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**Datasheet for the decision
of 6 March 2018**

Case Number: T 0730/15 - 3.3.07

Application Number: 07732397.0

Publication Number: 2018159

IPC: A61K9/28

Language of the proceedings: EN

Title of invention:
Colonic drug delivery formulation

Patent Proprietor:
UNIVERSITY COLLEGE LONDON

Opponent:
Saur-Brosch, Roland

Headword:
Colonic drug delivery/UNIVERSITY COLLEGE LONDON

Relevant legal provisions:
EPC R. 99(2)
EPC Art. 54(2), 56
RPBA Art. 12(4)

Keyword:

Admissibility of appeal - (yes)

Evidence submitted with the grounds of appeal - admitted (yes)

Novelty - main request (yes)

Inventive step - main request (yes)



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Case Number: T 0730/15 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 6 March 2018

Appellant: UNIVERSITY COLLEGE LONDON
(Patent Proprietor) Gower Street
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Representative: Beck Greener
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Appellant: Saur-Brosch, Roland
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Decision under appeal: Interlocutory decision of the Opposition
Division of the European Patent Office posted on
3 February 2015 concerning maintenance of the
European Patent No. 2018159 in amended form.

Composition of the Board:

Chairman J. Riolo
Members: A. Usuelli
R. Winkelhofer

Summary of Facts and Submissions

- I. European Patent 2 018 159 was opposed on the grounds that its subject-matter lacked novelty and inventive step and it was not sufficiently disclosed.

The following documents were among those cited during the first-instance proceedings:

D1: WO 99/25325

D8: GB 2 367 002

D11: US 5,422,121

D15: Declaration of Mr John Michael Newton of 4 September 2014

D17c: Final report of further experimental studies signed by Prof. Abdul Basit (19 November 2014) and Dr Roberto Bravo (20 November 2014)

- II. The appeals of the patent proprietor and of the opponent lie against the decision of the opposition division according to which the subject-matter of auxiliary request 2 met the requirements of the convention. The decision was based on the patent as granted as the main request and two auxiliary requests filed during the oral proceedings held on 26 November 2014.

Claim 1 of the patent as granted read as follows:

"1. A delayed release drug formulation for delivery of a drug to the colon comprising a particle with a core and a coating for the core, the core comprising a drug and the coating comprising a mixture of a first material which is susceptible to attack by colonic bacteria and a second material which has a pH threshold at pH 5 or above, wherein the first material comprises

a polysaccharide selected from the group consisting of starch; amylose; amylopectin; chitosan; chondroitin sulfate; cyclodextrin; dextran; pullulan; carrageenan; scleroglucan; chitin; curdulan and levan, wherein release of the drug is delayed until the colon and wherein the pH threshold of the second material is the pH below which it is insoluble and at or above which it is soluble".

Claim 1 of auxiliary request 1 read as follows:

"1. A delayed release drug formulation for delivery of a drug to the colon comprising a particle with a core and a coating for the core, the core comprising a drug and the coating comprising a mixture of a first material which is susceptible to attack by colonic bacteria and a second material which has a pH threshold at pH 6.5 or above, wherein the first material comprises a polysaccharide selected from the group consisting of starch; amylopectin; chitosan; chondroitin sulfate; cyclodextrin; dextran; and carrageenan, wherein release of the drug is delayed until the colon and wherein the pH threshold of the second material is the pH below which it is insoluble and at or above which it is soluble".

Claim 1 of auxiliary request 2 differed from claim 1 of auxiliary request 1 in that the pH threshold of the second material was set to 7 or above (instead of 6.5 or above).

III. According to the decision under appeal:

(a) The information disclosed in the patent was sufficient to enable the skilled person to prepare the compositions of claim 1 of the patent. The

requirement of sufficiency of disclosure was therefore met. The claims were novel over D1 since this document did not disclose compositions comprising a coating containing a material having a pH threshold at pH 5 or above.

- (b) Document D11 was the closest prior art for the assessment of inventive step. The compositions disclosed in this document were characterised by the presence of guar gum in the coating. The compositions of the patent differed from those disclosed in D11 in the type of polysaccharide contained in the coating. The results disclosed in D17c were not sufficient to show that the effect of improving the targeted drug release to the colon could be obtained throughout the entire scope of the claim 1, as maintained by the patent proprietor. The technical problem was the provision of an alternative delayed release dosage form for delivery of a drug to the colon. Document D8 suggested using some of the polysaccharides recited in claim 1 of the opposed patent in the preparation of coatings for colonic-targeted formulations. The skilled person would have replaced the guar gum used in the coating of the compositions of D11 with one of the polysaccharides of D8. The subject-matter of the patent was therefore obvious.

- (c) The experimental results of D17c were insufficient to show any improvement over D11 also with regard to the subject-matter of auxiliary request 1, particularly in view of the fact that claim 1 covered compositions wherein the coating contained a polymer having a pH threshold at 6.5. Thus, auxiliary request 1 did not comply with the

requirement of inventive step substantially for the same reason as the main request.

- (d) The subject-matter of claim 1 of auxiliary request 2 was limited to compositions wherein the coating contained a material having a pH threshold at pH 7 or above. On the basis of the results disclosed in document D17c, the objective technical problem was the provision of a formulation with improved targeted colonic delivery in comparison to the formulations of the prior art. The prior art did not suggest replacing the guar gum used in D11 with one of the polysaccharides recited in claim 1 of auxiliary request 2 in order to solve this problem. The requirement of Article 56 EPC was therefore met.

IV. In the statement setting out the grounds of appeal submitted on 15 June 2015 the appellant-patent proprietor requested to set aside the decision of the opposition division and to maintain the patent on the basis of a new main request or, alternatively, on the basis of one of nine auxiliary requests.

Claim 1 of the new main request was identical to claim 1 of auxiliary request 1 considered by the opposition division (see point II above).

The following document was filed by the appellant-patent proprietor with the statement setting out the grounds of appeal:

D24: Report of further experimental studies

- V. The admissibility of the appeal of the appellant-patent proprietor was questioned by the appellant-opponent in its submission of 5 January 2016.
- VI. In a communication pursuant to Article 15(1) RPBA issued on 24 January 2018, the board expressed the opinion that the statement setting out the grounds of appeal of the appellant-patent proprietor met the requirements of Rule 99(2) EPC. It furthermore observed that the main request appeared to be novel over D1 and to comply with the requirements of inventive step.
- VII. The appellant-patent proprietor's arguments can be summarised as follows:

(a) Admissibility of its appeal

In the statement setting out the grounds of appeal the appellant-patent proprietor had clearly explained why it disagreed with the conclusions of the opposition division on inventive step. The requirements of Rule 99(2) EPC were therefore complied with and the appeal was admissible.

(b) Novelty

Document D1 did not anticipate the subject-matter of the patent. As confirmed by Mr Newton in its declaration, the reference on page 5 of D1 to Eudragit® L was an error. Moreover, D1 did not disclose compositions containing one of the polysaccharides recited in claim 1.

(c) Inventive step

Document D11 was the closest prior art for the assessment of inventive step. The compositions defined in the main request differed from the composition disclosed in example 5 of D11 in the nature of the polysaccharide used in the coating. The experimental data submitted by the appellant-patent proprietor demonstrated that replacing guar gum used in D11 with one of the polysaccharides recited in claim 1 provided an improved site specific drug release to the colon. Since none of the cited documents suggested that using any of the polysaccharides identified in the main request would have enabled such an improvement over guar gum, the claims of the main request were inventive.

VIII. The appellant-opponent's arguments can be summarised as follows:

(a) Admissibility of the appeal of the appellant-patent proprietor

In the statement setting out the grounds of appeal the appellant-patent proprietor did not identify any error in the decision of the opposition division. The appeal of the appellant-patent proprietor was therefore to be rejected as inadmissible.

(b) Novelty

Claim 1 of the main request was not novel over D1 which disclosed compositions that could contain Eudragit® L in the coating. It was not important whether the reference to Eudragit® L was an error. What was

relevant was the information that the skilled person would have derived from D1.

(c) Inventive step

The composition of example 5 of D11 was the closest prior art for the assessment of inventive step. The person skilled in the art would have realised by reproducing this example that the coating solution was too viscous. He would have therefore replaced guar gum with an alternative polysaccharide such as starch that did not cause the same increase of viscosity. In this manner he would have obtained the compositions of the main request without any inventive effort. The fact that replacing guar gum with starch resulted in other advantages was to be regarded as a bonus effect. In any case, the experiments carried out by the patent proprietor to show an improvement in the release of the active ingredient to the colon were not convincing. Indeed, the comparative compositions containing guar gum would have performed as the compositions according to claim 1 if the thickness of the coating had been increased. The comparative composition used in the experiments of the appellant-patent proprietor was not an exact reproduction of the composition of example 5 of D11. It was in any case obvious to replace in the coating of the composition of example 5 guar gum with starch since in D8 it was explained that these two materials were substantially equivalent as components of coatings of formulations suitable for colonic drug delivery.

IX. The appellant-patent proprietor requests that the decision under appeal be set aside and that the patent be maintained on the basis of the main request, or

alternatively, on the basis of one of auxiliary requests 1 to 9, all filed with the grounds of appeal.

- X. The appellant-opponent requests that the decision under appeal be set aside and the patent be revoked, and that the appeal of the patent proprietor be rejected as inadmissible.

Reasons for the Decision

1. Admissibility of the appeal of the appellant-patent proprietor
 - 1.1 In the appellant-opponent's view, the appeal of the patent proprietor is inadmissible because the statement setting out the grounds of appeal does not indicate why the decision of the opposition division would be erroneous.
 - 1.2 The opposition division came to the conclusion that the then pending auxiliary request 1 (corresponding to the current main request) did not comply with Article 56 EPC. The board notes that the appellant-patent proprietor explains in the statement setting out the grounds of appeal why, in its view, the current main request meets the requirements of Article 56 EPC (paragraphs 26 to 107). The central argument in the decision of the opposition division with regard to the then pending auxiliary request 1 was based on the consideration that claim 1 encompassed coating materials that dissolved at pH 6.5 (point 3.4.1.b of the decision). This argument is clearly addressed in the statement setting out the grounds of appeal starting from point 94 wherein the appellant-patent proprietor discusses the new experiments reported in

D24, made in reply to the criticism expressed by the opposition division in point 3.4.1.b.

For these reasons the statement of grounds of appeal of the patent proprietor fulfils the requirements of Rule 99(2) EPC. The appeal of the appellant-patent proprietor is therefore admissible.

2. Admissibility of document D24

2.1 The appellant-patent proprietor submitted the experimental report D24 with the statement setting out the grounds of appeal.

The experiments of D24 address some criticism expressed by the opposition division in its decision as to the effectiveness of the formulations containing a material with a pH threshold of 6.5 in delivering the active ingredient to the colon (see also point 1.2 above).

2.2 Hence, since the experiments of D24 have been filed in reaction to some conclusions made by the opposition division in its decision, it cannot be affirmed that they should have been submitted at an earlier stage of the proceedings (Article 12(4) RPBA).

2.3 In view of the above, D24 is admitted into the appeal proceedings.

Main request

3. Sufficiency of disclosure

3.1 The appellant-opponent did not submit any argument in relation to the requirement of sufficiency of

disclosure and there is no reason to overrule the conclusion of the opposition division in this regard.

4. Novelty

4.1 In the appellant-opponent's opinion document D1 anticipates the subject-matter of the main request. This document relates to formulations suitable for delivering an active ingredient to the colon. The formulations are coated with a film-forming composition comprising an amylose alcohol-complex and an insoluble film-forming polymer (page 3, lines 4 to 20).

4.2 The board considers that the composition of claim 1 of the main request differs from the compositions of D1 in the requirement of containing a polysaccharide selected from the group consisting of starch, amylopectin, chitosan, chondroitin sulfate, cyclodextrin, dextran, and carrageenan. In this regard it is noted that according to paragraph [0025] of the patent, starch is a mixture of amylose and amylopectin, i.e. it is not amylose.

4.3 The board furthermore agrees with the opposition division and with the appellant-patent proprietor that the compositions of D1 do not contain in the coating a material which has a pH threshold at pH 6.5 or above, (i.e. a material soluble at pH 6.5 or above) as required by claim 1 of the main request. On page 5 (line 28) of D1, reference is made to Eudragit L®, a soluble polymer which is cited as a suitable coating material in paragraph [0036] of the patent in suit. However, document D1 relates to compositions in which the coating contains an insoluble polymer, i.e. a polymer having a solubility of less than 1% w/v also at pH 7.2 (see first paragraph of page 5). A skilled

person would therefore immediately recognise that the reference in D1 to Eudragit L® is clearly erroneous, since this polymer is not insoluble as required by the general teaching of D1. Indeed, in document D15 one of the inventors of D1 confirms that the reference to Eudragit L® is a mistake.

4.3.1 According to the established case law of the boards of appeal, the technical disclosure in a prior art document must be considered as a whole. The individual parts of a document cannot be considered in isolation from the others but must be seen in their overall context. Moreover a prior art disclosure is to be interpreted from the standpoint of the skilled person possibly disregarding information which would be understood to be wrong (see Case law of the Boards of Appeal of the European Patent Office, 8th edition 2016, I.C.4.1). Hence, the appellant-opponent's position according to which the mere reference in D1 to Eudragit L® would be sufficient to conclude that the material used in the compositions of D1 is the same as the second material of claim 1 is not convincing.

4.4 Thus, the main request is novel over D1.

5. Inventive step

5.1 Closest prior art

5.1.1 The board agrees with the opposition division that document D11 is the closest prior art. This document relates to pharmaceutical compositions suitable for releasing an active ingredient in the region of colon. The compositions contain a shell material surrounding the active ingredient wherein the shell material comprises a polysaccharide that decomposes in the

colon, and a film forming polymer (column 2, lines 28 to 33).

In the composition disclosed in example 5 of D11 the shell material contains Eudragit S 100® as film forming polymer and guar gum as polysaccharide that decomposes in the colon. Eudragit S 100® is used in example 1 of the patent in suit as material for the coating. The composition defined in the main request differs from the one of example 5 of D11 mainly in the nature of the polysaccharide contained in the coating.

5.1.2 Document D1, suggested by the appellant-opponent as an alternative closest prior art, is a less promising starting point for the assessment of inventive step since the coating of the compositions disclosed therein contains a different polysaccharide and a different polymer compared to the coating of the composition of claim 1.

5.2 Technical problem

5.2.1 The appellant-patent proprietor has carried out various experiments with the aim of showing that the compositions according to claim 1 provide a more specific release of the active ingredient to the colon than the composition of example 5 of D11. Particularly relevant in the present context are the experiments disclosed in documents D17c and D24.

5.2.2 The appellant-opponent disputes the relevance of these experiments with the argument that the composition for comparison with the compositions of claim 1 is not identical to the composition of example 5 of D11.

5.2.3 In this respect the board agrees with the appellant-patent proprietor that the disclosure of example 5 is silent with regard to various details of the composition. The experiments made by the appellant-patent proprietor appear to be a genuine attempt to reproduce the teaching of D11. It is observed in particular that compositions with different thickness of the coating have been prepared in order to take into account the fact that D11 does not provide any explicit information in this regard (see e.g. parts 5 and 6 of D24).

5.2.4 Moreover, no matter whether the experiments carried out by the appellant-patent proprietor are based on an exact reproduction of D11, they represent a piece of evidence that must be assessed and taken into account for the definition of the technical problem.

Particularly relevant in this regard are the experiments which allow an assessment of the effects arising from the distinguishing feature, i.e. the replacement of guar gum with the polysaccharides of claim 1. These are in particular the experiments disclosed in parts 2 and 3 of D17c and in D24. In these experiments the compositions tested differ only in the nature of the polysaccharide.

5.2.5 The results of these experiments show that the formulations containing one of the polysaccharides of claim 1 provide improved site specific release of the active ingredient to the colon. The results disclosed in part 5 of D24 show that the formulations according to claim 1 release the active ingredient to the colon also when the polymer used has a pH threshold of 6.5.

5.2.6 In the appellant-opponent's opinion the formulations with guar gum would perform as the formulations of claim 1 of the main request if the thickness of the guar gum coating were increased. However, if the guar gum coating provides the same site specific release as the coatings of claim 1 only when it is thicker than the coatings of claim 1, it means that the latter are more effective. Hence, this reasoning of the appellant-opponent does not invalidate the conclusion that the coatings containing one of the polysaccharides of claim 1 perform better than the coating of the composition of example 5 of D11.

5.2.7 In the light of these considerations the technical problem is defined as the provision of a formulation with improved targeted colonic delivery.

5.3 Obviousness

5.3.1 None of the cited documents teaches to solve the problem defined in point 5.2.7 above by replacing in the composition of example 5 of D11 guar gum with one of the polysaccharides recited in claim 1 of the main request.

5.3.2 The appellant-opponent argues that on the basis of the teaching of document D8, the skilled person would have considered using starch instead of guar gum in the composition of example 5 of D11.

This argument is not convincing for the following reasons:

Document D8 describes compositions that release the active ingredient in the colon. These compositions comprise a core and a coating system containing *inter*

alia microparticles made of a dietary fibre (page 4, lines 18 to 23) which can be selected for instance from guar gum, carrageenan (see page 9 last paragraph) or starch (page 5, lines 24 to 27). Document D8 does not indicate that carrageenan and starch, which are recited also in claim 1 of the main request, provide better results than guar gum in terms of targeted delivery to the colon. Thus, the skilled person faced with the problem formulated in point 5.2.7 above would not be motivated on the basis of the teaching of D8, to replace in the composition of D11 guar gum with carrageenan and starch.

- 5.3.3 The appellant-opponent further argues that the skilled person would have replaced in the composition of D11 guar gum with a different polysaccharide, such as starch, in order to reduce the viscosity of the coating composition. Any further advantage deriving from this modification, such as the improved targeted release to the colon, should be regarded as a mere bonus effect.

In this respect the board notes that there is no indication in D11 that there may be a serious problem with the viscosity of the coating solution used in example 5. In contrast, the fact that example 5 describes the preparation of a formulation containing guar gum in the coating and provides the results of a dissolution test performed with this formulation indicates that a composition can effectively be coated with a solution containing guar gum.

- 5.3.4 In any case, even assuming, in the appellant-opponent's favour, that the skilled person would have encountered problems in processing the coating composition of example 5 due to the viscosity of guar gum, then the advantages in terms of improved targeted delivery to

the colon could be regarded as a bonus effect only if the skilled person, when addressing the problem of viscosity, had no alternative to replacing guar gum with one of the polysaccharides of claim 1. Only in such a "one-way-street" situation, the effect on the delivery of the drug to the colon, could be regarded as a "bonus effect" that would not render the subject-matter of the claim inventive (see Case Law of the Boards of Appeal of the EPO, 8th Edition 2016, I.D.10.8).

However, in the present case there is no indication that any possible problem of viscosity could only be solved by replacing guar gum with one of the polysaccharides recited in claim 1. In contrast, D11 indicates (column 5, lines 14-20) that any problems with high viscosity of the coating solutions would be overcome by using suspensions or dispersions of the components in the liquid phase. Hence, even assuming that the skilled would have encountered problems when reworking example 5 of D11 due to the viscosity of the solution, he would have not necessarily decided to use one of the polysaccharides of claim 1 instead of guar gum.

It follows that the technical effect arising from the use of the polysaccharides recited in claim 1 cannot be regarded as a bonus effect.

5.4 Therefore, the subject-matter claimed in the main request meets the requirements of Article 56 EPC.

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 the main request filed with the statement setting out the grounds of appeal on 15 June 2015 and a description to be adapted thereto.

The Registrar:

The Chairman:



S. Fabiani

J. Riolo

Decision electronically authenticated