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Datasheet for the decision of 17 July 2024

Case Number: T 1163/22 - 3.2.02

Application Number: 11737698.8

Publication Number: 2528499

IPC: A61B5/0205, A61B5/0452, A61B5/08

Language of the proceedings: EN

Title of invention:
ELIMINATION OF THE EFFECTS OF IRREGULAR CARDIAC CYCLES IN THE DETERMINATION OF CARDIOVASCULAR PARAMETERS

Patent Proprietor:
Edwards Lifesciences Corporation

Opponent:
Dieckhoff, Beate

Headword:

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

Keyword:
Grounds for opposition - insufficiency of disclosure (no)
Inventive step - (yes)

Decisions cited:
T 0983/18

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 1163/22 - 3.2.02

D E C I S I O N
of Technical Board of Appeal 3.2.02
of 17 July 2024

Appellant: (Opponent)	Dieckhoff, Beate Dünnwalder Grenzweg 20 51375 Leverkusen (DE)
Representative:	Lohmanns, Bernard Benrather Schlossallee 49-53 40597 Düsseldorf (DE)
Respondent: (Patent Proprietor)	Edwards Lifesciences Corporation One Edwards Way Irvine, CA 92614 (US)
Representative:	Eisenführ Speiser Patentanwälte Rechtsanwälte PartGmbB Postfach 31 02 60 80102 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 28 February 2022 rejecting the opposition filed against European patent No. 2528499 pursuant to Article 101(2) EPC**

Composition of the Board:

Chairman	M. Alvazzi Delfrate
Members:	D. Ceccarelli
	N. Obrovski

Summary of Facts and Submissions

I. The opponent appealed against the Opposition Division's decision to reject the opposition against the European patent.

II. Oral proceedings took place on 17 July 2024.

The appellant requested that the decision under appeal be set aside and that the patent be revoked.

The respondent requested that the appeal be dismissed (main request) or that the patent be maintained on the basis of one of auxiliary requests 1 to 3, filed with the reply to the statement of grounds of appeal on 23 November 2022, and auxiliary requests 4 to 6, filed on 18 August 2023.

III. The following documents are mentioned in this decision:

D1: US 2005/0187481 A1
D4: US 2005/0124903 A1

IV. Independent claims 1 and 15 of the main request read as follows:

1. "A computer-implemented method of determining a cardiovascular parameter comprising the steps:

receiving a waveform dataset corresponding to an arterial blood pressure, or a signal proportional to, or derived from, the arterial blood pressure signal;
identifying individual cardiac cycles in the waveform dataset;

measuring waveform characteristics for the individual cardiac cycles;
determining if the individual cardiac cycles are regular cardiac cycles or irregular cardiac cycles;
characterized in that
measuring a respiratory parameter which is a respiratory-induced variation in the waveform dataset caused by respiration;
creating a modified waveform dataset containing the waveform characteristics of the regular cardiac cycles and the waveform characteristics of the irregular cardiac cycles wherein the waveform characteristics of the irregular cardiac cycles are replaced with estimated waveform characteristics, wherein replacing the waveform characteristics of the irregular cardiac cycles with estimated waveform characteristics comprises:
determining, based on the waveform characteristics of regular cardiac cycles, pseudo-starting points and/or pseudo-ending points for the irregular cardiac cycles which have longer durations than regular cycles, and directly measuring or calculating waveform parameters/characteristics of the irregular cardiac cycle based on the pseudo-starting points and/or pseudo-ending points; and
calculating a cardiovascular parameter using the modified waveform dataset, wherein the cardiovascular parameter is a parameter reflecting preload dependence and fluid responsiveness, such as stroke volume variation, pulse pressure variation, systolic pressure variation, stroke volume, cardiac output, systemic vascular compliance, cardiac flow,

cardiac flow velocity, vascular compliance, or vascular elastance."

15. "A computer-readable medium storing computer-executable instructions which, when loaded into and executed by a processing system, cause the processing system to carry out the method of any of the previous claims."

Claims 2 to 14 are dependent claims.

V. The appellant's arguments, where relevant to this decision, can be summarised as follows.

Sufficiency of disclosure

The invention as defined in claims 1 and 15 of the main request was not sufficiently disclosed. The claims were overly broad, such that they could not put into practice across the whole scope. They only presented a vague idea of identifying longer cardiac cycles and replacing them with shorter ones, which was a task that was always to be addressed.

The feature of "determining, based on the waveform characteristics of regular cardiac cycles, pseudo-starting points and/or pseudo-ending points for the irregular cardiac cycles which have longer durations than regular cycles" covered a variety of non-workable embodiments. Selecting arbitrary pseudo-starting and pseudo-ending points did not improve the calculation of cardiovascular parameters. The pseudo-points needed to shorten the duration of an irregular cycle in order to cut out irregular data and had to be within a given range of the mean/median pressure difference and mean/median time period for regular cycles in order to

provide an accurate result, but this was not defined in claims 1 and 15. Accordingly, the claims covered embodiments which could lengthen, rather than shorten, the irregular cycle. This would not "eliminate the effect of irregular cardiac cycles" as intended (paragraph [0059] of the patent).

Moreover, the claims did not specify either waveform characteristics or the calculation for determining the pseudo-point "based on" the waveform characteristics. The term "waveform characteristic" covered a wide variety of different parameters. The description listed as many as 51 different examples of waveform characteristics; however, the description only provided support for a specific embodiment according to which pseudo-points were allocated to pressure values found within a pre-established range of a mean or median time duration and a pre-established range of a mean or median pressure difference, which were only four different combinations of waveform characteristics of regular cardiac cycles. According to the established case law of the boards of appeal, sufficiency of disclosure presupposed that the person skilled in the art was able to obtain substantially all the embodiments falling within the ambit of the claims. In the recent decision T 983/18, it was stated that gaps in the disclosure could not be filled by an undue number of experiments amounting to a research program. The protection obtained by the patent had to be commensurate with the disclosed teaching and should not cover non-working embodiments. For claim 1 of the main request, however, this was the case, as the scope of a claim was defined by its wording and the description could not imply limitations which were not present in the claim. As a consequence, the claim was not limited to pseudo-starting or pseudo-ending points that

shortened the duration of the cardiac cycle or to waveform characteristics limited to time and pressure parameters. If the Board came to the conclusion that the invention as defined in claims 1 and 15 was sufficiently disclosed, it was to identify at least one embodiment according to these claims in the description.

Inventive step

The subject-matter of claims 1 and 15 of the main request lacked an inventive step when starting from D1.

If it was considered that D1 did not disclose the features of determining, based on the waveform characteristics of regular cardiac cycles, pseudo-starting points and/or pseudo-ending points for the irregular cardiac cycles which have longer durations than regular cycles, and directly measuring or calculating waveform parameters/characteristics of the irregular cardiac cycle based on the pseudo-starting points and/or pseudo-ending points, these distinguishing features covered a wide variety of embodiments that did not provide the purported technical effect of improving the accuracy of the measurement of preload dependence and fluid responsiveness in situations of high-frequency occurrence of irregular cardiac cycles by eliminating the effect of irregular cardiac cycles (paragraph [0059] of the patent).

Since the distinguishing features did not provide a technical effect and therefore did not solve a technical problem across their whole scope, they could not contribute to the inventive step of the claims according to the established case law of the boards of

appeal. It followed that the subject-matter of claims 1 and 15 was not inventive over D1 alone.

Even if it was considered that the distinguishing features solved a technical problem, the subject-matter of claims 1 and 15 of the main request was not inventive over the combination of D1 with D4.

D4 disclosed a method in which stroke volume or cardiac output was determined from the standard deviation (or an approximation of standard deviation) of a waveform of arterial pressure (abstract and paragraphs [0038] to [0041] and [0054]). The time window for the determination could coincide with a single heart cycle (paragraph [0045]) and could be shortened if an irregular cycle was detected (paragraphs [0046] to [0048]). Paragraph [0055] disclosed calculating derivatives over an interval of a cardiac cycle between the start and the first dicrotic point, to avoid spurious values from irregular cycles being used from after the dicrotic point. This amounted to the determination of a pseudo-ending point that was different from the actual ending point of the cardiac cycle. The detection of an irregular cycle and the determination of the pseudo-ending point would necessarily be based on waveform characteristics of regular cardiac cycles. There was no technical difference between pseudo-starting/ending points used to define a window over which a calculation was performed and the starting/ending points of a sampling window that initially corresponded to the start and end of a cardiac cycle and was subsequently adapted so that it did not conform to the starting/ending point of the cardiac cycle. It followed that D4 disclosed the distinguishing features and the person skilled in the art would have implemented them in the method according

to D1 in order to improve the accuracy of the calculation of cardiovascular parameters.

VI. The respondent's arguments, where relevant to this decision, can be summarised as follows.

Sufficiency of disclosure

The invention as defined in claims 1 and 15 of the main request was disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

Paragraphs [0087] to [0090] of the patent disclosed in detail when and how pseudo-starting points and/or pseudo-ending points were determined.

The claims did not extend to selecting pseudo-starting and pseudo-ending points which extended an irregular cardiac cycle. It was clear to the person skilled in the art that, if the duration of an irregular cycle was extended, the amount of unsuitable data within that cycle would be increased and would additionally comprise data from neighbouring cycles, which made no technical sense. The person skilled in the art would not contemplate such a meaningless embodiment.

The determination of the pseudo-starting and pseudo-ending points based on the waveform characteristics was also sufficiently disclosed. The description explained how pseudo-starting and pseudo-ending points could be calculated from the median or mean time duration using range factors (e.g. range start factor, range stop factor etc.). In addition, the use of the standard deviation of the duration of regular cycles was described. Furthermore, the person skilled in the art

would also contemplate using time factors derived from the pressure waveform other than the median or mean time of the duration of the whole regular cycle. The same applied to pressure factors. The person skilled in the art could easily use a pressure characteristic of a waveform of a regular cycle to find a suitable pseudo-starting or pseudo-ending point. For example, the median or mean pressure difference between the diastolic pressures of two adjacent cycles, or the maximum difference as described in paragraph [0087] of the patent, could be considered. It was also within the competence of the person skilled in the art to use the maximum, median or mean difference between the diastolic pressure of regular cardiac cycles and the mean arterial pressure, since, for all regular cardiac cycles, such a difference was within a certain range. In this context the term "waveform characteristics" was limited to pressure or time parameters since a pressure waveform representing a cardiac cycle was a measurement of pressure values over time.

Inventive step

The subject-matter of claims 1 and 15 of the main request was inventive.

D1 did not disclose the determination of pseudo-starting points and/or pseudo-ending points for irregular cardiac cycles which have longer durations than regular cycles, and directly measuring or calculating waveform parameters/characteristics of the irregular cardiac cycle based on the pseudo-starting points and/or pseudo-ending points.

The appellant's argument that these distinguishing features were not associated with a technical effect

across their whole scope because they covered non-working embodiments could not succeed, as the technical effect that the data relating to irregular cardiac cycles could be used for the evaluation of a patient's health status was provided for all (working) embodiments falling within the scope of the claims.

D4 did not disclose determining pseudo-starting and/or pseudo-ending points for irregular cardiac cycles which had longer durations than regular cycles. Hence, its combination with D1 could not render the subject-matter of the claims obvious.

Reasons for the Decision

1. The subject-matter of the patent

The patent relates to a computer-implemented method of determining a cardiovascular parameter from arterial blood pressure and corresponding computer-readable medium storing instructions for carrying out the method.

According to the patent (paragraph [0001]) cardiovascular parameters such as stroke volume (SV), cardiac output (CO), end-diastolic volume, ejection fraction, stroke volume variation (SVV), pulse pressure variation (PPV), and systolic pressure variations (SPV) are important not only for diagnosis of disease, but also for "real-time" monitoring of serious conditions (paragraphs [0002] and [0012] to [0017] provide definitions of these parameters). Obtaining these parameters from arterial blood pressure is advantageous because blood pressure can be accurately measured with minimal or no invasion (paragraph [0006]).

The method according to claim 1 of the main request comprises receiving a waveform dataset corresponding to an arterial blood pressure, or a signal proportional to, or derived from, the arterial blood pressure signal; identifying individual cardiac cycles in the waveform dataset; measuring waveform characteristics for the individual cardiac cycles; and determining if the individual cardiac cycles are regular cardiac cycles or irregular cardiac cycles.

A cardiac cycle is the performance of the human heart from the beginning of one heartbeat to the beginning of the next. It consists of two periods: systole and diastole. During systole the heart muscle contracts and pumps blood to the body. During diastole the heart muscle relaxes and refills with blood. Due to the pumping action of the heart the arterial blood pressure varies during a cardiac cycle. At the beginning of systole, for a short time both the mitral valve (through which blood flows into the left ventricle) and the aortic valve (through which the blood flows from the left ventricle to the body) are closed. In that time pressure builds up in the left ventricle of the heart and the arterial pressure does not vary significantly. After that time the aortic valve opens and the blood is pumped out of the left ventricle, which causes a rapid and strong increase in arterial pressure followed by a decrease when almost all the blood is expelled. At the beginning of diastole the aortic valve closes. For a short time in which the mitral valve is also still closed there is an increase in the arterial blood pressure, followed by a decrease during the rest of diastole, with both the aortic valve and the mitral valve being open. Figure 1 of the patent shows this pressure change, which repeats itself

regularly during successive cardiac cycles. Hence, the variation of pressure over time makes it possible to identify the cardiac cycles.

The claimed method further comprises measuring a respiratory parameter which is a respiratory-induced variation in the waveform dataset caused by respiration. It further comprises creating a modified waveform dataset containing the waveform characteristics of the regular cardiac cycles and the waveform characteristics of the irregular cardiac cycles wherein the waveform characteristics of the irregular cardiac cycles are replaced with estimated waveform characteristics by determining, based on the waveform characteristics of regular cardiac cycles, pseudo-starting points and/or pseudo-ending points for the irregular cardiac cycles which have longer durations than regular cycles.

The method further comprises directly measuring or calculating waveform parameters/characteristics of the irregular cardiac cycle based on the pseudo-starting points and/or pseudo-ending points and calculating a cardiovascular parameter using the modified waveform dataset.

The cardiovascular parameter is a parameter reflecting preload dependence and fluid responsiveness, such as stroke volume variation, pulse pressure variation, systolic pressure variation, stroke volume, cardiac output, systemic vascular compliance, cardiac flow, cardiac flow velocity, vascular compliance, or vascular elastance.

The creation of the modified waveform dataset is intended to mitigate the effect of the occurrence of

irregular cardiac cycles on the accuracy of the measurement of the cardiovascular parameter.

2. Sufficiency of disclosure

The appellant argued that the invention as defined in claims 1 and 15 of the main request was not sufficiently disclosed.

2.1 A first line of argument was that the claims were overly broad and could not be put into practice across their whole scope. This was because the claims did not define the pseudo-starting and/or pseudo-ending points. To improve the accuracy of a measurement, which was the aim of the patent, the pseudo-points could not be selected arbitrarily.

The Board is not convinced by this argument.

The claims specify that the pseudo-starting and pseudo-ending points are determined to replace the waveform characteristics of irregular cardiac cycles which have longer durations than regular cycles with estimated waveform characteristics. This is done after measuring waveform characteristics of individual cardiac cycles and determining if the individual cardiac cycles are regular or irregular. The estimated waveform characteristics of the irregular cardiac cycles together with the waveform characteristics of the regular cardiac cycles are used to create a modified waveform set, from which a cardiovascular parameter is calculated.

For the person skilled in the art this inherently means that the pseudo-starting and pseudo-ending points, with the estimated waveform characteristics, must simulate

regular cardiac cycles.

The description of the patent, the disclosure of which forms the basis for assessing sufficiency, confirms this, as it sets the aim of eliminating the effect of irregular cardiac cycles (paragraph [0059]) and discloses appropriate methods for achieving it (for example paragraph [0090] and Figure 15). It is irrelevant whether or not the claim wording, when read purely literally, might include embodiments with estimated waveform characteristics which may lengthen or otherwise worsen the effects of the irregular cycles. Such embodiments make no technical sense and are excluded from the scope of the claims by the person skilled in the art, who reads the claims in context, using common general knowledge and while trying to make technical sense out of them.

2.2 A second line of argument was that claims 1 and 15 did not specify the kind of "waveform characteristics" of the regular cardiac cycles and how the pseudo-points could be established from them. The description disclosed only a few waveform characteristics which could lead to the determination of the pseudo-points; however, many other waveform characteristics fell within the scope of the claims. It followed that the invention could not be performed across all the claimed embodiments.

The Board agrees with the appellant that sufficiency of disclosure presupposes that the person skilled in the art can carry out the invention substantially across the whole breadth of the claimed subject-matter.

However, this is the case for the current claims 1 and 15 of the main request, as understood by the person

skilled in the art.

In paragraphs [0064] to [0072], the patent discloses several time and pressure (for example the location of a dichrotic notch versus the diastolic pressure) parameters of the waveform, the analysis of which may make it possible to establish whether or not a cardiac cycle is regular. It also discloses several ways of creating a modified waveform (paragraphs [0087] to [0089]). The claims are an acceptable generalisation of this disclosure. The person skilled in the art, in view of the teaching of the patent and the common general knowledge, would have been able to establish pseudo-points on the basis of further usable waveform characteristics, bearing in mind that the pseudo-points should be selected to mitigate the effects of irregular cardiac cycles on the calculation of the cardiovascular parameters. This is a matter of mathematics which does not require undue burden, let alone a research program. Hence, the findings in T 983/18, as cited by the appellant, are not relevant to the current case. In this respect it is noted, as the respondent pointed out, that the waveform characteristics are limited to time and pressure parameters as the waveform is a plot of pressure versus time.

As regards the identification of at least one embodiment falling under the scope of the claims in the description, the appellant herself identified such an embodiment according to which pseudo-points are allocated to pressure values found within a pre-established range of a mean or median time duration and a pre-established range of a mean or median pressure difference (paragraphs [0087] to [0089] of the patent).

Finally, the appellant's assertion that the idea underlying the invention as defined in the claims was a task that was always to be addressed is merely an unsubstantiated allegation, which is to be rejected as such.

2.3 In conclusion the appellant's objections of insufficient disclosure (Article 100(b) EPC) do not prejudice the maintenance of the patent on the basis of the main request.

3. Inventive step

The appellant submitted that the subject-matter of claims 1 and 15 of the main request lacked inventive step when starting from D1.

3.1 D1 discloses a method for determining a cardiovascular parameter, such as stroke volume variation, on the basis of a waveform dataset corresponding to arterial blood pressure according to the preamble of claim 1 (paragraph [0037]). It also discloses methods for excluding deviant values from the waveform dataset (paragraphs [0077] to [0080] and [0087] to [0095]).

D1 does not disclose the determination of pseudo-starting points and/or pseudo-ending points for irregular cardiac cycles which have longer durations than regular cycles, and directly measuring or calculating waveform parameters/characteristics of the irregular cardiac cycles based on the pseudo-starting points and/or pseudo-ending points.

These features have the technical effect that the data relating to irregular cardiac cycles can still be used for the evaluation of a patient's health status. Hence,

they address the objective technical problem of improving the accuracy of the determination of the cardiovascular parameter.

The appellant's argument that the distinguishing features did not provide the technical effect because they covered a variety of non-working embodiments is not convincing, because such embodiments do not fall within the scope of the claim as read in context by a person skilled in the art in view of the common general knowledge (as explained above for sufficiency).

Hence, the subject-matter of claims 1 and 15 is inventive in view of D1 alone.

3.2 The appellant argued that D1 in combination with D4 would have rendered the subject-matter of claims 1 and 15 obvious.

D4 discloses a method in which stroke volume or cardiac output is determined from the standard deviation (or an approximation of standard deviation) of a waveform of arterial pressure (paragraphs [0038] to [0041] and [0054]) during subsequent time windows, each possibly corresponding to a single heart cycle (paragraph [0045]); however, according to paragraphs [0046] to [0048], a time window can be expanded or contracted if the average pressure during the time window differs absolutely or proportionately from the average pressure of the previous time window by more than a threshold amount.

As the Opposition Division noted in the impugned decision (point 16.5.2), D4 does not disclose the distinguishing features of claim 1 over D1 because the adjustment of the single time windows does not imply

the determination of pseudo-starting and/or pseudo-ending points for irregular cardiac cycles which have longer durations than regular cycles. In D4 the duration of a cardiac cycle is not taken into account for the adjustment of the time window. The general shortening of the time windows as suggested in paragraph [0055] of D4 does not involve the determination of irregular cardiac cycles at all. The appellant's allegation that there was no technical difference between the disclosure of D4 and the distinguishing features is not acceptable, since the distinguishing features involve different computation of the cardiovascular parameters. The claimed computation takes into account the single irregular cardiac cycles which have longer durations than regular cycles. This may also lead to improved accuracy.

It follows that the combination of D1 with D4 would have not rendered the subject-matter of claims 1 and 15 of the main request obvious.

3.3 In conclusion the appellant's objections of lack of inventive step (Article 100(a) EPC) do not prejudice the maintenance of the patent on the basis of the main request.

4. Since none of the appellant's objections prejudices the maintenance of the patent on the basis of the main request, the appeal must be dismissed.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

A. Chavinier-Tomsic M. Alvazzi Delfrate

Decision electronically authenticated