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Case Number: T 0810/10 - 3.3.02

Application Number: 99921398.6

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Language of the proceedings: EN

Title of invention:
GUIDED DEVELOPMENT AND SUPPORT OF HYDROGEL-CELL COMPOSITIONS

Patent Proprietor:
VBI Technologies, L.L.C.

Opponent:
Richter, Wolfgang

Headword:
Tissue-forming structure/VBI TECHNOLOGIES

Relevant legal provisions:
EPC Art. 54(2), 56
RPBA Art. 12(4)

Keyword:
Novelty (no)
Inventive step - obvious alternative
Late-filed request - same amendment not admitted in first-instance proceedings

Decisions cited:
G 0007/93

Catchword:

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Case Number: T 0810/10 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 16 March 2017

Appellant: (Patent Proprietor)	VBI Technologies, L.L.C. 910 Louisiana, Suite 3000 One Shell Plaza Houston, TX 77002 (US)
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Representative:	Ricker, Mathias Wallinger Ricker Schlotter Tostmann Patent- und Rechtsanwälte Partnerschaft mbB Zweibrückenstrasse 5-7 80331 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 5 February 2010 revoking European patent No. 1076533 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman	A. Lindner
Members:	T. Sommerfeld
	L. Bühler

Summary of Facts and Submissions

I. European patent 1076533, based on application 99921398.6, entitled "Guided development and support of hydrogel-cell compositions" and published as international application WO 1999/055252, was granted with 37 claims.

II. Opposition was filed against the granted patent, the opponent requesting revocation of the patent in its entirety. The grounds for opposition were lack of novelty and inventive step (Articles 54(2) and 56 EPC and Article 100(a) EPC), as well as exclusion from patentability (Article 53(a) EPC in combination with Rule 23d(c) EPC 1973 and Article 100(a) EPC).

III. By its decision announced at oral proceedings, the opposition division revoked the patent under Article 101(3)(b) EPC.

The opposition division decided that the main request and the sixth auxiliary request lacked clarity (Article 84 EPC), and that the first, second, fourth, fifth and sixth auxiliary requests lacked novelty (Article 54 EPC). The third auxiliary request was not admitted into the proceedings (Article 114(2) EPC and Rule 116 EPC).

IV. The patent proprietor (appellant) lodged an appeal against that decision. With the statement of the grounds of appeal, the appellant requested that the patent be maintained according to the main request or one of four auxiliary requests, all filed with the grounds of appeal.

Claim 1 of the **main request** reads as follows:

"1. A tissue forming structure comprising:
a permeable, biocompatible support structure having a predetermined shape that corresponds to the shape of desired tissue; and
a hydrogel-cell composition at least partially filling the support structure, wherein the hydrogel-cell composition is a suspension of tissue precursor cells in a hydrogel, said cells not including human embryonic cells,
for use in therapy."

Claim 1 of the **first auxiliary request** differs from claim 1 of the main request by insertion of the following feature (underlined) and deletion of "for use in therapy":

"1. A tissue forming structure comprising:
a permeable, biocompatible support structure having a predetermined shape that corresponds to the shape of desired tissue and that provides structural integrity sufficient to resist external stresses from the environment and surrounding tissues during growth of new tissue; and ..."

Claim 1 of the **second auxiliary request** differs from claim 1 of the first auxiliary request by re-insertion of the feature "for use in therapy" (as in the main request).

Claim 1 of the **third auxiliary request** differs from claim 1 of the main request as shown:

"1. A tissue forming structure comprising:
a permeable, biocompatible support structure having a predetermined shape that corresponds to the shape of

desired tissue and is selected from natural and synthetic sponges, pieces of coral, hydroxyapatite, or a matrix of metallic, inorganic, ceramic or plastic struts; and
a hydrogel-cell composition at least partially filling the support structure, wherein the hydrogel-cell composition ~~is a suspension of~~ comprises a hydrogel and tissue precursor cells~~ in a hydrogel~~, said cells not including human embryonic cells~~,~~
~~for use in therapy~~."

Claim 1 of the **fourth auxiliary request** differs from claim 1 of the third auxiliary request by re-introduction of the following features of the main request: definition of the hydrogel-cell composition and "for use in therapy".

V. The opponent (respondent) replied to the grounds of appeal, requesting that the appeal be dismissed. New documents were submitted, *inter alia* E11.

VI. The appellant replied to the respondent's submissions, maintaining its requests.

VII. Oral proceedings before the board took place as scheduled. At the end of the oral proceedings, the chairman announced the board's decision.

VIII. The documents cited during the proceedings before the opposition division and the board of appeal include the following:

E1 Sittinger et al. 1996, Biomaterials 17, 237-242
E4 Sittinger et al. 1995, Laryngo-Rhino-Otol. 74, 695-699
E6 DE 4431598

E11 Weber and White 1972, Science 176, 922-924

IX. The appellant's submissions, in so far as relevant for the decision, may be summarised as follows:

Main request and second auxiliary request - novelty

E6 did not disclose directly and unambiguously that tissue precursor cells were still present in the structure that was used for implant. Two stages were disclosed in E6 (column 1, line 55 ff.) but, even for the first stage, tissue rather than tissue precursor cells was mentioned. Even if the extracellular matrix may not have been completely formed, in any case there were no longer tissue-forming cells. The use of tissue precursor cells for therapy was hence not disclosed in E6. In the implants according to the patent, the structural integrity was conferred by the support structure, while in E6 it was provided by the extracellular matrix, the support structure being degraded during the *in vitro* cultivation. The structure with the features as claimed was disclosed in the prior art but was not for use in therapy.

Concerning the second auxiliary request, the added feature meant that the support structure had to be chosen according to its mechanical properties. In contrast, the support structure of E6 should be form-stable in the *in vitro* stage but not necessarily *in vivo*, since it was degraded already during *in vitro* cultivation.

First, third and fourth auxiliary requests - admissibility

The opposition division had not exercised its discretion wrongly but its reasons for not admitting the third auxiliary request were no longer valid for the present first auxiliary request, which had been submitted already with the grounds of appeal. The opponent had had plenty of time to react to it - which it had in fact done, extensively. The present third and fourth auxiliary requests further specified the claimed subject-matter and could thus therefore not be considered divergent but rather they were convergent.

Third and fourth auxiliary requests - inventive step

E6 was the closest prior art, and the problem was not to provide an alternative but an implant that guided development and shape of the new tissue, allowed vascularisation, and resisted external stresses from the environment and surrounding tissues. These properties were not achieved by E6, because the support structure, independently of its mechanical properties, was subsequently degraded (column 1, lines 7 to 9 and 25 to 26; column 2, lines 28 and 29). To solve this problem, the skilled person would not consider using the materials of E11, because E6 taught away from it. E6 required degradable materials, in order to avoid the problems with other materials disclosed in E1 (first page, left column, lines 3 to 10) and in E4 (first page, right column). E11 did not disclose that these materials could be used as support structure for hydrogen-cell compositions. As regarded the fourth auxiliary request, the aspect of vascularisation became even more relevant and was a clear advantage not taught by the prior art.

X. The respondent's arguments may be summarised as follows:

Main request and second auxiliary request - novelty

Although E6's implants developed to some extent *in vitro*, they still had to contain undeveloped cells, because the extracellular matrix developed further *in vivo*, meaning that the tissue continued to form (E6, column 1, lines 21 to 27, 52 ff.). A hydrogel-cell composition with cells in suspension was disclosed in E6 at column 1, lines 4 to 13 and 42 to 45; column 2, lines 28 to 60. Moreover it was apparent from the application (page 7, lines 13 to 14) that the added feature was rather just a definition of what was already in the granted claim. Since E6 disclosed implants, these were clearly meant for use in therapy. E6 referred to "tissue formation" ("Gewebebildung") *in vivo* (column 1, lines 64 to 66), which implied the presence of tissue precursor cells.

Concerning the second auxiliary request, the additional feature was also disclosed in E6, which characterised the support structure as "formstabil" (column 1, line 10). Since the tissue and the environment were not defined at all in the patent, the mechanical properties provided no limitation and the feature was in fact almost a "non-feature".

First, third and fourth auxiliary requests - admissibility

The first auxiliary request corresponded to the third auxiliary request filed during oral proceedings before the opposition division, which had not been admitted because it had been filed too late and *prima facie* did not solve the novelty issue. Additionally, this request was divergent because it lacked the feature "for use in

therapy" and the definition of the hydrogel-cell composition. The third and fourth auxiliary requests should not be admitted either, because they were not convergent.

Third and fourth auxiliary requests - inventive step

E6 was the closest prior art and the sole difference was that instead of a polymer mesh other support structures were used. There was no technical effect for this feature, either in the patent or on file, and so the technical problem was the provision of an alternative to E6; the alleged properties of the invention were not novel over E6. Since E11 (e.g. abstract) already disclosed the suitability of the claimed materials for tissue in-growth, the claimed solution was obvious. In line with E1, the skilled person would choose materials which were natural and degradable, such as natural coral and hydroxyapatite.

XI. The appellant (patent proprietor) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request, or, alternatively, of one of the first to fourth auxiliary requests, all filed with the statement of grounds of appeal.

The respondent (opponent) requested that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible.

2. Main request

2.1 Novelty

2.1.1 E6 discloses implants produced from cell cultures and comprising a support structure which is a degradable, three-dimensional, form-stable structure having a preformed shape corresponding to the desired form of the tissue (abstract; column 1, lines 6 to 12). Tissue precursor cells are suspended in a nutrition solution which also includes materials such as agarose or other hydrogels (column 3, first paragraph and lines 22 to 23; claim 8). Moreover, the structures of E6 are designated implants, which are, by definition, used for therapeutic purposes.

2.1.2 Hence E6 discloses a "tissue forming structure" with all features as claimed and is thus novelty-destroying for the subject-matter of claim 1.

2.1.3 The appellant did not dispute that E6 discloses a tissue-forming structure with all the features as claimed, but argued that said structure merely corresponded to the first phase of development (which takes place *in vitro*) and was not used for therapy: instead, the structure which was used for *in vivo* implantation in E6 was the structure resulting from the *in vitro* first phase, which no longer had any precursor cells in suspension, but rather comprised a tissue formed of cells interconnected by an intracellular matrix. The use for therapy of a structure comprising tissue precursor cells was hence, according to the appellant, not disclosed in E6.

2.1.4 The board notes that, although not stated in E6, it is implicit that the structure which is to be implanted does in fact contain tissue precursor cells, because,

as stated in E6 (e.g. column 1, lines 26 and 27 and lines 64 to 66), the tissue continues to develop *in vivo* - which requires the presence of tissue precursor cells. Moreover, E6 states that implantation takes place when the intracellular matrix has developed at least partially ("zumindest teilweise": column 1, lines 22 to 24; claim 1 at line 54) rather than completely, again implying that tissue development continues after implantation. In this respect, it is noted that claim 1 is not limited to structures in which all cells have to be tissue precursor cells; hence the existence of formed tissue in the structure which is implanted is not excluded from the scope of the claim.

2.1.5 The main request is thus not allowable for lack of novelty (Article 54(2) EPC).

3. First auxiliary request

3.1 Admissibility

3.1.1 According to Article 12(4) RPBA, the board has the discretionary power to hold inadmissible facts, evidence or requests which could have been presented or were not admitted in the first-instance proceedings. In the case of a discretionary decision of the first instance not to admit a request, it is not the function of the board to review all the facts and circumstances of the case as if it were in the place of the first-instance department, in order to decide whether or not it would have exercised such discretion in the same way. A board should only overrule the way in which the first-instance department has exercised its discretion if the board comes to the conclusion either that the first-instance department in its decision has not

exercised its discretion in accordance with the right principles or that it has exercised its discretion in an unreasonable way, and has thus exceeded the proper limits of its discretion (G 7/93, OJ EPO 1994, 775, reasons 2.6).

3.1.2 Claim 1 of the first auxiliary request comprises the functional feature that the support structure "provides structural integrity sufficient to resist external stresses from the environment and surrounding tissues during growth of new tissue". This feature, which was introduced into the third auxiliary request submitted at oral proceedings before the first instance, was considered by the opposition division to be *prima facie* unclear and not able to solve the novelty problems; the opposition division therefore decided not to admit the third auxiliary request into the proceedings.

3.1.3 The appellant has not argued that the opposition division exercised its discretion wrongly in not admitting the third auxiliary request into the proceedings. Nor can the board discern any improper exercise of discretion by the opposition division in that respect. Therefore, the board, in the exercise of its own discretionary power according to Article 12(4) RPBA, decides not to admit the first auxiliary request into the proceedings.

4. Second auxiliary request

4.1 Admissibility

4.1.1 There were no objections from the respondent concerning admissibility of this request. Although claim 1 of this request contains the same feature which led the opposition division not to admit the then third

auxiliary request, the board decided not to raise an admissibility objection of its own motion. This request is thus admitted into the proceedings (Article 12(4) RPBA).

4.2 Novelty

4.2.1 Claim 1 of the second auxiliary request differs from claim 1 of the main request solely by the further characterisation of the support structure by the above mentioned functional feature. The board considers that any support structure fulfils, by definition, the functional requirement of providing structural integrity. That said structural integrity should be "sufficient to resist external stresses from the environment and surrounding tissues during growth of new tissue" is implicit in the use of the support structure in the present case, which is in the context of a "tissue forming structure", i.e a structure where growth of new tissue takes place, used for implantation. Hence the board comes to the conclusion that this feature is nothing more than a functional definition of a "support structure" in the context of an implant as in E6 or of a tissue-forming structure of the patent, and as such cannot render the subject-matter novel over E6.

4.2.2 The appellant's arguments that the present claim comprised functional requirements - in terms of mechanical properties of the support structure - which were not disclosed in E6 are not convincing. E6 clearly discloses a support structure which is stable ("formstabil"). While E6 states that the support structure is degradable ("resorbierbar") and that, at some point during the implantation stage, it may indeed be completely absorbed, it is nevertheless still

present at the time of implantation (column 1, lines 24 to 27). Contrary to the appellant's submissions, there is no disclosure in E6 that the support structure is absorbed already before implantation and that its support function is then (solely) fulfilled by the newly developed extracellular matrix.

4.2.3 The second auxiliary request is hence not allowable for lack of novelty (Article 54(2) EPC).

5. Third and fourth auxiliary requests

5.1 Admissibility

5.1.1 The board is not convinced by the respondent's arguments that the third and fourth auxiliary requests are not convergent and should hence not be admitted into the proceedings. The amendments made in claim 1 of these requests constitute alternative limitations to the subject-matter of claim 1 of the main request, in a *bona fide* attempt to overcome the outstanding novelty objections. The board thus decides to admit these requests into the proceedings (Article 12(4) RPBA).

5.2 Inventive step

5.2.1 The patent discloses methods of generating new tissue in patients, by delivering a liquid hydrogel-cell composition, comprising tissue precursor cells, into a permeable, biocompatible support structure (paragraph [0004]). These methods improve the quality of the new tissue growth and increase the range of tissue shapes and structures that can be grown (paragraph [0005]).

5.2.2 Document E6, which also aims at providing methods to produce implants out of cell cultures, can be

considered the closest prior art. The difference to the claimed subject-matter is that a support structure made of the materials as claimed is not disclosed. In the absence of any technical effect associated with this difference (see also below), the technical problem has to be formulated as the provision of alternative tissue-forming structures. The board is satisfied that the technical problem is solved by the subject-matter as claimed.

5.2.3 It hence has to be assessed whether the claimed solution is inventive. E6 teaches the use of polymer fibres ("Polymerfasern") for the support structure. Porous polymer meshes are among the alternatives described in the patent as suitable for the support structures (e.g. paragraph [0037]) and are in fact the ones which are used in the examples of the patent. The other possible materials - which are the ones claimed - are listed in the above-mentioned paragraph as equally suitable alternatives. As evidenced by e.g. document E11 (abstract), said materials as well as their suitability for tissue in-growth were in fact known. Hence the board comes to the conclusion that the skilled person would arrive at the claimed subject-matter without inventive skill.

5.2.4 The appellant formulated the technical problem as being the provision of an implant that guided development and shape of the new tissue, allowed vascularisation, and resisted external stresses from the environment and surrounding tissues. The board however notes that these advantages, listed in paragraph [0027] of the patent, are not restricted to the structures as claimed but rather to any support structure, including those made out of polymer meshes (paragraph [0037], lines 36 and 37) which were used in E6. In fact, the same advantages

are also disclosed, at least implicitly, in E6: also with the tissue-forming structure of E6 cells are kept viable and allow growth of new tissue, and the permeable support structure provides a shape and structure for the solidifying hydrogel-cell composition while still allowing nutrients and waste products to diffuse (E6, claim 1). The support structure serves to guide the development and shape of the new tissue, since it is modelled according to the desired shape: "entsprechend der gewünschten Form des Implantates vorgeformt" (column 1, lines 10 to 12); at the same time it has, by definition, the ability to resist external stresses from the environment and surrounding tissues (see section 4.2.1). As already discussed above (section 4.2.2), the support structure according to E6 may be degraded *in vivo* at some point in time but not before it has performed these functions for as long as required.

5.2.5 A further argument of the appellant was that the prior art, in particular earlier documents E1 and E4, taught away from using these materials. The board notes however that the problems of using synthetic materials disclosed therein may apply to some of the materials claimed but certainly not to all, since the claim also includes natural materials (such as natural coral) and even materials which are naturally present within the human body (hydroxyapatite).

5.2.6 The third and fourth auxiliary requests are thus not allowable for lack of inventive step (Article 56 EPC).

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

N. Maslin A. Lindner

Decision electronically authenticated