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Datasheet for the decision of 20 January 2022

Case Number: T 1773/16 - 3.3.01

Application Number: 08725256.5

Publication Number: 2137537

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Language of the proceedings: EN

Title of invention:
Compositions and Uses for Treating Multiple Sclerosis

Patent Proprietor:
Biogen MA Inc.

Opponents:
Zentiva k.s.
Hexal AG
G. L. Pharma GmbH
European Oppositions Limited
Generics [UK] Limited
ZAKLADY FARMACEUTYCZNE POLPHARMA S.A.
Gallafent, Antony Xavier
Actavis Group PTC ehf (opposition withdrawn)
Synthon B.V.
Forward Pharma A/S (opposition withdrawn)

Headword:

Dimethyl fumarate or Monomethyl fumarate for treatment of multiple sclerosis/BIOGEN

Relevant legal provisions:

EPC Art. 123(2)
RPBA Art. 13(1)

Keyword:

Amendments - allowable (no)
Late-filed main request - admitted (no)

Decisions cited:

T 1480/16, T 0995/18, T 0981/17, T 1792/19, T 0914/18, T 1857/19, T 0306/18, T 0197/08

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Case Number: T 1773/16 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 20 January 2022

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Representative:	Prins, Hendrik Willem Arnold & Siedsma Bezuidenhoutseweg 57 2594 AC The Hague (NL)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 13 June 2016 revoking European patent No. 2137537 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman	A. Lindner
Members:	M. Pregetter
	P. de Heij

Summary of Facts and Submissions

I. European patent No. 2137537 is based on European patent application No. 08725256.5, which was filed as an international application published as WO2008/097596.

Claims 1 and 7 as granted read as follows.

"1. A pharmaceutical composition for use in treating multiple sclerosis, the composition consisting of:
(a) dimethyl fumarate or monomethyl fumarate, and
(b) one or more pharmaceutically acceptable excipients,
wherein the composition is to be administered orally to a subject in need of treatment for multiple sclerosis, and wherein the dose of dimethyl fumarate or monomethyl fumarate to be administered is 480 mg per day.

7. Dimethyl fumarate or monomethyl fumarate for use in treating multiple sclerosis, wherein the dimethyl fumarate or monomethyl fumarate is the only neuroprotective compound to be administered, and wherein the dimethyl fumarate or monomethyl fumarate is to be orally administered to a subject in need of treatment for multiple sclerosis at a dose of 480 mg per day."

II. The patent was opposed under Article 100(a), (b) and (c) EPC on the grounds that the claimed subject-matter lacked novelty and an inventive step, was not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art, and extended beyond the content of the application as filed. The validity of the priority was also

questioned.

In the course of the opposition proceedings, the patent proprietor submitted an amended main request and auxiliary requests 1a, 1b and 2, all filed on 14 January 2016.

The opposition division revoked the patent. The subject-matter of the dependent claims of the main request and of auxiliary request 1b were found to contravene the requirements of Article 123(2) EPC. The subject-matter of auxiliary requests 1a, 1b and 2 lacked an inventive step.

III. The patent proprietor appealed this decision. With its statement setting out the grounds of appeal, it re-submitted the sets of claims of the main request and of auxiliary requests 1a, 1b and 2.

Claim 1 of the main request and of auxiliary request 1a is identical to claim 1 as granted. Claim 6 of the main request and claim 5 of auxiliary request 1a are identical to claim 7 as granted.

Claim 1 of auxiliary requests 1b and 2 differs from claim 1 as granted in that monomethyl fumarate has been deleted. Claim 4 of auxiliary request 1b and claim 3 of auxiliary request 2 differ from claim 7 as granted in that monomethyl fumarate has been deleted.

IV. In a communication sent pursuant to Article 15(1) RPBA 2007, the board indicated, *inter alia*, which technical features were crucial for the discussion of the amendments in light of the decision under appeal and the submissions of the parties.

V. Oral proceedings before the board took place on 19 and 20 January 2022.

Respondents 3 (opponent 3), 7 (opponent 7) and 9 (opponent 9) were not represented, as had been announced on 4 January 2022, 17 January 2022 and 14 January 2022, respectively.

During the oral proceedings, the appellant (patent proprietor) filed a new main request and renamed the previous main request and auxiliary requests 1a, 1b and 2 as auxiliary requests 1, 2a, 2b and 3, repectively.

Claim 1 of the new main request is identical to claim 7 as granted.

VI. The appellant's arguments, insofar as they are relevant to the present decision, may be summarised as follows.

Admission of the new main request

The Rules of Procedure of the Boards of Appeal 2007 applied since the summons were issued in 2019. Subsequent postponements due to the coronavirus pandemic did not change this fact.

The new main request was admissible. It was based on a granted claim that had been in the proceedings from the beginning. The mere deletion of an independent claim and the dependent claims related thereto did not constitute an amendment of the appeal case. Even if the RPBA 2020 were found to apply, there is a multitude of case law that comes to the conclusion that the deletion of claims does not constitute a change of case (T 1480/16, T 995/18, T 981/17, T 1792/19, T 914/18, T 1857/19 and T 306/18). The board therefore did not

have discretion to not admit the claim request into the proceedings.

In addition, the conclusion of the board on the allowability of the amendments had not been foreshadowed in its preliminary opinion. The appellant could not be expected, in an exceptionally complicated case such as the present one, to file auxiliary requests addressing each and every objection. The appellant thus had the right to discuss a claim that had always been on file and which, despite having been discussed together with claim 1 of auxiliary request 1 (the former main request), had nevertheless not been treated as being equivalent to this claim. This could be seen from point 20 of the grounds of appeal.

Amendments

The mere fact that the application as filed concerned several aspects was not crucial. Each of the aspects could be claimed separately.

Claim 1 of auxiliary request 1 was directly and unambiguously derivable from paragraph [0116], which contained all of the technical features of claim 1, with the exception of the disease, and from paragraph [0001], which clearly indicated that multiple sclerosis was the preferred disease to be treated. The fact that the application as filed contained other embodiments was irrelevant.

The dose of 480 mg per day was not a selection in paragraph [0116]. The natural convergence of the nested ranges in this passage, which converged from broad to narrow, indicated a preference for this value. The lower end point of the narrowest and thus preferred

range was explicitly disclosed and could not be considered to be a selection from a list of some length. A further indication for the preference of 480 mg per day was the fact that it was disclosed as the lower end point of a range having 720 mg per day as the higher end point. Since the person skilled in the art was aware that 720 mg per day was an effective dose of DMF for the treatment of multiple sclerosis, they would have been aware that this range did not represent a mere alternative.

The term "consisting of" in claim 1 was clearly derivable from the application as filed. In paragraphs [0019] and [0063], the term "at least one" was disclosed with reference to DMF and MMF, "one" providing a literal basis for a single active compound. As paragraph [0116] referred only to DMF or MMF, the doses disclosed in this paragraph related to DMF or MMF only. Also, the examples were based on the activity with one compound only and showed that DMF or MMF alone provided an effect on which the treatment of hallmark characteristics of multiple sclerosis relied. The application as filed thus clearly pointed to a preference of treatment by DMF or MMF alone. As supported by the findings of T 197/08, the use of the term "consisting of" was thus justified. In sum, monotherapy was not a selection. Even if methods 4 and 5 were considered to represent a list, monotherapy was clearly the preferred option. It was established case law that preferred technical features can be combined.

VII. The respondents' arguments, insofar as they are relevant to the present decision, may be summarised as follows.

Admission of the new main request

In response to the appellant's request to postpone the oral proceedings, new summons had to be issued after the entry into force of the RPBA 2020. These thus applied.

The set of claims of the new main request should not be admitted. It was late-filed, at the end of the first day of the oral proceedings, and could have been submitted earlier, for example in response to the board's communication pursuant to Article 15(1) RPBA 2007, which flagged the issues for discussion in the context of added matter. The filing of this set of claims was a clear amendment to the appellant's case. Claims 1 and 6 of the former main request (now auxiliary request 1) had been discussed and treated together throughout the proceedings. Claim 1 of the new main request, which was identical to claim 6 of auxiliary request 1, could thus not be expected to overcome any of the issues of claim 1 of auxiliary request 1. As a consequence of having discussed and treated claims 1 and 6 of auxiliary request 1 together, any handling of claim 6, now claim 1 of the new main request, in a different manner would constitute a change of case.

Amendments

The application as filed focused on the screening of compounds, with the aim of identifying and evaluating

neuroprotective compounds (title and paragraphs [0008] and [0009]). DMF and MMF were used as comparator compounds for these new compounds to be identified (claim 9). Treating multiple sclerosis was not preferred and there was no basis for treating multiple sclerosis with DMF or MMF. All further passages had to be understood with this in mind.

To arrive at the claimed subject-matter, several selections had to be made. Apart from the choice of DMF or MMF as the active agent, these included the selection of DMF or MMF as the only active agent and the selection of the dose of the active agent(s).

Nothing in paragraph [0116] pointed to a preferred daily dose of 480 mg. The value of "480" was merely the end point of one of the ranges which clearly converged on the value of 720. The value of "480" was thus neither preferred nor individualised.

The disclosure in paragraph [0116] described the "co-usage" of DMF or MMF with other therapeutic agents as a possibility and thus was not clearly directed to mono-therapies. Method 4 (see paragraphs [0009], [0019] or [0063]), using the wording "at least one compound" or "at least one neuroprotective compound", did not clearly point to a mono-therapy either, since a selection of "one" from "at least one" was required. Method 5 (see paragraph [0009]) even explicitly related to combination therapy. The term "consisting of" thus required a selection.

The examples could not provide any guidance as to preferred doses or compositions consisting of DMF or MMF and one or more excipients. None of the examples described a pharmaceutical formulation or the treatment

of multiple sclerosis. The examples concerned the mechanistic background.

In sum, the subject-matter of claim 1 of the main request was the result of a multitude of selections including the selection of the dose of 480 mg per day and the term "consisting of".

VIII. The parties' final requests were as follows.

The appellant requested that the decision under appeal be set aside and that the patent be maintained on the basis of the set of claims of the new main request filed during the oral proceedings, or, alternatively, on the basis of auxiliary requests 1, 2a, 2b or 3, which were filed as the main request and auxiliary requests 1a, 1b and 2, respectively, with the statement of grounds of appeal.

Respondents 1 to 6 and 9 requested that the appeal be dismissed. Respondent 9 requested in addition that the case be remitted to the opposition division if the board arrived at the decision that any of the claim requests comprised an inventive step.

Respondent 7 did not submit a request.

Reasons for the Decision

1. The appeal is admissible.

2. The oral proceedings before the board took place in the absence of Respondents 3, 7 and 9, which had been duly summoned but had chosen not to attend. According to Rule 115(2) EPC and Article 15(3) RPBA, the board was not obliged to delay any step in the proceedings,

including its decision, by reason only of the absence from the oral proceedings of any party duly summoned which was treated as relying only on their written case. Hence, the board was in a position to announce a decision at the conclusion of the oral proceedings, as provided for by Article 15(6) RPBA.

3. *Admission of new main request*

3.1 The former main request (now auxiliary request 1) contains two independent claims. Claim 1 is directed to a composition consisting of dimethyl fumarate or monomethyl fumarate and one or more pharmaceutically acceptable excipients for use in treating multiple sclerosis, wherein the composition is to be administered according to a certain dosage regimen. Claim 6 of the former main request is identical to claim 7 as granted and claims dimethyl fumarate or monomethyl fumarate, wherein these compounds are the only neuroprotective compounds to be administered, for use in treating the same disease according to the same dosage regimen. In the new main request, claim 1 and its dependent claims 2 to 6 as well as claims 11 and 12 have been deleted. Claim 6 of the former main request has been renumbered to become claim 1 of the new main request.

3.2 The respondents argued that the filing of the new main request constituted a change of the appellant's case. The appellant insisted that the new main request did not constitute a change of case, because it had merely deleted claim 1 and its dependent claims and claims 11 and 12. The remaining claims were identical to the subject-matter that had been part of the main request which had been filed with the statement of grounds of appeal. Therefore, the board did not have discretion to

not admit the new main request.

3.3 The appellant's view cannot be accepted. In the board's opinion, any new claim request may, and often will, represent a change of the party's case because it may involve an assessment of the allowability of subject-matter or of arguments, which assessment has not been part of the case before. In the case at hand, it had been argued by the respondents that claims 1 and 6 of the former main request did not meet the requirements of Article 123(2) EPC, *inter alia*, because the claimed subject-matter was an undisclosed combination of different features disclosed in the application as filed. The appellant had replied to this, and included in its reply further added-matter issues (concerning the dosage regimen and the disease to be treated), not making a distinction between claims 1 and 6 (see, for example, the statement of grounds of appeal, point V.1, and appellant's letter dated 27 October 2017, point I. 1, especially point I.1.5). The appellant pointed to the reference to paragraph [0063] of the application as filed in the statement of grounds of appeal at point 20. This reference should be read in the context in which it was made, i.e. that the use of dimethyl fumarate or monomethyl fumarate was disclosed as a monotherapy in a preferred embodiment of the application as filed. It does not alter the conclusion that no distinction between claims 1 and 6 had been made.

Admitting the new main request into the proceedings would thus have involved an examination during oral proceedings as to whether the added-matter objections raised by the respondents would have to be regarded differently for the subject-matter of claim 6 than for the subject-matter of claim 1. This had not been

addressed before, and therefore constitutes a new line of defence on the part of the appellant, which represents a change of the appellant's case.

3.4 In addition, the board does not concur with the appellant's conclusion, drawn from the cited case law, that the deletion of claims can never represent a change of case.

On the contrary, in case T 1480/16 the board explicitly states that the admission of auxiliary request 5 is at the discretion of the board, as stipulated in Article 13(1) RPBA. The board sees no reason for not admitting the request as - and this is different from the case at hand - no new discussion would have been needed (Reasons 2.2 and 2.3). An analogous conclusion is reached in T 995/18 and T 1792/19.

In case T 981/17, the board again bases its conclusion on the admissibility of the factual situation (see Reasons 3.2).

In case T 914/18, the board does not consider a deletion of the claimed subject-matter to be an amendment of a party's case, "provided the deletion ... do not lead to a fresh case". The deletion was "without shedding new light on the remaining subject-matter and without other consequences on the parties' respective appeal cases" (see Reasons 4.1).

In case T 1857/19, the board took the view that as the deletion of a claim led to the limitation of the claims to a claim category which was the principal subject of the discussion, the factual and legal framework of the appeal was not changed (Reasons 1.1).

Similarly, in case T 306/18 the board held that the deletion of an independent claim was a change of case. However, as no new issues were to be considered, the factual and legal framework of the appeal procedure was not changed (Reasons 5.1.1 and 5.1.4).

The case law has thus by no means adopted an approach in which the deletion of claimed subject-matter can never be regarded as a change of case. In fact, none of the decisions cited by the appellant provides support for such an approach. Quite the opposite, it demonstrates that the deletion of claims in a newly presented claim request can or cannot constitute a change of case, depending on the circumstances of the case, and that its admission is subject to the discretion of the board in accordance with Article 13(1) RPBA or, as the case may be, Article 13(1) RPBA 2007.

3.5 In the case at hand, the summons to oral proceedings was notified on 12 April 2019 and thus before the entry into force of the RPBA 2020 (referred to as "RPBA" in this decision). In accordance with Article 25(3) RPBA 2020, Article 13 RPBA 2007 applies to the present case. This is not affected by the fact that the oral proceedings were postponed twice.

3.6 In exercising its discretion, the board decided not to admit the new main request since it was presented at a very late stage of the proceedings, would entail a fresh discussion of the issue of added matter and because the deletion of claims 1 to 6 and 11 and 12 would prima facie not overcome the added matter objections against the former main request (now auxiliary request 1). It is of no relevance that the conclusion of the board regarding added matter had

allegedly not been foreshadowed in its communication pursuant to Article 15(1) RPBA. The appellant is required to present its complete case in view of the objections put forward by the respondents in their written submissions, irrespective of whether or not the board has preliminarily agreed with those objections. The preliminary opinion of the board expressed in its communication, in particular in point 7, could not in any case cause the appellant to be surprised by the conclusions of the board on the issue of added matter.

3.7 In conclusion, the board, exercising its discretion under Article 13 (1) RPBA 2007, decided to not admit the new main request into the proceedings.

4. *Auxiliary request 1 - amendments (Article 123(2) EPC*

The appellant argued that the subject-matter of claim 1 of auxiliary request 1 could be directly and unambiguously derived from the combination of paragraphs [0001] and [0116] of the application as filed.

The decision will focus on two technical features of claim 1 of auxiliary request 1, namely the technical features relating to the terms "consisting of" and "480 mg per day", which are crucial for the board's findings with regard to Article 123(2) EPC.

4.1 *"consisting of"*

Claim 1 defines a composition consisting of dimethyl fumarate or monomethyl fumarate and one or more pharmaceutically acceptable excipients for use in treating multiple sclerosis, wherein the composition is to be administered according to a certain dosage

regimen. This wording excludes the presence of any further active agents, e.g. active agents suitable for treating multiple sclerosis by the same or by a different mechanism of action, in addition to dimethyl fumarate or monomethyl fumarate.

Since dimethyl fumarate is defined in claim 1 of all the claim requests in the proceedings, the further reasoning will focus on dimethyl fumarate for the sake of simplicity.

4.1.1 Paragraph [0116] deals with the dosing of DMF. "DMF" is taken to be an abbreviation of dimethyl fumarate. However, the present decision does not come to a conclusion on whether there is a basis in the application as filed for the term "dimethyl fumarate" in claim 1 of auxiliary request 1.

Paragraph [0116] states that effective doses will vary depending on the route of administration, excipient usage and the possibility of co-usage with other therapeutic treatments including use of other therapeutic agents. This is followed by suggestions for an effective dose of DMF. Thus, the suggestions for effective doses are not restricted in any way to mono-treatment. Neither the fact that the doses are linked to oral treatment nor the absence of any indication pointing to possible further active agents justifies such a reading. The disclosure of paragraph [0116] starts with more general statements regarding doses and then leads on to more specific values of doses to be used in a dosage regimen. However, this "zooming in" relates merely to the doses of DMF to be administered and not to the possibility of administering (or not) further active agents. A second medical use based on the administration of a composition necessarily

consisting of dimethyl fumarate and (an) excipient(s) cannot be derived from this passage.

4.1.2 The appellant has argued that since the examples exclusively disclose the use of a single active agent, either DMF or MMF, these would back up the term "consisting of" and point to a preference of treatment by DMF or MMF alone.

However, the examples do not relate to the treatment of multiple sclerosis as such or to formulations that are to be orally administered in such a treatment. Examples 1 and 2 are carried out using cell cultures and report on the finding that DMF and MMF are Nrf2 agonists. Example 3, in an animal model of multiple sclerosis, administers DMF or MMF by subcutaneous injection and determines Nfr2 activation. The examples (merely) show a proof of concept relating to the background discussed in paragraphs [0002] to [0008] of the application as filed.

The situation thus differs from T 197/08, where the examples, which were considered in the context of the overall disclosure of the application as filed, included, apart from examples relating to the synthesis of the active compounds and pharmacological assays, formulation examples. These formulation examples contained the claimed compound as the sole active ingredient showing that monotherapy was the only administration form envisaged in the application as filed (reasons 3.3).

4.1.3 The application as filed describes five methods (paragraph [0009]). Two of these methods are methods of treating a neurological disease. While method 4 describes that "at least one compound" is administered,

method 5 relates to the administration of at least two active agents. Method 4 is further discussed in paragraphs [0019] and [0063]. Here, the administration of "a therapeutically effective amount of at least one neuroprotective compound" is disclosed, followed by the possibility that this compound or these compounds is/ include dimethyl fumarate or monomethyl fumarate ("(e.g., DMF or MMF)"). There is no doubt that the term "at least one neuroprotective compound" includes, but is not limited to, the possibility that precisely one such compound is administered. Therefore, a conscious selection of precisely one compound has to be made in order to arrive at a claim wording using the term "consisting of".

4.1.4 In sum, the application as filed discloses the possibility that dimethyl fumarate (or monomethyl fumarate) is used in mono-treatments. However, this treatment form is not highlighted in a way that would flag this treatment form as being clearly preferred. Furthermore, formulation examples consisting of a single pharmaceutical active agent are not disclosed. Consequently, the application as filed does not directly and unambiguously disclose a composition consisting of dimethyl fumarate (or monomethyl fumarate) and (an) excipient(s) for treating a neurological disease/multiple sclerosis as a preferred embodiment. To arrive at the claimed subject-matter mono-treatment needs to be selected.

4.2 *"480 mg per day"*

The dose of 480 mg per day is disclosed in paragraph [0116] of the application as filed in a sentence relating to oral dosages for DMF and MMF. Several ranges are listed, from the broadest range of

0.1 g to 1 g per day, to two more restricted ranges, to a range of 480 mg to 720 mg per day, followed by a dose of 720 mg per day and a sentence describing how the dose of 720 mg could be administered in sub-doses for separate administration over the day. None of the ranges or values is linguistically qualified as being preferable over any of the others, for example by terms such as "preferred", "especially preferred" or "most preferred". However, based on the fact that the list of ranges of doses is followed by a single dose, namely the dose of 720 mg, it can be clearly derived that the most preferred dose is 720 mg per day. Conversely, it follows from the manner in which the dose of 720 mg per day is presented that the range of 480 mg to 720 mg per day does not disclose the most preferred dose/dosage regimen.

4.2.1 The appellant argued that end points in general and the two end points of the narrowest range in particular were singled out and would be considered to be preferred embodiments.

The complete sentence in paragraph [0116] reads: "For example, an effective dose of DMF or MMR [sic] to be administered to a subject orally can be from about 0.1 g to 1 g per pay [sic], 200 mg to about 800 mg per day (e.g., from about 240 mg to about 720 mg per day; or from about 480 to about 720 mg per day; or about 720 mg per day)". There are thus several ranges with several end points. The lower end point of the narrowest range is without doubt the value "480 mg". However, this narrowest range is not the most preferred disclosure; the most preferred disclosure is the disclosure of 720 mg on its own. While the end points are values that are explicitly disclosed as such, the mere fact that a value is the end point of a range does not

automatically render it the most preferred value. In the case at hand, the value of "480 mg" is just the end point of a less preferred range and its inclusion into a claim is thus to be considered a selection.

4.2.2 Furthermore, the appellant argued that the value "480 mg" was disclosed as the lower end point of a range whose higher end point was the value that the person skilled in the art would recognise as being known to be effective.

The board fails to see that in a context where the higher end point of this range, 720 mg per day, was clearly singled out and thus stressed, the knowledge of the person skilled in the art would have led them to consider the value of 480 mg as being highlighted in any way. Instead the person skilled in the art would have found their knowledge confirmed by the manner in which the dose of 720 mg is disclosed.

4.2.3 Consequently, the dose of 480 mg is not disclosed as being the preferred dose; rather, it is merely, like the mono-treatment, the result of a selection.

4.3 The respondents brought forward further lines of argument. However, in view of the conclusion reached by the board above, a discussion thereof is not crucial for the present decision.

4.4 In sum, neither a composition consisting of a sole active agent in the form of dimethyl fumarate (or monomethyl fumarate) and (an) excipient(s) nor a method of treatment administering 480 mg per day of dimethyl fumarate (or monomethyl fumarate) is clearly preferred in the application as filed. The combination of these two features is thus not the combination of two

preferred embodiments. Moreover, these two features are not explicitly disclosed in combination in the application as filed. Consequently, the combination of these two features constitutes a double selection of features and is therefore not directly and unambiguously derivable for the person skilled in the art from the application as filed.

4.5 The subject-matter of claim 1 of auxiliary request 1 contravenes the requirements of Article 123(2) EPC.

4.6 Auxiliary request 2a

Claim 1 of auxiliary request 2a is identical to claim 1 of auxiliary request 1. The same argumentation as presented in points 4.1 to 4.4 above applies.

The subject-matter of claim 1 of auxiliary request 2a contravenes the requirements of Article 123(2) EPC.

4.7 Auxiliary requests 2b and 3

The subject-matter of claim 1 of auxiliary requests 2b and 3 is restricted to dimethyl fumarate as the active agent. The argumentation provided for claim 1 of auxiliary request 1 above, see points 4.1 to 4.4, applies *mutatis mutandis*.

The subject-matter of claim 1 of auxiliary requests 2b and 3 contravenes the requirements of Article 123(2) EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated