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Datasheet for the decision of 30 June 2014

Case Number: T 2458/09 - 3.3.02

Application Number: 02786241.6

Publication Number: 1562573

IPC: A61K31/18, A61K9/58, A61P13/08

Language of the proceedings: EN

Title of invention:
PHARMACEUTICAL PELLETS COMPRISING TAMSULOSIN AND A PROCESS FOR MAKING THE SAME

Patent Proprietor:
Synthon B.V.

Opponents:
Zentiva k.s.
EGIS Gyógyszergyár Nyrt
Astellas Pharma Inc. and Astellas B.V.

Headword:
Pharmaceutical dosage form comprising multiple unit pellets of tamsulosin/SYNTHON

Relevant legal provisions:
EPC Art. 56
RPBA Art. 12, 13

Keyword:
Admissibility of amendments to a party's case (no)
Admissibility of auxiliary request II (yes)
Admissibility of auxiliary request III (no)
Inventive step (no)

Decisions cited:
G 0001/92, T 0952/92

Catchword:

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Case Number: T 2458/09 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 30 June 2014

Appellant: (Patent Proprietor)	Synthon B.V. Microweg 22 6545 CM Nijmegen (NL)
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Representative:	Misander, Henriette Plougmann & Vingtoft A/S Sundkrogsgade 9 DK-2100 Copenhagen Ø (DK)
Respondent 2: (Opponent 2)	EGIS Gyógyszergyár Nyrt Keresztúri út 30-38 1106 Budapest (HU)
Representative:	Stolmár & Partner Blumenstraße 17 80331 München (DE)
Respondents 3: (Opponents 3)	Astellas Pharma Inc. 3-11 Nihonbashi-Honcho 2-chome Chuo-ku Tokyo 103-8411 (JP) and Astellas B.V. Elisabethhof 19 2353 EW Leiderdorp (NL)

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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted on 2 November 2009 revoking European patent No. 1562573 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman U. Oswald
Members: M. C. Ortega Plaza
R. Cramer

Summary of Facts and Submissions

I. European patent No. 1 562 573, based on European patent application No. 02786241.6, which was filed as international patent application published as WO 2004/043449, was granted with twenty claims.

Claim 1 as granted read as follows:

"1. A pharmaceutical dosage form comprising a plurality of pellets, wherein each pellet comprises:

a. a pellet core having a diameter within he range of 0.3-0.9 mm and comprising a tamsulosin hydrochloride, microcrystalline cellulose, a pharmaceutically acceptable water permeable acrylic polymer and water; and
b. an outer layer coat surrounding said core which comprises a pharmaceutically acceptable acid-resistant acrylic polymer, wherein wherein the mass of said outer layer coat, calculated on a dry pellet core basis, is within the range of 2.5-15%; and

wherein the plurality of pellets exhibits a dissolution release profile in simulated gastric fluid using Ph. Eur. basket method at 100 rpm which includes releasing less than 10% of the tamsulosin during the first two hours."

Dependent claim 5 as granted read as follows:

"5. The dosage form according to claim [*sic*] 1-4, wherein the composition of said outer layer coat comprises 25-75 mass% of said acid resistant acrylic polymer, calculated on a dry basis."

Dependent claim 9 as granted read as follows:

"9. The dosage form according to claim [*sic*] 1-8, wherein said coated pharmaceutically pellet exhibits a dissolution release profile in a phosphate buffer of pH 6.8 using Ph. Eur. basket method at 100 rpm which includes releasing 15-45% of the tamsulosin in 30 minutes."

II. Oppositions were filed and revocation of the patent in its entirety was requested, in particular pursuant to Article 100(a) EPC (opponent 1 for lack of novelty and opponents 1 to 3 for lack of inventive step). Moreover opponents 3 raised under paragraph 3.5 of their grounds for opposition dated 19 January 2007 objections against the reproducibility of the claimed subject-matter (Article 100(b) EPC).

III. The following documents were cited *inter alia* during the opposition and appeal proceedings:

D1 Several pages of a document relating to the approval package for "Application No. 0220579, Trade Name Flomax 0.4 mg capsules" before the FDA, US centre for drug evaluation and research

D3-D3a Leaflet Omnic^{R} (Yamamouchi) 0,4 mg long-acting capsules in the original Danish language and in the English translation

D4 English translation of Czech summary of product characteristics for Omnic^{R}, the Czech Medicines Agency, 14 April 1998

D6a to D6g Technical evidence and experimental reports submitted by opponent 1 during opposition proceedings

concerning the commercial product Omnic^{R} sold in the Czech Republic

D7 Physician's Desk reference, 1999, Flomax^{R}

D8 US 4772475

D10bis Handbook of Pharmaceutical Excipients, Pharmaceutical Press, third edition, 2000, edited by A.H. Kibbe

D11 EP-A-0080341

D21 Rote Liste 2002, reference 82 173, Omnic^{R} 0,4 [mg] Retard capsules

D24 Lehman et al., Pharmazeutische Verfahrenstechnik Band 1, 133-122, 1984
D24a Enlarged figure 7 of document D24

D25 Experimental data concerning granule size in Omnic^{R} submitted by opponents 3 with their letter dated 19 January 2007

D27 Memorandum by Mr Ariaans dated 14 August 2007

D29 Additional technical information concerning "Dissolution data" of Omnic^{R} 0.4 mg cps. submitted by opponent 1 with its letter dated 5 March 2009

D34 Copy of a document entitled "Function of eudragit in TSL pellets" by Mr Ariaans dated 19 November 2008, submitted by Synthon B.V. in connection with the utility model FI5842; (D34 was filed by opponent 1 on 9 July 2009, during opposition proceedings, as document D31)

D35 Declaration of Mr Elffrink dated 19 February 2010

D36 Überzogene Arzneiformen, H. Bauer, 1988, pages 74, 75, 137

D38 Handbook of Pharmaceutical Excipients, 1994, page 519

D39 Handbook of Pharmaceutical Excipients, 1994, page 63

D40 "*Declaration instead of oath*" of Mr de Jong dated 19 July 2010

D40a C.V. of Mr de Jong filed with respondents' 3 letter dated 23 June 2014

D41 Lehrbuch der pharmazeutischen Technologie, 1987, pages 178-179

D42 Hunnius Pharmazeutisches Wörterbuch, 1998, pages 258-259

D43 M. Morihara et al., Drug Development and Industrial Pharmacy, 2(86), 655-662, 2002

IV. The present appeal lies from a decision of the opposition division revoking the patent (Article 101(3) (b) EPC).

V. The decision under appeal is based on the main request and auxiliary request I, both filed at the oral proceedings before the opposition division.

Claim 1 of the main request differs from claim 1 as granted in that the following passage has been added after the expression "during the first two hours" at the end of the claim:

", and exhibits a dissolution release profile in a phosphate buffer of pH 6.8 using Ph. Eur. Basket method at 100 rpm which includes releasing 15-45% of the tamsulosin in 30 minutes."

Claim 1 of auxiliary request I reads as follows:

"1. A pharmaceutical dosage form comprising a plurality of pellets, wherein each pellet comprises:

a. a pellet core having a diameter within he range of 0.3-0.9 mm and comprising 0,05-5.0% mass of tamsulosin hydrochloride, 50-95% mass of microcrystalline cellulose, 2.5-25% mass of a pharmaceutically acceptable water permeable acrylic polymer [,] 2-10% mass of water; and
b. an outer layer coat surrounding said core which comprises a pharmaceutically acceptable acid-resistant acrylic polymer, wherein the mass of said outer layer coat, calculated on a dry pellet core basis, is within the range of 2.5-15%; and

wherein the plurality of pellets exhibits a dissolution release profile in simulated gastric fluid using Ph. Eur. basket method at 100 rpm which includes releasing less than 10% of the tamsulosin during the first two hours, and exhibits a dissolution release profile in a phosphate buffer of pH 6.8 using Ph. Eur. Basket method at 100 rpm which includes releasing 15-45% of the tamsulosin in 30 minutes."

VI. The opposition division considered that the subject-matter claimed in the main request was novel over the cited prior art, which also included the marketed product Omnic^{R} (a product commercialised in Europe by Yamanouchi at the effective filing date of the patent in suit). According to the opposition division "*it was undisputed*" that "Omnic^{R} was available to the public before the relevant priority date of the patent in suit" (this being in fact acknowledged in paragraph [0003] of the patent in suit).

In the opposition division's view "the subject-matter of claim 1 of the main request differed from Omnic^{R} at least in the mass of the outer layer coat". In this context, the opposition division considered that "*the data provided by opponent 1, especially D6c and D6d, seemed to be inconsistent and therefore not reliable*".

As regards inventive step, the opposition division considered that the product Omnic^{R} represented the closest prior art. The difference relied on the mass amount of the outer layer coat since the product Omnic^{R} fulfilled the dissolution profile requirements defined in claim 1. The opposition division defined the problem to be solved as "*to provide an alternative coated tamsulosin pellet having good release characteristics*". In the opposition division's opinion the claimed subject-matter related to an obvious alternative, since no effect could be linked to the "*slight*" increase in the mass of the outer layer coat, and thus it was "*an arbitrary modification resulting in an obvious alternative*". The opposition division also developed an alternative approach, where document D8 was defined as closest prior art, and also reached a negative conclusion on inventive step for the subject-matter

claimed in the main request in view of the content of documents D8 and D24.

As regards auxiliary request I, the opposition division considered that the invention claimed was sufficiently disclosed in the patent in suit. In particular, the opposition division cited paragraph [0017] which explained the term "dried core" as being one that has been substantially dried and has a residual solvent content (such as water) of 15% or less. Additionally, in the opposition division's opinion, the subject-matter claimed in auxiliary request I was novel, but lacked an inventive step for reasons analogous to those for the main request.

VII. The patentee (appellant) lodged an appeal against the opposition division's decision and also filed grounds thereto. With its statement of grounds of appeal the appellant filed the declaration of Mr Elffrink (D35) containing several annexes with experimental evidence. The appellant maintained its main request and auxiliary request I, both filed at the oral proceedings before the opposition division.

VIII. Respondent 2 filed with its letter dated 12 July 2010 a response to the grounds of appeal. As an annex thereto it filed document D36 and three pages of some enlarged reproductions of document D1. Respondent 2 argued that the subject-matter of the main request and auxiliary request I lacked an inventive step and gave reasons thereto.

IX. With a letter dated 13 July 2010 respondent 1 filed a response to the grounds of appeal. It filed as an annex thereto document D38 (renumbered by the board), and document D39 (renumbered by the board). Respondent 1

contested inventive step of the subject-matter claimed in the main request and auxiliary request I.

X. With a letter dated 22 July 2010 respondents 3 filed a response to the appeal. They filed as an annex thereto a declaration signed by Mr de Jong (renumbered by the board as D40), and documents D41 to D43 (renumbered by the board). Respondents 3 contested the inventive step of the subject-matter claimed in the main request and auxiliary request I.

Moreover, respondents 3 contested sufficiency of disclosure of claim 1 of auxiliary request I, in accordance with their submissions before the opposition division, i.e. the fractions specified in claim 1 of auxiliary request I were "to be calculated" on a dry pellet core and the claim did not specify what a dry pellet was. Thus, the amount of residual water (which could be 15% or less according to the description) significantly influenced the result of the calculation.

XI. With a letter dated 16 July 2012 signed by Mr Motsch the EPO was informed that the former representative of respondent 2 had died.

XII. With a letter dated 9 November 2012 the new representatives for respondent 2 informed the EPO that they had taken over representation for opponent Egis Gyógyszergyár Nyrt. With their letter dated 19 November 2012 they filed a "General Power of Attorney" signed on 30 October 2012.

XIII. A communication of the board pursuant to Article 15(1) RPBA was sent on 8 April 2014 as an annex to the summons to oral proceedings. In said communication the board made a summary of the case according to the state

of the file and expressed its preliminary opinion on some of the aspects which required particular attention. The board also annexed some printouts from www.astellas.com (eight pages).

XIV. With a letter dated 15 April 2014 respondent 1 announced that it would not be attending the oral proceedings scheduled for the 30 June 2014.

XV. With its letter dated 30 May 2014 respondent 2 contested for the first time during the appeal proceedings sufficiency of disclosure of the subject-matter claimed in claim 1 of the main request and novelty of the subject-matter claimed. Respondent 2 did not file with said letter any further experimental evidence or prior-art documents.

XVI. With a letter dated 23 June 2014 respondents 3 submitted a CV of Mr de Jong and a coloured copy of Fig. 14 of D6b.

XVII. On 30 June 2014 oral proceedings took place in the absence of respondent 1. In the course of the oral proceedings the appellant filed two auxiliary requests (auxiliary requests II and III).

Claim 1 of auxiliary request II differs from claim 1 of auxiliary request I in that the following expression can be read between the word "comprises" and the expression "wherein the mass" in feature b:

"25-75 mass % of acceptable acid-resistant acrylic polymer calculated on a dry basis".

Claim 1 of auxiliary III differs from claim 1 of auxiliary request II in that the following expression

has been added between the expression "permeable acrylic polymer" in feature a:

"which is an Eudragit L polymer".

XVIII. The respondents' arguments, as far as relevant for the present decision, may be summarised as follows:

a) *Admission of amendments to respondent 2's case filed with its letter of 30 May 2014*

Respondent 2 submitted that the representative who had filed the response to the appeal had died. Therefore, as new representatives for respondent 2 they could not have filed a complete case with the response to the statement of grounds of appeal.

Respondent 2 further submitted that novelty was not a fresh ground for opposition. Moreover, opponents 3 had filed Article 100(b) EPC as a ground for opposition in point 3.5 of their statement of grounds for opposition dated 19 January 2007. Therefore, the objections raised with respondent 2's letter of 30 May 2014 did not amount to the introduction of fresh grounds for opposition within the sense of Enlarged Board of Appeal decision G 1/95, OJ EPO, 1996, 615.

When asked by the board about the reasons for the belatedness of the objections raised for the first time with its letter of 30 May 2014, the representative of respondent 2 answered that the late filing was due to the fact that it had only taken over representation after the death of the former representative for respondent 2.

b) *Admission of auxiliary requests II and III filed in the course of the oral proceedings before the board*

Respondents 2 and 3 contested the admission of auxiliary request II since it had been late filed. Moreover, the request was not clearly allowable; in particular, the subject-matter claimed was not inventive.

Respondents 2 and 3 contested the admission of auxiliary request III. Auxiliary request III should have been filed much earlier. Its admission would compromise the fairness of the proceedings. The appellant (patentee) was alone responsible for the definitions of the subject-matter it claimed, which as repeatedly pointed out by the respondents throughout the oral proceedings was much broader than what had been actually exemplified.

c) *Inventive step (Article 56 EPC)*

Respondent 1 had contested in writing the inventive step of the subject-matter claimed in claim 1 of the main request and auxiliary request I. In particular, the commercial product Omnic^{R} was the closest prior art. In the light of what the skilled person knew from the leaflets of Omnic^{R} 0.4mg capsules and the routine experimentation on the public available Omnic^{R} capsules (*inter alia* D6a to D6g and D29 and pellets dissolution data provided by opponents 3 on 19 January 2007), the problem to be solved was the provision of an alternative to the known product. The solution was obvious in the light of the cited prior art.

Respondents 3 submitted that the opposition division had correctly concluded that the subject-matter claimed

in claim 1 of both the main request and auxiliary request I lacked an inventive step. The commercial product Omnic^{R}, which corresponded to Flomax^{R} in the USA, represented the closest prior art. The product Omnic^{R} (see also the leaflet D3) was acknowledged as relevant prior art in the patent in suit. In this context respondents 3 cited Enlarged Board of Appeal opinion G 1/92, OJ EPO 1993, 277 and the experimental data reports D6a to D6g and D29, which had been filed by respondent 1, showing that the product Omnic^{R} was analysable and reproducible. Respondents 3 further submitted that document D34, which concerned a technical report by Mr Ariaans for Synthon B.V., confirmed that the appellant had been able to have access to and analyse the product Tamsulosin 0.4mg retard capsules marketed by Yamamouchi (now Astellas). Board of appeal decision T 472/92, OJ EPO 1998, 161, related to a different situation where a product was sold only once or twice and thus was not easily accessible for the patentee in that particular case.

The question to be answered was what the skilled person could establish the composition and constitution of the product Omnic^{R} to be. The answer could be found in the light of the evidence filed mostly by respondent 1, *inter alia* documents D1, D3, D6a to D6g, D7, D21, D29 and D34.

If document D1 was incomplete, it was due to the fact that the skilled person at a date earlier than the priority date of the patent in suit would not have had access to the full authorisation dossier of Flomax^{R} before the FDA. That dossier was incomplete and contained blanked spaces in order to safeguard the trade secrets of Flomax^{R}'s manufacturer. Since the skilled person faced an incomplete disclosure in

document D1 he would have taken the commercial product Omnic^{R} and analysed it. The list of components appearing on page 281, section 6, of document D1 contained a blanked space for one of the components, followed in the next line by: "composed of methacrylic acid copolymer...". The skilled person would have read this component as being some kind of Eudragit^{R} polymer from Röhm Pharma. Table 2 on page 67 of document D1 should be read in the light of the list of components on page 281, having in principle the same order for the components. Therefore, the skilled person would conclude that Eudragit^{R} would be at the core of the granules. The next blanked space on Table 2 corresponded to one component of the granule coating. However, on page 6 of document D1 it was stated that the outer granule coating provided acid resistance. The skilled person would consider it to be probable that Eudragit^{R} polymer would be present in the core and in the enteric coating. Document D24 reflected the general knowledge of the skilled person about poly(meth)acrylic polymers in pharmacy. Document D24, page 121, left-hand column, lines 14 to 20, taught that Eudragit polymers could be employed in the same granules during their preparation by means of wet granulation and for their coating. Thus, the skilled person was aware that Eudragit^{R} polymers could be present at the same time in both the core and the outer coating of granules and thus he would start with this hypothesis when experimentally investigating the commercial product.

Respondents 3 also submitted that in their view document D34 confirmed their own findings that the thickness of the outer layer coat was the only difference from the pellets in Omnic^{R} 0.4 mg capsules.

Respondents 3 also referred to the declaration D40.

In addition to the submissions of respondents 1 and 3, respondent 2 developed an alternative problem-solution approach. Document D8 was the closest prior art and the problem to be solved was the provision of an alternative dosage form. The solution was obvious in the light of the content of document D8, considering the content of document D11, which was explicitly cited in document D8, and/or in combination with the teaching in document D24.

As regards the appellant's submissions about the thickness and function of the outer layer coat, respondents 2 and 3 commented on the breadth of the definitions given in claim 1 and compared them to the specific disclosure illustrated by the examples. In particular they pointed to the ranges of the diameter of the pellet core and the ranges of the mass amount of the outer layer. Therefore, the claim also included certain variations in relation to the actual thickness of the coating containing the enteric acrylic polymer and its function.

The respondents disagreed that the patent in suit disclosed that the dissolution release profiles were to be measured subsequently.

The respondents further submitted the following. The passage on page 121 of D24 concerned a general teaching which was not restricted to pH-independent Eudragit retard.

The skilled person following the general teaching in document D24 was able to perform a routine fine-tuning to achieve similar dissolution profiles to those of the closest prior-art product. That a routine fine-tuning

in relation to the amount of coating was made for achieving the targeted dissolution profile in simulated gastric acid was also shown in paragraph [0047] of the patent in suit. There was no direct correlation between the structural and functional features in the claim.

Moreover, the objections of lack of inventive step for claim 1 of the main request applied by analogy to claim 1 of auxiliary requests I and II. The amounts of the components were similar to those in the Omnic^{R} pellets and broadly defined. They were not associated to any particular effect. The proportions were also variable depending on the residual solvent content in the dry pellet core, and the calculations of the water content performed by respondent 1 according to the TGA method were reliable.

The definitions concerning the amount of acid-acrylic polymer in the coating of claim 1 of auxiliary request II overlapped with the recommended values in document D24.

XIX. The appellant's arguments, as far as relevant for the present decision, may be summarised as follows:

a) *Admission of amendments of respondent 2's case filed with its letter of 30 May 2014*

The appellant stated that although the amendments to a party's case were not conform with the legal provisions they did not expressly contest the admission of respondent 2's new objections since they had clear answers to all the objections.

b) *Admission of auxiliary requests II and III filed in the course of the oral proceedings before the board*

Auxiliary request II was first filed as a reaction to the discussions during the oral proceedings before the board. The amendments introduced were simple and easy to handle.

Auxiliary request III was filed in order to sort out any inconsistency between the appellant's submissions and the claim's wording in relation to the definition of the acrylic polymer in the pellet core.

c) *Inventive step (Article 56 EPC)*

The arguments in relation to Flomax^{R} and Omnic^{R} products were *ex-post-facto*. Moreover, what had been made available to the public did not correspond to a full disclosure of the structure and composition of the commercial product. In this context it cited decision T 952/92, OJ EPO 1995, 755. Document D1 was completely unreliable since it was incomplete and contained several inconsistencies. The skilled person would not have been able to extract any valuable information about the actual structure and constituents of the pellets since not only essential constituents had been blanked out but also their amounts (which had a bearing in discovering their function). The skilled person would not have made such a guess as submitted by respondents 3 in relation to document D1. Moreover, the only patent document cited in document D1 concerning dosage forms was document D8. Document D8 disclosed multiple unit pellets without enteric coating. Document D8 did not help to fill the gaps of document D1. On the contrary, it opened further questions concerning for instance the presence and amount of water.

As regards the product Omnic^{R} and the experimental results on file (mostly produced by respondent 1 although respondents 3 were the manufacturers of the commercial product) even if some Eudragit had been detected in respondent 1's experiments as being in the coating, the mere presence of some Eudragit did not prove that it provided the function of an enteric coating to the pellets. The pellets of the known products contained Eudragit in their core and did not have an enteric coating. The appellant's experimental results in D35 showed that calcium stearate and talc were the substances on the outer surface of the pellets. Calcium stearate and talc were used in pharmacy not only as lubricants and adjuvants but also for coating. In relation to calcium stearate the appellant cited document D42. The appellant further submitted that respondent 1's experimental data in D6d showed that after treatment with acetone the external surface layer partly remained. This was an indication that Eudragit did not form the outer layer coat. The Eudragit measurements performed in the pellets of Omnic^{R} following treatment with acetone could serve to assess the amounts of Eudragit in total but did not allow to differentiate coating/core.

Document D34 made presumptions and not only confirmations, in particular in relation to the outer surface layer and its constituents. In this context the appellant cited document D27 which showed that the external layer of the Omnic^{R} pellets was very thin and therefore not able to perform the function concerning an enteric coating, or to be responsible for the dissolution release profile in gastric acid.

The appellant also submitted that the dissolution release profiles were obtained by *in vitro* experiments

at two different pH values (simulated gastric fluid and pH 6.8), but in order to reproduce behaviour in the gastrointestinal tract they were to be measured subsequently. Later on in the discussion the appellant explained that the amount of outer coat comprising the acid-resistant acrylic polymer was chosen so that the dissolution profile at simulated gastric acid was attained. In physiological conditions the outer layer coat of granules disappeared first. The first test to be performed was that on simulated gastric fluid. There was a functional relationship between the structural and functional features in the claim.

Additionally, considering the teaching in document D24 and the particle size, the thickness of the surface layer of the Omnic^{R} pellets (even considering, for the sake of argument, that it contained a Eudragit acrylic polymer) was clearly insufficient to qualify as an enteric coating.

Moreover, the surface layer of calcium stearate and talc could have been used to reduce water permeability in the known pellets.

Therefore, document D8 represented the closest prior art since it was a more promising starting point. Document D8 concerned Tamsulosin dosage forms with multiple unit pellets which did not have an enteric coating. The pellets in document D8 contained in their core an enteric acrylic polymer of the Eudragit type. Document D11, which was cited in document D8, went against the teaching of document D8 since the granules had an enteric coating. The mention made in document D8 of the materials in document D11 did not mean that document D8 disclosed pellets having simultaneously an enteric core and an enteric coating.

The problem to provide an alternative dosage form was unexpectedly solved by means of an enteric acrylic polymer simultaneously in the core and the coating of the pellets. The skilled person would not have considered this as an obvious alternative since according to the teaching in document D8 one option excluded the other. Moreover, the passage on page 121 of document D24 only applied to the case in which the core contained a polymer such as Eudragit retard as defined in figure 2, i.e. an acrylic polymer which was not acid-resistant.

The skilled person would not have been able to predict the effect in the dissolution release profiles of the addition of an enteric coating to pellets containing in their core an enteric material. Moreover, Tamsulosin was not an acid-sensitive substance.

Document D40 was not available to the skilled person and did not reflect the knowledge of the skilled person. Therefore it should be disregarded.

The appellant stated that the arguments it had submitted for claim 1 of the main request applied *mutatis mutandis* to each claim 1 of auxiliary requests I and II. Moreover, the definitions in claim 1 of auxiliary request II matched the discussions concerning the functional features.

XX. The appellant (patent proprietor) requested that the decision under appeal be set aside and that the patent be maintained in amended form on the basis of the main request, or, alternatively, on the basis of auxiliary request I, both requests filed at the oral proceedings before the opposition division, or, on the basis of

auxiliary requests II or III filed during the oral proceedings on 30 June 2014 before the board.

The respondents (opponents) requested that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible.

2. The oral proceedings before the board took place in the absence of respondent 1, who was dully summoned but decided not to attend, as announced with its letter dated 15 April 2014.

As stipulated by Article 15(3) RPBA, the board shall not be obliged to delay any step in the proceedings, including its decision, by reason only of the absence at the oral proceedings of any party duly summoned who may then be treated as relying only on its written case.

3. Amendments to respondent 2's case filed with its letter dated 30 May 2014

Respondent 2's response to the appeal was filed with a letter dated 12 July 2010, which was received at the EPO on the same day (Article 12(1)(b) RPBA).

The new representatives for respondent 2 informed the EPO on 9 November 2012 that they had taken over the representation of respondent 2. With EPO Form 2575 they were informed that the amendment concerning the appointment of a new representative had been registered as from 22 November 2012, i.e. almost one and a half

years before the date of the oral proceedings before the board.

Respondent 2's letter dated 30 May 2014 (i.e. one month before the oral proceedings before the board), which was filed electronically on the same day, contains substantive amendments to its case since for the first time in appeal proceedings it contested sufficiency of disclosure of claim 1 of the main request and novelty of the subject-matter claimed in claim 1 of the two requests on file at that date.

Moreover, none of the respondents had contested the novelty of the subject-matter claimed in the main request and auxiliary request I in their replies to the appeal (Article 12(1)(b) RPBA), and only respondents 3 had contested claim 1 of auxiliary request I under Article 83 EPC in their reply to the appeal. Therefore, respondent 2's submissions filed with its letter of 30 May 2014 concerning objections of lack of novelty against the subject-matter claimed in the main request and auxiliary request I, and of lack of sufficiency of disclosure against the subject-matter of claim 1 of the main request raised new and complex issues for the first time at appeal proceedings shortly before the date fixed for the oral proceedings. Admission of the amendments to respondent 2's case filed with its letter of 30 May 2014 would have required adjournment of the oral proceedings, contrary to the need for procedural economy (Article 13(1) and (3) EPC).

Additionally, the amendments to respondent 2's case could and should have been filed earlier during the almost one-and-a-half-year period after the new representatives had taken over.

Moreover, the board's communication sent as an annex to the summons for oral proceedings on 8 April 2014 under Article 15(1) RPBA contained a summary of the case according to the state of the appeal file at that date and a preliminary opinion in relation to some of the issues discussed in the written file. According to the state of the file at the time of said board's communication, novelty of the subject-matter claimed was no longer contentious, and an objection of insufficiency of disclosure had been raised by respondents 3 only against the subject-matter in claim 1 of auxiliary request I.

Therefore, the substantive amendments to respondent 2's case filed with its letter dated 30 May 2014 are not justified by the board's communication sent as an annex to the summons either (Article 12(c) RPBA).

Consequently, the amendments to respondent 2's case are not admitted into the proceedings (Articles 12 and 13 RPBA).

4. Admission of auxiliary requests filed at the oral proceedings before the board

4.1 With its statement of grounds of appeal the appellant maintained the two requests serving as the basis for the opposition division's decision, i.e. the main request and auxiliary request I filed at the oral proceedings before the opposition division.

The appellant also chose not to file any further auxiliary requests as a precautionary measure in reaction to the respondents' replies (dated 12, 13 and 22 July 2010) to its grounds of appeal.

4.2 While Article 12(1)(c) RPBA provides that appeal proceedings shall be based on, in addition to the grounds of appeal and reply, any communication sent by the board and any answer thereto, this does not mean that the appellant has an unlimited right to file amended sets of claims as a reply to a board's communication, or that any set of claims filed after the board expresses a preliminary opinion either in written form before the oral proceedings or in oral form during those proceedings will automatically be admitted into the proceedings.

Article 13(1) RPBA provides that any amendment to a party's case after it has filed its grounds of appeal or reply may be admitted and considered at the board's discretion, and that discretion shall be exercised in view of *inter alia* the complexity of the new subject-matter submitted, the current state of the proceedings and the need for procedural economy. Additionally, the right of all parties to fair proceedings and equity has to be considered in *inter partes* appeal proceedings.

Additionally, Article 13(3) RPBA provides that amendments sought to be made after oral proceedings have been arranged shall not be admitted if they raise issues which the board or other party or parties cannot reasonably be expected to deal with without adjournment of the oral proceedings.

4.3 During the oral proceedings before the board, auxiliary request II was filed after the discussion concerning claim 1 of the main request and claim 1 of auxiliary request I. In particular, it was filed after the discussion of the subject-matter in claim 1 of auxiliary request I. There had been a discussion of the possible bearing the structural features had on the

functional features in said claim. The discussion about the existence of a functional link between the structural and the functional definitions in each claim 1 took place for the first time at the oral proceedings before the board and auxiliary request II was filed as a direct reaction thereto.

Additionally, the amendments introduced in auxiliary request II did not amount to a situation of fresh case and could be dealt with without postponement of the oral proceedings.

The respondents argued that auxiliary request II should not be admitted into the proceedings since it was not clearly allowable, due not only to formal requirements but also for lack of inventive step.

Whether an amended claim is not clearly allowable is one criterion for deciding on the admission of late-filed requests. However, the criterion of an amended claim not being clearly allowable does not include an in-depth assessment of inventive step.

Additionally, the respondents did not request an adjournment of the oral proceedings to prepare their position on the amendments introduced in auxiliary request II and the debate did not require lengthy discussions.

Therefore, auxiliary request II is admissible.

4.4 After announcing the admission of auxiliary request II the board discussed with the parties claim 1 of auxiliary request II.

Before closing the debate for all requests at the oral proceedings the board indicated that contrary to the appellant's submissions throughout the oral proceedings, the "pharmaceutically acceptable water permeable acrylic polymer" in feature "a" of claim 1 did not necessarily have to be acid-resistant (the board also cited paragraph [0015] of the patent in suit).

The filing of auxiliary request III was made in order to overcome any inconsistencies between the claim's wording and the appellant's submissions. However, the wording a patent proprietor chooses for the subject-matter claimed is within its sole responsibility. Moreover, the patent proprietor must be aware of the scope for which it has sought protection, in particular in the light of the definitions it has given in the description of its patent.

Additionally, throughout the oral proceedings the board had repeatedly signalled that the subject-matter claimed in each claim 1 had to be assessed in its broadest technically meaningful sense.

As regards the claim's construction, respondents 2 and 3 had insisted during the course of the oral proceedings that the subject-matter claimed in the main request and auxiliary request I was very broad in comparison to the pharmaceutical dosage forms and formulations illustrated by the examples in the patent in suit, and that the structural features in each claim 1 could not be separately correlated with the functional features.

It was as a reaction to these discussions that the appellant filed auxiliary request II at the oral

proceedings. It did, however, not submit any further auxiliary requests at that stage.

Auxiliary request III could and should have been filed earlier during the appeal proceedings. Moreover, admission of auxiliary request III at such a very late stage would have compromised the fairness of the proceedings.

The appellant submitted that it did not consider it to be necessary to file such a request earlier, since the opposition division was of the opinion that the polymer in feature "a" was the same as the polymer in feature "b". However, this does not discharge the appellant from its responsibility to provide arguments that are reflected by the claim's language. Moreover, claim 1 of each of the requests before the opposition division encompasses two options: either that the polymer in feature "a" is acid-resistant, or that it is not. Therefore, for the opposition division's decision to be substantiated it sufficed that one of the options encompassed by the claims was found to lack an inventive step.

Additionally, the opposition division's findings did not deprive the appellant of the opportunity of filing earlier in the appeal proceedings further auxiliary requests as a precautionary measure. The appellant did not need to wait for the outcome of the discussions at the oral proceedings before the board in relation to the main request and auxiliary requests I and II before filing auxiliary request III.

Consequently, auxiliary request III is not admitted into the proceedings (Articles 12 and 13 RPBA).

5. Claims' construction

5.1 Main request

5.1.1 Claim 1 of the main request relates to a controlled-release dosage form of the active drug tamsulosin hydrochloride, the dosage form comprising a plurality of pellets. The pellets in the pharmaceutical dosage form claimed are defined by means of structural and functional features.

5.1.2 The features defined in "a" in claim 1 require that the pellet core comprises tamsulosin hydrochloride, microcrystalline cellulose, a pharmaceutically water permeable acrylic polymer and water. Moreover, the pellet core has a diameter within the range of 0.3-0.9 mm.

The pharmaceutically acceptable water-permeable acrylic polymer present in the core does not have to be acid-resistant. This point is confirmed in paragraph [0015] of the patent in suit which states "The acrylic polymer in the core serves as a binder and a release-controlling agent. Preferably, the polymer is an acid-resistant acrylic polymer, which releases tamsulosin dependent upon the pH". This is also confirmed in paragraph [0020], lines 33 to 34, which states that "In a particular aspect of the invention, the "acrylic polymer" of the pellet used for the manufacturing of the pellet core is advantageously identical with the "acid-resistant acrylic polymer" of the pellet coating". Thus, claim 1 encompasses two options for the acrylic polymer in the core: (i) that it is acid-resistant (for instance being the same acrylic polymer as that employed in the outer layer coat); and (ii) that it is not acid-resistant.

The two examples in the patent in suit relate to pellets in which both the water-permeable acrylic polymer in the core and the acid-resistant acrylic polymer in the outer layer coat are the same acrylic polymer, namely Eudragit^{R} L 30 D-55. Thus, the examples illustrate the case in which the acrylic polymer in the pellet core is acid-resistant. However, the examples cannot serve to artificially restrict the subject-matter claimed, which has to be read in its broadest technically meaningful sense, which is confirmed in the patent in suit by paragraph [0015] of the description.

5.1.3 The features defined in "b" in claim 1 require that there is an outer layer coat surrounding the core defined in "a". The outer layer coat comprises a pharmaceutically acceptable acid-resistant acrylic polymer. The mass of said outer layer coat, calculated on a dry pellet basis, is defined in claim 1 as being within the range of 2.5-15%. However, claim 1 does not require that the outer layer coat be constituted only by the acid-resistant acrylic polymer. In paragraph [0020] of the patent in suit it is stated that "The outer **surface** layer can additionally contain other acid-resistant polymers,..., as well as other pharmaceutically acceptable excipients" (emphasis added). Moreover, calcium stearate and talc are explicitly named as ingredients of the "pellet coating" in the examples of the patent in suit, and thus they form part of the options for further ingredients in said outer layer coat surrounding the pellets; whether or not they are on the outer "surface" will depend on the manufacturing process.

5.1.4 As regards the functional features which have to be fulfilled by the pellets, they concern dissolution

release profiles *in vitro* which are to be measured at two different pH values: simulated gastric fluid and a phosphate buffer of pH 6.8.

In general terms, claim 1 requires that the dissolution release profiles are attainable by the pellets. Additionally, there is an interrelationship between the variations possible for the different structural elements characterising the pellets and their impact in attaining the functional definitions. In particular, it is generally known by the skilled person (as shown by document D24, page 120, middle column, paragraph entitled "Teilchengröße und Lackbedarf") that there is a relationship between the thickness of an acid-resistant acrylic polymer coat and the actual diameter of the spherical granules/pellets when providing an enteric coating to individual granules/pellets. This point is also confirmed in paragraph [0012] of the patent in suit, which acknowledges that the dissolution release profile in gastric fluid can be attained "by controlling, *inter alia*, the amount of coating in the pellet" and in paragraph [0019], lines 21 to 22 which states *inter alia* that "the amount of gastro-resistant coating based on acid-resistant acrylic polymers depends on the size of the pellet core to be coated. For example, the smaller the size of the pellets is, the more coating that is needed". Moreover, paragraph [0012] of the patent in suit states further that "the pellet core size and composition as well as the material and amount of the coating are so selected that the resulting coated collection of pellets exhibits at least one of the (following) release rates..." and that, preferably, "the pellets satisfy all (three) release rates".

Although the claim does not specify that the acid-resistant acrylic polymer in the outer layer coat surrounding the pellet core is responsible for attaining the dissolution release profile in simulated gastric acid, a technically meaningful reading of the claim allows the conclusion that the outer layer coat has a bearing on the dissolution release profile in simulated gastric fluid. However, in view of the variations allowed by the claim's wording, such as those regarding the pellet size (expressed as diameter ranges) and the actual thickness of the acid-resistant acrylic polymer coat, it cannot be concluded that there is a direct correlation between the presence of the acid-resistant acrylic polymer in the outer layer coat and the dissolution release profile in simulated gastric fluid. Similar considerations apply when establishing whether or not the outer layer coat is responsible for the dissolution release profile at pH 6.8 and what is the functional impact of the broadly defined water-permeable acrylic polymer present in the core (which may or may be not acid-resistant) on the dissolution release profiles defined in the claim.

Moreover, the claim does not specify that the dissolution tests have to be performed subsequently and thus it is not necessarily required that in order to measure the dissolution release profile at pH 6.8 the pellets have to be subjected first to a two-hour pretreatment in simulated gastric acid.

5.2 An analogous analysis to that given above in relation to claim 1 of the main request directly applies to claim 1 of auxiliary request I, which differs essentially from claim 1 of the main request in the specification of broadly defined mass ranges of the components in the pellet core calculated on a dry

pellet core basis. The expression "dried core" means a core that has been substantially dried and has a residual solvent content (water being the most suitable solvent in the pellet formation) from the production thereof of 15% or less (paragraph [0017]) in the patent in suit). Therefore, since the mass ranges for the components of the pellet core expressed in claim 1 of auxiliary request I are calculated on a dry pellet core basis, they are not absolute but relative values which depend on the residual amount of solvent in the dry pellet core, which may vary up to 15%.

5.3 Claim 1 of auxiliary request II differs from claim 1 of auxiliary request I in that the mass range of acid-resistant polymer comprised in the outer layer coat surrounding the pellets is specified as 25-75% calculated on a dry basis. However, the actual mass of said outer layer coat remains within the range of 2.5-15% calculated on a dry pellet core basis, and the defined amount of 25 to 75% mass of acid-resistant acrylic polymer on a dry basis is to be calculated relative to the coating layer (see paragraph [0021], line 40).

Therefore, the claim-construction given above for claim 1 of the main request and auxiliary request I applies *mutatis mutandis*.

6. Inventive step

6.1 Main request

The commercial product Omnic^{R}, manufactured by Yamamouchi and marketed in Europe since a date prior to the effective filing date of the patent in suit (this

is acknowledged in paragraph [0003] of the patent in suit), represents the closest prior art.

The product Omnic^{R} concerns long-acting or retard capsules (dosage form) containing multiple granulate units (multiple pellets) comprising 0.4mg tamsulosin hydrochloride (see package leaflets D3 and D4, and document D21). The capsule surface consists of gelatin and colourants (see D3 under the heading "Declaration" and D4 under the heading 6.1 List of excipients, Capsule). The multiple granulate units in the capsule comprise the active drug tamsulosin hydrochloride and the following excipients: microcrystalline cellulose, methacrylic acid copolymer, polysorbate, sodium lauryl sulphate, triacetin, calcium stearate and talc (see package leaflet D3 under the heading "Declaration"). The package leaflet D4 specifies that the methacrylic acid copolymer is methacrylic acid copolymer type C and that the polysorbate is polysorbate 80.

The entry in the "Rote Liste" 2001 (document D21) for "Omnic^{R} 0,4 Retardkapseln" specifies that they contain poly(acrylic acid, methacrylic acid) (ethyl,methyl/ acrylate, methacrylate) (1:1).

Respondents 3 (Astellas Pharma Inc. and its European subsidiaries emerging from a merger between Yamanouchi Pharmaceutical Co., Ltd. and Fusijawa Co., Ltd.) had already stated with their grounds of opposition that the Omnic^{R} products publicly available before the priority date of the patent in suit were the same as the Omnic^{R} products available today. To that effect they also submitted a declaration from Mr de Jong (D40, D40a) of Astellas Pharma Europe B.V., who had held a position in Yamamouchi Europe B.V. (a legal predecessor

of Astellas Pharma Europe B.V.), responsible for manufacturing processes of pharmaceuticals.

The dissolution release profiles in simulated gastric fluid and in a phosphate buffer of pH 6.8 of the granules/pellets contained in the Omnic^{R} capsules are within the ranges defined in claim 1 of the main request, as measured by respondents 3 (data provided in their letter dated 19 January 2007).

Moreover, it appertains to the general knowledge of the skilled person in the field of pharmacy that Eudragit^{R} methacrylic polymers and copolymers are commonly used (see document D24). The skilled person generally knows that the anionic methacrylic acid copolymers Eudragit^{R} L are acid-resistant at a pH of the gastric fluid and solubilise at a pH higher than 5.5 (intestinal fluid) (see document D24, page 117, figure 2). Eudragit^{R} L are methacrylic acid copolymers fulfilling the definitions for the methacrylic acid copolymer present in the product Omnic^{R} given in the leaflets D3 and D4, and in document D21 (see Handbook D10bis, point 5, structural definitions for Eudragit L and point 4, USP methacrylic acid copolymer type C).

Therefore, the skilled person in pharmacy possesses this technical knowledge when analysing experimentally the pellets of the product Omnic^{R} by means of routine experiments.

The experimental data provided by respondent 1 which had been carried out with the product Omnic^{R} 0.4, registered and sold in the Czech Republic since 1996 (batches manufactured in April 1998, September 2000 and February 2002) (documents D6a to D6g) are relevant. The experimental data obtained under the optical microscope

show that the content of the capsules is a plurality of pellets (spherical particles) with a majority of their diameters falling within the range of about 0.4 to about 0.8 mm (document D6a).

Respondents 3 had also provided with their letter of 19 January 2007 experimental data results showing measurements of the granules/pellets in the Omnic^{R} capsules. The pellet sizes fall within the range of about 0.50 to 0.79 mm.

Furthermore, the experimental data in document D6b using the NMR technique confirm the presence of the essential ingredients stated in the Omnic^{R} leaflets and show that the pellets contain *inter alia* Eudragit L (methacrylic acid copolymer). The FTIR (Fourier transformed infrared) spectra obtained after dissolution (extraction) experiments of unbroken/broken pellets with a phosphate buffer of pH 6.8 (a pH value at which Eudragit L products are soluble) show that the methacrylic acid copolymer present in the pellets had dissolved and that only the microcrystalline cellulose remained undissolved.

The experimental data in document D6d (scanning electron microscopy, SEM) show that the pellets of the product Omnic^{R} have an outer layer coat. Furthermore, the experimental data in documents D6d and D6e, obtained by means of treatment with acetone followed by physical release and/or chemical extraction, show that Eudragit L is present in the coating and in the core of the pellets. However, the experiments performed in document D6d do not allow any conclusion as to the actual mass amount of Eudragit L in the outer layer coat. In fact, respondent 1 does not deny in its comments on the experimental data in D6d and D6e that

the coating is formed not only by Eudragit L. What respondent 1 has submitted is that the main ingredients of the coating observed in its experiments are Eudragit L and triacetin. Moreover, these experimental results do not exclude the presence in the outer surface of the pellets of other ingredients such as calcium stearate and talc, as pointed out by the appellant.

In fact, the FTIR experimental data submitted by the appellant with the expert declaration D35 show that the material physically removed from the pellets contained in Omnic^{R} 0.4 (tamsulosin hydrochloride) capsules by means of "lightly" grinding the pellets with KBr powder in a mortar (in order to prepare a sample for IR spectroscopy) "consists mainly of calcium stearate and talc and no Eudragit or only a trace of Eudragit". These findings show which ingredients are present at the external surface of the pellets. However, these experimental data do not disprove that some Eudragit may be present in the layer coat surrounding the core of the pellets in the product Omnic^{R}.

Mr de Jong's declaration D40 about the manufacturing process, states that "the manufacturing of the Omnic^{R} capsules consisted and still consists of the following steps:
a) preparing core granules from tamsulosin HCl, microcrystalline cellulose and methacrylic acid copolymer by means of wet granulation;
b) coating the granules with a mixture of triacetin and methacrylic acid copolymer and
c) blending the dried granules with calcium stearate and talc as lubricants prior to filling the mixture so obtained into empty hard gelatin capsules."

However, declaration D40 is immaterial for determining the conclusions reached by the skilled person before the priority date of the patent in suit when establishing the nature and constitution of the pellets in the product Omnic^{R} by means of routine experiments.

The skilled person establishes by routine experimentation the physical and chemical constitution of the pellets in the product Omnic^{R} and not the function of the ingredients in a possible manufacturing process.

Therefore, as already indicated, the skilled person establishes that calcium stearate and talc are present at the surface of the pellets and thus that these two excipients form part of the external coating of the pellets of the product Omnic^{R}.

However, as already mentioned in paragraphs 5 ff. above concerning claim construction, calcium stearate and talc are also possible as ingredients of the pellet coating in the pellets according to the patent in suit. Depending on the manufacturing process these ingredients will or will not be at the outer surface of the "outer layer coat surrounding the pellet core". Claim 1 of the pending requests is not characterised by any particular product-by-process feature, and thus the outer surface of the pellet in the dosage form claimed is not specified in this respect.

There have been lengthy disputes between the parties about whether or not the outer layer coat in the pellets of the product Omnic^{R} can be considered to be an enteric coating and, if so, which ingredients perform that function (see for instance D27). However, it is to be stressed that the pellets in the product Omnic^{R}

fulfil the dissolution release profiles in claim 1 of all pending requests. It is also an established fact in the light of the evidence on file that the "coating" layer in the pellets of the product Omnic^{R} is thinner than in the pellets defined according to claim 1 of all pending requests. Furthermore, respondents 3 have acknowledged in their letter dated 19 January 2007 that the coating of the Omnic^{R} pellets "amounted to **less than 2.5%**, calculated on a dry pellet core basis" (emphasis added). Additionally, the technical submissions (D34) concerning "Function of Eudragit in TSL (Tamsulosin) pellets", submitted by Synthon B.V. (appellant in the present case) in connection with the Finnish utility model FI5842, stated that the "formulation type C" (see figure 1 in document D34, where formulation type C is shown as a pellet comprising in the core an enteric material and having a surface layer surrounding said core) represented the type of pellet marketed by Yamamouchi/Astellas, containing Tamsulosin (hydrochloride). D34 also states that those pellets marketed by Yamamouchi/Astellas "Eudragit has been mixed into the core" (mandatorily consisting of microcrystalline cellulose) and that they showed a "thin surface layer (1-2 µm)".

Therefore, the fact that the skilled person does not know with absolute certainty whether the external surface layer of the pellets in Omnic^{R} provides for acid-resistance, or which amount (if any) of Eudragit is in the coating, does not disqualify the product Omnic^{R} as closest prior art. The skilled person takes the information that has been made publicly available when selecting a particular prior art as starting point. This is the case for the publicly available commercial product Omnic^{R}, and it would have also been the case if the disclosure was in a written prior-art

document (in which the ingredients but not their actual function were explicitly mentioned). These findings are not in contradiction with the principles set out in Enlarged Board of Appeal decision G 1/92 and applied in decision T 952/92. Moreover, novelty of the claimed invention is not denied in the present decision; what is assessed is the information made available to the public by means of routine experimental analysis performed by the skilled person on the commercial product Omnic^{R}.

In view of the product characteristics, in particular the dissolution profiles of the pellets, the product Omnic^{R} and not the products specifically disclosed in document D8 is the most promising starting point.

6.1.1 In the light of the closest prior art, the problem to be solved is to provide an alternative controlled-release (or retard) dosage form of Tamsulosin hydrochloride.

The solution proposed in claim 1 of the main request relies on the outer layer coat (comprising an acid-resistant polymer) surrounding the core of the pellets, wherein the mass of the outer layer coat is within the range of 2.5-15%, calculated on a dry pellet core basis.

The problem has been plausibly solved in the light of the content of the description of the patent in suit.

It has now to be investigated whether the proposed solution is obvious in the light of the cited prior art.

As already mentioned, document D24 illustrates the general knowledge of the skilled person about methacrylic acid polymers (and copolymers) in pharmacy. Document D24 discloses that methacrylic acid polymers (and copolymers) are commonly used in peroral pharmaceutical dosage forms for the coating of *inter alia* granules and pellets, and for modifying the release of drugs (page 114, right-hand column). Eudragit^{R} acrylic copolymers from Röhm Pharma are disclosed as commonly used for forming coating films and for modifying the release profile of drugs in the digestive tract (page 115, middle column and table 2). Document D24 also teaches how to attain particular dissolution profiles by means of adequate choice of the methacrylic acid copolymers in the coating. Eudragit^{R} L/S are anionic methacrylic acid copolymers which are acid-resistant (i.e. resistant to gastric fluid) and dissolve at a pH above 5.5 (intestinal fluid) (document D24, page 117, Figure 2, right-hand column, last paragraph). Moreover, document D24 specifically teaches about the coating of small particles that can be filled into capsules or incorporated into tablets (page 118, right-hand column). Document D24 further teaches how controlled-release and retard effects can be achieved in multiple-unit technology (small particles), namely through coating of a core containing the drug and/or through matrix (or support) structures in which the drug is distributed (document D24, page 119, left-hand and middle columns and Figure 5). Document D24 further teaches that coating small particles with film-forming acrylic polymers is an effective and flexible way of providing suitable (pH-dependent) controlled release and retard release of the drug (page 119, middle column). Moreover, document D24 explains that routine fine-tuning in the choice of the film-forming acrylic polymer (to be chosen according to the dissolution

criteria to be attained at the physiological pH values of the gastrointestinal tract) and the thickness of the film easily enables the targeted dissolution release profiles to be achieved (page 119, middle column). In addition to this information, document D24 also explains that for enteric coating or for attaining "strong" retard coatings the coating should be about 2-3mg/cm^2; reference is made to the curve depicted in figure 7 (page 120, middle and right-hand columns). Figure 7 further illustrates the interdependency between particle size and required coating. Document D24 recommends that in case of small particles having a diameter within the range of 0.2 to 0.6 mm the amount of coating material should be within the range of 10 to 30% (page 120, middle column). Additionally, as shown by the enlarged figure 7 of document D24 (D24a), for pellets with a diameter within the range of 0.3 to 0.9 mm, the recommended amounts for the coating are about 7 to 23%.

Therefore, the solution proposed in claim 1 concerns generally recommended values in document D24. Document D24 further states that in practical terms the actual amount required for an effective polymer coating would be much lower, depending on the regularity of the particles and on the manufacturing process (page 120, middle column, last paragraph). Additionally, the specification of the mass range of 2.5 to 15% in claim 1 has not been linked to any particular technical effect beyond that generally attributable to acid-resistant polymer coatings. Therefore, the solution proposed in claim 1 is obvious for the skilled person in the light of the prior art knowledge.

6.1.2 As regards the appellant's submissions that the skilled person would not provide an enteric coating to pellets

with a core containing an enteric polymer, this argument relies on the view that the external surface of the pellets in the product Omnic^{R} is not able to provide an enteric coating to the pellets. In other words, the appellant submits that the coating in the pellets of Omnic^{R} does not provide the function necessary for attaining the release profile in simulated gastric fluid, either in view of its constituents or in view of its thickness. However, this aspect has already been taken into account in the definition of the solution which has been given above. Additionally, claim 1 of the main request does not require that the acrylic polymer in the core is acid-resistant (see point 5.1.2 above). In fact, the claim merely requires that the acrylic polymer in the core is water-permeable. Such a definition encompasses the retard acrylic polymers mentioned in document D24, page 117, figure 2. Granules with a Eudragit polymer in their core and a Eudragit polymer in their coating for retarding the drug release of the pellets are expressly mentioned in document D24, page 121, left-hand column.

Moreover, even if the acrylic polymer in the core of the pellets in claim 1 of the main request may be acid-resistant, document D24 teaches that the coated multiple units may also contain methacrylic copolymer in the core (figure 5 and page 121, left-hand column). This follows from the fact that document D24 teaches the skilled person that the choice of the methacrylic acid copolymer in the coating and/or core mainly depends on the functionality which he wishes to attain, i.e. the targeted dissolution release at different sites/pH of the gastrointestinal tract (page 119, middle column). Since Eudragit L methacrylic copolymers are able to provide a dual function, namely retard of dissolution of the drug in gastric fluid due to acid-

resistance, and release of the drug at a pH of the intestinal fluid due to dissolution of the polymer (page 117, figure 2), the skilled person contemplates the simultaneous use of Eudragit L in the core and the outer layer coat as an obvious alternative.

As regards further appellant's arguments, the lack of complete information in relation to the product Flomax^{R} (marketed in the US), as well as the inconsistencies detected in the incomplete document D1, cannot serve to call into question the publicly available commercial product Omnic^{R} (marketed in Europe) together with the information the skilled person has through routine experimental analysis, as detailed above.

Moreover, whether or not Omnic^{R} is a product according to the disclosure in document D8 is not relevant for the present decision. The skilled person is able to produce a product fulfilling the analytical results of Omnic^{R} by means of generally known methods in the art.

6.1.3 Consequently, the main request fails because claim 1 does not meet the requirements of Article 56 EPC.

6.2 Auxiliary request I

As regards claim 1 of auxiliary request I, the definitions of the mass amounts of the ingredients in the core of the pellets are considered to be add-on features which encompass the values in the pellets of Omnic^{R} (as experimentally shown by D6a to D6g, using the TGA method for water content). Moreover, the range of values given in claim 1 do not concern absolute values but vary relative to the residual content of solvent (unspecified in the claim), which may be up to 15% of the dry pellet core basis (paragraph [0017] of the

patent in suit). This relative nature of the mass amounts defined in claim 1 of auxiliary request I is of particular relevance in relation to the broad range for the mass of water, defined as 2-10% calculated on a dry pellet core basis (which contains up to 15% solvent, including water).

Therefore, the reasons given above in respect of claim 1 of the main request apply *mutatis mutandis* to claim 1 of auxiliary request I.

As a consequence, auxiliary request I fails for lack of inventive step of the subject-matter in claim 1 (Article 56 EPC).

6.3 Auxiliary request II

As regards claim 1 of auxiliary request II, the reasons given for claim 1 of the main request and claim 1 of auxiliary request I apply *mutatis mutandis*, since the mass of acid-resistant acrylic polymer, defined as 25-75 mass % calculated on a dry basis, is relative to the coating layer (paragraph [0021] of the patent in suit), which mass remains defined within the range 2.5-15% calculated on a dry pellet core basis.

Therefore, the mass amount of the acid-resistant acrylic polymer used in the layer coat derives in an obvious manner from routine fine-tuning (in consideration of the pellet core diameter) of the general teaching in document D24.

Correspondingly, auxiliary request II fails since claim 1 lacks an inventive step (Article 56 EPC).

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

N. Maslin U. Oswald

Decision electronically authenticated