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**Datasheet for the decision
of 26 October 2006**

Case Number: T 0906/04 - 3.3.02

Application Number: 95926054.8

Publication Number: 0723436

IPC: A61K 9/26

Language of the proceedings: EN

Title of invention:

Multiple unit tableted dosage form

Patentee:

AstraZeneca AB

Opponent:

Hexal Pharmaforschung GmbH

Headword:

Omeprazole multiple unit tableted dosage form/ASTRA ZENECA

Relevant legal provisions:

EPC Art. 52, 54, 56

Keyword:

"Main request: novelty (yes), selection in several directions;
inventive step (no), obvious solution in the light of closest
prior art"

"First and second auxiliary requests: novelty (yes); inventive
step (no), analogous reasons"

Decisions cited:

-

Catchword:

-



Case Number: T 0906/04 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 26 October 2006

Appellant: Hexal Pharmaforschung GmbH
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Decision under appeal: Interlocutory decision of the Opposition
Division of the European Patent Office posted
21 May 2004 concerning maintenance of the
European patent No. 0723436 in amended form.

Composition of the Board:

Chairman: U. Oswald
Members: M. C. Ortega Plaza
P. Mühlens

Summary of Facts and Submissions

- I. European patent EP-0 723 436, based on European application No. 95 926 054.8, which was filed as international application WO 96/01623, was granted on the basis of 21 claims.

Claim 1 as granted read as follows:

"1. An oral pharmaceutical multiple unit tableted dosage form comprising tablet excipients and individually enteric coating layered units of a core material containing active substance in the form of omeprazole or one of its single enantiomers or an alkaline salt of omeprazole or one of its single enantiomers, optionally the active substance is mixed with alkaline compounds and pharmaceutically acceptable excipients, the core material is covered with one or more layer(s), of which at least one is an enteric coating layer, characterised in that the enteric coating layer comprises a plasticizer in the amount of 20-50% by weight of the enteric coating layer polymer and that the enteric coating layer has mechanical properties such that the compression of the individual units mixed with the tablet excipients into the multiple unit tableted dosage form does not significantly affect the acid resistance of the individually enteric coating layered units."

- II. The following documents inter alia were cited during the proceedings:

(1) EP-A-0 247 983

(2) A. Sandberg et al, Eur. J. Clin. Pharmacol, 33 [Suppl], pages 3-7, 1988

(3) J.P. Dechesne, International Journal of Pharmaceutics, 37, pages 203-209, 1987

(4) Pharmaceutical Research, vol. 10, No. 10, October 1993 (Supplement), PDD 7397

(7) K. Lehmann, Drugs made in Germany 37, No. 2, pages 53-60 (1994)

III. Opposition was filed and revocation of the patent in its entirety was requested pursuant to Article 100(a) EPC on the grounds of lack of novelty and lack of inventive step (Articles 52, 54 and 56 EPC).

IV. The appeals lie from the interlocutory decision of the opposition division maintaining the patent in amended form (Articles 102(3) and 106(3) EPC) on the basis of the sets of claims of auxiliary request 1 filed with the letter of 13 April 2004.

V. The opposition division considered that the subject-matter claimed in the main request (claims as granted) met the requirements of novelty (Articles 52 and 54 EPC), but lacked inventive step (Article 56 EPC).

According to the opposition division's findings, document (1) represented the closest prior art and the problem to be solved lay in the provision of an alternative dosage form of omeprazole. In the opposition division's view, the solution related to a multiple unit tableted dosage form comprising enteric coated omeprazole units compressed into a tablet, wherein the enteric coating comprised 20-50% plasticizer. The solution was found to be obvious by

the opposition division in the light of the teaching of document (1).

As regards auxiliary request 1, the opposition division considered that the amended claims met the requirements of Article 123(2) and (3) EPC. Furthermore, the opposition division considered that the objection raised by the opponent within the meaning of Article 84 EPC against the functional definition appearing in the characterising part of claim 1 was outside the framework of the opposition procedure since the objected definition was already present in claim 1 as granted.

According to the opposition division's findings the subject-matter claimed in auxiliary request 1 was novel and involved an inventive step.

In particular, the opposition division considered that the closest prior art document (1) neither alone nor in combination with other documents rendered obvious the subject-matter claimed.

- VI. The patent proprietor (appellant patentee) and the opponent (appellant opponent) lodged an appeal against said decision and filed grounds of appeal.

- VII. The appellant patentee filed with its grounds of appeal a copy of the submissions made during opposition proceedings with its letter of 13 April 2004, which contained some additional technical data, and a copy of the amended sets of claims corresponding to the auxiliary requests 1 to 4.

In particular, claim 1 of the first auxiliary request merely differed from claim 1 of the set of claims as granted in the following feature at the end of the claim:

" and in that the amount of the enteric coating layered pellets constitutes less than 60% by weight of the total tablet weight."

Additionally, claim 1 of the fourth auxiliary request merely differed from claim 1 of the set of claims as granted in the following features at the end of the claim:

", the individually enteric coating layered units are further covered with an over-coating layer comprising pharmaceutically acceptable excipients and in that the amount of enteric coating layered pellets constitutes less than 60% by weight of the total tablet weight."

- VIII. The appellant opponent and the appellant patentee filed counterarguments to the other party's appeal.
- IX. A board's communication which conveyed the board's preliminary opinion was sent to the parties as an annex to the summons to attend oral proceedings.
- X. Both appellants filed responses to the board's communication before the oral proceedings.
- XI. Oral proceedings took place on 26 October 2006. During the oral proceedings the appellant patentee withdrew its second and third auxiliary requests filed with the letter of 13 April 2004 and renumbered the set

of claims of the fourth auxiliary request filed with the said letter as second auxiliary request.

- XII. The appellant opponent objected to the novelty of the subject-matter of claim 1 of the main request vis-à-vis the content of document (1) and made reference to its written submissions.

The appellant opponent submitted that the amount of plasticizer appearing in claim 1 of all requests was expressed as a percentage by weight in relation to the content of enteric polymer in the enteric coating layer and not in relation to the total amount of polymer(s) in the enteric coating layer. It cited paragraph [0035] of the patent in suit. Therefore, the relative amount of plasticizer present in the formulations of document (7) had to be calculated in that way.

Moreover, in the appellant opponent's view, claim 1 of the main request lacked an inventive step. In its opinion, the opposition's division findings were correct with respect to the main request, in particular the choice of document (1) as closest prior art and the definition of the technical problem to be solved. Additionally, when considering the acid resistance requirements set out in paragraph [0019] of the patent in suit it had to be concluded that the problem addressed by the patent in suit was not solved within the scope claimed. In this context the appellant opponent referred to the acid resistance test results shown in Table I for the tablets according to example 10 (page 18 of the patent in suit) and to the acid resistance test results shown in Table 3 for experiment 2 (additional tests filed in opposition

proceedings by the patentee, copy of which was filed as an annex to the appellant patentee's grounds of appeal).

Additionally, the appellant opponent stated that when considering the appellant patentee's statement in respect of paragraph [0019] of the patent in suit it was clear that claim 1 also encompassed pharmaceutical forms without a restriction in relation to their acid resistance value. Hence, acid resistance test values similar to that shown for the tablets of reference example III were possible for the pharmaceutical forms claimed.

Furthermore, according to the appellant opponent's submissions MUPS (multiple units pellets system) tablets had been commonly known to the skilled person as illustrated by documents (2) and (7). The skilled person was aware that the pellets undergo mechanical stress conditions due to the compression forces when tableting, and it was self-evident and trivial that softer materials withstand better mechanical stress than harder materials. Hence, the skilled person was in a position to know that flexibility/hardness were essential criteria when selecting the enteric coating in order to avoid brittleness. The appellant opponent further cited documents (3) and (7) to support its view that it belonged to the prior art's knowledge that flexibility depended on the amount of plasticizer. Moreover, it submitted that document (7) disclosed the use of tableting excipients in amounts of 20 to 50% to reduce the stress of the coating during the tableting process.

The appellant opponent objected to auxiliary request 1 on the grounds of insufficiency of disclosure (Article 83 EPC). In particular, it addressed its arguments against the expression beginning with "the enteric coating layer has mechanical properties such that..." and ending with "enteric coating layered unit".

The appellant opponent also raised an objection within the meaning of Article 123(3) EPC against claim 1 of the first auxiliary request, since the introduction of the feature concerning the maximum amount of pellets present in the tablet had an influence on the meaning of the definition concerning the nature of the enteric coating of the pellets appearing in the claim.

The appellant opponent maintained its objection of lack of novelty against claim 1 of the first auxiliary request with analogous reasoning as for the main request.

As regards inventive step, the appellant opponent put forward analogous arguments as for the main request.

In the appellant opponent's view, the problem to be solved lay in the provision of a further oral pharmaceutical form containing pellets with omeprazole as active substance.

Additionally, it mentioned document (2) for illustrative purposes and the paragraphs under the heading "Conclusions" in document (7). As shown by document (7) (explicitly mentioning the use of 20-50% of tableting excipients), the skilled person was aware of the use of tableting excipients to reduce

compression stress of the pellets and to fill the interspace in the tablets. Thus, the choice of the appropriate amounts of excipients was a routine matter for the skilled person.

The appellant opponent contested the second auxiliary request on the ground of lack of inventive step. It submitted that to provide the pellets with an over-coating was a conventional measure in the field of omeprazole formulations. Moreover, the over-coating layer did not contribute to the solution of the technical problem as defined by the appellant patentee.

XIII. The appellant patentee referred to its written submissions in favour of the novelty of the subject-matter claimed in claim 1 of the main request. In particular, it stressed that document (1) disclosed neither enteric coated pellets with 20% plasticizer nor tablets containing such pellets.

Asked by the board whether it considered the feature appearing in all requests (namely that "the enteric coating layer has mechanical properties such that the compression of the individual units mixed with the tablet excipients into the multiple unit tableted dosage form does not significantly affect the acid resistance of the individually enteric coating layered units") an explanatory feature or an additional technical feature, the appellant patentee answered that it was not a limitation in itself and that it was more an explanation than a "product-by-process" feature.

As regards the expression "a plasticizer in the amount of 20-50% by weight of the enteric coating layer

polymer", appearing in claim 1 of all requests, the appellant patentee stated that the amount of plasticizer was expressed in relation to the total of polymer(s) included in the enteric coating layer. In its opinion, this reading of the claim's wording was not in contradiction with paragraph [35] of the patent in suit which explicitly mentioned the optional presence of further polymers as components of the enteric coating layer(s).

As regards inventive step, the appellant patentee contested the opposition division's findings in relation to the main request. However, the appellant patentee agreed on the choice of document (1) as the closest prior art.

The appellant patentee stressed that ensuring that acid resistance did not decrease by more than 10% during compression of pellets into tablets (paragraph [0019] of the patent in suit) was a prerequisite only for preferred formulations. Moreover, this paragraph referred to the decrease in acid resistance when tableting and not to a specific acid resistance value.

Additionally, although experiment 2, provided with the additional data during opposition proceedings (copy of which was submitted with the grounds of appeal), did not concern the best results, the improvement attained over the prior art (reference example I of the patent in suit) was very significant.

Questioned by the board, the appellant patentee stated that the formulation of the pellets used for reference example I was that of example 2 of document (1). The

appellant patentee stressed that reference example I was not a reworking of example 2 of document (1).

Furthermore, the appellant patentee stressed that the teaching of document (7) concerned the elongation at break as a valid parameter when choosing the polymer for the coating. However, in its opinion, this teaching was contradicted by the facts in the patent in suit. The appellant patentee cited example 4 of the patent in suit in order to prove that amounts close to 20% of plasticizer (about 23%) also provided good results, whereas such positive results were not to be expected from document (7). Document (7) showed for Eudragit^R L 30 D an elongation at break of 14% (Table 6, page 59), i.e. far below the recommended values, and taught that there was no significant increase in flexibility if the amount of plasticizer was increased above 15%. Moreover, formulation N°6 of document (7), which contained about 10% plasticizer, was not appropriate for enteric coating of an acid labile substance such as omeprazole since it led to a quick release of ASA (acetyl salicylic acid), this meaning that acid and water would enter the pellet containing the active drug (document (7), point 2.2.3, page 56, fig. 11, fig. 14, conclusions on page 60). Therefore, in the appellant patentee's view, the combination of the teaching of document (7) with that of document (1) would not lead to the claimed invention.

Hence, the appellant patentee denied that increasing flexibility was trivial since elongation was not a reliable parameter.

The appellant patentee also pointed to reference example III in order to show that when using formulation N°9 of document (7) one has to go a step further, increasing the amount of tableting excipients over the teaching of document (7) (i.e. 70% instead of 30%), in order to achieve an acid resistance in tablets of 82%.

The appellant patentee also stressed that owing to the sensitivity of omeprazole even small quantities of water and/or acid will cause a rapid decay of the active drug and hence the requirements to be fulfilled by the formulations of the state of the art (documents (3), (4) and (7)) which did not concern omeprazole were different. In this context, it added that even the best embodiment of document (3) would be insufficient for the survival of omeprazole since the ASA escaped the net provided by the enteric coating by as much as 6.5% in 2 hours.

In relation to document (4) the appellant patentee mentioned that there was no specification of plasticizer and that the only teaching was that if the film was too hard the pellets could break. Moreover, document (4) did not represent the average knowledge of the formulation practitioner.

As regards the first auxiliary request, the appellant patentee contested the introduction of the opposition ground relating to sufficiency of disclosure as too late filed. Moreover, if this new ground was to be admitted into the proceedings it further requested remittal of the case to the department of first instance for further prosecution.

The appellant patentee stated that the amendment introduced in claim 1 of the first auxiliary request did not change the nature of the pellets and hence related to a restriction of the scope claimed.

As regards inventive step, the appellant patentee stated that the fact that the skilled person would not be prevented from considering increasing the amount of excipients in the tablets was irrelevant for assessing obviousness, since reference example III showed that even increasing the amount of excipients to about 70% by weight did not achieve an improvement in acid resistance for the formulations according to document (7).

The appellant patentee stated that "it takes both increasing the amounts of plasticizer and excipients" to attain the adequate acid resistance test results.

The appellant patentee also referred to the additional technical data filed during opposition proceedings (a copy of which was filed with the grounds of appeal), which, in its opinion, supported the existence of an improvement in the acid resistance achieved by increasing the amount of plasticizer and the amount of excipients. There was no suggestion in the prior art concerning combining both features. Moreover, document (7) discloses the use of 30% of tableting excipients in the case of enteric coating polymers.

The appellant patentee summarised its position as follows: it was not enough to adapt the coating or to adapt the amount of tableting excipients disclosed in

document (7) in order to achieve acid resistance test results better than 80%. The examples according to the patent in suit displayed values higher than 80% with the exception of example 6 of the patent in suit and the example shown in experiment 2 of the additional data filed during the opposition proceedings. The appellant patentee stressed that an improvement was shown for the combination of features appearing in claim 1 of the first auxiliary request which was not obvious in the light of the prior art.

As regards the second auxiliary request, the appellant patentee referred to paragraph [0037] of the patent in suit. The use of an over-coating layer was intended to prevent agglomeration of pellets owing to the stickiness caused by the high amounts of plasticizer used. This was reflected in the reference examples, paragraph [0099] of the patent in suit. Moreover, the appellant opponent had not provided evidence for the obviousness that over-coating layers did indeed belong to the prior art knowledge.

XIV. The appellant (opponent) requested that the decision under appeal be set aside and that the patent be revoked and that the patent proprietor's appeal be dismissed.

The appellant (patentee) requested that the opponent's appeal be dismissed and that the patent be maintained as granted (main request) or on the basis of the first auxiliary request filed with letter of 13 April 2004 or on the basis of the second auxiliary request filed as fourth auxiliary request with letter of 13 April 2004.

Reasons for the decision

1. The appeal is admissible.
2. Having regard to point XIII, second paragraph, above, the feature "the enteric coating layer has mechanical properties such that the compression of the individual units mixed with the tablet excipients into the multiple unit tableted dosage form does not significantly affect the acid resistance of the individually enteric coating layered units" appearing in claim 1 of all requests must be regarded as an explanatory feature and not as a limiting feature.

As regards the dispute concerning the definition of the amount of plasticizer in the enteric coating layer appearing in claim 1, the board considers that the fact that the percentage is expressed as "by weight of the enteric coating layer polymer" means that all polymer constituents of the enteric coating layer are included.

Furthermore, the board sees no contradiction with the information given in paragraph [0035] which makes clear that the enteric coating layer may be constituted by more than one single polymer.

Moreover, as clearly expressed in the description of the patent in suit, with the expression "individual units" employed in the claims "is meant small beads, particles, granules or pellets, in the following referred to as pellets" (paragraph [0018] of the patent in suit).

3. *Main request*

- 3.1 Document (1) discloses an "enteric coated form of omeprazole, which is resistant to dissolution in acid media and which dissolves rapidly in neutral to alkaline media and which has good stability during long-term storage." (page 4, lines 25-28)

The dose form of document (1) is characterised in that "(c)ores containing omeprazole mixed with alkaline compounds or an alkaline compound are coated with two or more layers, whereby the first layer/layers is/are soluble in water or rapidly disintegrating in water and consist(s) of non-acidic, otherwise inert pharmaceutically acceptable substances. This/these first layer/layers separates/separate the alkaline core material from the outer layer, which is an enteric coating." (page 4, lines 29-36)

Second paragraph, under the heading "Detailed disclosure of the invention", reads: "The powder mixture is then formulated into small beads i.e. pellets, tablets, hard gelatine or soft capsules by conventional pharmaceutical procedures. The pellets, tablets or gelatin capsules are used as cores for further processing."

Under the heading "Enteric coating layer" the following can be read: "The enteric coating layer is applied on to the sub-coated cores by conventional techniques such as, for instance, pan coating or fluidized bed coating using solutions of polymers in water and/or suitable organic solvents or by using latex suspensions of said polymers. As enteric coating polymers can be used, for

example cellulose acetate phthalate, hydroxypropyl methylcellulose phthalate, polyvinyl acetate phthalate, carboxymethylethylcellulose, co-polymerized methacrylic acid/methacrylic acid methyl esters such as, for instance, compounds known under the trade name Eudragit^R L 12,5 or Eudragit^R L 100 (Röhm Pharma), or similar compounds used to obtain enteric coatings. The enteric coating can also be applied using water-based polymer dispersions, e.g. Aquateric^R (FMC Corporation), Eudragit^R L100-55 (Röhm Pharma), Coating CE 5142 (BASF). The enteric coating layer can optionally contain a **pharmaceutically acceptable plasticizer** such as, for instance, cetanol, triacetin, citric acid esters such as, for instance, those known under the trade name Citroflex^R (Pfizer), phthalic acid esters, dibutyl succinate or similar plasticizers. **The amount of plasticizer is usually optimized for each enteric coating polymer(s) and is usually in the range of 1-20% of the enteric coating polymer(s).**" (*emphasis added*)
(page 7, lines 16-34)

Under the heading "Final dosage form" the following can be read: "The final dosage form is either an enteric coated tablet or capsule or **in the case of enteric coated pellets**, pellets dispensed in hard gelatin capsules or sachets or **pellets formulated into tablets.**" (*emphasis added*) (page 8, lines 22-24)

- 3.2 Although document (1) discloses generically tablets containing omeprazole which have been formulated from enteric coated pellets comprising a plasticizer in the enteric coating layer in amounts of 20% as the preferred higher limit, the skilled person has to perform selections in several directions in order to

arrive at the subject-matter of claim 1 of the main request.

- 3.3 The enteric coated pellets containing omeprazole specifically disclosed in document (1) are dispensed in capsules and contain less than 20% plasticizer by weight of the enteric coating layer polymer (independently of how it is calculated).

Correspondingly, tablets formulated from enteric coated pellets have not been specifically disclosed in document (1).

- 3.4 Consequently, the subject-matter claimed in claim 1 of the main request is novel over the content of document (1) (Article 54 EPC).

- 3.5 As regards the assessment of inventive step (Article 56 EPC), the following has been considered:

- 3.5.1 Document (1) represents the closest prior art. This has not been disputed by the parties.

In the light of this prior art the problem to be solved lies in the provision of a further oral pharmaceutical form containing enteric coated pellets with omeprazole as active substance.

The solution defined in claim 1 relates to a tableted dosage form characterised by the fact that the enteric coating layer of the pellets comprises a plasticizer in the amount of **20-50%** by weight of the enteric coating layer polymer.

The board is satisfied that the problem has been plausibly solved in the light of the content of the description, in particular the examples.

Therefore, it has to be assessed whether the proposed solution is obvious in the light of the prior art.

3.5.2 As becomes evident from the reading of the contents of document (1) quoted in point 3.1 above, document (1) discloses multiple units systems, wherein the multiple units are enteric coated pellets. Enteric coated pellets formulated into tablets are among the final dosage forms disclosed in document (1) (page 8, lines 22-24).

Furthermore, document (1) teaches under the heading "Enteric coating layer" which polymers should preferably be chosen for the enteric coating layer, which coating technique may be used and finally how to modify the enteric coating layer by addition of a plasticizer.

Claim 1 of the main request is silent about the chemical nature of the enteric coating layer, although it becomes evident from the claim's wording that at least a polymer and a plasticizer are present. The enteric coating polymers disclosed in document (1) for the enteric coating layer correspond to those or are encompassed by the enteric coating polymer classes listed in paragraph [0033] of the patent in suit. Moreover, the plasticizers disclosed in document (1) appear within the list of plasticizers given in paragraph [0034] of the patent in suit.

Therefore, the proposed solution **as defined in claim 1** of the main request merely amounts to the choice concerning the presence of a plasticizer in the amount of 20-50% by weight of the enteric coating layer polymer.

This solution is, however, foreseen by the teaching of document (1) which discloses the presence of a plasticizer usually in amounts of 20%.

Although document (1)'s teaching concerns the use of a plasticizer in amounts going from zero to a non-specifically stated maximum (which will depend inter alia on workability), document (1) states that the choice of the appropriate amounts is made within the (usual) optimization measures to be undertaken for each of the specific enteric coating polymer(s) (page 7, lines 32-34).

Nothing else is disclosed in the patent in suit which even acknowledges what appears as self-evident to the skilled person in the light of the teaching of document (1), namely that "(t)he amount of plasticizer is optimized for each enteric coating layer formula, in relation to selected enteric coating layer polymer(s), selected plasticizer(s) and the applied amount of said polymer(s)" (paragraph [0035]).

It has to be stressed that none of these elements and factors (with the exception of a minimum amount for the plasticizer expressed as a percentage relative to the enteric coating layer polymer) characterise the enteric coating layer as defined in claim 1 of the main request, which encompasses the enteric coating layers

generically disclosed in document (1). Hence, the **claimed solution** amounts to a mere repetition of the prior art general teaching, since the amount of 20% is explicitly disclosed in document (1).

Therefore, the subject-matter of claim 1 of the main request lacks an inventive step (Article 56 EPC).

3.5.3 The appellant patentee put forward the argument that the formulations according to the patent in suit show improved acid resistance test results over the prior art formulations.

Within this context the appellant patentee clarified that the coated pellets used for reference example I are those of example 2 of document (1). However, example 2 of document (1) relates to enteric coated pellets which are filled into hard gelatine capsules, i.e. the specific enteric coated pellets used in example 2 (plasticizer less than 10%) are suitable for being dispensed in a capsule but are not required to be suitable for undergoing compression stress when tableting. This and nothing else is shown by reference example I (test results in Table II of the patent in suit) which uses enteric coated pellets suitable for being dispensed in capsules for tableting purposes.

The fact that tableted forms containing enteric coated pellets are not **specifically** disclosed in document (1) does not reduce the teaching of the document to the examples, which illustrate preferred realisation modes. The person skilled in formulation technology was aware that in contrast to pellets to be dispensed in capsules, enteric coated pellets for a tableted form have to be

able to undergo mechanical stress conditions due to the compression forces when tableting.

The proposed solution as defined in claim 1 merely chooses the presence of a plasticizer in an amount of 20% but this is a standard measure specifically disclosed in document (1) for the fine tuning of the enteric coating polymer. Therefore, in the absence in the claim of a definition of the constitution of the enteric coating layer, choosing the content of plasticizer as 20% merely amounts to the reproduction of the teaching of document (1) for which the skilled person only requires routine experimentation.

As regards reference example II, it relates to lansoprazole instead of omeprazole, hence it cannot be used for comparison purposes.

Moreover, in relation to reference example III, the results obtained for the tablets compressed from pellets with the enteric coating formulation No 9 of document (7) cannot serve as an indication of the presence of an inventive step **for the subject-matter claimed** since the **closest prior art document (1)** explicitly teaches that the amount of plasticizer is **optimized for each enteric coating polymer** and explicitly mentions 20% as preferred. In contrast to the teaching of document (1), the formulation of document (7) contains a combination of enteric and non-enteric polymers for the enteric coating layer which results in very different amounts of plasticizer (lower than 10% in relation to the coating layer polymer) and thus implies lower total amounts of enteric coating polymer in the enteric coating layer.

As regards the additional tests filed during the opposition proceedings by the patent proprietor (copy of which was filed with its grounds of appeal) they cannot serve as an indication of the presence of an inventive step **for the subject-matter claimed** which encompasses any enteric coating layer formulation with 20% plasticizer expressed in relation to undefined enteric coating layer polymer(s). The reasons are as follows: the two formulations tested include 30% plasticizer (instead of 20%, which is the value known from document (1) and included in claim 1 of all requests) and do not use any of the plasticizers explicitly suggested in document (1).

These tests were intended to demonstrate an effect over the enteric coating formulations disclosed in another prior art, namely document (3), which is not the closest prior art.

Additionally, the skilled person in the field of formulation technology knows that the nature and amount of enteric coating polymer(s), the nature of the plasticizer, the thickness of the enteric coating layer, the presence and choice of other constituents (such as other polymers or other additives) in the enteric coating layer influence the chemical and mechanical properties of the enteric coating layer which are responsible for the acid resistance and the behaviour under compression stress of the enteric coated pellets. This is also confirmed in several paragraphs of the patent in suit (inter alia [0035], [0036]). Therefore, single test results of very specific enteric coating layer formulations cannot be extrapolated to make

credible the presence of an improvement effect for a very broadly defined claim.

4. *First auxiliary request*

4.1 Procedural matters (admissibility of the introduction of the objection under Article 83 EPC)

The set of claims of the first auxiliary request served as the basis for the interlocutory decision of the opposition division. Surprisingly, during the oral proceedings before the board, i.e. two years after filing of the appeal, the appellant opponent raised for the first time an objection within the meaning of Article 83 EPC against claim 1 of the set of claims of this auxiliary request.

Although amended claims filed during opposition and opposition appeal proceedings have to meet the requirements of the European Patent Convention in order to be found allowable, the objection raised by the appellant opponent within the meaning of Article 83 EPC relates to an unallowable attempt to introduce a new ground of opposition during appeal proceedings in respect of a feature which was already present in the claims as granted and which meaning has not changed in the context of the amendment introduced in the claim.

Therefore, such a late filing is not justified and would amount to the introduction of a new ground of opposition in appeal proceedings without the consent of the patent proprietor. Consequently, this new ground of opposition is not admitted into the proceedings.

4.2 Article 123 EPC

The appellant opponent did not object to the amended set of claims under Article 123(2) EPC. The board has no reason to differ.

As regards the objection under Article 123(3) EPC raised by the appellant opponent, it does indeed concern the presence in claim 1 of the feature "the enteric coating layer has mechanical properties such that ... individually enteric coating layered units", which was already present in claim 1 as granted. Moreover, said feature is non-limiting but self-explanatory. Therefore, the protection conferred has not been extended.

Therefore, the nature of the pellets or of their enteric coating is not changed in amended claim 1 of the first auxiliary request with respect to claim 1 of the granted version (main request).

Consequently, the introduction of the feature concerning the maximum amount of pellets in the tablet relates to a restriction of the scope claimed and hence claim 1 of auxiliary request 1 does not contravene the requirements of Article 123(3) EPC.

4.3 Novelty

The analysis made for the subject-matter of claim 1 of the main request applies mutatis mutandis to claim 1 of the first auxiliary request.

In conclusion, the subject-matter of claim 1 of the first auxiliary request is novel over document (1).

5. *Inventive step*

- 5.1 The tableted form claimed in claim 1 of the first auxiliary request merely differs from claim 1 of the main request in that "the amount of the enteric coating layered pellets constitutes less than 60% by weight of the total tablet weight". This means that the minimum contents of tableting excipients is about 40% by weight.

Therefore, the assessment made for the main request with respect to the requirements of inventive step applies *mutatis mutandis* to the first auxiliary request.

Additionally, the board is convinced that it belongs to the common general knowledge of the skilled person in formulation technology at the priority date of the contested patent to know that tablets formulated from coated pellets or units (i.e. MUPS technology) contain tableting excipients.

Tableting excipients fulfil several functions: *inter alia*, they fill the interspace between the pellets and they reduce the stress of the coated units during the tableting process.

Document (7), which relates to a publication in a pharmaceutical journal ("Drugs in Germany"), illustrates and confirms this point.

Thus, it can be read in document (7): "To reduce the stress of the coatings during the tableting process and

to fill the interspace, admixture of about 20-50% of usually tableting excipients is useful" (page 60, left-hand column).

It can be seen that apart from the confirmation of this general knowledge, document (7) makes a general recommendation in respect of relative amounts of excipients to be used in MUPS tablets.

Therefore, the solution proposed in claim 1 of the first auxiliary request merely reflects the usual measures undertaken by the formulation technologist when producing the MUPS tablets disclosed in document (1).

- 5.2 The appellant patentee cited the following passage of document (7): "When approximately 30% of tableting excipients including disintegrants are mixed together with the coated particles and compressed, the interspace is filled and the coatings are separated so that the tablets disintegrated rapidly and damage of particles and change of release profiles can be reduced to a significant level."

However, this recommendation directly applies to the enteric coating layers specifically disclosed in document (7) and does not represent a prejudice sufficient to deter the skilled person from applying the general recommendation of 20-50% given in the same document for MUPS coating formulations.

The appellant patentee referred to the additional examples filed during opposition proceedings as proof of the existence of an improved effect for the

formulations according to the patent in suit but, as already mentioned for the main request, the test results for the two formulations tested are not conclusive for the scope claimed. Apart from the fact that they illustrate punctual enteric coating layer identities, whereas the claim is silent about the constitution of the enteric coating layer, the specific formulations tested include 30% plasticizer whereas the claim relates to amounts of 20% plasticizer. The board is not satisfied that the results can be extrapolated from one single value to another. On the contrary, the nature and amounts of plasticizer have to be fine-tuned for each enteric coating polymer (as known from document (1) and acknowledged in the patent in suit).

Furthermore, the appellant patentee acknowledged at the oral proceedings before the board that both the amounts of plasticizer in the enteric coating layer and the amounts of tableting excipients play a major role in attaining adequate acid resistance test results for the tablets.

5.3 Consequently, claim 1 of the first auxiliary request lacks an inventive step (Article 56 EPC).

6. *Second auxiliary request*

6.1 No formal objections were raised against the second auxiliary request and the board sees no reason to differ.

6.2 The subject-matter claimed in the second auxiliary request is novel for analogous reasons as for the

previous requests since a novelty-bringing feature suffices to satisfy the requirements of novelty.

- 6.3 As regards inventive step, the assessment made for the main request with respect to the requirements of inventive step applies mutatis mutandis to the second auxiliary request.
- 6.4 The subject-matter claimed in the second auxiliary request merely differs from claim 1 of the first auxiliary request in that "the individually enteric coating layered units are further covered with an over-coating layer comprising pharmaceutically acceptable excipients". It is to be noted that the requirement set by the claim's wording is only of a physical nature, i.e. the mere presence of a further coating layer over the enteric coating layer.

Multiple-layered pellet technology, where several coating layers concentrically cover an inert core containing the active substance, is commonly used in the field of omeprazole. This is reflected by the content of document (1), including its analysis of background art. Indeed, the presence of other layers such as a separating layer (not specifically reflected by the claims' wording) is a prerequisite for formulations containing acid labile substances, such as omeprazole, when using acidic enteric coating polymers.

As regards the addition or not of an over-coating layer, it has to be said that there is no functional requirement for enteric coating pellets that the enteric coating is the upper layer of the pellets. Therefore, the physical existence of an over-coating

layer can only be seen as an additional novelty-bringing feature over the MUPS disclosed in document (1). If the over-coating layer is to be linked to a function, then it has to be stressed that such function is not reflected by the claim's wording either in form of functional features or in the nature of chemical constituents of the over-coating layer.

Moreover, an inspection of the patent in suit shows that the presence of an over-coating layer was disclosed as optional since, according to the patent in suit, the enteric coating-layered pellets encompassed by the claims do not necessarily agglomerate.

"Pellets covered with enteric coating layer(s) **may** further be covered with one or more over-coating layer(s)... The materials for over-coating layers are chosen among pharmaceutically acceptable compounds such as, for instance sugar, polyethylene glycol, polyvinylpyrrolidone, polyvinyl alcohol..... Additives such as plasticizers, colorants, pigments, fillers, anti-tacking agents....may also be included into the over-coating layer(s). Said over-coating layer **may** further prevent **potential** agglomeration of enteric coating layered pellets, further protect the enteric coating layer towards cracking during compaction process and enhance the tableting process." (*emphasis added*) (paragraph [0037] of the patent in suit)

6.5 Hence, the subject-matter claimed in claim 1 of the second auxiliary request lacks an inventive step (Article 56).

6.6 The appellant patentee cited the reference examples, where it is stated: "The separating layer, enteric coating layer and the over-coating layer are sprayed onto pellets in a fluid bed apparatus. The over-coating layer is applied to prevent sticking of pellets before tableting."

First of all, the reference examples I to III do not concern examples illustrating the "invention".

Moreover, the possible preventing function vis-à-vis potential agglomeration of pellets achieved by an over-coating layer containing hydroxypropyl methylcellulose and magnesium stearate is not denied. What is denied is that the mere presence of an over-coating layer involves an inventive step, since to add an over-coating layer is to be seen as a conventional measure in multiple layered pellets technology.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chairman:

A. Townend

U. Oswald