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**Datasheet for the decision  
of 18 February 2015**

**Case Number:** T 1164/11 - 3.2.02

**Application Number:** 06118619.3

**Publication Number:** 1752190

**IPC:** A61M37/00

**Language of the proceedings:** EN

**Title of invention:**

Medical apparatus for cutaneous administration of medicaments

**Applicant:**

C.I.R.C.E S.R.L.

**Headword:**

**Relevant legal provisions:**

EPC Art. 83

**Keyword:**

Sufficiency of disclosure - (no)

**Decisions cited:**

**Catchword:**



**Beschwerdekammern  
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Case Number: T 1164/11 - 3.2.02

**D E C I S I O N**  
**of Technical Board of Appeal 3.2.02**  
**of 18 February 2015**

**Appellant:** C.I.R.C.E S.R.L.  
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**Decision under appeal:** **Decision of the Examining Division of the  
European Patent Office posted on 2 February 2011  
refusing European patent application No.  
06118619.3 pursuant to Article 97(2) EPC.**

**Composition of the Board:**

**Chairman** E. Dufrasne  
**Members:** C. Körber  
D. Ceccarelli

## **Summary of Facts and Submissions**

- I. On 2 February 2011 the Examining Division posted its decision to refuse European patent application No. 06118619.3 under Article 83 and Rule 42(1)(e) EPC.
- II. An appeal was lodged against this decision by the applicant by notice received on 30 March 2011, with the appeal fee being paid on the same day. The statement setting out the grounds of appeal was received on 16 May 2011.
- III. By communication of 20 November 2014, the Board forwarded its provisional opinion and summoned to oral proceedings.
- IV. With letter of 9 February 2015, the appellant submitted further evidence, arguments and an amended fourth auxiliary request.
- V. Oral proceedings were held on 18 February 2015.

The appellant declared that the amended fourth auxiliary request filed with letter 9 February 2015 was its sole request. It requested that the impugned decision be set aside and that a patent be granted on the basis of this request.

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

"Group 1)":

I.M. Rufino et al.: "Cryo Laser Phoresis as enhancer of skin penetration: Potential application in cosmetics" (undated)

"Group 2)":

C. Silva: "Local application of ganglioside GM1 with lasericed by the criopass therapy method improves peripheral nerve regeneration in rats. Final Report" (16 December 2007)

"Group 3)":

E. Finati: "Melatonin: a pleiotropic molecule of natural origin. Evaluation of the different therapeutic activities in animal models and/or human patients and a study of the metabolic-biochemical pathways related to them." Dottorato di Ricerca in Biochimica, XXV ciclo, BIO/10, Università degli Studi di Milano, Anno Accademico 2012-2013.

VII. Claim 1 of the appellant's sole request reads:

"A medical apparatus for cutaneous administration of medicaments comprising:

- a supporting frame (100);
  - an energy emitter (9) in engagement with the frame (100) and active on the molecules of at least one medicament to cause penetration of same into a skin region to be treated (10); and
  - a medicamentous solution (3) adapted to be positioned between the energy emitter (9) and the skin region to be treated (10), said solution (3) comprising a matrix containing said medicament,
- characterised in that it further comprises a container (2) to hold the medicamentous solution (3), said solution (3) comprising escina, being at the solid state, having a temperature included between -15°C and -22°C, and being slidable along a longitudinal axis of

the container (2); said energy emitter (9) being an electromagnetic wave generator (11) emitting a laser light of a wavelength comprised in the range of 600 to 650 nm."

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

Since the application related to a "device invention", the most suitable definition of the skilled person should be a technician who would realize such a device. A skilled person of this kind would certainly be capable of assembling the claimed device. The effects achievable with this device were self-evident, even without knowledge of the real phenomena occurring in the skin.

Combining the flow of coherent photonic energy with scattering of the same through the block of solid ice might achieve at least one of these three effects: reduction or elimination of the ablative effect on the stratum corneum of the skin, decrease or elimination of the patient's pain, i.e. an anaesthetic effect in case of residual ablative action of the partially scattered laser beam, or temporary modification of the lipoidal pathway and/or hydrophilic pathway, for example by heating/inducing molecular vibrations with the laser beam energy.

The experiments reported in "group 1)" were conducted on samples of human skin and employed a permeation-enhancing machinery with the commercial name "CRYO LASER PHORESIS" (CLP), produced and sold by the applicant, as could be seen from the penultimate paragraph of page 2. This machine actually corresponded in structural and functional terms to the claimed device. The samples of human skin were tested in

suitable receptacles, so-called "franz cells". Two sets of tests had been performed for different active principles (sodium diclofenac and caffeine). For diclofenac, consumption or "residuality" over the area of the human skin sample after the application with or without CLP was evident from page 7. Layer-by-layer content of the substance throughout the stratum corneum of the human skin sample could be seen at pages 9 and 11. Moreover, deep-wise concentration of substance in the epidermis/dermis region of the sample could be derived from page 13.

Further experimental evidence was retrievable in the "Group 2)" document, and this evidence was considered to be in proportion to the efficacy in local drug delivery, as to be seen from the comparison of the results achieved for the three groups of animal experiments (1) to (3) indicated in the first paragraph of page 2 of this document. Group (1) was exposed to the synergic effect of the combination "laser beam + iced/solid medical substance", group (2) was laser-treated with only iced (neutral) gel with no "charging" of the medical substance in the iced block itself, and group (3) was a control group. A 25% increase in "reconnected nerve fibres" was observed for group (1).

The "Group 3)" document gave a direct verification of the "performance level" of the invention, along with another (perhaps more plausible) scientific hypothesis about the penetration-enhancement mechanism underlying the "Cryopass" machine. At pages 50 to 52 different experimentation techniques for assessing therapeutical properties of melatonin were described. Pages 66 to 67 reported trans-dermal melatonin delivery through application of the claimed device. The choice of the CLP machine/device for these laboratory essays revealed

its high efficiency in transdermal drug delivery. Pages 80 to 84 demonstrated the combined effect of laser through the ice block containing suspended melatonin. It had been assessed with substantially evident differences in terms of "descriptive parameters" related to the so-called oncostatic situation in the three groups of animal samples. This implied that the drug (melatonin) delivery to the oncogenic region was greatly enhanced by the functional synergy of the invention's components, as clearly stated in the last paragraph on page 97 and the first two paragraphs of page 98.

In view of all these results, a surprising effect related to the use of the "CLP" device had been not only revealed, but experimentally certified, independently of any theoretical hypothesis on the physical effects underlying the phenomenon of transdermal penetration. With regard to the last observation, it was to be noted that all the (different) "enhancement mechanisms" cited in the abstracts could merely be considered as hypotheses, since the experimental nature of the studies performed did not delve into the theoretical details but simply assessed and verified the actual/factual presence of parametrically evaluable results. The effective use of the claimed device in the experimental testing procedures clearly demonstrated the sufficiency of the disclosure. The quantitative parameters mentioned in the description and claims (temperature of the iced block, composition of the iced block containing at least an active substance to be trans-dermally delivered, laser beam power and wavelength, association of the iced block to the laser beam and so on) had been used by the experimental operators, and therefore they

had been easily conceived and made available by the construction/assembly of the device/machine itself.

A correct interpretation of the expression "an energy transmitter [...] active on the molecules of at least one medicament to cause penetration of same into the skin region to be treated" in claim 1 should be interpreted in terms of "intended use" and not in terms of coherence with one or more scientific theories. The verification of scientific theories was not the object of the experimental studies, but it was demonstrated that the combined effect of iced block and laser beam actually enhanced permeation, either directly (energization of outer electronic orbitals or whatever else) or indirectly (widening of the inter-cellular pathways, inhibition of the receptors on the surfaces of the inter-cellular pathways, change in cellular membrane permeability, ablation of the stratum corneum and so on).

### **Reasons for the Decision**

1. The appeal is admissible.
2. Sufficiency of disclosure

Claim 1 relates to a medical apparatus comprising a number of components. The Board agrees that the skilled person would be able to assemble the claimed apparatus. However, this does not necessarily imply that the claimed invention is sufficiently disclosed within the meaning of Article 83 EPC.

The requirement of sufficiency of disclosure in Article 83 EPC is based on the consideration that the grant of a patent is only justified if the information comprised



in the patent application and generally available technical knowledge enable the skilled person successfully to put into practice the subject-matter of the claimed invention. It is not the purpose of the patent system to grant a monopoly for technical speculations that cannot be realised at the time of filing.

In addition to the components of the claimed device, the subject-matter of claim 1 also comprises the feature of "an energy emitter (9) [...] active on the molecules of at least one medicament to cause penetration of same into a skin region to be treated (10)". At the end of the claim it is further defined that the energy emitter is "an electromagnetic wave generator (11) emitting a laser light of a wavelength comprised in the range of 600 to 650 nm". The application is silent with regard to the power or intensity of the laser beam and the duration of its delivery.

The Board does not accept the appellant's view that this feature "should be interpreted in terms of 'intended use' and not in terms of coherence with one or more scientific theories". The feature relates to the function of the claimed energy transmitter, describing its interaction with the molecules of the medicament contained in the matrix of a solidified medicamentous solution which also forms part of the claim. Accordingly, this feature of the claim has to be taken into consideration when assessing whether the claimed invention is sufficiently disclosed.

The feature requires that the laser light must be "active" on the molecules to cause their penetration into the skin. In the Board's view, this must be understood as a direct interaction between the light

and the molecules, and not as a possible effect of the light on the skin which has an indirect influence on the molecules that would somehow enhance their penetration through the skin (e.g. inhibition of receptors in channels in the skin, widening of inter-cellular pathways, change in cellular membrane permeability, ablation of the stratum corneum). The wording of the claim clearly states "active on the molecules" and not "active on the skin" or something similar. The direct interaction is also emphasised in the corresponding paragraph [0052] of the description, where it is stated that "the laser light will **only** act on the molecule crystals constituting the medicament" [emphasis added]. On the other hand, the description is silent on any influence on the skin resulting in an indirect interaction of the above-mentioned kind.

Accordingly, the question arises of what nature this interaction between the laser light and the molecules is and how it could effect the penetration of the molecules into the skin. In the cited paragraph of the description (which is the only one dealing with this interaction) it is further stated that the "molecules are therefore pushed and introduced through the epidermis into the skin region 10 to be treated". However, in line with what is stated in the impugned decision, the Board is not aware of a known physical mechanism according to which light is able to push molecules of a medicament, contained in the matrix of a solidified medicamentous solution, into the skin. The well-established effect of "radiation pressure" is not applicable to the present situation, as convincingly explained in point 2.3 of the Reasons of the impugned decision. This is not contested by the appellant, who does not rely on this effect as a possible explanation.

Instead, the appellant referred to "energization of outer electronic orbitals or whatever else". It is indeed known that (laser) light, i.e. photons, can interact with the electrons of a molecule, resulting in their elevation to a higher energy level, but only if the incident wavelength corresponds to the available energy states, resulting in absorption. Consequently, this kind of interaction would not occur if the respective molecules do not have absorption bands in the claimed range of wavelengths of 600 to 650 nm. According to the established jurisprudence ("Case Law of the Boards of Appeal of the EPO", 7<sup>th</sup> edition (2013), II.C.4.4), the disclosure is only sufficient if it allows the invention to be performed in the whole range claimed. Since claim 1 is directed to molecules of medicaments of any kind, this criterion is not fulfilled. In the application only one single example of a medicament is indicated ("escina-based medicamentous solution" in paragraph [0053]).

But even if absorption occurs, it remains entirely unresolved how the excited energy state of the molecules could result in their penetration into the skin, which would imply the directional movement of the molecules on a macroscopic scale. Accordingly, the Board has serious doubts regarding the claimed interaction of the (laser light) energy emitter with the molecules and the claimed result of penetration of the molecules into the skin.

The appellant admitted that there might be a lack of scientific explanation, but stated that nevertheless a "surprising effect" was achievable with the claimed device "without knowing the real phenomena occurring in the skin". The Board accepts that it may not be possible to provide a scientifically sound explanation

and that the invention may still be sufficiently disclosed if such an unexpected effect is convincingly demonstrated. However, the original application is devoid of any test results or experimental evidence that could give an indication of light-induced enhancement of penetration of medicament molecules into the skin.

With its letter of 9 February 2015, i.e. after submitting its statement of grounds of appeal, the appellant presented three documents relating to experimental testing in order to demonstrate the effects achievable with the claimed device. All these documents were established well after the priority date of the present application. Even though sufficiency of disclosure must, in principle, be established at the priority date, post-published documents can be used as evidence that the claimed concept can be put in practice ("Case Law of the Boards of Appeal of the EPO", 7<sup>th</sup> edition (2013), II.C.5.8). Accordingly, the Board decided to consider these documents (in spite of their late filing).

"Group 1)":

The penultimate paragraph of page 2 of this document refers to a technique "called Cryo Laser Phoresis (CLP) ... developed by CIRCE. Srl, Italy", i.e. the present appellant. It is further stated that it "consists in a device that emits radiation on the polar or apolar molecules of an active ingredient [...]" without, however, indicating any further details about this device. The cited reference at the end of this paragraph does not reveal anything in this regard either. Section 3 ("Materials and Methods") at pages 3 to 4 mentions a "cryoapplicator", a frozen gel and a

laser, again without indicating any further details. Accordingly, in the absence of a description of further details about the features of the device used in this document, it cannot be established that the results described therein can be attributed to the device as claimed.

"Group 2)":

This is a colour copy of a piece of evidence already submitted in the first instance examination proceedings and dealt with in point 4.1 of the Reasons of the impugned decision. It refers to "the Cryopass Therapy Method" performed with a "gel in the LASERICEMED tube", the gel comprising 50mg/ml of porcine ganglioside GM1. Since further details of the device are not revealed, it again cannot be established that the results described in this document can be attributed to the device as claimed. Even if this were to be the case, the three test groups defined in the first paragraph of page 2 of this document are not suitable as proof that laser radiation has contributed to the active delivery of the medicine (which would have required a comparison of the application of the medicine in a test group with laser radiation and another one without, as correctly observed in the impugned decision).

"Group 3)":

This document comprises more than 100 pages and appears to be a manuscript of a doctoral thesis about melatonin (MLT).

The apparatus ("Lasericemed-cryoRx") depicted in Figure 14 at page 50 looks similar to that of the "medical machine" shown Figure 1 of the present patent

application, but the photograph fails to reveal any details about the claimed apparatus (corresponding to what is shown in Figures 2A and 2B of the application). Paragraph 3 of page 51 mentions a low power laser "(source 635 nm, power 50 mW, laser safety class 3R)", apparently forming part of a "the cryo-applicator". In this context it is mentioned that skin lesions are avoided due to the laser, an effect unrelated to what is stated in the present application. The following paragraph merely mentions that "active principles" penetrated into certain tissues in 15-20 min, "with a maximum observed in the genital muscle of 6 cm ( $\pm$  4 mm) (n=6 patients)" including a reference to "Criopass terapia" and the appellant's and the inventor's names, dated 8 June 2012. No further information is revealed in this passage with respect to the claimed device and effect.

In the cited passage at pages 66 and 67 it is stated that 15 ml of a suspension comprising a certain amount of melatonin were transferred into the cryo-applicator, frozen to  $-20^{\circ}\text{C}$ , and the frozen stick connected to "a laser source", which gave the energy to penetrate the cutaneous barrier and deliver the active principle to the target area, was rubbed on the back of an animal, where tumors were xenografted, for 2.5 min. Due to the use of the indefinite article "a", it remains unclear whether the laser previously mentioned in the passage of pages 50 and 51 was used.

The results on tumour growth presented in the cited passage at pages 80 to 84 relate to a comparison of an untreated control group ("Ctrl") with a group "treated with laser alone" and a group "treated with topical MLT", apparently also termed as "transdermal MLT by cryolaser". Again these results are not adequate to

prove that laser radiation has contributed to the active delivery of melatonin (which would have required a comparison of the application of medicine in a test group with laser radiation and another one without, as mentioned above).

Finally, the lower half of page 97 refers to a "novel and patented technique named cryoRx" (without, however, indicating any patent number). A meaningful comparison of results relating to the claimed effect is again missing. Instead, an increase in the systemic circulation is mentioned.

Accordingly, the results presented in this document do not demonstrate the claimed effect and it is not even certain that these results can be attributed to the device as claimed.

It follows that none of the three documents presented by the appellant demonstrate that the claimed device was able to achieve the alleged surprising effect of penetration into the skin achieved by laser irradiation active on the molecules of a medicament.

In the absence of a plausible explanation of the claimed effect and without any test results or experimental evidence demonstrating that this effect is achievable with the claimed device, the Board must conclude that the claimed invention is not disclosed in a manner sufficiently clear for it to be carried out by the person skilled in the art, in breach of Article 83 EPC.

**Order**

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

The appeal is dismissed.

The Registrar:

The Chairman:



D. Hampe

E. Dufrasne

Decision electronically authenticated