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**Datasheet for the decision  
of 16 December 2014**

**Case Number:** T 1605/13 - 3.3.07

**Application Number:** 07837876.7

**Publication Number:** 2061433

**IPC:** A61K9/127, A61K9/16, A61K9/50,  
A61K9/51, A61K31/70, A61K47/26,  
A61K47/48, A61K48/00

**Language of the proceedings:** EN

**Title of invention:**  
COMPOSITIONS FOR ENHANCING TRANSPORT THROUGH MUCUS

**Patent Proprietor:**  
JOHNS HOPKINS UNIVERSITY

**Opponent:**  
Vectura Limited

**Relevant legal provisions:**  
EPC Art. 123(2)

**Keyword:**  
Amendments - extension beyond the content of the application  
as filed (yes)



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Case Number: T 1605/13 - 3.3.07

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.07**  
**of 16 December 2014**

**Appellant:** JOHNS HOPKINS UNIVERSITY  
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**Decision under appeal:** **Decision of the Opposition Division of the  
European Patent Office posted on 8 May 2013  
revoking European patent No. 2061433 pursuant to  
Article 101(3) (b) EPC.**

**Composition of the Board:**

**Chairman** J. Riolo  
**Members:** D. Semino  
P. Schmitz

## Summary of Facts and Submissions

I. The appeal of the patent proprietor (appellant) lies against the decision of the opposition division announced at the oral proceedings on 23 April 2013 to revoke European patent 2 061 433. The patent was granted on the basis of 17 claims, claim 1 reading as follows:

"1. A particle comprising an outer surface and one or more surface-altering moieties disposed on the outer surface that reduce mucoadhesion of the particle, wherein

(a) the mass of the surface-altering moiety makes up at least  $1/3400$  of the mass of the particle, and/or

(b) the surface-altering moiety is present on the outer surface at a density of greater than 0.01 units per nanometer squared."

II. A notice of opposition was filed in which revocation of the patent in its entirety was requested on the grounds of lack of novelty and of inventive step, of insufficiency of disclosure and of extension of the subject-matter beyond the content of the application as filed (Article 100(a), (b) and (c) EPC).

III. The decision was based on 6 sets of claims filed as main request during oral proceedings on 23 April 2013 and as auxiliary requests I to V with letter of 15 April 2013.

Claim 1 of the main request had the following wording:

"1. A particle comprising a core, an outer surface and one or more surface-altering moieties disposed on the outer surface that reduce mucoadhesion of the particle, wherein the surface-altering moiety is present on the outer surface at a density of greater than 0.01 units

per nanometer squared, wherein the surface-altering moiety is a poloxamer, wherein said core is  
(i) a pharmaceutically acceptable polymer core;  
(ii) a core having one or more bioactive agents; or  
(iii) a pharmaceutically acceptable polymer core,  
wherein a bioactive agent is encapsulated in the core;  
and  
wherein the surface-altering moiety is disposed on the outer surface by adsorption or covalent linkage."

Claim 1 of auxiliary requests I to V corresponded to claim 1 of the main request unamended (auxiliary request I), with the specification that "said particle is greater than 50 nm in diameter" (auxiliary request II), with a limitation to option (iii) (auxiliary request III), with a redefinition of the claimed object as a composition comprising a particle according to claim 1 of the main request and a "sacrificial polymer, wherein the sacrificial polymer is not physically or chemically associated with the particle and promotes the transport of the particle through mucus" (auxiliary request IV) and with a redefinition of the claimed object as an ophthalmic formulation comprising a particle according to claim 1 of the main request (auxiliary request V).

IV. The decision under appeal can be summarised as follows:

- a) Original claim 6, on which claim 1 of the main request was based, was part of a list of six independent product claims defining the particle through different technical features, so that, to start with claim 6, one had to choose already from the list of independent claims. The feature that "the surface-altering moiety is disposed on the outer surface by adsorption or covalent linkage" had also to be selected among a number of

alternatives. The choice of "poloxamer" was a further selection from a long list of surface-altering agents.

b) In summary, a selection from at least two lists was necessary to arrive at the subject-matter of claim 1 of the main request, which could not be directly and unambiguously derived from the application as originally filed. The main request therefore did not fulfill the requirements of Article 123(2) EPC.

c) None of the auxiliary requests fulfilled the requirements of Article 123(2) EPC for the same reasons as the main request. On top of that, the added features were either selections from further lists (auxiliary requests II, III and V) or had no basis in the original application (auxiliary request IV).

V. The appellant lodged an appeal against that decision. With the statement setting out the grounds of appeal, the appellant filed 5 sets of claims as main request and auxiliary requests I to IV.

The main request corresponded to the main request on which the decision was based.

Auxiliary requests I, III and IV corresponded to auxiliary requests I, III and V on which the decision was based. Auxiliary request II corresponded to auxiliary request II on which the decision was based with the replacement of the term "50 nm" in claim 1 with "100 nm".

- VI. In a communication sent in preparation of oral proceedings the Board with regard to the issue under Article 123(2) EPC for claim 1 of the main request expressed the preliminary view that the "choice of the product of independent claim 6 among equally relevant alternatives is already a first selection that the skilled person has to make to come to the subject-matter of claim 1 of the main request" (paragraph 1.1 ) and stated that the "issues outlined for the main request appear to equally apply to claim 1 of all auxiliary requests" (paragraph 2).
- VII. Oral proceedings were held on 16 December 2014.
- VIII. The arguments of the appellant can be summarised as follows:

*Main request - amendments*

- a) The contribution of the application on which the patent in suit was based was the provision of particles modified with surface-altering moieties with decreased mucoadhesion and increased mobility in mucus. This technical effect was achieved by modifying the particles so as to achieve a higher concentration of surface moieties on their surface. Independent claims 1 to 6 of the application as filed defined the product achieving this effect either by directly quantifying the reduced mucoadhesion or the increased mucosal transport or by defining the amount of surface altering moieties. They defined therefore one and the same product by means of different parameters. This was confirmed by the particles prepared in the example section, where a single batch of particles was described which was characterised by

all the parameters of the six independent claims. Claims 1 to 6 were therefore alternative definitions of the same particles and the choice of claim 6 could not be seen as a selection from a list. The only selection which had to be made to come to the subject-matter of claim 1 of the main request was therefore the selection of poloxamer as the surface-altering moiety, which material was given some prominence in the description (page 31) and could be seen as a preferred one, being a derivative of polyethylene glycol. On that basis the requirements of Article 123(2) EPC were met.

*Auxiliary requests - amendments*

- b) The same arguments as to the combination of the parameter of original claim 6 and poloxamer applied for claim 1 of the auxiliary requests.

IX. The arguments of the opponent (respondent) can be summarised as follows:

*Main request - amendments*

- a) Claim 1 of the main request was based on claim 6 of the original application, which was one of six independent claims defining the particles through different technical features. The selection of one of a number of independent claims is according to the jurisprudence equivalent to a selection from a list. The six parameters used in the six independent claims depended on different characteristics of the particles and did not describe the same property, so that it was not credible on a scientific basis that they defined one and the same product. This was confirmed by

the examples in the original application, which described one batch, but analysed the properties of particles with three different sizes and showed that particles were produced which fulfilled the conditions of some of the independent claims, but not of others. While some overlap among the independent claims was present, the claims had a different scope and defined different products. Poloxamer as the surface-altering moiety was just one member of a very long list which was given no prominence in the original application and could not be considered as a polyethylene glycol derivative. Therefore the combination of original independent claim 6 with poloxamer resulted from a selection of two lists and was not directly and unambiguously derivable from the application as originally filed, so that the requirements of Article 123(2) EPC were not met.

*Auxiliary requests - amendments*

- b) The same arguments as to the combination of the parameter of original claim 6 and poloxamer applied for claim 1 of the auxiliary requests.
- X. The appellant requested that the decision under appeal be set aside and that the case be remitted to the first instance on the basis of the main request or one of auxiliary requests I to IV, all filed with the statement setting out the grounds of appeal.
- XI. The respondent requested that the appeal be dismissed.

**Reasons for the Decision**

*Main request - amendments*



1. Claim 1 of the main request combines *inter alia* the feature that "the surface-altering moiety is present on the outer surface at a density of greater than 0.01 units per nanometer squared" with the one that "the surface-altering moiety is a poloxamer".
  - 1.1 While it is not disputed that a basis for the former feature is to be found in the characterising part of original claim 6 and in the corresponding part of the description (last paragraph of page 3) and that poloxamer is mentioned as a possible surface-altering moiety on pages 31 and 36, the crucial issue concerns whether the combination of the two features is directly and unambiguously derivable from the original application.
  - 1.2 Original claim 1 is one of the six independent claims of the original application which identify six alternative embodiments of the invention. All these embodiments refer to a particle comprising an outer surface and one or more surface-altering moieties disposed on the outer surface, but are characterised by different properties in terms of relative or absolute diffusivity (original claims 1 and 2), zeta potential (original claim 3), mass of the surface-altering moiety with respect to the mass of the particle (original claim 4), adsorption of fluorescently labeled avidin (original claim 5) and density of the surface-altering moiety on the outer surface (original claim 6). A similar disclosure is present in the original description (last two paragraphs on page 3 and first four paragraphs on page 4).
  - 1.3 While some overlap may be present among the different embodiments, it is not technically credible that the subject-matter covered by the six independent claims

defines one and the same product. Indeed, the six parameters, each one with a specific range, are not different measures of the same property, but define different physical characteristics of the particles.

- 1.4 If one compares the parameters of claims 4 and 6, which both refer in some ways to the quantity of surface altering moieties, it is immediately apparent that the parameter of claim 4 (the mass of the surface-altering moiety with respect to the mass of the particle) depends on the dimension of the particle and its density (which determine its mass) and on the mass of the surface-altering moiety, while the parameter of claim 6 (the density of the surface-altering moiety on the outer surface measured in units per nanometer squared) depends on the quantity of the surface-altering moiety and on the outer surface of the particle. Depending on the kind of particle, its size, its shape and its material, it may therefore well be that particles with the same value of one of the two parameters have quite different values of the other. Therefore a correspondence between a range of one parameter and a range of the other is technically not possible.
- 1.5 This is even more evident for parameters such as the diffusivity (relative or absolute), the zeta potential and the avidin adsorption, which depend not only on the quantity of the surface-altering moiety (be it expressed by a mass ratio or by a surface density), but also on the chemical of physical properties of the chosen moiety and on its interactions with the particle material, which strongly affect the diffusional, electrical and adsorption properties of the particles.
- 1.6 The fact that the six products of the six independent claims may not define one and the same product, which is

already without doubts from a technical point of view, is confirmed by the examples in the application as filed, which show that 100 nm particles modified with polyethylene glycol do not fall under original claim 1, having a diffusivity which is reduced 2000 times with respect to the one in water (page 62, lines 30 to 31), nor under original claim 2, having a diffusivity of around  $10^{-3} \mu\text{m}^2/\text{s}$  at a time scale of 1 s (figure 2B), but fulfill the requirements of zeta potential and avidin adsorption of original claims 3 and 5 (data in figure 8).

- 1.7 The six independent claims formulated in the original application are therefore six alternative embodiments of the invention and correspond to a list of alternative products. As to the embodiment of claim 6, there is no indication in the application as filed that it is for any reason a preferred one. Therefore the choice of the product of independent claim 6 among equally relevant alternatives is already a first selection that the skilled person has to make to come to the subject-matter of claim 1 of the main request.
- 1.8 As to poloxamer as the surface-altering moiety, it is mentioned twice in the application as filed, namely in the paragraph bridging pages 31 and 32 (last line of page 31) and in the one bridging pages 35 and 36 (line 14 of page 36). In the first case it is one of the examples of one of several classes of compounds which are indicated as possible surface-altering moieties. In the second case it is a member of a long list of polymers which may be employed. In both cases no preference or prominence is given to poloxamer as a surface-altering moiety.

- 1.9 The question whether poloxamer may be considered as a polyethylene glycol derivative is irrelevant to the present analysis. Even if the term derivative were interpreted in a very broad sense, so as to extend to a triblock copolymer such as poloxamer (which is doubtful), there is no mention in the application as filed of poloxamer as a specific polyethylene glycol derivative, so that the generic citations of polyethylene glycol derivatives in the application as filed would not provide any further basis for the specific surface-altering moiety.
- 1.10 The combination of a density of the surface-altering moiety at greater than 0.01 units per nanometer squared with poloxamer as the surface-altering moiety results therefore in a specific embodiment made out from the selection of two not preferred elements out of two separate lists, which is not directly and unambiguously derivable from the application as originally filed. Such an embodiment remains hidden in the original application and is a novel selection with respect to it.
- 1.11 The requirements of Article 123(2) EPC are therefore not met.

*Auxiliary requests I to IV - amendments*

2. Claim 1 according to auxiliary requests I to IV corresponds to claim 1 of the main request unamended (auxiliary request I), with the specification that "said particle is greater than 100 nm in diameter" (auxiliary request II), with a limitation to option (iii) (auxiliary request III), and with a redefinition of the claimed object as an ophthalmic formulation comprising a particle according to claim 1 of the main request (auxiliary request V).

- 2.1 As claim 1 according to all auxiliary requests includes the wording of original claim 6 in combination with the specification that the surface-altering moiety is a poloxamer, the requirements of Article 123(2) EPC are not met for all auxiliary requests for the same reasons as outlined for the main request (see point 1, above).

*Conclusion*

3. As all requests on file do not meet the requirements of Article 123(2) EPC, there is no reason for the Board to decide on any other point and the appeal is to be dismissed.

**Order**

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

The appeal is dismissed.

The Registrar:

The Chairman:



S. Fabiani

J. Riolo

Decision electronically authenticated