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# Datasheet for the decision of 30 September 2014

**Case Number:** T 1721/10 - 3.3.07

**Application Number:** 03766483.6

**Publication Number:** 1534304

**IPC:** A61K33/00, A61P25/04

**Language of the proceedings:** EN

**Title of invention:**
AN ANALGESIC AGENT FOR NEWBORN OR FETAL SUBJECTS

**Patent Proprietor:**
Imperial Innovations Limited

**Opponent:**
L AIR LIQUIDE SOCIETE ANONYME POUR L ETUDE ET L EXPLOITATION DES PROCEDES GEORGES CLAUDE

**Headword:**

**Relevant legal provisions:**
EPC Art. 56

**Keyword:**
Inventive step - main request (yes)

**Decisions cited:**

**Catchword:**

Europäisches Patentamt
European Patent Office
Office européen des brevets

**Beschwerdekammern**
**Boards of Appeal**
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**Case Number: T 1721/10 - 3.3.07**

# D E C I S I O N
# of Technical Board of Appeal 3.3.07
# of 30 September 2014

| | |
|---|---|
| **Appellant:** (Patent Proprietor) | Imperial Innovations Limited<br>52 Princes Gate<br>South Kensington<br>London, Greater London SW7 2PG (GB) |
| **Representative:** | Clyde-Watson, Zöe<br>D Young & Co LLP<br>120 Holborn<br>London EC1N 2DY (GB) |
| **Respondent:** (Opponent) | L AIR LIQUIDE SOCIETE ANONYME POUR L ETUDE ET L EXPLOITATION DES PROCEDES GEORGES CLAUDE<br>75 QUAI D ORSAY<br>75321 PARIS CEDEX 07 (FR) |
| **Representative:** | Pittis, Olivier<br>L'Air Liquide, S.A.<br>Direction de la Propriété Intellectuelle<br>75, Quai d'Orsay<br>75321 Paris Cedex 07 (FR) |
| **Decision under appeal:** | **Interlocutory decision of the Opposition Division of the European Patent Office posted on 14 June 2010 concerning maintenance of the European Patent No. 1534304 in amended form.** |

**Composition of the Board:**

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| **Chairman** | D. Semino |
| **Members:** | A. Usuelli |
| | P. Schmitz |

## Summary of Facts and Submissions

I. The appeal of the patent proprietor (appellant) lies against the decision of the opposition division to maintain European patent No 1 534 304 in amended form.

II. The patent was opposed under Article 100(a) EPC on the grounds that its subject-matter lacked novelty and inventive step. The following documents were among those cited during the opposition proceedings:

D1: Prog. Neuro-Psychopharmacol. & Biol. Psychiat. 2000, 24, 1357-1368
D2a: British Journal of Anaesthesia, 1998, 81, 742-747
D13: Developmental Brain Research, 1986, 24, 261-270
D14: Developmental Brain Research, 1991, 64, 72-76
D15: Anest. Analg. 2000, 91, 6-10
D16: Pain, 2002, 100, 7-18

III. The decision of the opposition division was based on a set of claims filed with letter of 15 May 2009 as main request and on an auxiliary request filed on 22 February 2010.

Independent claims 1 and 11 of the main request, which were identical to the corresponding claims of the granted patent, read as follows:

"1. Use of xenon in the preparation of a medicament for providing analgesia in a newborn subject and/or a fetal subject."

"11. Use of xenon in the preparation of a medicament to be administered to the mother of a fetal subject for providing analgesia in fetal subject, wherein the xenon

is in a therapeutically effective amount for both the mother and the fetal subject."

IV. The decision of the opposition division can be summarised as follows:

a) The main request met the requirements of Article 54 EPC.

b) The closest prior art for the assessment of inventive step was represented by document D2a. The subject-matter of the invention differed from the disclosure of D2a in that xenon was used for the treatment of newborn subjects instead of adults. The technical problem was seen in the provision of a gas providing analgesia in newborn subjects. Knowing from D2a that xenon produced an analgesic effect in adults and being aware of the safety of this gas in newborns in view of the teaching of document D1, the skilled person would have tested the analgesic properties of xenon also in newborns. Claims 1 and 11 of the main request were therefore considered to lack inventive step in the sense of Article 56 EPC.

c) No objections were raised by the opponent against the auxiliary request. This request was therefore considered to comply with the requirements of novelty and inventive step.

V. The appellant lodged an appeal against that decision. With the statement setting out the grounds of appeal sent on 22 October 2010 he requested, as the Board interpreted it, as main request the maintenance of the patent as granted and as auxiliary request the

maintenance of the patent in accordance with the request allowed by the opposition division.

VI. The opponent (respondent) replied to the grounds of appeal with a letter dated 4 February 2011 in which the objection of lack of inventive step against the granted claims was maintained. With letter of 17 March 2014 he informed the Board that he would not attend the oral proceedings scheduled for the 30 September 2014.

VII. In a communication sent on 7 May 2014, the Board submitted its observations in particular with regard to the requirements of Article 56 EPC.

VIII. On 1 August 2014 the appellant submitted a new set of claims as first auxiliary request. The previous auxiliary request became the second auxiliary request.

IX. On 30 September 2014 oral proceedings were held before the Board in the absence of the respondent. With regard to inventive step, it was discussed in particular whether the neural pathways of rats in the third and fourth week after birth could be considered as fully developed in the light of D13, D14 and D15.

X. As far as relevant for the present decision, the appellant's arguments can be summarized as follows:

The technical problem in the light of document D2a was the provision of a new medical use of xenon as an analgesic agent. The closest prior art disclosed the use of xenon as an analgesic in adult humans, without providing any teaching or suggestion that this gas was capable of providing analgesia also in newborn and fetal subjects. None of the cited documents disclosed medicaments capable of providing analgesia in newborn

or fetal subjects. D1 was concerned with the potential adverse effects of xenon or nitrous oxide in neonatal rats. However, this document made no reference whatsoever to the possibility of xenon acting as an analgesic agent. Moreover, D13 to D16 taught that as a result of immature pain pathways, analgesics that are effective in adults such as nitrous oxide may not necessarily be effective in newborn or fetal subjects. In particular, the authors of D15 reported that up to postnatal day 15, rats showed no analgesic effect to nitrous oxide and only by postnatal day 29 they exhibited a comparable analgesic effect to that seen in adults. In D14 it was explained that stimulation-produced analgesia in rats could be elicited starting at day 21, but not earlier and that supraspinal modulation of nociception was however still immature at 3 weeks after birth. Accordingly, there was a general prejudice that would have discouraged the skilled person from investigating the use of xenon as an analgesic agent in newborn or fetal subjects.

XI. As far as relevant for the present decision, the respondent's arguments can be summarized as follows:

The document representing the closest prior art for the assessment of inventive step was D2a, which disclosed the use of xenon as analgesic agent for adults. Starting from this document the technical problem underlying the invention was to provide an analgesic treatment for newborns and fetal subjects. Nothing would have dissuaded the skilled person at least from testing xenon on this group of patients. Indeed, the teaching of D1 that xenon is a safe gas for newborns and does not affect the neuronal development, would have encouraged the skilled person to do so. There was no prejudice against the use of xenon in young

patients. Documents D13 and D14 indicated that the neuronal pathways are functionally developed after 18 to 21 days from the birth. This teaching was confirmed by documents D15 and D16 which showed that nitrous oxide started to be effective as analgesic agent after the third week. Since the patent defined the newborns as subjects in the first four weeks after birth, the arguments of the appellant as to the existence of a prejudice against the use of xenon for the treatment of pain in newborn subjects were not justified.

XII. The appellant requested that the decision under appeal be set aside and that the opposition be rejected. Subsidiarily, he requested that the patent be maintained on the basis of the first auxiliary request filed with letter of 1 August 2014, or of the second auxiliary request as maintained by the opposition division.

XIII. The respondent requested that the appeal be dismissed.

## Reasons for the Decision

*Main request - Granted patent*

1. *Claim 1 - Inventive step*

1.1 The invention addresses the problem of providing an analgesic agent which is suitable for use in newborn and fetal subjects ([0001] of the patent).

*Closest prior art*

1.2 The Board agrees with the parties and with the opposition division that the closest prior art is represented by document D2a, which describes the

results of an experimental study comparing the analgesic potency of xenon and nitrous oxide in twelve adults ranging from 22 to 30 years (page 742, paragraph "Subjects and method"). It was not disputed by the parties that the distinguishing feature of the subject-matter of claim 1 over the disclosure of D2a is represented by the group of patients treated with xenon, namely newborn and fetal subjects.

*Technical problem*

1.3 The technical problem underlying the patent in suit in the light of document D2a can be seen in the provision of a new medical use of xenon as analgesic agent.

1.4 The effectiveness of xenon in the new medical use, namely the treatment of pain in newborn and fetal subjects is supported by the experimental data disclosed in examples 1 and 2, in table 1 and in the figures of the patent. These data relate to experiments performed on rat pups of 7, 19 or 28 days. The experiments consist in injecting formalin to the animals in order to cause a nociceptive response, and subsequently to expose them to xenon. The results show that xenon suppresses the nociceptive response even in very young rats (see [0071]).

The efficacy of xenon as analgesic agent for newborn and fetal subjects has never been contested by the respondent.

1.5 In view of the above, the Board considers that the technical problem defined in paragraph 1.3 has been plausibly solved by the provision of the medical use of xenon defined in claim 1.

*Obviousness of the solution*

1.6 As a preliminary remark, the Board notes that none of the documents in the proceedings discloses therapeutic agents which are capable of providing a satisfactory level of analgesia in newborn or fetal subjects. In other words, xenon appears as the first effective analgesic agent for these groups of patients.

There are also no documents directly suggesting the possibility of using xenon as analgesic agent for newborn ad fetal subjects. Document D1 in particular, cannot represent such a document as maintained by the respondent. Indeed, this document describes experiments in which fetal and neonatal rats are exposed to an atmosphere containing xenon (abstract, point 2). It is reported that the gas is safe and does not affect the neuronal development (abstract, point 4). However, the authors of D1 uses xenon as anesthetic agent and nothing is said in this document as to the analgesic properties of this substance. Accordingly, document D1 does not address the problem of providing a further medical use of xenon as analgesic agent. It follows that D1 does not provide any relevant teaching to the skilled person faced with the technical problem defined in paragraph 1.3 above.

1.7 In the light of these considerations, the obviousness issue amounts to the assessment of whether the skilled person would decide to test the effectiveness of xenon as analgesic agent in newborn or fetal subjects, for the sole reason of being aware of the analgesic properties of this gas in the adults.

1.8 In this respect the Board observes that documents D13 to D16 consistently teach that certain results obtained

in the treatment of pain in adults cannot be automatically extrapolated to neonatal or fetal subjects. In particular, D15 and D16 report the results of experiments performed on rats to assess the analgesic properties of nitrous oxide, which is a substance presenting some similarities to xenon in that they are both gas exhibiting analgesic and anesthetic properties (see D2a and D1). The authors of D15 affirm that nitrous oxide has no analgesic effect in newborn rats at postnatal day 15 and starts exhibiting an analgesic effect comparable to that seen in adult rats at postnatal day 29 (abstract). Since the development of the central nervous system is much faster in rats than humans, the authors of D15 conclude that nitrous oxide may not be an effective analgesic in humans at least until toddler stage (page 9, first paragraph of left column). Similar conclusions are drawn in document D16 where it is stated that adult-like antinociceptive responses to nitrous oxide are present only in rats older than 3 weeks, namely 23- and 29-day old rats (abstract).

An explanation for the absence of analgesic activity of nitrous oxide in newborn rats is provided by documents D13 and D14. In both articles it is underlined that the pathways associated with nociception are not functionally developed in newborn rats. For instance, the authors of D14 observe that the stimulation-produced analgesia which activates these pathways can be elicited starting at 21 days after birth but not earlier and add that supraspinal modulation of nociception is however still immature at 3 weeks after birth (abstract). They conclude that there is no descending control of nociceptive reflexes prior to 3 weeks after birth (page 75, last paragraph). In D13 it is remarked that despite an early anatomical

maturation, the dorsolateral funiculus which is part of an endogenous analgesic system, has a slow functional development (paragraph bridging pages 267 and 268).

1.9 The above analysis suggests that the skilled person at the priority date was aware of the difficulties in providing an effective analgesic treatment for newborn or fetal subjects. He knew that a gas useful in the treatment of pain in adults, such as nitrous oxide, was ineffective in newborns. He was aware of the physiological differences between adults and newborns, in relation to the mechanisms involved in pain control. In the Board's opinion, in the light of the teachings of D13 to D16 the skilled person would have avoided to make any simplistic analogy between adults and newborn subjects. Accordingly, he would not have been encouraged to test xenon as a possible analgesic agent for newborn subjects, for the sole reason that this gas was known to be effective in adults. Quite to the contrary, the teaching of D13 to D16 would have cast strong doubts as to the possibility of using xenon for treating pain in these groups of patients with a reasonable expectation of success.

1.10 It is evident that a newborn subject at some point of its life will start to behave like an adult in respect of the sensitivity to the analgesic agents. This will have an impact on the attitude of the skilled person as to the possibility of using xenon as analgesic. In this respect it is observed that in documents D13 to D16 the point of time in which the physiological developments of rats is complete and the exposure to nitrous oxide starts to provide analgesic effect is roughly allocated between the third and the fourth week after the birth (see 1.8 above). The respondent remarked that in accordance with the description the term newborn

embraces subjects in the first four weeks after birth and therefore also rats of three weeks of age, for which the analgesic activity of xenon is to be expected in the light of D13 to D16.

In the Board's opinion the prior art suggests that the physiological maturation of a newborn subject is a process that requires a certain time to arrive at completeness and that it cannot have a precisely defined end-point. Since the issue concerns the development of living beings, the person skilled in the art would not even expect such a precise information. More relevant for him would be the general teaching derivable from D13 to D16 that nitrous oxide does not work as analgesic agent in newborn and fetal subjects for physiological reasons. This teaching would result in a very cautious attitude towards the possibility of using xenon as an effective analgesic agent in subjects whose physiological development may not yet be complete, such as newborn subjects in their first four weeks of life.

1.11 On that basis the subject-matter of the patent is considered to comply with the requirements of Article 56 EPC.

2. *Claim 11 - Inventive step*

This claim relates to the use of xenon for providing analgesia in fetal subjects by administering the gas to the mother. Since the use of xenon as analgesic agent for fetal subjects is inventive (see 1.1 to 1.11 above) and neither the respondent, nor the appealed decision have provided additional arguments for claim 11, also the use defined in this claim is considered to comply with the requirements of Article 56 EPC.

**Order**

**For these reasons it is decided that:**

1. The decision under appeal is set aside.

2. The opposition is rejected.

The Registrar: The Chairman:

S. Fabiani D. Semino

Decision electronically authenticated