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**Datasheet for the decision
of 10 March 2025**

Case Number: T 0213/23 - 3.3.07

Application Number: 17740398.7

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A61K33/00, A61P7/08

Language of the proceedings: EN

Title of invention:
ISOTONIC CRYSTALLOID AQUEOUS SOLUTION

Patent Proprietor:
Oller Duque, Lara

Opponent:
Laboratoires Quinton International, SL

Headword:
ISOTONIC CRYSTALLOID AQUEOUS SOLUTION/Oller Duque, Lara

Relevant legal provisions:
EPC Art. 83, 54, 56

Keyword:
Sufficiency of disclosure - (yes)
Novelty - (yes)
Inventive step - (yes)



Beschwerdekammern

Boards of Appeal

Chambres de recours

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Case Number: T 0213/23 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 10 March 2025

Appellant: Laboratoires Quinton International, SL
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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 1 December 2022
rejecting the opposition filed against European
patent No. 3490526 pursuant to Article 101(2)
EPC.**

Composition of the Board:

Chairman A. Usuelli
Members: D. Boulois
A. Jimenez

Summary of Facts and Submissions

- I. European patent No. 3 490 526 B1 was granted on the basis of a set of 12 claims.

Independent claim 1 as granted read as follows:

"1. Isotonic crystalloid aqueous solution, comprising Na⁺ ions in a range comprised between 50 and 200 mmol/L, K⁺ ions in a range comprised between 1 and 10 mmol/L, Cl⁻ ions in a range comprised between 50 and 200 mmol/L, characterized in that it has nitrate ions or nitrite ions or mixtures thereof in a range comprised between 0.0001 mmol/L and 1 mmol/L and at least a chemistry element selected from: Li, Be, B, Al, Si, P, Sc, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Br, Rb, Sr, Y, Zr, Mo, Pd, Ag, Sn, Sb, I, Cs, Ba, Ce, Au, Tl, Pb, Bi, Th and U."

- II. The patent had been opposed under Article 100 (a) and (b) EPC on the grounds that its subject-matter lacked novelty and inventive step and was not sufficiently disclosed.
- III. The appeal lies from the decision of the opposition division to reject the opposition.
- IV. The documents cited during the opposition proceedings included *inter alia* the following:

D1: US 6680305 B1

D2: US 2006/182815 A1

D3: Garnacho et al.

D8: Laboratory Tests 2015
D9: Laboratory Tests Jan-Jun. 2016
D10: L'Eau de Mer... 1904 Rene Quinton Book
D11: Dictionary Vidal 1966
D12: Dictionary Vidal 1975
D16: WO 2009/105164 A2
D17: US 8945823 B2
D18: WO 2005/004884 A2
D19: Oller et al.
D20: Stomato-quinton Proof of commercialization
D21: Laboratory Assay 04/02/2021 Stomato-quinton tests
D22: Analysis of Seawater 2006
D24: Article of the New York Times (year 2008)
disclosing the similarity between blood plasma and sea
water
D25: Non-final Office Action of the parallel
application US 2021/0308179 A1
D26: US 20040076687 A1 cited in the document D25
D27: US 20160067278 A1 cited in the document D25
D28: LENNTECH (Composition of Seawater, Major ion
composition of seawater) cited in D25
D29: Magazine - Water Condition & purification, January
2005 cited in D2

V. According to the decision under appeal, D22 was admitted into the proceedings, since it was intended to be filed with the notice of opposition and was submitted as soon as possible after realising this error. Furthermore, D22 disclosed the analysis of seawater and was considered relevant for the proceedings. D24-D29 were not admitted in the proceedings, since they were late filed and not considered *prima facie* relevant for the proceedings.

The requirements of Article 83 EPC were met. Claim 1 was directed to a product and the skilled person was

well aware how to prepare this composition in particular in view of the description and common general knowledge. The alleged synergistic technical effect did not play a role for the evaluation whether the product could be prepared.

The claimed subject-matter was novel over D10 with reference to documents D11, D12 and D15. It was also novel in view of the product "Stomato-Quinton" referred to in D20, with a reference to D8, D9, and D21.

D1 was considered to represent the closest prior art and the problem over D1 was the provision of a solution for the treatment of haemorrhagic shock. The claimed solution was inventive over D1 combined with D10.

- VI. The opponent (hereinafter the appellant) filed an appeal against said decision.
- VII. The patent proprietor (hereinafter the respondent) replied to the statement of grounds of appeal by its letter dated 14 August 2023.
- VIII. A communication from the Board, dated 8 October 2024, was sent to the parties. In it, the Board expressed its preliminary opinion that the claimed invention was sufficiently disclosed and was novel over the cited documents.

With regard to inventive step, the Board mentioned that the claimed subject-matter appeared to be inventive over D10 in combination with D11 or D12. With D1 as closest prior art, the problem was defined as the provision of an improved blood substitute composition, and it was questionable whether it would be obvious in view of a combination with the teaching of D2.

- IX. With letters dated respectively 6 and 7 February 2024, the respondent and the appellant informed the Board that they will not attend the oral proceedings. In consequence, the oral proceedings were cancelled.
- X. The arguments of the appellant may be summarised as follows:

Main request - Sufficiency of disclosure

The contested patent did not disclose how to produce the isotonic aqueous solution of the claimed invention. The patent proprietor failed to teach how to adjust the different ions to the claimed ranges, when starting from a combination of seawater and "*aqua fontana*". In this context it was observed that nitrate and nitrite seemed not to be commercially available.

Moreover, the composition according to claim 1 as granted did not work in the whole area claimed, in particular in view of the alleged synergistic effect. The only example of the patent could not provide support for all the possible claimed embodiments. In the appellant's view, the presence of magnesium was necessary to facilitate the neutralisation of reactive oxygen species (ROS); reference was made to D19 on page 10.

Main request - Novelty

D10, D11 and D12 referred to the same product, named "Plasma de Quinton". The product was defined as isotonic and was mainly composed by an isotonic solution of seawater (pH 7,2). In documents D11 and D12, it was disclosed that René Quinton demonstrated in

1904 that the seawater could be a blood substitute. This was an explicit cross-reference to the document D10. The composition of the seawater ("plasma de Quinton") could be found on pages 218-219 of D10.

The product named "Stomato-Quinton" was an isotonic solution of seawater, and was a practical embodiment of the known "Plasma de Quinton" which was authorised by the Spanish Government on 29.04.2015 (see e.g. D20). D8, D9 and D21 provided the analysis of the components of these products.

Main request - Inventive step

The product "Plasma de Quinton" was clearly used as a blood substitute and could be the closest prior art. Documents D11 and D12 disclosed that it was possible to replace the blood of an animal with "Plasma de Quinton". Therefore, D10, in view of D11 and D12 with an explicit reference to the document D10, disclosed that the product could be used as a blood substitute. The concentration of the different elements could be easily changed with distilled water, as Mr Quinton disclosed in D10, page 164-165. In addition, in the claimed invention there was no direct technical effect associated with the concentration of the different ions. In fact, those wide ranges were quite usual in the natural form of the seawater.

D1 disclosed the development of new physiologically acceptable aqueous solutions for use as plasma substitute (column 2, lines 5-11). The isotonic solution comprised sodium, potassium, calcium, chloride ion, and magnesium (e.g., claim 7). The solution was used for the treatment of hemorrhagic shock (example

6). The skilled person in the art would have combined D1 and D2 to solve the objective technical problem.

XI. The arguments of the respondent may be summarised as follows:

Main request - Sufficiency of disclosure

Regarding sufficiency of disclosure, the respondent agreed with the conclusion of the opposition division in points 3.1 to 3.9 of the reasons of its decision.

Main request - Novelty

The novelty attacks from the appellant were systematically based on the combination of different documents, and this was contrary to EPO practice where conformance of all features of the claim had to be present in one single document. In addition, D8, D9 and D21 were not valid evidence. The subject-matter claimed in claim 1 was clearly new vis-à-vis the prior art presented.

Main request - Inventive step

D10, D1 and D2 were already discussed during the opposition proceedings with regard to inventive step and both attacks starting from D10 or D1 were dismissed.

XII. Requests

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

The respondent (patent proprietor) requests that the appeal be dismissed.

Reasons for the Decision

1. Main request - Sufficiency of disclosure

- 1.1 Claim 1 as granted relates to a composition comprising Na⁺ ions, K⁺ ions, Cl⁻ ions, nitrate or nitrite ions, and at least a chemistry element selected from: Li, Be, B, Al, Si, P, Sc, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Br, Rb, Sr, Y, Zr, Mo, Pd, Ag, Sn, Sb, I, Cs, Ba, Ce, Au, Tl, Pb, Bi, Th and U.

Claims 9-12 are medical use claims directed to the composition of claim 1 for use respectively as a vasodilator, in the treatment of hemorrhagic shock or in acute normovolemic hemodilution, as intravenous fluid replacement and in the the prevention of ischemia-reperfusion injury.

- 1.2 The Board concurs with the conclusion of the opposition division that a skilled person would not have any difficulty in preparing the composition of claim 1, in particular in view of the description of the contested patent and the common general knowledge. The claimed composition is a simple blend of known minerals and ions which does not present any particularity.

This is confirmed by the teaching of several documents cited in the opposition proceedings, such as *inter alia* D1, D3, D16 or D17, which disclose the same type of composition comprising blends of minerals and by the composition of the commercial product Plasmalyte used as comparative composition in the contested patent; as shown in Table 2 of the contested patent, the product

Plasmalyte comprises *inter alia* Na⁺, K⁺ and Cl⁻ in the same concentrations as in the claimed composition which indicates that the skilled person would not have any difficulty to adjust the different ions to the claimed ranges.

The use of nitrite or nitrate in pharmaceutical compositions is also known from instance from documents D2 or D18; the argument of the appellant that nitrate and nitrite seemed not to be commercially available is therefore not credible and cannot be followed, and the skilled person would not see any difficulty in adding nitrites or nitrates to compositions comprising other elements.

Consequently, the skilled person would not have no difficulty in preparing the composition of claim 1.

- 1.3 The contested patent provides an example wherein a solution according to the claimed invention shows an effect *inter alia* on the restoration of the microcirculation and the ability to dissolve and carry oxygen (see Tables 2-4 and par. [0037]-[0044], [0047] of the specification). The effect shown is superior to the effect shown by the Plasmalyte solution. Hence, the pharmacological activity of the composition has been shown in a convincing way. Having regard to these data, the Board considers it credible that the composition of claim 1 can be used in the treatment of the medical indications of claims 9-12 which are linked to the use of the claimed composition as blood substitute. For these reasons, claims 9-12 are sufficiently disclosed.

The argument of the appellant that the composition according to claim 1 as granted does not work in the whole area in view of the absence of magnesium which is

necessary to facilitate the neutralisation of reactive oxygen species (ROS), is neither proven, nor credible. In the Board's view, there is no evidence to suggest that the presence of magnesium or of any other specific element is essential for achieving the pharmacological effect or for the preparation of a blood substitute. This is shown for instance by D3, which discloses in Table 1 several commercial preparations of blood substitute or resuscitation fluids that do not contain magnesium:

Table 1 Composition of the crystalloids and comparison with plasma.

Composition	0.9% NaCl	Plain Ringer solution	Ringer acetate	Ringer lactate	Plasma-Lyte® 148	Isofundin®	Plasma
Na ⁺ , mmol/l	154	147	130	131	140	145	135-145
Cl ⁻ , mmol/l	154	155	112	112	98	127	98-105
K ⁺ , mmol/l	-	4	5	5.4	5	4	3.5-5
Ca ²⁺ , mmol/l	-	4	1	1.8	3	2.5	2.5
Mg ²⁺ , mmol/l	-	-	1	-	-	1	1.5-2.5
Lactate, mmol/l	-	-	-	28	-	-	-
Acetate, mmol/l	-	-	27	-	27	24	-
Others, mmol/l	-	-	-	-	Gluconate 23	Malate 5	Bicarbonate 24-28
Osmolarity, mOsm/l	308	309	276	277	295	309	291
pH	4.5-7.0	5-7.5	6.0-8.0	5.0-7.0	4.0-8.0	5.1-5.9	7.35-7.45

The fact that in D19, it was shown that the composition Oxsealife, containing nitrate and nitrite supporting the physiological generation of nitric oxide, magnesium and trace amounts of transition metals that may facilitate neutralisation of ROS, is effective on recovery from haemorrhagic shock, cannot constitute an evidence that a composition without magnesium would not be active.

1.4 Consequently, the Board does not see any reason to overrule the decision of the opposition division. Accordingly, the claimed invention is sufficiently disclosed.

2. Main request - Novelty

2.1 The appellant considers that the claimed subject-matter lacks novelty over the product "Plasma de Quinton" in view of documents D10, D11 and D12, as well as over the product "Stomato-Quinton" in view of document D20, as well as documents D8, D9, D21.

2.2 Product "Plasma de Quinton"

D10 is a book published in 1904 and written by Mr Quinton. It indicates that the composition of seawater is different depending on its origin (see page 217). Page 219 of D10 shows the composition of seawater of different origins, while page 223 indicates that seawater contains nitrite or nitrate. The Table of D10 reproduced by the appellant on page 21 of its statement of grounds of appeal gives the concentrations of elements in seawater which do not fall under the scope of the claim. For instance, it can be easily calculated from the amounts of NaCl in 1L of seawater of different sources that the concentration of chlorine or sodium, is above 400 mmol/L.

D11 and D12 refer to the product "Plasma de Quinton" and to the book of Mr Quinton of 1904 (D10)

D11 and D12 are extracts of the "Dictionnaire Vidal" from respectively 1966 and 1975. They indicate that the "Plasma de Quinton" is a **dilution** of natural seawater which can be either isotonic or hypertonic, and which can be used as blood reconstitution product. None of these documents gives however the exact composition of the product "Plasma de Quinton". Furthermore, none of these documents indicates how much the seawater was diluted to obtain the product Plasma de Quinton.

Consequently, it is not possible to conclude that the product "Plasma de Quinton" is novelty-destroying in the absence of any precise qualitative or quantitative information on its constituents.

The product "Plasma de Quinton" is therefore not novelty-destroying for claim 1 of the main request.

2.3 The product "Stomato-Quinton"

Document D20 discloses on page 6 the **buccal composition** "Stomato-Quinton" and indicates on pages 7-8 that the product is a blend of 71,43 ml of seawater and 178,57 ml of mineral water or a blend of 714,29 ml of mineral water and 285,71 ml of seawater. **There is no further indication of the qualitative and quantitative composition of the product.** The document does indeed not give any further information with regard to the nature and origin of the used seawater and mineral water, which renders impossible to draw any conclusion regarding the composition of the product, in view of the possible variations in terms of the composition of seawater as shown in D10. **Moreover, there is no indication that the product is isotonic and this document cannot be novelty-destroying already for this reason alone.**

The appellant referred furthermore to documents D8, D9 and D21 to provide the analysis of the components of the product "Stomato-Quinton". Documents D8 and D9, dated 2015 and 2016 respectively, present analysis reports of the product "Stomato-Quinton 250 ml" in relation to their concentration in mineral elements. However, they are silent about the possible presence of nitrate or nitrite. Additional tests were performed in January 2021 to demonstrate the presence of nitrates

and some metals in the product "Stomato-Quinton 250 ml". These tests are disclosed in D21.

The Board shares the concerns of the opposition division with regard to the disclosure of documents D8, D9 and D21, their relation with the disclosure of D20 and their interrelation. Neither the sample denominations and descriptions, nor the dates of reception of the samples (in particular the date of reception of the sample of D21) coincide in the documents. Since there is furthermore no evidence that the composition of the product "Stomato-Quinton" has been kept unchanged between 2015 and 2021, it is not possible to combine fragmented information from such documents together to come to the conclusion that the claimed composition was known. In other words, there is no clear information about the composition of the product of D10.

Consequently, the product "Stomato-Quinton" is not novelty-destroying for the claimed subject-matter.

3. Main request - Inventive step

- 3.1 The claimed invention relates to an isotonic crystalloid aqueous solution used to replace fluids, primarily blood, which does not present oncotic pressure *per se* and which intends to yield better results than the already known blood substitute solutions or a solution of ionic solutes (cf. par. [0001]-[0006] and [0008] of the specification). Said solution can be used as vasodilator, in the treatment of hemorrhagic shock or in acute normovolemic hemodilution, as intravenous fluid replacement or for use in the prevention of ischemia-reperfusion injury (cf. claims 9-12).

3.2 The opposition division considered that D1 or D3 could be considered as closest prior art instead of D10. The appellant considers that D10 is a suitable closest prior art and assesses inventive step over D1 in its statement of grounds of appeal. Even if it appears that D10 cannot be a suitable starting point for the assessment of inventive step, the Board will provide some comments starting from this document.

3.3 D10 as closest prior art

D10 is a book dated 1904 and relating to seawater which comprises 519 pages. The appellant cited page 459 as possible starting point, where it is disclosed that seawater can be injected to treat different diseases, without any mention of the use as blood substitute. There is furthermore no information, neither in D10, nor in D11/D12 on the degree of dilution of the seawater in the product "Plasma de Quinton" or of the origin of the seawater, and therefore on the final concentration of all possible elements originating from seawater. In the Board's view, assessing inventive step starting from a document that does not provide any clear information regarding the composition and pharmacological properties of the relevant product can only be made with the benefit of hindsight.

Accordingly, the Board considers that the claimed invention is inventive over D10. In the Board's view, there is indeed no teaching in any of documents D10, D11 or D12 to adapt or change the concentrations of the seawater elements in order to arrive at the claimed subject-matter. The argument of the appellant that the different elements can be easily changed with distilled

water is a clear *ex post facto* analysis and cannot be followed.

The claimed subject-matter is inventive over D10 in combination with D11 or D12.

3.4 D1 as closest prior art

3.4.1 D1 discloses physiologically acceptable **aqueous solutions for use as plasma substitute** comprising a carboxylic acid as a dynamic buffering system, an oncotic agent selected from a simple sugar or hydroxyethylstarch (hetastarch), and a buffer (column 2, lines 5-11; col. 5, lines 21-40; claim 1). The isotonic solution comprises sodium, potassium, calcium, chloride ion, and magnesium (e.g., claim 7).

Example 1 of D1 discloses a composition L comprising inter alia:

- Na⁺ 143 at mM
- Ca⁺⁺ at 2.5 mM
- Mg⁺⁺ at 0.45 mM
- K⁺ at 3.0 mM
- Cl⁻ at 124 mM
- glucose an lactate.

The composition HL of example 1 comprises additionally hetastarch. The solution HL can be used for the treatment of haemorrhagic shock as disclosed in example 6.

The differences between claim 1 and D1 is the addition of:

- a) nitrate ions or nitrite ions or mixtures thereof in a range comprised between 0.0001 mmol/l and 1 mmol/l and

b) and at least a chemistry element selected from: Li, Be, B, Al, Si, P, Sc, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Br, Fib, Sr, Y, Zr, Mo, Pd, Ag, Sn, Sb, I, Cs, Ba, Ce, Au, TI, Pb, Bi, Th and U.

3.4.2 The opposition division defined the problem as the provision of a solution for the treatment of hemorrhagic shock.

During the opposition proceedings, the appellant defined the problem over D1 as how to generate vasodilation to improve perfusion and oxygenation of tissues and how to produce redox potential without deleterious effects on the organism (cf. point 5.4 of the decision of the OD).

In its statement of grounds of appeal, the appellant did not define clearly the problem over D1, but mentioned that the technical effects linked with the presence of nitrite and/or nitrate ions are the prevention and treatment of conditions associated with the cardiovascular system, for example, high blood pressure, pulmonary hypertension, cerebral vasospasm, and tissue ischemia-reperfusion injury and the provision of methods to increase blood flow to tissues, for example, to tissues in regions of low oxygen tension. Moreover, the appellant considers that there was no direct technical effect associated with the concentration of the different ions (cf. point 5.2.1 of the statement of grounds of appeal).

As mentioned by the Board in its communication expressing its preliminary opinion, the treatment of haemorrhagic shock, as claimed in claim 10 is not the only medical application that the patent intends to treat, since the subject-matter of claims 9, 11 and 12

relates also respectively to the use as a vasodilator, as an intravenous fluid replacement or in the prevention of ischemia-reperfusion injury.

- 3.4.3 According to the teaching of the contested patent, the underlying mechanism of action of the claimed isotonic crystalloid solution is the interaction between the nitrite/nitrate ions and the presence of metals or metalloids in the composition. **Nitrates and nitrites will open or reconnect capillaries collapsed** to the systemic circulation via the nitric oxide pathway and **the chemical elements will "sweep" the detritus generated during the time of "disconnection" from the systemic circulation**, in particular by neutralization of the oxygen reactive species via their potential to reduce the reactive oxygen species (cf. par. [0012]-[0014] of the specification). It is the synergy of both characteristics which explains the results obtained in the experimental tests shown in the contested patent. These effects are experimentally shown in the contested patent in paragraphs [0038]-[0050] and Tables 3-5. The Board notes that the same explanation is given in the post-published document D19, which shows that a composition according to the claimed invention provides a greater capillary recruitment and enhanced clearance of acidic tissue metabolites (see for instance the Abstract or the "Discussion").

The patent provides a comparison between a composition according to the invention shown in Table 1 and the Plasmalyte® solution which does not comprise any nitrite/nitrate and/or metal, but includes acetate and gluconate (cf. Table 2 of the specification). The solution of the present invention showed an effect comparable to the administration of whole blood and a clear improvement with regard to the Plasmalyte®

solution (see par. [0043] and [0044] of the specification). **A loop oedema was observed at the intestinal level in the animals treated with Plasmalyte, while this was not the case of the animals treated with the claimed solution or with whole blood.** In the Plasmalyte group, the lactic acid level remained furthermore above baseline lactic acid level which is a clear indicator that **the microcirculation was not restored** (see also Tables 3 and 4 of the specification).

The solubility coefficient of oxygen in the solution was also shown to be superior to the results obtained with Plasmalyte and even to the blood plasma, which shows the higher capacity of the composition of the invention to dissolve and carry oxygen (see par. [0047]).

A further comparison with blood transfer was disclosed in paragraph [0045] which showed **a similar effect in reference to the analysis of microcirculation and lactic acid washing;** the lactic acid level returned to normality in over two hours. The lactic acid washing is the clinical expression of the effective restoration of the microcirculation (cf. also par. [0039]-[0040]).

Moreover, in the group of animals treated with the solution of the present invention, a higher consumption of bases (bicarbonate) was observed when compared with whole blood and Plasmalyte groups, showing that the solution of the present invention **improves metabolic management in bleeding patients since the microcirculation is "cleaned" from acid metabolites** (cf. par. [0050]).

In the Board's view, the results shown for the product Plasmalyte can be extrapolated to the compositions disclosed in D1 which also do not contain any nitrite/nitrate and/or metalloid. Accordingly, it is shown that the claimed composition provides an improved effect and shows similar effects to the administration of whole blood. The effects shown by the claimed composition are the occurrence of an effective restoration of the microcirculation, an effective lactic acid washing and a better oxygen solubility, when used as blood substitute.

Similar results were shown in the post-published document D19, which demonstrates that a solution according to the claimed invention has a superior effect in haemorrhagic shocks than Plasmalyte (see the Abstract).

In view of these results, the Board is of the opinion that the problem over D1 should be defined as the provision of an improved blood substitute composition.

- 3.4.4 It remains to determine whether the claimed solution, i.e. the addition to the composition of D1 of nitrate or nitrite ions or mixtures thereof in a specific concentration and at least one of the claimed chemistry element, for obtaining an improved blood substitute composition is obvious.

The plasma substitute disclosed in D1 has a different mechanism of action, in particular in view of the presence of an oncotic agent, while the claimed invention refers to solutions used to replace fluids, which does **not** present oncotic pressure *per se* (cf. par. [0008] of the specification). There is no suggestion or incentive in D1 to add other compounds

such as a metal compound or a known vasodilator, such as a nitrite or a nitrate, or to replace the oncotic agent in the disclosed compositions. Accordingly, the claimed solution appears to be inventive over D1.

During the appeal proceedings, the appellant considered that the solution was obvious in view of D2. D2 discloses the use of sodium nitrite as vasodilator to prevent or treat conditions associated with the cardiovascular system, such as high blood pressure, pulmonary hypertension, cerebral vasospasm and tissue ischemia-reperfusion injury (see par. [0008]). Nitrite can be administered in solution of a buffer, which can be a phosphate buffer, which is also one of the claimed element (see [0022] and [0150]); the concentration of nitrite in the solution is comprised between 0.6 to 240 μM , which correspond also to the claimed amount.

In the Board's view, it is common general knowledge that nitrite and nitrates have a vasodilatory effect. This is confirmed by D2 which discloses parenteral compositions which comprise nitrite ions in a buffer. D2 does however not relate to blood or plasma substitute used for fluid resuscitation and it appears difficult to establish a link between the teaching of D2 and the disclosure of D1. Moreover, the compositions of D2 aim to induce vasodilation and/or increasing blood flow in a subject, and D2 does not mention the effects shown in the contested patent, such as the restoration of the microcirculation which is the core of the claimed invention. Finally, there is no indication in D2 to add mineral elements for the neutralization of the oxygen reactive species.

The claimed solution is therefore not obvious also when considering the teaching of D2.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:



B. Atienza Vivancos

A. Uselli

Decision electronically authenticated