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Datasheet for the decision of 18 January 2018

Case Number: T 0937/14 - 3.3.01

Application Number: 09728199.2

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Language of the proceedings: EN

Title of invention:
USE OF RIBOSE IN FIRST RESPONSE TO ACUTE MYOCARDIAL INFARCTION

Applicant:
Bioenergy Inc.

Headword:
Ribose in first response to myocardial infarction/BIOENERGY

Relevant legal provisions:
EPC Art. 56

Keyword:
Inventive step - (no)

Decisions cited:

Catchword:

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Case Number: T 0937/14 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 18 January 2018

Appellant: (Applicant)	Bioenergy Inc. 13840 Johnson Street NE Ham Lake, MN 55304 (US)
Representative:	Lucas, Brian Ronald Lucas & Co. 135 Westhall Road Warlingham, Surrey CR6 9HJ (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 12 December 2013 refusing European patent application No. 09728199.2 pursuant to Article 97(2) EPC**

Composition of the Board:

Chairman	A. Lindner
Members:	M. Pregetter
	M. Blasi

Summary of Facts and Submissions

I. The present appeal lies from the decision of the examining division refusing European patent application No. 09 728 199.2, filed as an international application published as WO 2009/123742.

II. The following documents, cited during the examination and appeal proceedings, are referred to below:

(1) US 4,719,201

(7) Befera et al., J. Surg. Res., 2007, 137(2), 156

(11) Petch, European Heart Journal, 1998, 19(8), 1140-1164

(12) McCarty, Medical Hypotheses, 1983, 11(4), 449-465

(13) download from the Medscape website, entitled "Myocardial Infarction", 3 pages, filed with letter of 17 January 2018

(14) download from the Mayo Clinic, entitled "First aid: Heart attack", 4 pages, filed with letter of 17 January 2018

III. The decision under appeal was based on the set of claims filed with the letter received on 23 October 2013.

The examining division considered that said set of claims did not comply with the requirements of Article 84 EPC. Furthermore, claim 1 lacked novelty in view of documents (1), (7) and (12). No inventive step was acknowledged, starting from either document (1) or

(7) as the closest prior art.

IV. With its statement of grounds of appeal, the appellant submitted an amended main request, corresponding essentially to the set of claims considered in the decision under appeal.

Claim 1 reads as follows:

"1. D-ribose for use in the treatment of a human patient presenting at first response with an acute myocardial infarction, wherein the D-ribose is to be administered during first response care."

V. With the summons to oral proceedings dated 16 October 2017, the board issued a communication under Article 15(1) RPBA indicating a need to discuss the phrase "in the treatment of a human patient presenting at first response with an acute myocardial infarction". The communication also briefly analysed the content of document (1).

VI. With letter dated 15 December 2017 the appellant submitted auxiliary requests 1 and 2.

Claim 1 of auxiliary request 1 reads as follows:

"1. D-ribose for use in the treatment of a human patient presenting at first response with an acute myocardial infarction, wherein the D-ribose is to be administered immediately during first response care for stabilization of the heart following AMI until other interventions can be instituted."

Claim 1 of auxiliary request 2 has the following wording:

"1. D-ribose for use in the treatment of a human patient presenting at first response with an acute myocardial infarction (AMI), wherein the D-ribose is to be administered immediately during first response care for stabilization of the heart following AMI until other interventions can be instituted, and wherein administration is either orally as a 3% solution to be sipped by the patient until at least ten grams of ribose have been ingested over at least one hour or intravenously at a dosage of pyrogen-free D-ribose of 50-300 mg/kg/hour."

VII. The appellant informed the board on 16 January 2018 that it would not be represented at oral proceedings and filed auxiliary request 3 together with further arguments with letter dated 17 January 2018.

Claim 1 of auxiliary request 3 reads as follows:

"1. D-ribose for use in the treatment of a human patient whose cardiac function is in the process of compromising resulting from acute myocardial infarction, wherein the administered D-ribose is for effectively stabilising the heart prior to any surgical intervention, and wherein administration is either orally as a 3% solution to be sipped by the patient until at least ten grams of ribose have been ingested over at least one hour or intravenously at a dosage of pyrogen-free D-ribose of 50-300 mg/kg/hour."

VIII. Oral proceedings were held on 18 January 2018 in the absence of the appellant.

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

"First response"

The term "first response" had a clear meaning and defined the administration of D-ribose to a specific group of patients, i.e. those who had just suffered a myocardial infarction, immediately once medical help was available. First responders might be ambulance personnel and hospital casualty reception, and triage on arrival at hospital was also included. First-response care defined a time of administration that existed as a practical reality and was widely recognised in the medical profession. First response would be understood as covering broadly the period between arrival of an ambulance where the AMI attack had happened and early treatment of the patient in the hospital emergency room.

In the letter dated 17 January 2018 the appellant referred to the curriculum vitae of Dr John StCyr, a retired cardiovascular surgeon of substantial experience and reputation and the first-named inventor in the application under consideration. The appellant went on to state: "On his [Dr John StCyr's] initiative the words "first response" are used in the title of the subject application and some nine times in the description. In particular, clearly and unequivocally addressing his medical colleagues, he explains at page 2 lines 25-27: "The need remains for a method to stabilize MI patients immediately at first response, so that myocardial stability and function can be restored, thus allowing surgical intervention if indicated." It is plain, almost beyond argument, that Dr StCyr was referring to a clinical situation and time period that

they would recognise and understand as a clinical reality and whose understanding could be taken for granted. It is submitted that his choice of language as a skilled practitioner in this field of medicine is convincing evidence of these facts and should be given substantial weight when considering the clarity of this term. The alternative view is that Dr StCyr was talking nonsense to his professional colleagues which is neither a credible nor an attractive approach".

Inventive step

The closest prior art was the equipment and knowledge possessed by first responders prior to the invention. The actions of ambulance personnel and those in the emergency department of a hospital were summarised in document (13), including immediate administration of aspirin and nitroglycerin, immediate defibrillation and administration of intravenous medications.
Document (14) confirmed said practices and taught to administer medications selected from a list not including ribose as "immediate steps". The problem was to provide improved or at least alternative medication for administration to an ischaemic patient at first response. None of the cited prior-art documents disclosed or suggested the employment of ribose for that purpose. Alternatively, document (11) could be seen as the closest prior art. Starting from document (11) the problem was whether anything and if so what should be added to the range of drugs and other substances for use in first-response care for the immediate treatment of acute myocardial infarction. Example 4 of the application emphasised the benefits of administration of ribose at first response. None of the prior-art documents pointed to this solution. The objection of lack of inventive step was based on a

hindsight interpretation of particular passages of the prior-art documents.

Document (1) had been represented over-broadly by the examining division. Said document did not refer in any way to the treatment of a human patient at first response. The statement in column 1, lines 58 to 61, concerned unblocking blocked blood vessels, i.e. reperfusion, but not necessarily simultaneous ribose administration. There was no suggestion in document (1) of either administering ribose orally or administering it through the general circulation and still less doing so for a human subject in the immediate aftermath of an AMI and immediately at first response. Such an interpretation could only be made with knowledge of the subject-matter of the claims under consideration, i.e. with impermissible hindsight.

X. The appellant's final requests were as follows:

The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the claims of the main request filed with the statement of grounds of appeal, or alternatively on the basis of one of the sets of claims filed as auxiliary requests 1 and 2 with letter dated 15 December 2017 or as auxiliary request 3 with letter dated 17 January 2018.

Reasons for the Decision

1. The appeal is admissible.

2. The oral proceedings before the board took place in the absence of the appellant, who had been duly summoned

but chosen not to attend, as announced with letter of 16 January 2018. According to Article 15(3) RPBA, the board is not obliged to delay any step in the proceedings, including its decision, by reason only of the absence at the oral proceedings of any party duly summoned who may then be treated as relying only on its written case. 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. *Main request*

3.1 *"First response"*

The term [treatment at] "first response" has no precise general meaning. In everyday spoken language the term includes efforts by lay rescuers and by medical professionals, e.g. ambulance staff. The application as filed specifies that "first response to assist a heart attack patient may be emergency medical technicians, ambulance staff, hospital receiving staff or clinic office staff" (page 2, lines 11 to 12). It may be assumed that emergency medical technicians, ambulance staff and hospital receiving staff are professionals with (some) medical training. "Clinic office staff" have not necessarily received special medical training. On the other hand, hospital receiving staff will be capable of providing medical treatment that blends smoothly into all further required measurements and goes well beyond any measures that can be taken by laymen. No further information concerning the definition of "first response" is on file.

Consequently, the term "first response" as used in independent claim 1 can be linked neither to a clear beginning, i.e. it is not clear which efforts, if any,

by lay rescuers are included, nor to a clear ending, i.e. a point in time when the later stages of medical treatment start. The term "first response" thus defines a very broad period of time with no clear beginning or end. It can however be understood that "first response" means a period of time right at the beginning of medical treatment. Further examination will be based on this meaning.

3.2 *Inventive step*

3.2.1 The present invention relates to administration of D-ribose to patients suffering an acute myocardial infarction presenting at first response. The D-ribose will assist in the stabilisation of the heart as a precursor to adenosine triphosphate ("ATP", see application as filed, page 1, lines 13 to 17, page 2, lines 25 to 27, page 3, lines 3 to 4).

3.2.2 Closest prior art

In the decision under appeal the examining division considered either document (1) or document (7) to represent the closest prior art. The appellant considers that the most promising starting point is the equipment and knowledge possessed by first responders. Alternatively, it considers document (11) to be the closest prior art.

The contents of these starting points for the problem-solution approach are discussed in the following paragraphs:

(a) Document (1) defines a method for reducing the recovery time of tissue function following ischaemic insult due to myocardial infarction by

administering ribose (claims 1, 3 and 5). The description mentions the administration of ribose by intravenous infusion (column 4, lines 20 to 29).

The description of document (1) explains that organ function is dependent on an adequate supply of energy and mentions ATP in this context (column 1, lines 12 to 21). During ischaemia, cellular ATP will be consumed and usually cannot adequately be replenished (column 1, lines 24 to 28). Significant ischaemia is said to occur during heart attacks (column 1, lines 34 to 41). In such cases a prompt reversal of the ischaemic state due to the myocardial infarction is important (column 1, lines 58 to 61).

Document (1) then explains that in the mechanisms responsible for the recovery of myocardial cells from ischaemia the availability of precursors for quickly restoring ATP levels is important (column 2, lines 1 to 20). The introductory part ends with the finding that there is a need for a method of treatment of ischaemic tissue which rapidly restores normal cellular ATP levels and maintains these levels until tissue has permanently recovered (column 3, lines 11 to 17).

It is thus clear from the introductory part of document (1) that quick and immediate action ("prompt"; "reduction in the ATP recovery time"; "rapidly restores normal cellular ATP levels") is required (column 1, lines 58 to 61; column 2, lines 32 to 37; column 3, lines 11 to 17).

Document (1) thus introduces its invention by describing the perfusion of the ischaemic heart

tissue with ribose to restore and maintain ATP levels. These passages are followed by the statement in column 3, lines 53 to 60, that ribose infusion is a method not limited to extreme situations such as those accompanying cardiac surgery, but also to be used in any situation in which hypoxia threatens tissue function.

(b) Document (7) discloses a test carried out on an animal model. Rats are treated with ribose before and after the induced myocardial infarction. A link to human patients is implied in the introduction and the conclusion.

(c) The appellant considers the equipment and knowledge possessed by first responders to be an appropriate starting point for the assessment of inventive step. In this context the appellant has filed documents (13) and (14). The board notes that documents (13) and (14) disclose the measures that were taken or were to be taken when a heart infarction was suspected at the time of the publication of documents (13) and (14) and not at the time prior to when the application under consideration was filed. Nevertheless, the contents of these documents will now be briefly discussed. Document (13) teaches immediate administration of aspirin, nitroglycerin and oxygen. After initial stabilisation, beta blockers are to be given. Coronary angiography and percutaneous coronary intervention and defibrillation are further mentioned. The board notes that in the last paragraph of document (13) the administration of "intravenous (IV) medication" is taught in order to "salvage jeopardized ischemic myocardium". The type of medication is however not disclosed. Thus,

although agents to "salvage" the myocardium are disclosed, D-ribose is not specifically mentioned. Document (14) starts off by advising you to call an emergency number. Administration of aspirin and nitroglycerin and, if necessary, cardiopulmonary resuscitation and/or defibrillation are to be effected. The list of medications to be administered includes aspirin, thrombolytics, anti-platelet agents, blood-thinning medications, pain relievers, nitroglycerin, beta blockers and ACE inhibitors. As can be seen from this list, document (14) does not disclose the administration of ribose.

(d) Document (11) is a report commissioned by the European Society of Cardiology and the European Resuscitation Council to supplement the existing advice available on the management of myocardial infarction and other forms of acute heart attack, with special reference to the pre-hospital phase (page 1140, right column, first paragraph). It provides support for the need for early intervention, i.e. pre-hospital, following AMI (page 1141, right column, last paragraph). It does not discuss ribose.

Taking into consideration that the introductory passages and the passages relating to the background of the invention both in the application as filed and in document (1) discuss ribose, its role in the energy cycle as a constituent of ATP and its action in hearts suffering from ischaemia, the board comes to the conclusion that document (1) represents the closest prior art. The disclosure of document (1) is closer to the application as filed than the set of facts considered under point (c) above. The board also notes

that document (1) is cited in the application as filed (page 6, lines 16 to 23).

3.2.3 The difference between claim 1 of the main request and document (1) lies in the expression "presenting at first response".

Although the term "first response" has no well-defined meaning, it has to be construed, in the present case, as defining a period of time right at the beginning of medical treatment, i.e the very first phase of the treatment of AMI, see point 3.1 above. The difference over document (1) can thus be described as the selection of a period of time in the treatment of a patient that is at the very beginning of said treatment.

3.2.4 The problem to be solved can thus be seen as finding a point in time to administer ribose in the effective treatment of AMI.

3.2.5 Claim 1 of the main request defines administration during first-response care as the solution to the problem of finding a point in time.

From the data presented and the background information disclosed in the application as filed it is plausible that the administration of ribose to a patient suffering from AMI at a very early stage of treatment will have positive effects. There is however no data showing that such treatment during first-response care has any advantages compared with treatment initiated at early stages of e.g. hospital treatment. Example 4B explicitly mentions treatment on admission to hospital care (page 15, lines 8 to 10).

The closest prior art, i.e. document (1), already indicates that it is advantageous to promptly reverse ischaemia and to rapidly restore normal cellular ATP levels. To achieve these goals, document (1) teaches the administration, e.g. intravenously, of ribose. It is thus obvious for the skilled person to start the administration of ribose at the earliest possible moment. The earliest possible moment in emergency treatment is at first response. Consequently, the skilled person, following the teaching of document (1), would arrive at the subject-matter of claim 1 of the main request without employing inventive skill.

3.2.6 The subject-matter of claim 1 of the main request does not involve an inventive step.

3.2.7 *Further argument - hindsight*

The appellant has argued that, on the basis of a proper reading and analysis of the documents cited, only hindsight could lead to a finding of lack of inventive step.

It is established case law that the closest prior art for assessing inventive step is normally a prior-art document disclosing subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention and having the most relevant technical features in common (Case Law of the Boards of Appeal of the European Patent Office, 8th edition 2016, I.D.3.1).

Point 3.2.2 above includes a detailed analysis of the documents and passages that led to the selection of the closest prior-art document. In section (a), document (1) is discussed in detail. The board considers that

the sum of the disclosure of the introductory parts, the brief description of the invention, the detailed description of the invention and the claims led to the selection of this document as the closest prior art. There is thus no impermissible hindsight involved.

4. *Auxiliary request 1*

The same line of argument as given under point 3.2 above also applies to claim 1 of auxiliary request 1. The expression "for stabilisation of the heart" is already reflected in document (1) in column 3, lines 11 to 17, where it is stated that the method of document (1) should lead to permanent tissue recovery.

The subject-matter of claim 1 of auxiliary request 1 does not involve an inventive step.

5. *Auxiliary request 2*

Claim 1 of auxiliary request 2 differs from claim 1 of auxiliary request 1 in comprising additional features relating to oral or intravenous administration of certain doses.

Intravenous administration is already suggested in document (1) in column 4, lines 20 to 25. Determination of the optimum dose is part of the routine work of a person skilled in the art. The application as filed acknowledges that the claimed range of doses for intravenous administration is comparable to the doses that are known to provide benefit (page 15, lines 17 to 18). In the absence of data linking a surprising effect to the doses claimed, these doses cannot lead to the acknowledgement of an inventive step.

The subject-matter of claim 1 of auxiliary request 2 does not involve an inventive step.

6. *Auxiliary request 3*

Auxiliary request 3 is admitted into the proceedings. In view of the board's decision with regard to inventive step, it is not necessary to come to a conclusion concerning Articles 123(2), 84 and 54 EPC.

Claim 1 of auxiliary request 3 defines the "treatment of a human patient whose cardiac function is in the process of compromising resulting from acute myocardial infarction". D-ribose is administered for "effectively stabilising the heart prior to any surgical intervention". The administration scheme is the same as in claim 1 of auxiliary request 2.

Any person suffering an acute myocardial infarction is in a situation where his or her cardiac function is compromised. Claim 1 of auxiliary request 3 explicitly specifies that stabilisation of the heart precedes surgical intervention. It does not limit the treatment to first-response care.

Document (1) is still considered to represent the closest prior art, cf. point 3.2.2 above. The board notes that document (1) provides for the possibility of surgical intervention. The last sentence of the "brief description of the invention" states that the method of document (1) need not be limited to extreme situations such as those accompanying cardiac surgery, thus indicating that situations with and without the need for surgery are encompassed by the teaching of document (1) (column 3, lines 56 to 60).

The difference between claim 1 of auxiliary request 3 and the closest prior art arises from additional features relating to oral or intravenous administration of certain doses.

The line of argument given for claim 1 of auxiliary request 2 in view of the doses to be administered intravenously also applies to claim 1 of auxiliary request 3.

The subject-matter of claim 1 of auxiliary request 3 does not involve an inventive step.

Order

For these reasons it is decided that:

1. The appeal is dismissed.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated