering from
ischemia-reperfusion produced only a modest lowering of the free fatty acid level.

- The administration of GLP-1 to patients suffering from ischemia-reperfusion would have caused deleterious side effects such as an increase in heart rate and a decrease of the blood pressure.

- Making and testing the huge range of "GLP-1" compounds and "biologically active analogues thereof" as recited in claim 1 to identify compounds effective in ameliorating organ tissue injury caused by reperfusion of blood flow constituted an undue burden, contrary to Article 83 EPC.

- It was impossible for a clinician to distinguish between ischemia-induced tissue damage and reperfusion-induced tissue damage. As a consequence, all patients would be treated identically regardless of whether reperfusion injury was actually treated.

Article 54 EPC

- The claimed medical use lacked novelty over the disclosure in document D1 or document D3.

Article 56 EPC

- Claim 1 lacked an inventive step in view of the combination of documents D4 and D5; or in view of document D6 taken in combination with document D5; or in view of document D3 taken in combination with document D22 or in view of document D22 alone.
VIII. The appellant (patent proprietor) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request filed with its letter of 15 June 2006.

The respondent (opponent) requested that the appeal be dismissed or that the decision under appeal be set aside and the case remitted to the department of first instance for further prosecution.

Reasons for the Decision

Admissibility of documents D20 to D25 into the proceedings

1. On 6 September 2010, i.e. exactly one month before the oral proceedings, the respondent filed documents D20 to D25. The appellant objected to these documents being admitted into the proceedings as having been filed too late and as being irrelevant.

The board considers these documents filed by the respondent to be merely a reaction to the submissions and statements filed by the appellant. They do not introduce new issues or arguments going beyond those already put forward by the respondent in its answer to the Grounds of Appeal, but merely support arguments already put forward in relation to the objection of insufficiency of disclosure.

Therefore, the board considers it appropriate to exercise its discretion under Article 114(2) EPC to admit documents D20 to D25 into the proceedings.
**Article 123(2) EPC**

2. The respondent maintains that the sentence "said treatment does not include the co-administration of glucose" in claim 1 contravenes Article 123(2) EPC.

In the board's view, however, there is a direct and unambiguous basis for the wording in claim 1 "said treatment does not include the co-administration of glucose" in the passage on page 8, line 31 to page 9, line 2 and on page 9, lines 15-16 of the published WO application as filed.

Moreover, it can be derived from page 16, lines 19-20 ("The GLP-1 infusion can be coadministered with glucose.."); emphasis added) and from the combination of claims 1 and 5 of the published WO application as filed that the co-administration of glucose is optional.

In conclusion, claim 1 does not contain added subject matter and meets the requirements of Article 123(2) EPC.

3. Finally, at the oral proceedings the respondent no longer pursued the argument that the statement ("however such treatment still requires the administration of glucose and even potassium in some cases"), added by the appellant in paragraph [0015] in connection with the disclosure of prior art document D3 (WO 98/08531), infringed Article 123(2) EPC.

In any case, this amendment pertaining to the representation of prior art document D3 affects neither the disclosure content of the application as filed nor the definition of any feature addressed in the claims.
Therefore, the board does not consider that this amendment gives rise to an objection under Article 123(2) EPC.

Article 83 EPC

4. The respondent argued that the patent contained neither examples nor in vitro or in vivo data showing that GLP-1 achieved the claimed therapeutic effect on reperfusion injury and that such therapeutic effect had only been shown in post-published documents D11, D12, D14 and D18, which could not be used to show that GLP-1 could achieve the claimed therapeutic effect.

5. However, the claimed medical use is based on the experimental evidence that GLP-1, when administered to healthy humans, reduces the free fatty acid (FFAs) levels to less than 10% of the control values (see paragraph [0019] of the patent: "It has been discovered, and is one of the bases of this therapeutic invention that GLP-1 suppresses FFA beyond what is expected for insulin which is at the 50% of suppression, and GLP-1 can be as high of 90% suppression of FFA" and paragraph [0028]: "Indeed, preliminary data in healthy volunteers indicate that an intravenous GLP-1 infusion will reduce fasting plasma FFA levels to < 10% of control values").

The patent in suit also provides the putative mechanism of action of GLP-1 (see paragraph [0019]) based on the fact that FFAs cause myocardial stunning (which is a reversible and temporary impairment of the myocardial contractile function: see page 4, lines 2-5 of the patent) and slow down recovery from the reperfusion therapy.
6. The respondent objected (see document D20, paragraph 10) that this experimental evidence was obtained on healthy human volunteers having physiological conditions different from patients experiencing myocardial infarction.

However, the board firstly notes that the respondent did not provide any evidence in support of its view that the FFAs levels in healthy volunteers were far different from that of patients undergoing reperfusion therapy. Secondly, this technical information that fasting plasma FFAs could be reduced in humans to less than 10% of control values went beyond mere in vitro protein assays or in vitro cell-based models or in vivo experiments conducted on animal models. Therefore, in the board's view, this experimental finding (together with the finding that FFAs had a direct toxic effect during the reperfusion period) made plausible the ability of GLP-1 to ameliorate tissue damage caused by reperfusion injury.

7. Moreover, since the patent itself already provides a clear experimental teaching that GLP-1 or a biologically active analogue thereof is useful in ameliorating tissue injury caused by reperfusion of blood flow following ischemia, no need arises to consider post-published documents D11, D12, D14 and D18.

8. It was the respondent's view that post-published document D12 showed that the presence of an inhibitor of DPPIV (the latter is dipeptidylaminopeptidase IV, an enzyme which cleaves intact GLP-1 (GLP-1 (7-36)) into GLP-1 (9-36)) was necessary in order to obtain
therapeutically effective concentrations of intact GLP-1. Thus, the patent in suit was not enabled because it lacked this feature, which was fundamental for the skilled person to reproduce the invention.

In the board's judgement, however, the fact that the results reported in post-published document D12 use valine pyrrolidide (VP) as inhibitor of GLP-1 breakdown by DPPIV do not demonstrate that the claimed subject matter is not enabled in the case where no DPPIV inhibitor is co-administered because no experiments were conducted in document D12 with GLP-1 in the absence of a DPPIV inhibitor.

Further, post-published documents D11 (see the final sentence of the abstract: "We conclude that GLP-1 enhances recovery from ischemic myocardial stunning after successful reperfusion") and D14 (see line 4: "GLP-1 has been shown to decrease cardiac ischemia-reperfusion injury in rats in vivo...") show that when GLP-1 is administered in the complete absence of a DPPIV inhibitor, it still reduces reperfusion injury.

9. In a different line of argument, the respondent maintained that post-published document D21 demonstrated that Liraglutide (a GLP-1 analogue) failed to ameliorate tissue injury caused by reperfusion.

The experiment described in document D21 involves glucose (see page 2/8, r-h column, line 17) and thus it does not reflect the medical use according to claim 1. Moreover, other passages of this document (see page 2/8, l-h column, lines 11-12; page 5/8, l-h column, lines 11-13 and 16-18) show that GLP-1 analogues are
indeed effective in ameliorating tissue injury caused by reperfusion.

10. The respondent also argued that post-published document D22 showed that the administration of GLP-1 to patients suffering from ischemia-reperfusion produced only a modest lowering of the free fatty acid level (10% of the normal fasting level). Document D22 discloses the administration of GLP-1 (7-36 amide) to diabetic patients followed by measurements of various factors including non-esterified fatty acids (NEFAs, another acronym for FFAs). The respondent is of the opinion that the lower panel of Figure 2 shows that the lowering of the free fatty acid level (NEFA) is much less than the 90% mentioned in the patent.

The board notes that the NEFA concentration (see the lower panel of Figure 2) is about 0.3 mmol/l at t = 0 and 0.1 mmol/l at t = 120 min. This represents a decrease of 66%, which cannot be termed as a "modest lowering of the free fatty acid level in the order of 10% of the normal fasting level", as the respondent argues. The decrease "-26.3 +3.1 mmol/l x 1/min" referred to in the third full paragraph on the r-h column on page 743 of document D22 is apparently erroneous (it should have read "-26.3 +3.1 μmol/l x 1/min"; emphasis added), but once the "mmol" are corrected to "μmol", this figure confirms the decrease of 66% at t = 120 min, which is compatible with the expression used in the patent in suit "...can be as high as 90% suppression of FFA" (see page 4, line 13).

11. The respondent also drew attention to the fact that the administration of GLP-1 to patients suffering from
ischemia-reperfusion would cause deleterious side effects such as an increase in heart rate (see documents D21, D24 and D25) and a decrease of blood pressure (see document D23, page 10/29, under "Blood pressure").

As regards a decrease of blood pressure, document D23 contradicts the statements in document D21 (see page 3/8, r-h column, under "Hemodynamic date) that "Liraglutide did not affect MABP (figure 2)" and in document D24 (see page 710, lines 2-3) "The results show that this peptide produces an increase in heart rate without affecting systemic blood pressure".

As for the increase in heart rate, the experiment described in document D21 involved glucose (see page 2/8, r-h column, line 17) and thus this experiment does not mirror the medical use according to claim 1. Moreover, the experiments described in document D24 use 35 pmol min\(^{-1}\)kg\(^{-1}\) IV of the GLP-1 analogue, whereas the patent uses only 0.1 pmol to 10 pmol min\(^{-1}\)kg\(^{-1}\) IV. Therefore, it cannot be excluded that the increase in heart rate might depend on the higher GLP-1 concentrations.

In any case, post-published documents D11, D12, D14 and D18 show that GLP-1 analogues can achieve the claimed therapeutic effect without deleterious side effects.

12. Finally, in the respondent's view, a further major insufficiency problem lay in the impossibility for a clinician to distinguish between ischemia-induced tissue damage and reperfusion-induced tissue damage. As a consequence, the clinician would be unable (except
for post-treatment histological examination) to clearly identify patients requiring treatment for reperfusion injury, with the consequence that all patients undergoing an ischemic event would be treated identically, regardless of whether reperfusion injury is actually treated. The respondent further noted that the patent in suit did not assist in the identification of reperfusion injury-prone patients, but merely focussed on patients undergoing an ischemic event (see paragraphs [0046] and [0047]).

Firstly, the parties do not dispute that acute myocardial infarction (AMI) and reperfusion injury are two distinct clinical frames. AMI results from the occlusion of the artery supplying the heart muscle with blood, resulting in an interruption of oxygen supply, which is known as ischemia. During ischemia, cells of the heart muscle may die. Reperfusion injury refers to damage to tissue caused when blood supply returns to the tissue after a period of ischemia.

Secondly, not all ischemia events will result in reperfusion injury and vice-versa: prompt reperfusion may result in no evidence of myocardial infarction damage, whereas reperfusion injury may not occur in the case of ischemia with TIMI 0 (the TIMI flow represents blood flow following an acute myocardial infarction, as quantified by the "Thrombolysis In Myocardial Infarction (TIMI) Study Group grading", in which the TIMI grades range from 0 to 3, with TIMI 0 representing no distal blood flow and TIMI 3 representing complete perfusion of the vessel and thrombolysis success).
Moreover, in the case of STEMI (ST segment elevation myocardial infarction), reperfusion injury may not be clinically relevant (myocardial infarction (MI) is generally classified as either non-ST segment elevation MI (NSTEMI), or ST segment elevation MI (STEMI), corresponding to the "old" non-Q wave MI and Q-wave MI, respectively; for an example of the "old" usage, see e.g., document D3, page 19, lines 21-23).

In view of the foregoing, the board does not consider that AMI and reperfusion injury overlap to the extent that the clinician would be unable to clearly identify patients requiring treatment for reperfusion injury. Rather, the clinician is able to clearly establish when a treatment to ameliorate reperfusion injury is clinically appropriate or not.

13. Finally, the respondent was of the opinion that making and testing the huge range of "GLP-1" compounds and "biologically active analogues thereof" as recited in claim 1 to identify compounds effective in ameliorating organ tissue injury caused by reperfusion of blood flow constituted an undue burden, contrary to Article 83 EPC.

Paragraph [0032] of the patent defines the biologically active analogues of GLP-1 as molecules that bind to the GLP-1 receptor protein such as GLP-1-(7-36) amide and exert the same biological effect on insulin secretion as GLP-1-(7-36) amide. Paragraphs [0026] and [0028] of the patent provide more details as to the biological effect, namely the stimulation of insulin release and the inhibition of glucagon secretion, leading to the reduction in circulating FFA levels. Paragraph [0042] of the patent provides a detailed explanation as to how
the skilled person can determine GLP-1 activity. Paragraph [0032] of the patent provides a vast list of scientific and patent literature relating to the production of useful analogues of GLP-1, which are also listed in paragraphs [0034] to [0036] of the patent.

Thus, in the board's view, arriving at biologically active analogues of GLP-1 would not represent any undue burden for the average skilled person using the information provided in the patent in suit (which devotes paragraphs [0025] to [0044] to this), supplemented by common general knowledge.

Novelty

14. In the respondent's view, the claimed medical use lacked novelty over the disclosure in document D1 or document D3. The respondent argued that documents D1 and D3 disclosed the treatment of stroke or myocardial infarction, respectively, by administering GLP-1 without co-administration of glucose. While such treatment was intended to reduce tissue damage caused by ischemia, however, this treatment was indistinguishable from the claimed treatment. The respondent took the fact that paragraphs [0046] and [0047] of the patent only dealt with treating myocardial infarction as corroboration of its opinion.

The brain ischemia described in document D1 is never followed by a resumption of blood flow (reperfusion), so that no reperfusion injury (and hence no treatment of this disease) can arise. As regards document D3, the board arrived at the conclusion (see point 12 supra) that myocardial ischemia injury and reperfusion injury
did not overlap to the extent that the clinician would be unable to clearly identify patients requiring treatment for reperfusion injury. Therefore, the claimed medical use is distinguishable from the treatment of stroke and acute myocardial infarction disclosed in document D1 and D3, respectively. As a result, the claims are novel over each of documents D1 or D3.

**Article 56 EPC**

15. The respondent argued lack of inventive step of the claimed subject-matter in view of (i) the combination of documents D4 and D5; (ii) document D6 taken in combination with document D5; (iii) document D3 taken in combination with document D22 and (iv) document D22 alone or together with common general knowledge.

**Closest prior art**

*Documents D3, D4 and D22*

16. Document D3 relates to the use of GLP-1 for normalizing blood glucose level in diabetic patients suffering from myocardial infarction (see document D3, page 4, lines 19-33). Document D4 discloses post-ischemic insulin and glucose administration to rats resulting in a reduction in CA1 hippocampal glutamate-induced necrosis (see Abstract and page 650, 1-h column, lines 19 and 22 from the bottom). Document D22 is concerned with investigating on the effects of GLP-1 (7-36 amide) on the levels of plasma glucose (and other metabolites) in Type II diabetic patients. None of these documents relates to ameliorating injury caused by reperfusion following a period of ischemia.
**Document D6**

17. This document can be considered to be the closest prior art as it describes the reduction of mortality rates following the ischemia and reperfusion of myocardial tissue upon administration of glucose, insulin and potassium ("GIK") (see the abstract, under "Conclusions"). It is stated on page 2231, 1-h column, lines 2-4, that "This effect [i.e., the mortality reduction and other benefits] was more impressive and reached statistical significance in patients who underwent reperfusion strategies".

**Problem to be solved**

18. Departing from document D6, the problem to be solved can be seen as the provision of an alternative therapy for ameliorating injury caused by reperfusion following a period of ischemia. The proposed solution is a treatment with GLP-1, or a biologically active analogue thereof, without co-administration of glucose (see present claim 1).

The medical use claimed in the present patent differs from the medical use as disclosed in document D6 in that a different compound (GLP-1 instead of insulin) is used and by the absence of glucose. It should be decided whether or not the proposed solution follows from the prior art in an obvious manner.
Document D6 taken in combination with document D5


20. Document D6 fails to suggest the use of anything other than GIK (glucose-insulin-potassium). The skilled person would not be motivated to modify the methods described in document D6 by substituting GIK with GLP-1 and eliminating the administration of glucose.

21. If the skilled person departing from document D6 came across document D5, he/she would not be directed to the claimed subject-matter by substituting GIK with GLP-1 and eliminating the administration of glucose. This is because document D5: (i) related to a completely different problem, namely that of increasing the in vivo half-life of GLP-1 when used for the treatment of Type II diabetics via stimulation of insulin secretion, which problem was of little relevance to the clinical situation described in document D6; and (ii) failed to suggest that GLP-1 analogues might be used for treating reperfusion injury.

Document D3 taken in combination with document D22.


Document D3 relates to the use of GLP-1 for normalizing blood glucose level in diabetic patients suffering from myocardial infarction (see point 16 supra). It is stated on page 2, lines 10-17 that FFAs damage myocardium during myocardial infarction.
Document D22 is concerned with investigating the effects of GLP-1 (7-36 amide) on the levels of plasma glucose (and other metabolites) of type 2 diabetic patients (see point 16 supra). It is stated on page 743, r-h column, of this document that during administration of GLP-1, plasma non-esterified fatty acids (NEFAs, another acronym for FFAs) significantly decreased.

The respondent argues that, although documents D3 and D22 have no bearing on the treatment of reperfusion injury, combining these two teachings with the common general knowledge referred to in the patent on page 4, lines 2-13 that reperfusion-induced myocardial stunning and reperfusion ventricular arrhythmias were due to high plasma FFAs would direct the skilled person to the claimed subject-matter in an obvious way.

However, there is no evidence before the board that the link between high FFAs and reperfusion injury (mentioned on page 4, lines 2-13 of the patent) was common general knowledge before the priority date of the patent in suit. The respondent failed to cite any literature to this effect, which in any case would have shown that a combination of at least three documents was required to arrive at the claimed subject-matter. This would hardly have suggested obviousness.

*Document D22 alone or together with common general knowledge*

23. The respondent further argued lack of inventive step in the light of document D22, either alone or together with common technical knowledge.
In view of the missing link between high FFAs and reperfusion injury (see point 22 supra), the skilled person would not arrive at the claimed subject-matter in an obvious way by departing from document D22.

Combination of documents D4 and D5


Document D4 discloses post-ischemic insulin and glucose administration to rats resulting in a reduction of in CA1 hippocampal glutamate-induced necrosis (see point 16 supra).

Even assuming that document D4 taught an amelioration of reperfusion injury, the skilled person was not thereby motivated to replace glucose and insulin with GLP-1 and eliminating the administration of glucose, for the reasons highlighted in point 21 supra.

In summary, the claimed subject-matter does not follow from the prior art in an obvious way.
Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to maintain the patent on the basis of claims 1 to 11 of the main request filed with the appellant's letter of 15 June 2006 and the description as granted.

The Registrar: The Chairman:

P. Cremona C. Rennie-Smith