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Datasheet for the decision of 19 December 2012

Case Number: T 0015/09 - 3.2.02

Application Number: 01932895.4

Publication Number: 1278564

IPC: A61M 5/172, A61M 15/00, A61M 16/01, A61B 5/11

Language of the proceedings: EN

Title of invention:
System for adaptive drug delivery

Patent Proprietor:
Universiteit Gent

Opponent:
Hovorka, Roman, Dr.

Headword:
-

Relevant legal provisions:
EPC Art. 54, 56, 83, 84, 114(2), 123(2), 123(3)
EPC R. 139
RPBA Art. 12(2), 13(1), 13(3)

Relevant legal provisions (EPC 1973):
-

Keyword:
"Obvious correction (no - main request and auxiliary request 2a)"
"Added subject-matter (yes - auxiliary request 1)"
"Admissibility of late-filed request (yes - auxiliary request 2b new)"
"Admissibility of late-filed document (no)"
"Added subject-matter (no - auxiliary request 2b new)"
"Extension of scope of protection (no - auxiliary request 2b new)"
"Clarity and support (yes - auxiliary request 2b new)"
"Sufficiency of disclosure (yes - auxiliary request 2b new)"
"Novelty (yes - auxiliary request 2b new)"
"Inventive step (yes - auxiliary request 2b new)"

Decisions cited:
G 0003/89

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0015/09 - 3.2.02

D E C I S I O N
of the Technical Board of Appeal 3.2.02
of 19 December 2012

Appellant: (Patent Proprietor)
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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 6 November 2008 revoking European patent No. 1278564 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman: E. Dufrasne
Members: C. Körber
M. Stern

Summary of Facts and Submissions

I. On 6 November 2008 the Opposition Division posted its decision to revoke European patent No. 1278564 for extension of scope of protection and lack of novelty. The fifth auxiliary request was not admitted into the proceedings.

II. An appeal was lodged against this decision by the patent proprietor by notice received on 17 December 2008, with the appeal fee being paid on the same day. The statement setting out the grounds of appeal was received on 16 March 2009.

III. By communication of 10 September 2012, the Board forwarded its provisional opinion to the parties and summoned them to oral proceedings.

IV. Oral proceedings were held on 19 December 2012.

The final requests of the parties were as follows:

The appellant (patent proprietor) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request, or, in the alternative, on the basis of one of the auxiliary requests 1 and 2a, all filed on 5 December 2012, the "auxiliary request 2b new" filed during the oral proceedings, or the auxiliary requests 3a to 4b filed on 5 December 2012. Auxiliary request 2b filed on 5 December 2012 was withdrawn during the oral proceedings.

The respondent (opponent) requested that the appeal be dismissed.

V. The following documents are of importance for the present decision:

D24: E. Mortier et al.: "Closed-loop controlled administration of propofol using bispectral analysis", Anaesthesia 53 (1998), 749-754;

D25: J. Schüttler and H. Schwilden: "Feedback control of intravenous anesthetics by quantitative EEG" in: "Control and automation in anaesthesia" (Eds.: H. Schwilden and H. Stoeckel), Springer-Verlag, Berlin (1995), 194-207.

VI. The independent claims of the **main request** read:

"1. A system for controlling the administration of medication to a patient to achieve and maintain a target effect in said patient, the system comprising:
a sensor package (104) having one or more sensors (608, 610, 612), said sensors (608, 610, 612) being configured to sense an attribute of said patient (116) and to provide a parameter indicating the attribute being sensed;
a medication delivery unit (112) configured to administer said medication to said patient (116) to achieve a concentration of said medication in said patient (116); and
a medication delivery controller (108) having an input coupled to said sensor package (104) and an output coupled to said medication delivery unit (112), said medication delivery controller (108) being configured

to accept said one or more parameters from said sensor package (104), wherein the medication delivery controller is configured to calculate an individual patient response profile to determine a target concentration level of said medication to achieve said target effect, and to control said medication delivery unit (112) to deliver said medication at a rate determined to achieve said target concentration level of said medication in said patient (116), and wherein said individual patient response profile defines the patient's (116) individualized response to said medication,
characterized in that said medication delivery controller is configured to shift the individual patient response profile to adapt to changing patient conditions."

"8. A medication delivery controller (108) for controlling the administration of medication to a patient (116) to achieve and maintain a target effect in said patient (116), the controller comprising:
a sensor interface (826) configured to receive one or more patient parameters from a sensor package (104),
a processor (808) coupled to said sensor interface (826), and
a data output port coupled to said processor (808),
wherein said processor (808) is configured to calculate an individual patient response profile to determine a target concentration level of said medication to achieve said target effect and to determine a medication delivery rate to achieve said target concentration level of said medication in said patient, and wherein said individual patient response profile

defines the patient's (116) individualized response to said medication, and
wherein said data output port is coupled to said processor (808) to forward instructions to a medication delivery unit (112) to deliver said medication at said medication delivery rate determined by said processor, characterized in that said processor is configured to shift the individual patient response profile to adapt to changing patient conditions."

Claims 2 to 7 and 9 to 16 are dependent claims.

Independent claim 8 of **auxiliary request 1** reads:

"8. A medication delivery controller (108) for controlling the administration of medication to a patient (116) to achieve and maintain a target effect in said patient (116), the controller comprising:
a sensor interface (826) configured to receive one or more patient parameters from a sensor package (104),
a processor (808) coupled to a data interface (818), and
a data output port coupled to said processor (808),
wherein said processor (808) is configured to calculate an individual patient response profile to determine a target concentration level of said medication to achieve said target effect and to determine a medication delivery rate to achieve said target concentration level of said medication in said patient, and wherein said individual patient response profile defines the patient's (116) individualized response to said medication, and
wherein said data output port is coupled to said processor (808) to forward instructions to a medication

delivery unit (112) to deliver said medication at said medication delivery rate determined by said processor, characterized in that said processor is configured to shift the individual patient response profile to adapt to changing patient conditions."

Claim 1 is identical to claim 1 of the main request. Claims 2 to 7 and 9 to 16 are dependent claims.

The independent claims of **auxiliary request 2a** read:

"1. A system for controlling the administration of medication to a patient to achieve and maintain a target effect in said patient, the system comprising:
a sensor package (104) having one or more sensors (608, 610, 612), said sensors (608, 610, 612) being configured to sense an attribute of said patient (116) and to provide a parameter indicating the attribute being sensed;
a medication delivery unit (112) configured to administer said medication to said patient (116) to achieve a concentration of said medication in said patient (116); and
a medication delivery controller (108) having an input coupled to said sensor package (104) and an output coupled to said medication delivery unit (112), said medication delivery controller (108) being configured to accept said one or more parameters from said sensor package (104), wherein the medication delivery controller is configured:
to calculate a first individual patient response profile to determine a first concentration level of said medication to achieve said target effect, and to control said medication delivery unit (112) to deliver

said medication at a rate determined to achieve said first concentration level of said medication in said patient (116), and wherein said individual patient response profile defines the patient's (116) individualized response to said medication, characterized in that
said medication delivery controller is configured to adapt to changing patient conditions by:
determining whether the patient's response to said first concentration level of said medication has changed;
computing a second patient response profile reflecting the patient's new individualized response to said medication, said computation comprising determining an operating point representing a measured effect of said first concentration level of medication on said patient and shifting said first patient response profile until said shifted patient response profile intersects said operating point; and
using said second patient response profile to determine a new concentration level of medication to maintain said target effect in said patient."

"8. A medication delivery controller (108) for controlling the administration of medication to a patient (116) to achieve and maintain a target effect in said patient (116), the controller comprising:
a sensor interface (826) configured to receive one or more patient parameters from a sensor package (104),
a processor (808) coupled to said sensor interface (826), and
a data output port coupled to said processor (808),
wherein said processor (808) is configured to calculate an individual patient response profile to determine a

target concentration level of said medication to achieve said target effect and to determine a medication delivery rate to achieve said target concentration level of said medication in said patient, and wherein said individual patient response profile defines the patient's (116) individualized response to said medication, and
wherein said data output port is coupled to said processor (808) to forward instructions to a medication delivery unit (112) to deliver said medication at said medication delivery rate determined by said processor, characterized in that said processor is configured to adapt to changing patient conditions by being configured to:
determine whether the patient's response to said first concentration level of said medication has changed;
compute a second patient response profile reflecting the patient's new individualized response to said medication, said computation comprising determining an operating point representing a measured effect of said first concentration level of medication on said patient and shifting said first patient response profile until said shifted patient response profile intersects said operating point; and
use said second patient response profile to determine a new concentration level of medication to maintain said target effect in said patient."

Claims 2 to 7 and 9 to 16 are dependent claims.

The independent claims of **"auxiliary request 2b new"** filed during the oral proceedings read:

"1. A system for controlling the administration of medication to a patient to achieve and maintain a target effect in said patient, the system comprising:
a sensor package (104) having one or more sensors (608, 610, 612), said sensors (608, 610, 612) being configured to sense an attribute of said patient (116) and to provide a parameter indicating the attribute being sensed;
a medication delivery unit (112) configured to administer said medication to said patient (116) to achieve a concentration of said medication in said patient (116); and
a medication delivery controller (108) having an input coupled to said sensor package (104) and an output coupled to said medication delivery unit (112), said medication delivery controller (108) being configured to accept said one or more parameters from said sensor package (104), wherein the medication delivery controller is configured:
to calculate a first individual patient response profile to determine a first concentration level of said medication to achieve said target effect, and to control said medication delivery unit (112) to deliver said medication at a rate determined to achieve said first concentration level of said medication in said patient (116), and wherein said individual patient response profile defines the patient's (116) individualized response to said medication,
characterized in that
said medication delivery controller is configured to adapt to changing patient conditions by:
determining whether the patient's response to said first concentration level of said medication has changed;

computing a second patient response profile reflecting the patient's new individualized response to said medication, said computation comprising determining an operating point representing a measured effect of said first concentration level of medication on said patient and shifting said first patient response profile until said shifted patient response profile intersects said operating point; and
using said second patient response profile to determine a new concentration level of medication to maintain said target effect in said patient."

"7. A medication delivery controller (108) for controlling the administration of medication to a patient (116) to achieve and maintain a target effect in said patient (116), the controller comprising:
a sensor interface (826) configured to receive one or more patient parameters from a sensor package (104),
a processor (808) coupled to a data interface (818), and
a data output port coupled to said processor (808),
wherein said processor (808) is configured to calculate a first individua1 patient response profile to determine a first concentration level of said medication to achieve said target effect and to determine a medication delivery rate to achieve said first concentration level of said medication in said patient, and wherein said individual patient response profile defines the patient's (116) individualized response to said medication, and
wherein said data output port is coupled to said processor (808) to forward instructions to a medication delivery unit (112) to deliver said medication at said medication delivery rate determined by said processor,

characterized in that said processor is configured to adapt to changing patient conditions by being configured to:
determine whether the patient's response to said first concentration level of said medication has changed;
compute a second patient response profile reflecting the patient's new individualized response to said medication, said computation comprising determining an operating point representing a measured effect of said first concentration level of medication on said patient and shifting said first patient response profile until said shifted patient response profile intersects said operating point; and
use said second patient response profile to determine a new concentration level of medication to maintain said target effect in said patient."

Claims 2 to 6 and 8 to 14 are dependent claims.

VII. The appellant's arguments are summarised as follows:

The phrase "a processor coupled to said data interface (818)" in claim 8 as granted was clearly and unambiguously erroneous. Not only was there no antecedence for "said" data interface, neither was there any context for a data interface in the structure of the claim as a whole. It was immediately apparent to the skilled reader that the correction to be made was one of "a data interface (818)" or "said sensor interface (826)". These were the only two reasonable alternatives. If the word "said" were to be replaced by "a", the data interface was left on a limb: it was there merely as an observation that the controller had one. The data interface had no explained function in

the claim. Its inclusion in the claim was quite arbitrary, and indeed not plausible. The skilled reader recognised that the processor had to be coupled to the sensor interface in order to process the patient parameters and deliver the logical sequence of operations set out in the claim. On the other hand, a coupling between a data interface and the processor was technically meaningless and unexplained. It left in doubt how the processor received information from the sensor package, thus leaving a hole between the processor and sensor package. It had to be inferred that processor and sensor interface were coupled. Such a coupling made perfect sense in the technical context of the claim, and it was immediately evident that nothing else would have been intended than what was offered as the correction, as required by Rule 139 EPC. This was also evident from the file history. At the beginning of the examination proceedings, the phrase "a processor coupled to said data interface" in original claim 22 had already been replaced by "a processor coupled to said sensor interface", but was afterwards reversed when new representatives took over the case who did not have access to the original document. If the correction was allowable under Rule 139 EPC, this was merely declaratory of the factual position of the documents properly understood prior to the correction being sought (G 3/89, Reasons, point 4), and there was no requirement to consider whether or not the correction was in breach of Article 123(3) EPC.

The basis for the amendment of the characterising part of claim 1 of auxiliary request 1 could be found in the 3rd paragraph of page 12 and the first two paragraphs of page 13 of the application as published. In view of

the fact that in the penultimate paragraph of page 4 it was stated that the new patient response profile was calculated, without mentioning the additional requirement that the shifted profile intersected the new operating point, the amendment was not an intermediate generalisation in breach of Article 123(2) EPC.

Auxiliary request 2b new was filed in response to the respondent's late-filed objections under Articles 83, 84 and 123(2) EPC, raised only in its letter dated 15 November 2012. The appellant was entitled to react by filing amendments in order to overcome these objections.

The amendments included in claim 1 of this request were supported by original claims 9 and 20. Maintaining a target effect implied that it had been previously achieved.
The expression "shifting said first patient response profile until said shifted patient response profile intersects said operating point" in claim 1 was clearly to be understood as relating to a mere translation of the profile without changing its shape, amounting to a simple coordinate transformation, as described in connection with Figures 5B and 5C. It was within the skilled person's comprehension to extend this teaching to more than two dimensions.

The term "determined" in paragraph [0029] was not in contradiction with the term "shifted" in claim 1. The requirement of support in Article 84 EPC could not be understood to mean that the exact terminology of the claims had to be used throughout the description.

Figures 5B and 5C disclosed two working embodiments of how the patient response profile was shifted in a two-dimensional system. The skilled person was able to extrapolate this teaching to a more than two-dimensional system. A one-dimensional "profile" was technically meaningless. Accordingly, the requirements of Article 83 EPC were met.

Document D25 was cited as reference [22] in D24 in the context of updating and individualising model parameters and should thus be admitted into the proceedings.

The statement at page 750, left-hand column, 3rd paragraph of D24 left open which ones of the various model parameters in the functional relationship representing the model, such as E_0 or C^{γ}_{50} in the Hill equation, were "updated and individualised". Moreover, D24 was entirely silent as to how such an updating was to be performed. There were many possibilities of computing a second patient response profile, but there was no disclosure whatsoever in D24 regarding the specific kind of a second patient response profile obtained by shifting the first patient response profile until the shifted patient response profile intersected the new operating point as defined in claim 1.

The advantage of shifting the patient response profile was that such a mere coordinate transformation was simple and could be performed rapidly. The profile did not have to be altered entirely, but merely repositioned. The invention made it possible to quickly return a patient to a desired target effect of a drug

after a departure from the individualised profile had been established. D24 did not address this problem and gave no hint towards shifting the response profile as claimed. The solution according to claim 1 was therefore not obvious to the skilled person when starting from D24.

VIII. The respondent's arguments are summarised as follows:

With regard to the replacement of the expression "a processor (808) coupled to said data interface (818)" in claim 8 as granted by "a processor (808) coupled to said sensor interface (826)" in claim 8 of the main request, it was not immediately evident that nothing else would have been intended than what was offered as the correction, as required by Rule 139 EPC. The alternative "a processor (808) coupled to a data interface (818)" was equally plausible and technically meaningful. The proposed correction was therefore not allowable under Rule 139 EPC. Moreover, the deletion of the feature "data interface" in claim 8 as granted extended the scope of protection, in breach of Article 123(3) EPC. Claim 8 of auxiliary request 2a was objectionable for the same reasons.

The characterising part of claim 1 of auxiliary request 1 represented an intermediate generalisation since shifting of the individual patient response profile was only disclosed in combination with the limitation that the shifted patient response profile intersected the new operating point. Without this limitation the claim encompassed undisclosed subject-matter, for instance shifting of the profile into a new area of operation, in breach of Article 123(2) EPC.

Auxiliary request 2b new was filed late during the oral proceedings and comprised subject-matter which was not present in the set of claims as granted. Moreover, original claims 9 and 20, which related to this new subject-matter, had not been searched. The submission of this request at this stage of the proceedings prevented the respondent from performing a search regarding the newly introduced features. It was an abuse of procedure and should not be admitted.

Claim 1 of auxiliary request 2b new was in breach of Article 123(2) EPC since original claim 9 included the limitation that the target effect was maintained at the first concentration level of the medication, which was no longer present in claim 1. Furthermore, the feature that the individual patient response profile was adaptable to adapt to changing patient conditions has been deleted. Moreover, the original description disclosed the shifting of the profile only in two dimensions. The passage bridging pages 11 and 12, cited by the appellant in support of the amendment, stated that the profile was replotted based on a current operating point. The deletion of these features also amounted to unallowable intermediate generalisations.

The deletion of the feature in claim 1 as granted that the individual patient response profile was adaptable to adapt to changing patient conditions extended the scope of protection, in breach of Article 123(3) EPC.

The expression "shifting said first patient response profile until said shifted patient response profile intersects said operating point" in claim 1 was not

clear under Article 84 EPC since Figure 5B did not in fact depict a "shift" of the profile but an extension of the curve to the right. Further, at the end of paragraph [0046] it was mentioned that the new patient response profile was calculated and redrawn, thus casting further doubt on what had to be understood by "shifting". Moreover, the meaning of the expression "shifting" a "profile" was entirely unclear in a more than two-dimensional space.

The phrase at the beginning of paragraph [0029] stated that a new response profile was "determined". This was broader than the term "shifted" used in claim 1, which was thus not supported by the description as required by Article 84 EPC.

The disclosure was insufficient and incomplete since it did not clearly describe how the shifting of the profile was actually performed. In addition to what was shown in Figures 5A to 5C, there were further possibilities of shifting the profile, resulting in different values of the new concentration of medication (C_2). The value of C_2 in Figure 5B was not identical to that in Figure 5C. Moreover, the disclosure was entirely silent about how to shift the profile in a one-dimensional or more than two-dimensional system, which was also within the scope of the claim. Accordingly, the requirements of Article 83 EPC were not fulfilled.

The late submission of document D25 during the oral proceedings did not allow the respondent to present its technical analysis. It would be unfair if D25 were admitted into the proceedings.

In addition to the features of the preamble of claim 1, D24 also disclosed those of its characterising part, as became apparent in particular from page 750, left-hand column, 3rd and 4th paragraphs. As also described in the patent specification, the measured BIS was used as control variable, and the adaptive-model-based controllers used a PK-PD model. Accordingly the medication delivery controller of D24 was configured to adapt the individual patient response profile to adapt to changing patient conditions. An "updating" of the response profile as disclosed in D24, i.e. a recalculation, would necessarily result in some kind of "shift" of the profile, and a new operating point would necessarily be reached thereby. The Hill curve describing the profile was patient-dependent and necessarily maintained its shape, for instance when a second medication attenuated the drug effect. Accordingly, D24 was novelty-destroying for claim 1.

As disclosed at page 751, left-hand column, 1st and 2nd paragraph, the controller of D24 was clearly configured to adapt the response profile to changing patient conditions. In case of a departure from the response profile, there were only two alternatives for updating the model parameters of D24, namely to either shift or recalculate the patient response profile. Accordingly, shifting the profile was an obvious selection which the skilled person would consider without any inventive step. Moreover, the Hill equation was a well-known model for describing the course of the patient response profile, and the hint in D24 to update its model parameters would directly instruct the skilled person that the profile was to be shifted.

Reasons for the Decision

1. The appeal is admissible.

2. Main request - amendments

Claim 8 of the patent as granted defines "a processor (808) coupled to said data interface (818)". This expression has now been replaced by "a processor (808) coupled to said sensor interface (826)". It is to be established whether this amendment is allowable as a correction of an error under Rule 139 EPC, as requested by the appellant.

It is undisputed that claim 8, referring to "said data interface", comprises an obvious mistake since the data interface lacks an antecedent basis in the claim. The question to be decided is whether the correction according to claim 8 of the main request is "obvious in the sense that it is immediately evident that nothing else would have been intended than what is offered as the correction", as required by Rule 139 EPC.

In order to correct the obvious mistake, there are at least two alternative possibilities: (a) the word "said" could be replaced by "a", or (b) the term "said data interface (818)" could be replaced by "said **sensor** interface (**826**)" [emphasis added], as defined in present claim 8 (wherein the sensor interface (826) is previously defined). It is to be noted that alternative (b) requires the replacement of not only the word "data" by "sensor" but also of reference numeral 818 by 826.

Both alternatives are supported by Figure 8, showing both the data interface (818) and the sensor interface (826) coupled to the processor (808). It may be agreed that alternative (b) "makes perfect sense", as argued by the appellant, since patient parameters received by the sensor package (104) can be entered via sensor interface (826) into the processor (808) in order to calculate the individual patient response profile, as defined further on in the claim. However, this changes the technical meaning of the claim substantially, since one structural feature of the claimed system is deleted and replaced by an entirely different one. This is not the case for alternative (a), which merely involves a small linguistic correction of the claim wording. Particularly in view of paragraphs [0063] to [0065] of the patent specification (corresponding to lines 3 et seq. of page 18 and the first paragraph of page 19 of the application as published (WO-A-01/83007)), alternative (a) is also technically meaningful: it is stated that the data interface (818) can be utilised as a conduit for providing data such as patient attributes to the medication delivery controller, thereby providing additional or enhanced functionality. As described in paragraphs [0031] to [0035], such patient attributes are used for calculating the individual patient response profile. The fact that alternative (a) leaves a "hole" between the processor and the sensor package, leaving in doubt how the processor receives information from the sensor package, as argued by the appellant, is not relevant in this respect since the claim does not require that the processor is configured to calculate the individual patient response profile **on the basis of patient parameters received by the sensor package.**

Therefore, there exist at least two ways in which the error in claim 8 could have been corrected. Both alternatives (a) and (b) are perfectly plausible. Accordingly, it cannot be said that only alternative (b) and nothing else would have been intended. As stated at the end of point 6 of the Reasons of G 3/89 (OJ EPO 1993, 117), if there is any doubt that nothing else could have been intended than what is offered as the correction, a correction cannot be made. Therefore, this correction is not obvious in the sense required by Rule 139 EPC and hence not allowable.

The fact that during the examination proceedings a corresponding amendment to original claim 22, replacing "a processor coupled to said data interface" by "a processor coupled to said sensor interface", was reversed when new representatives took over the case is not considered to be relevant here. A change of representatives does not legitimise the correction. Moreover, the applicant/patent proprietor/appellant had finally approved the (erroneous) text of the patent for grant.

3. Auxiliary request 1 - amendments

The characterising part of claim 1 states that the medication delivery controller is configured to shift the individual patient response profile to adapt to changing patient conditions. The appellant's argument that the second paragraph of page 12 and the first two paragraphs of page 13 of the original application provide a basis for this amendment is not accepted by the Board. The disclosure in these passages is to be

understood in context as referring to Figures 5A to 5C which show that the individual patient response profile is shifted **until the shifted patient response profile intersects the new operating point P_S**. This additional limitation is also mentioned explicitly in the first sentence of page 13 and in original claim 20.

The penultimate paragraph of page 4 does not provide a sufficient basis for the amendment. This passage states that the controller calculates a new patient response profile, without referring to the above-mentioned additional limitation but also without using the term "shifting". **Calculating** a **new** profile is not equivalent to shifting the profile, since the shape of the profile is not necessarily maintained, as is the case when the profile is shifted (according to the understanding of the term explained further in point 5.3 below).

It follows that shifting of the profile is not disclosed in isolation, but only in combination with the additional limitation of the shifted profile intersecting the new operating point. Without this limitation the wording of the claim encompasses subject-matter which has not been disclosed, for instance shifting of the profile into a new area of operation. Therefore the subject-matter of claim 1 of auxiliary request 1 represents an intermediate generalisation which is in breach of Article 123(2) EPC.

4. Auxiliary request 2a - amendments

Claim 8 of auxiliary request 2a also comprises the feature "a processor (808) coupled to said sensor

interface (826)" which is present in claim 8 of the main request and which is not allowable as an obvious correction under Rule 139 EPC, as detailed in point 2 above.

5. Auxiliary request 2b new

5.1 Admissibility

The present request was filed during the oral proceedings in response to objections under Articles 83, 84 and 123(2) EPC against inter alia previous auxiliary request 3 (corresponding to present auxiliary request 1) filed by the appellant with its statement of grounds of appeal. These objections were late-filed since they were raised by the respondent only in its letter dated 15 November 2012, but not in its counter-statement filed on 30 July 2009 in response to the appellant's statement of grounds.

It would not be equitable not to allow the appellant to file amendments in an attempt to overcome such late-filed objections. Such a reaction is justified in response not only to patentability issues, for instance resulting from newly introduced prior-art documents, but to any admitted late-filed objection.

Claims 1 and 7 comprise features of original claims 9 and 20 of the application as published which were not searched, as can be seen from the International Search Report. The respondent's argument that it did not have sufficient time to perform a search for prior art disclosing the unsearched features included in independent claims 1 and 7, which correspond to those

filed as auxiliary request 2b with the appellant's letter dated 5 December 2012, i.e. relatively shortly before the date of the oral proceedings, is not accepted by the Board. When raising an objection under Article 123(2) EPC regarding an intermediate generalisation (as detailed in point 3 above), the respondent must be prepared for the appellant to try to overcome it by adding the "missing" features. The inclusion of the features of original claims 20 and 9 (on which claim 20 depends) addresses this objection. Moreover, at least the feature of shifting the response profile was already present in the independent claims of auxiliary requests 2 to 11 filed with the statement of grounds of appeal.

From the above it follows that it would not be equitable to disregard auxiliary request 2b new under Article 114(2) EPC. Accordingly, it is admitted into the proceedings.

5.2 Amendments

5.2.1 Basis

Claim 1 is based on claim 1 as granted in combination with original claims 9 and 20.

According to claim 1 the controller is configured to calculate a first individual patient response profile to determine a first concentration level of the medication to **achieve** the target effect, whereas original claim 9 refers to using the first patient response profile to determine a first concentration level of the medication to **maintain** the target effect.

In the Board's view, maintaining a target effect implies that it has been previously achieved. Moreover, the first paragraph of both present claim 1 and original claim 9 requires controlling the administration of medication to a patient to **achieve and maintain** a target (or "desired") effect in the patient.

The deletion from granted claim 1 of the feature that the individual patient response profile is adaptable to adapt to changing patient conditions is supported by the fact that this feature is not present in original claim 3 wherein the corresponding feature "patient response profile defin[ing] the patient's individualized response to said medication" is introduced without the additional requirement of adaptability to changing patient conditions.

It may be agreed that the original description discloses the shifting of the profile only in **two dimensions**. It is further correct that in the passage bridging pages 11 and 12 it is stated that the profile is **replotted** based on a current operating point. However, the fact that claim 1 does not comprise these limitations does not represent an intermediate generalisation in breach of Article 123(2) EPC, since original claim 20 does not comprise these limitations either and thus provides support for the amendment.

Accordingly, the Board is satisfied that the requirements of Article 123(2) EPC are met.

5.2.2 Scope of protection

The feature in claim 1 of the patent as granted that the "individual patient profile [is] adaptable to adapt to changing patient conditions" has been further specified by the inclusion of the additional features in the characterising part of present claim 1. Moreover, the claim begins by explicitly stating that the medication delivery controller is configured to "adapt to changing patient conditions". Accordingly, the existing features have been maintained and the scope of protection has been limited by additional features, and there is no extension in breach of Article 123(3) EPC.

5.3 Clarity

In the Board's view, the expression "shifting said first patient response profile until said shifted patient response profile intersects said operating point" in claim 1 is to be understood as referring to a mere translation of the first profile, maintaining its shape, as described in paragraphs [0045] to [0048], [0091] and [0092] and depicted in two dimensions in Figures 5A to 5C. Firstly, from a literal point of view, the formal reference to **said** shifted patient response profile indicates that the shape of the profile is maintained. The fact that it is mentioned at the end of paragraph [0046] that "a new patient response profile 500 is calculated", i.e. **re**calculated, and reference is made to "**re**drawing patient response profile 500" [emphasis added] cannot be seen to imply that the new profile has a different shape. The skilled reader recognises that a mere coordinate transformation

is meant (which also requires some recalculation). The respondent's argument that Figure 5B does not depict a "shift" of the profile but an extension of the curve to the right is not accepted by the Board, since the drawing is only schematic and the skilled reader understands from the corresponding part of the description that such an extension is not intended. The Board is further of the opinion that the expression "shifting said first patient response profile" is within the skilled person's comprehension also in a more than two-dimensional space. Accordingly, the wording of the claims is clear within the meaning of Article 84 EPC.

5.4 Support

In paragraph [0019] it is stated that the object of the invention is achieved by "a system for controlling the administration of a medication according to the characterizing portion of the appended claims", i.e. referring to the claims rather than repeating their wording, as is usual practice. The respondent objects that the phrase at the beginning of paragraph [0029] under the headings "DETAILED DESCRIPTION OF THE INVENTION" and "1. Overview of the Invention", stating that a new response profile is "determined", is broader than the term "shifted" used in claim 1, the claim thus not being supported by the description. In the Board's view, however, this requirement of Article 84 EPC does not mean that the exact terminology of the claims must be used throughout the description, particularly in the part relating to the detailed description of the specific embodiments. The term "determined" in paragraph [0029] is not in contradiction with the term

"shifted" in claim 1. In view of the statement in paragraph [0019], the claims are supported by the description as required by Article 84 EPC.

5.5 Sufficiency of disclosure

Paragraphs [0045] to [0048] in combination with Figures 5B and 5C disclose two working embodiments of how the patient response profile is shifted in a two-dimensional system, namely horizontally in the X direction (Figure 5B) or vertically in the Y direction (Figure 5C). It is further mentioned that the profile could also be shifted in both the X and the Y directions. Accordingly, the description clearly indicates at least one way for the skilled person to carry out the invention ("Case Law of the Boards of Appeal of the EPO", 6th ed. 2010, II.A.3b)). The fact that further possibilities of shifting the profile may exist, resulting in different values of the new concentration of medication (C_2), as demonstrated by the drawings submitted by the respondent during the oral proceedings, is of no relevance since claim 1 merely refers to "a new concentration level of medication". The respondent further objected that the value of C_2 in Figure 5B is not identical to that in Figure 5C. However, the drawings are only schematic, and nowhere in the description is it stated that the values of C_2 have to be identical. In a two-dimensional system the response profile is represented by a curve, as explicitly stated in paragraph [0035], representing the desired effect of the medication on the patient as a function of the concentration of medication (paragraph [0020] and Figures 5A to 5C). The Board has no doubt that the person skilled in the art is able to extend

this teaching to further dimensions (e.g. if additional medications are involved), as covered by the scope of the claim. On the other hand, the Board does not accept the respondent's interpretation that the response profile could be represented by a single value only, since such a one-dimensional "profile" would be technically meaningless. Accordingly, the invention is disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art, as required by Article 83 EPC.

5.6 Admissibility of D25

During the oral proceedings, the appellant submitted document D25, cited as reference [22] in D24 in the context of updating and individualising model parameters. D25 is a research publication comprising 14 pages, and the technical evaluation of its teaching by the respondent and the Board would require adequate time, thus resulting in a delay of the proceedings which would not be conducive to procedural economy. In view of the fact that the novelty objection vis-à-vis D24 was already raised in the first-instance opposition proceedings, it could and should have been presented much earlier, in particular with the statement of grounds of appeal (Article 12(2) RPBA). Pursuant to Article 13(1) and (3) RPBA, the Board considers it equitable to exercise its discretion not to admit this document at such a late stage of the proceedings.

5.7 Novelty

D24 undisputedly discloses the features of the preamble of claim 1, in particular (page 751, left-hand column,

1st and 2nd paragraph) the calculation of a first individual patient response profile as defined in the last paragraph of the preamble of claim 1. In analogy to what is described in paragraphs [0010] and [0038] to [0042] of the patent in suit, the first individual patient response profile defining the patient's individualised response to the medication is determined in an open-loop mode, with the bispectral index (BIS) representing the "parameter indicating the attribute being sensed" as defined in the 2nd paragraph of claim 1. The functional relationship between the propofol target effect and site concentration as determined in D24 corresponds to the "first individual patient response profile" in claim 1.

At page 750, left-hand column, 3rd paragraph it is stated that adaptive-model-based controllers using a PK-PD model "compare the set-point of the control variable with the value actually measured. This comparison is used not only to correct dosing but also to update and individualise the model parameters [22]." (as mentioned at page 751, left-hand column, 1st paragraph, the measured BIS is used as control variable). In the next paragraph of page 750 it is stated that "a patient-individualised adaptive model-based control of propofol by BIS ... with a PK-PD model" was used.

In the Board's view, this passage does not anticipate the medication delivery controller being configured to adapt to changing patient conditions in the specific manner defined in the characterising part of claim 1, in particular by "shifting said first patient response

profile until said shifted patient response profile intersects said operating point".

"[C]ompar[ing] the set-point of the control variable with the value actually measured ... to correct dosing" corresponds to changing the concentration level of medication along the first individual patient response profile in a closed-loop mode. "[U]pdat[ing] and individualis[ing] the model parameters" can be understood as relating to the parameters of, for instance, the Hill curve as represented by equation (1) in paragraph [0073] of the patent in suit, representing an example of a PD (pharmacodynamic) model. However, the statement in D24 leaves open which ones of the various model parameters in the functional relationship representing the model, such as the Hill equation, are "updated and individualised". Even if this statement in D24 is understood as corresponding to "computing a second patient response profile reflecting the patient's new individualized response to said medication, said computation comprising determining an operating point representing a measured effect of said first concentration level of medication on said patient" as defined in claim 1, there are many possible ways of computing such a second patient response profile, but there is no disclosure in D24 of the specific second patient response profile as defined in the claim, namely the one obtained by "shifting said first patient response profile until said shifted patient response profile intersects said operating point" (with the term "shifting" meaning a mere translation of the first profile, as explained in point 5.3 above).

The respondent's argument that the teaching of D24 does not exclude a shift of the profile as defined in claim 1 is not sufficient to challenge novelty. Such a shift would have to be directly and unambiguously derivable from the document, which is not the case here. The submission that the Hill curve is patient-dependent and necessarily maintains its shape, for instance when a second medication attenuates the drug effect, is a mere assertion for which no evidence has been presented.

Accordingly, D24 does not anticipate all the features of claim 1 of auxiliary request 2b new. Its subject-matter is novel within the meaning of Article 54 EPC.

5.8 Inventive step

Document D24 (co-authored by the inventors of the patent in suit) is undisputedly the closest prior art.

When the BIS value measured departs from what it should be, D24 suggests updating the model parameters (loc. cit.). There are two conceivable ways of performing such an update. One way would be to measure a further response profile in the open-loop mode and to determine the new model parameters therefrom. This is time-consuming and may not be practical or even possible, as explained in paragraph [0046] of the patent in suit. Another way is to calculate new model parameters without performing an additional measurement. No guidance is given in D24 in this regard. There are many possibilities to calculate new model parameters, and the skilled person cannot derive any information from D24 as to which ones of the model

parameters are to be recalculated and how this is to be done.

The advantage of computing a second patient response profile by shifting the first patient response profile as defined in the characterising part of claim 1 is that such a mere coordinate transformation is simple and can be performed rapidly. The first profile does not have to be altered entirely, but merely repositioned.

The objective technical problem underlying the distinguishing features of claim 1 is to quickly return a patient to a desired target effect of a drug after a departure from the individualised profile has been established.

D24 gives no hint towards the specific solution according to claim 1 and of its advantages. The Board does not accept the respondent's argument that there are only two possible ways to update the model of D24, namely either to shift or to recalculate the patient response profile, and that shifting the profile is an obvious selection, since such an argumentation is based on hindsight. In the appeal proceedings no other prior-art documents were cited by the respondent against claim 1.

It follows that the solution according to claim 1 of auxiliary request 2b new is not obvious from D24. Its subject-matter is based on an inventive step within the meaning of Article 56 EPC.

5.9 Independent claim 7 is directed to a medication delivery controller. The features of its characterising part correspond to those of claim 1. The reasoning presented above in points 5.2 to 5.5, 5.7 and 5.8 also applies mutatis mutandis to claim 7.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to maintain the patent on the basis of:

   – claims 1 to 14 of the "auxiliary request 2b new", filed during the oral proceedings;

   – description: pages 2, 7, 8 and 10 to 16 of the patent as granted; pages 3, 3a, 4 to 6 and 9 filed during the oral proceedings;

   – figures 1 to 9 of the patent as granted.

The Registrar: The Chairman:

D. Hampe E. Dufrasne