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Datasheet for the decision of 18 April 2019

Case Number: T 1537/16 - 3.3.07

Application Number: 10700730.4

Publication Number: 2379063

IPC: A61K9/28, A61K31/215, A61P17/06, A61K9/20, A61K31/225

Language of the proceedings: EN

Title of invention:
PHARMACEUTICAL FORMULATION COMPRISING ONE OR MORE FUMARIC ACID ESTERS IN AN EROSION MATRIX

Patent Proprietor:
FWP IP APS

Opponents:
Generics [UK] Limited
Biogen MA Inc.
Wohldorff GmbH

Headword:
PHARMACEUTICAL FORMULATION COMPRISING ONE OR MORE FUMARIC ACID ESTERS IN AN EROSION MATRIX/FWP IP APS

Relevant legal provisions:
EPC Art. 56, 54, 100(b), 100(c)

Keyword:
Main request - Inventive step (No)
Auxiliary request 1 - Amendments (yes)
Auxiliary request 1 - Sufficiency of disclosure (Yes)
Auxiliary request 1 - Novelty (Yes)
Auxiliary request 1 - Inventive step (Yes)

Decisions cited:

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

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Case Number: T 1537/16 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 18 April 2019

Appellant: (Opponent 1)	Generics [UK] Limited (trading as Mylan) Albany Gate Darkes Lane Potters Bar Hertfordshire EN6 1AG (GB)
Representative:	Elkington and Fife LLP Prospect House 8 Pembroke Road Sevenoaks, Kent TN13 1XR (GB)
Party as of right: (Opponent 3)	Wohldorff GmbH Neuer Wall 72 20354 Hamburg (DE)
Representative:	Simandi, Claus Badehausallee 55 27476 Cuxhaven (DE)
Respondent: (Patent Proprietor)	FWP IP APS Østergade 24 A 1100 København K (DK)
Representative:	HGF Limited 4th Floor Merchant Exchange

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Manchester M1 5WG (GB)

Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted on 7 June 2016 rejecting the opposition filed against European patent No. 2379063 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman A. Usuelli

Members: D. Boulois
C. Schmidt

Summary of Facts and Submissions

I. European patent No. 2 379 063 was granted on the basis of a set of 21 claims.

Independent claim 1 as granted read as follows:

"1. A pharmaceutical formulation in the form of an erosion matrix tablet comprising:
i) 10 % to 80 % by weight of one or more fumaric acid esters selected from di-(C_1 -C_5)alkylesters of fumaric acid and mono-(C_1 -C_5)alkylesters of fumaric acid, or a pharmaceutically acceptable salt thereof, as an active substance;
ii) 1-50 % by weight of one or more rate-controlling agents; and
an enteric coating, wherein said enteric coating is applied at a level of 1.5 - 3.5 % by weight of the core,
wherein erosion of said erosion matrix permits controlled or sustained release of said active substance."

II. The patent was opposed under Article 100(a), (b) and (c) EPC, on the grounds that its subject-matter lacked novelty and inventive step, was not sufficiently disclosed and extended beyond the content of the application as filed.

III. The documents cited during the opposition proceedings included the following:

D1: WO 2006/037342
D5: US 6 509 376
D6: US 6 355 676
D10: WO 2007/042034

D15: Handbook of Pharmaceutical Excipients, 4th Edition, page 289
D19: US 2004/002544
D20: Pharmaceutics, The Science of Dosage Form Design
D26: "Comparative trials on disintegration behavior of DMF tablets", ConsuPharm GmbH
D28: Reply to the Int. Search Opinion filed in response to the communication pursuant Rule 161 EPC
D39: Declaration of Prof. Dr. A Fahr
D40: Eudragit RS 30D, product information sheet (Evonik)
D41: Second Declaration of C. Galetzka

IV. The present appeal lies from the decision of the opposition division to reject the oppositions (Article 101(2) EPC).

V. According to the decision under appeal, D39 and D40 were admitted into the proceedings. D41 was not admitted, since the technical data disclosed therein could have been produced earlier by the patentee.

The opposition division considered that claim 1 as granted had a basis in original claim 19 with reference to original claim 1 and the main request fulfilled the requirements of Article 123(2) EPC for this reason.

According to the opposition division, the patent provided the skilled person with specific working examples, and the skilled person was able to carry out the invention according to the claims. The opposed patent was therefore sufficiently disclosed.

As regards novelty, neither example 16 of D1, nor example 1 of D10, example 2 of D5 and example 2 of D6 disclosed tablets containing an enteric coating applied

at a level of 1.5-3.5 % by weight of the core. The subject-matter of the main request was therefore novel.

As regards inventive step, the opposition division considered example 16 of D1 as the closest prior art, rather than the marketed product Fumaderm or other embodiments of D1, D10, D5, D6, and D19 cited by opponents 01, 02 and 03. D1 did not disclose an erosion matrix tablet and the coating disclosed therein did not show the claimed level of 1.5-3.5% by weight of the core. No improvement over the prior art was convincingly demonstrated and the problem was formulated as the provision of an alternative composition. The claimed solution was not obvious since not suggested in any cited document.

VI. Opponents 01 (hereinafter the appellant), 02 and 03 filed an appeal against said decision.

VII. With its statement of grounds of appeal dated 17 October 2016, opponent 03 submitted a new document:
D42: Declaration of Dr. Podpetschnig-Fopp

VIII. In its reply to the statements of ground of appeal dated 28 February 2017, the patentee (hereinafter the respondent) requested to dismiss the appeal and maintained its auxiliary requests 1-3 filed during the opposition proceedings with letter dated 5 February 2016. It also submitted a document:
D42bis: Second Declaration by Christin Galetzka dated 1 April 2016

Independent claim 1 of auxiliary request 1 was further restricted by the specification as regards the rate-controlling agent, namely **"wherein the rate-controlling agent is a water-soluble polymer"**.

IX. With a letter dated 10 March 2017, opponent 02 withdrew its opposition against the patent.

X. With a letter dated 15 May 2017, opponent 03 (hereinafter party as of right) withdrew its appeal.

XI. With a letter dated 14 February 2018, the respondent submitted new documents:

D43: Counter-Declaration of Professor Martini
D44: Davies and Gloor et al, J. of Pharm. Sciences, 1971, vol.60, No 12, 1869-1874
D45: Ritschel W.A., Chapter 2: Peroral Solid Dosage Forms with Prolonged Action on Drug Design, Drug Design, Edoted by E.J. Ariens, Vol. IV(1973), pages 64 and 65
D46: Zimmermenn I., Pharmazeutische Technologie – Industrielle Herstellung und Entwicklung von Arzneimitteln, Springer (1998), Pages 387-388
D47: York P., Chapter: Tablet lubricants in "Materials Used in Pharmaceutucal Formulation", Edited by A.T. Florence, 1984, pages 49-51
D48: Guignon et al., Fluid Bed Encapsulation of Particles and Practice, Drying Technology 20(2), 419-447, 2002
D49: Evonik Röhm GmbH, Eudragit Application Guidelines, 11th edition (Sep. 2009), Ch. 2, pages 9-11
D50: Handbook of Pharmaceutical Excipients, Second Edition (1994), pages 424-427

XII. With a letter dated 27 June 2018, the appellant submitted a new document:

D51: Modern Pharmaceutics, 4th Edition, 2002, page 294

XIII. In a communication pursuant to Article 15(1) RPBA, the Board stated inter alia that the closest prior art for assessing inventive step was D1 and not D10. The Board also stated that the only distinguishing feature between the subject-matter of claim 1 of the main request and example 16 of D1 was the amount of enteric coating, and that claim 1 of the main request did not appear to involve an inventive step.

XIV. With a letter dated 28 March 2019, the respondent filed new auxiliary requests 3-7 and a new document:
D52: Pharmaceutics, Second Edition 2002, pages 289-305

XV. Oral proceedings took place on 18 April 2019, in the absence of the party as of right to the appeal proceedings as announced previously by letter.

XVI. The arguments of the appellant and the party as of right to the proceedings may be summarised as follows:

Main request - Inventive step

According to the appellant, D1 was the closest prior art, and the only difference with the claimed subject-matter was the amount of enteric coating. No effect was shown over D1 as regards said difference and the problem had to be formulated as the provision of an alternative composition.

Claim 1 was not limited by any kind of release, such as a zero-order release as argued by the respondent.

The claimed enteric coating was not unusually thin. The limitation of claim 1 only related to the amount of enteric coating, and not on said thickness, which was dependent on the size and the density of the core.

Hence, the claimed amount was just an arbitrary proportion of the coating which was dependent on the density of the core, the important factor being the density of the core.

Moreover, D20 mentioned that a 2-3 weight % of coating was a normal coating.

The claimed solution was therefore obvious.

The party as of right to the proceedings considered in its written submissions that example 16 of D1 was the closest prior art. The amount of enteric coating was the only difference between the claimed subject-matter and example 16 of D1. D42 showed that compositions comprising an enteric coating at weight ratios different from the claimed 1.5-3.5% still could achieve a release profile of zero order. This showed that the amount of enteric coating did not provide any technical contribution as regards the problem of the contested patent and that this feature was not essential for the assessment of inventive step. The amount of enteric coating did not provide any particular effect and the choice of an amount as claimed was obvious. Moreover, the content of D26 could not be taken in account, since it did not prove that the formulations of D1 did not comprise an erosion matrix.

Auxiliary request 1 - Sufficiency of disclosure

According to the appellant, the patent did not provide a specific definition of an erosion matrix and did not teach how to select the relevant excipients. Moreover the patent did not specify under which conditions the tablets of example 16 of D1 were supposed to

disintegrate. The tests in D26, which compared the compositions of the patent and D1 used particular conditions of crushing forces and disintegration medium, for which there was however no basis in the contested patent.

The coating was also not sufficiently disclosed, since the claims were not limited to any type of enteric coating, with any mass density and excipients. The patent did not make it credible that 1.5% by weight of the core of an enteric coating would be effective for any core.

Auxiliary request 1 - Inventive step

According to the appellant, this request was limited to a rate-controlling agent which was water-soluble. The comparative example was still not corresponding to the formulation disclosed in D1. The objective technical problem was still an alternative formulation and the claimed invention was not inventive.

XVII. The arguments of the respondent may be summarised as follows:

Main request - Inventive step

D10 was a better closest prior art than D1 since it was filed one year later; moreover, its example 1 corresponded to example 16 of D1. The claimed invention was inventive over D10.

As regards the disclosure of D1, the differences with the claimed composition and D1 were the presence of an erosion matrix and the amount of enteric coating. The

enteric coating was thin, and disintegrated quickly for this reason, and allowed a further controlled release of the erosion matrix. The process involved in the claimed tablets was an erosion process which was not the case in D1 or D10, which involved a diffusion process as shown in D39. The polymer used in example 16 of D1 could indeed not allow an erosion and also not a zero order release.

Moreover, example 16 of D1 disclosed the preparation of tablets comprising multiples units, namely dimethyl fumarate (DMF) granulates and placebo granulates, followed by a compression of said units and coating. The kind of release could not be an erosion but rather a diffusion release, through ethyl cellulose. As it was taken from D26, the tablets of example 16 of D1 disintegrated within about three minutes.

A diffusion release as provided in D1 was different from the release of the claimed formulations, since it depended on the square root of the time span, while for erosion there was a linear relationship between cumulative drug amount and time span. Thus, tablets according to example 16 of D1 and tablets according to the claimed invention differed in their release profiles, as illustrated by Figure 1 of the patent showing a zero order release and Figure 2 of D1 showing a different release.

Moreover, the prior art tablets had a higher enteric coating level. This showed that high amounts of enteric coating were necessary to avoid a quick disintegration of the tablets core disclosed in example 16 of D1, which had a release mediated by diffusion.

The problem to be solved was the provision of an improved pharmaceutical formulation having a reduced variability of pharmacokinetic parameters. This was shown by example 43 of the contested patent.

D1 did not teach or suggest DMF formulations with a thin enteric coating and an erosion matrix, more particularly in view of the problem to be solved. The claimed solution was therefore not obvious.

Auxiliary request 1 - Inventive step

Claim 1 had been restricted by the nature of the rate-controlling polymer, namely a water-soluble polymer. In D1 ethylcellulose was used as rate-controlling polymer and this polymer is obviously water-insoluble. PEG 400 was a liquid component used as binding agent in the composition of example 16. The problem remained the same and the claimed invention was inventive for the same reasons than the main request.

XVIII. Requests

The appellant requested that the decision under appeal be set aside and that the patent be revoked. The appellant further requested that auxiliary requests 4 to 7 be not admitted into the proceedings.

The party as of right to the proceedings requests that the decision under appeal be set aside and the patent be revoked.

The respondent requested that the appeal be dismissed or that the decision under appeal be set aside and that the patent be maintained on the basis of one of auxiliary requests 1 to 7 filed with letter dated 5

February 2016 (auxiliary requests 1 and 2) and with letter dated 28 March 2019 (auxiliary requests 3 to 7).

Reasons for the Decision

1. Main request - Inventive step

1.1 The invention relates to a pharmaceutical formulation of one or more fumaric acid esters in an erosion matrix.

1.2 The opposition division considered D1 as the closest prior art, in view of example 16. The respondent's position is that example 5 of D10 should rather be the closest prior art.

1.2.1 D1 relates to controlled release compositions of a fumaric ester comprising a fumaric ester, a polymer, such as ethylcellulose or a methacrylic acid copolymer, and hydrophilic excipients (see D1, page 33, lines 7-19).

More specifically, D1 discloses in example 16 tablets prepared by compression of a DMF-granulate comprising ethyl cellulose and polyethylene glycol 400, and a placebo granulate comprising lactose, microcrystalline cellulose and PVP. The amount of hydrophilic excipients in the final tablet is about 4.6% by weight of PEG 400 and 19% by weight of lactose. Said tablets are enteric coated according to example 4 of D1, at an amount of polymeric material of about 6 mg/cm^2 of the tablet, thus with an amount of enteric coating of around 6.5-6.9% by weight, as calculated by the respondent. Figure 2 shows the release of the DMF core tablet without enteric coating of example 16; said Figure

shows in particular that the tablets of example 16 do not present a quick disintegration profile but a continuous release over time.

D1 suggests also very generally the preparation of matrix compositions of multiple units, wherein the active, namely DMF, is embedded in a matrix of cellulose and cellulose derivatives, such as hydroxy propyl cellulose (see D1, page 13).

Hence, the only distinguishing feature between the subject-matter of claim 1 of the main request and example 16 of D1 is the amount of enteric coating which is comprised between 1.5-3.5% by weight in the core in the compositions of the invention, instead of around 6.5% by weight of the core in example 16 of D1.

The terminology used in claim 1 of the main request to define the tablet core, as regards the functional terms "erosion matrix" and "rate-controlling polymer", does in particular not make possible to distinguish between the core tablet of the claimed invention from the core tablet disclosed in example 16 of D1, which also discloses the presence of a rate-controlling polymer.

1.2.2 The Board could also not follow the argumentation of the respondent that:

a) D1 did not relate to erosion matrices,
b) the eroding matrix of claim 1 of the main request necessarily provides a zero order release profile, which is not the case of D1,
c) the tablets disclosed in D1 were multiple units systems, contrary to the tablets disclosed in the contested patent.

As regards point a), D1 discloses explicitly a dosage form in the form of a matrix system (see D1, page 13, l. 15-21). The matrix of example 16 comprising a certain amount of hydrophilic excipients, such as lactose and PEG 400, and a rate-controlling polymer, namely ethylcellulose, which is a water-insoluble polymer. It results that the matrix system of example 16 of D1 undergoes at least partially an erosion of said hydrophilic excipients, and that the drug is released at least partially by dissolution. The presence of a water-insoluble rate-controlling polymer in the tablet of example 16 cannot constitute a further difference, since claim 1 of the main request does not specify the nature of the rate-controlling polymer, which can also be a water-insoluble polymer.

As regards point b), claim 1 is not limited to any specific kind of release profile, in particular not a zero order profile as argued by the respondent, and does also not refer to any speed of release. The respondent relied on D26 to show that tablets according to example 16 of D1 disintegrate quickly while tablets according to the invention dissolve slowly; this comparison is contrary to the teaching of Figure 2 of D1 and is anyway irrelevant as long as the terminology used in claim 1 encompasses also compositions of core tablets as disclosed in D1. The description of the contested patent mentions furthermore several kinds of alternative possible types of release profile different form a zero order release profile (see par. [0162] or [0166] of the specification).

Moreover, an eroding matrix is not necessarily a matrix with a zero order release. Said term is not necessarily connected with specific release properties, it only defines a way of releasing by slow dissolution.

Finally, as regards point b), it is true that Figure 1 of the contested patent shows the release of tablets having a zero order release. Said Figure 1 however refers to specific examples of the patent, namely examples 16, 18, 20 and 22 having specific tablet formulations comprising in particular hydroxy propyl cellulose, a water-soluble polymer, as rate-controlling agent of the matrix. The functional feature "rate-controlling polymer" remains a general term which does not reflect the specific type of (water-soluble) polymers used in said examples.

Consequently, the erosion matrix and supposedly linked release profile cannot constitute a further difference between the claimed subject-matter and the disclosure of D1.

As regards point c), even if it is true that D1 disclose a tablet core constituted by two different types of granulates, the compression of said granulates forms a final matrix which cannot be distinguished from the matrix system of claim 1 of the main request. Several examples of the contested patent show in any case also a compression of different types of granulates (cf. inter alia examples 11, 13, 21, 22 of the contested patent). This feature cannot therefore constitute a further difference between the claimed subject-matter and the disclosure of D1.

1.2.3 As regards D10, the disclosure of example 1 corresponds to example 16 of D1, with a lower amount of enteric coating, but still higher than the claimed upper limit of 3.5% by weight. The teaching of said specific example does therefore not bring new technical

information in comparison to the teaching of example 16 of D1.

As regards example 5 of D10 which was put forward by the respondent, the Board notes that said example comprises a matrix formed by the combination of a granulate comprising DMF in the hydrophobic polymer Eudragit RS with a second granulate comprising lactose, cellulose and PVP. The active agent is thus clearly embedded in a granulate with an hydrophobic polymer without any hydrophilic component, and clearly cannot be released through erosion. The teaching of said example 5 of D10 is therefore remote from the subject-matter of claim 1 of the main request. Consequently, example 5 of D10 cannot constitute the closest prior art for assessing inventive step.

1.3 Thus, document D1 shows the largest number of similarities with the claimed subject-matter and this document represents the closest state of the art.

1.4 According to the respondent, the technical problem is seen as the provision of an improved pharmaceutical formulation with a reduced variability of its pharmacokinetic parameters, i.e a reduced variability of AUC and C_{max}.

1.5 The respondent refers to example 43 of the patent to support said effect, and also to the data of D28.

1.5.1 Example 43 and D28 refer to the compositions of examples 18 and 22 of the contested patent and provide a comparison as to the variability in AUC and C_{max} vis-à-vis the prior art Fumaderm® formulation. The Fumaderm® formulation is given in paragraph [0004] of the contested patent, and appears to correspond to the

composition of example 5 of D10, and is very different from the tablet disclosed in example 16 of D1. Said comparative tests are therefore irrelevant and cannot serve as the support for the existence of any technical effect over D1.

Hence, the contested patent and D28 do not provide any evidence that the technical problem as alleged by the respondent has been solved. It is thus not possible to establish the existence of an improvement over the prior art.

Consequently, in the absence of any experimental evidence, the presence of an improvement as to a reduced variability of its pharmacokinetic parameters, i.e a reduced variability of AUC and C_{max}. has not been credibly demonstrated and the technical problem must be reformulated as the provision of an alternative composition. This was also the position of the appellant.

1.6 Since the problem consists in the provision of an alternative composition, it belongs to the normal activity of the skilled person to accomplish routine modifications, such as the modification of the amount of enteric coating. The choice of a weight coating level of 1-5-3.5% is considered as an arbitrary choice in the absence of any demonstrated effect linked thereto. There is also no technical prejudice as to use an enteric coating at such low level.

Moreover, D1 discloses that the pH-controlled release provided by the enteric coating should be such that at the most 5% by weight of the fumaric acid ester should be released within the first two hours, which corresponds also to the desired release profile of the

claimed invention (see par. [0132] or Figure 1 of the contested patent and see pages 16-21 of D1). The skilled person would therefore adapt the amount of weight coating to reach this desired release profile, including the claimed 1.5-3.5% by weight of the core.

The claimed solution is therefore obvious.

1.7 It follows that the composition of claim 1 of the main request does not involve an inventive step.

2. Auxiliary request 1 - Amendments

Claim 1 of auxiliary request 1 differs from claim 1 as originally filed by the following added features:

a) “an enteric coating, wherein said enteric coating is applied at a level of 1.5-3.5% by weight of the core”;
b) "wherein the rate-controlling agent is a water-soluble polymer".

Feature a) finds an explicit and direct basis in the preferred embodiment of dependent claim 19 as originally filed.
Feature b) finds also an explicit and direct basis in the preferred embodiment of dependent claim 5 as originally filed.

The requirements of Article 123(2) EPC are met.

3. Auxiliary request 1 - Sufficiency of disclosure

Sufficiency of disclosure has been objected as to:
a) The enteric coating,
b) The rate-controlling polymer,

c) The erosion matrix tablet and the release by erosion.

As regards point a), a skilled person understands what is meant by enteric coating which is a commonly known type of coating. The skilled person would also be able to identify an enteric coating in view of the description of the contested patent (see description of the specification, paragraph [0129] and examples) and to adapt its weight level. Examples 27a, 27b, 28, 29a, or 29b disclose for instance tablets which are enteric coated at a weight ratio as claimed. Moreover, the experimental tests D42, which have been submitted by the party as of right, show the preparation of tablets coated with 1.0%, 1.8%, 3.5%, 4.5% and 6% by weight the tablet core of enteric coating; said tests confirm that coating a tablet by an enteric coating in a specific weight ratio is repeatable and of routine nature.

As regards point b), the description and the examples provide sufficient teaching as to the nature and amounts of the rate-controlling polymer (see the description of the specification, paragraph [0077]-[0090] and the examples).

As regards point c), erosion matrices are commonly known in the field of pharmacy, as confirmed for instance by the teaching of D1 (see D1, page 10, line 8). Even if the functional feature present in claim 1 appears to be very broad, the skilled person would not have any difficulty to repeat the claimed invention and to check its release; the erosion is seen as a degradation or erosion of the matrix which allows a release of the fumaryl acid ester.

4. Auxiliary request 1 - Novelty

Example 16 of D1 was mentioned as possibly novelty-destroying disclosure. As mentioned above for the assessment of inventive step of claim 1 of the main request, Example 16 of D1 discloses a tablet comprising an enteric coating at a level of about 6.5% by weight of the tablet core. Hence, said example cannot be novelty-destroying for the subject-matter of claim 1.

5. Auxiliary request 1 - Inventive step

5.1 Claim 1 of auxiliary request 1 has been amended in comparison to claim 1 as granted by the feature "wherein the rate-controlling agent is a water-soluble polymer".

5.2 D1 remains the closest prior art and discloses in example 16 a composition which comprises ethylcellulose, a water-insoluble polymer, as rate-controlling polymer, and around 6% by weight of an enteric coating. This document does therefore not disclose the presence a water-soluble rate-controlling polymer in the tablet core combined with an enteric coating at a level of 1.5-3.5% by weight of the tablet core.

5.3 The respondent maintained that the problem to be solved was the provision of an improved pharmaceutical formulation with a reduced variability of its pharmacokinetic parameters, i.e. a reduced variability of AUC and C_{max}.

The appellant also still maintained that the problem was the provision of an alternative formulation.

5.3.1 As stated above for the main request, Example 43 of the contested patent and D28 do not provide any comparison with D1 and/or evidence that the technical problem alleged by the respondent has been solved. It is thus not possible to establish the existence of an improvement over the prior art on the basis of said example 43 and document D28.

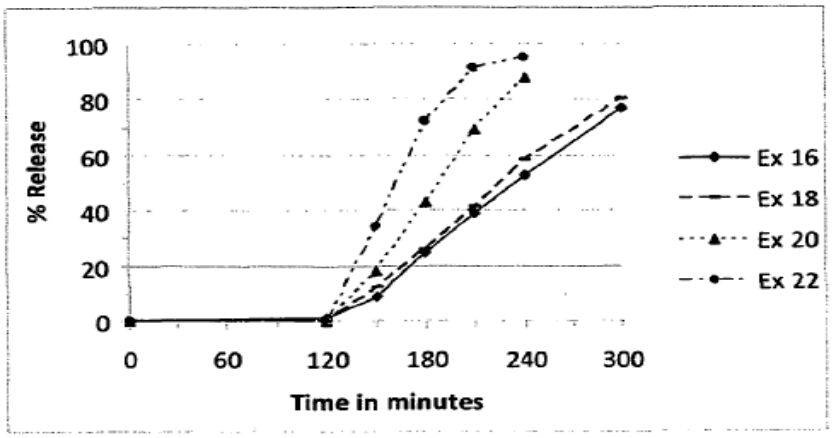
Consequently, as for the main request, the problem as posed by the respondent cannot be the problem to be solved.

5.3.2 In the present case, contrary to claim 1 of the main request which referred generally to a "rate-controlling agent", claim 1 of auxiliary request 1 has been restricted to a water-soluble rate-controlling polymer.

In this respect, the Board notes that Figure 1 of the contested patent, which gives the dissolution profile of the compositions disclosed in examples 16, 18, 20, and 22, shows that the release profile of the compositions was of a zero order when the rate-controlling polymer is a water-soluble polymer, after a delay due to the enteric coating.

In all examples 16, 18, 20 and 22 hydroxypropyl cellulose was used a rate-controlling water-soluble polymer.

Figure 1



On the other hand, the dissolution profile of example 16 of D1 is shown in Figure 2 of the same document, and shows a release profile of an uncoated tablet core of example 16 of D1, which is different from a zero order release.

2/3

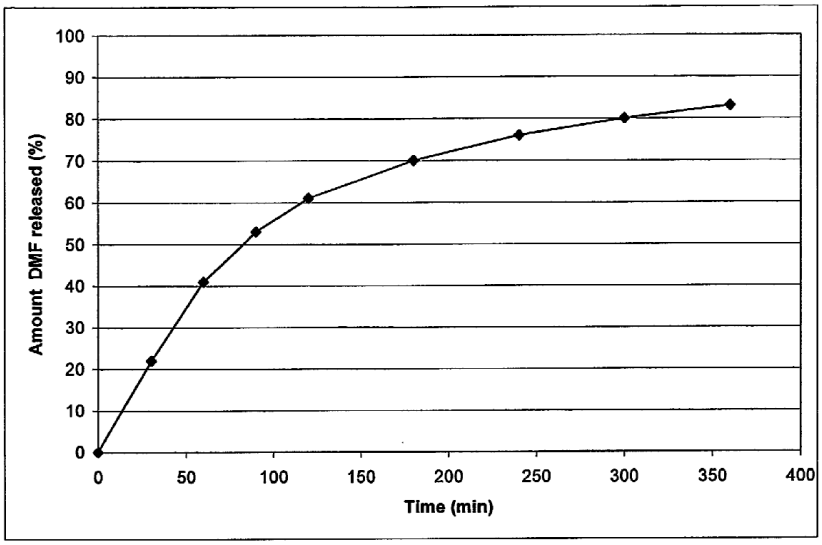


Fig. 2

5.3.3 Hence, it is clear that the distinct nature of the rate-controlling agent shows an effect on the release of the fumaric acid ester from the core tablet.

Accordingly, the technical problem is the provision of a pharmaceutical formulation showing a zero order release.

5.4 It remains to determine whether the combination of a tablet core comprising a water-soluble rate-controlling polymer and an enteric coating at a level of 1.5-3.5% by weight is an obvious solution of this problem.

Figure 2 of D1 shows the corresponding release profile of the tablet core of example 16, which is not a zero order release profile. None of the release profiles disclosed in Figures 1-3 of D1 and corresponding to various formulations such as capsules and tablets, show a zero order release.

There is also no teaching in D1 on how to obtain a core tablet or a final coated tablet showing a zero order release. The use of a water-soluble rate-controlling polymer or of a lower amount on enteric coating was in particular not suggested or disclosed in D1 for this purpose. As reminded by the respondent through its citation D52, the obtention of a formulation with a zero order release is in any case difficult to achieve (see D52, page 293).

Hence, the combination of a thinner enteric coating, which dissolves in principle quicker in the gastrointestinal tract and a water-soluble rate-controlling polymer in the core matrix, in order to obtain a composition providing a zero order release after dissolution of the enteric coating, is neither

disclosed, nor suggested in D1 or in any other document.

Consequently, the skilled person, seeking an alternative to the composition of example 16 of D1, would not have arrived at the technical solutions claimed in auxiliary request 1, namely the combination of an erosion matrix with a water-soluble rate-controlling polymer and a thin enteric coating.

5.5 Accordingly, the subject-matter of claim 1 of auxiliary request 1 is inventive over the prior art.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the Opposition Division with the order to maintain the patent on the basis of the first auxiliary request, filed with letter dated 5 February 2016 and a description to be adapted.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated