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**Datasheet for the decision  
of 13 December 2017**

**Case Number:** T 0860/11 - 3.3.01

**Application Number:** 00914455.1

**Publication Number:** 1143943

**IPC:** A61K31/428, A61P35/00

**Language of the proceedings:** EN

**Title of invention:**

USE OF p53 INHIBITORS FOR THE TREATMENT OF SIDE EFFECTS OF  
CANCER THERAPY

**Patent Proprietor:**

THE BOARD OF TRUSTEES  
OF THE UNIVERSITY OF ILLINOIS

**Opponent:**

Eleos Inc.

**Headword:**

p53 inhibitors/UNIVERSITY OF ILLINOIS

**Relevant legal provisions:**

EPC R. 99(2)  
EPC Art. 83

**Keyword:**

Admissibility of opponent's appeal - (yes)  
Sufficiency of disclosure - (no)

**Decisions cited:**

**Catchword:**



**Beschwerdekammern**

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Case Number: T 0860/11 - 3.3.01

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.01**  
**of 13 December 2017**

**Appellant:** THE BOARD OF TRUSTEES  
(Patent Proprietor) OF THE UNIVERSITY OF ILLINOIS  
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**Representative:** Daniels, Jeffrey Nicholas  
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**Decision under appeal:** **Interlocutory decision of the Opposition**  
**Division of the European Patent Office posted on**  
**17 February 2011 concerning maintenance of**  
**European patent No. 1143943 in amended form.**

**Composition of the Board:**

**Chairman** A. Lindner  
**Members:** M. Pregetter  
L. Bühler

## **Summary of Facts and Submissions**

- I. European patent No. 1143943 is based on European patent application No. 00914455.1, filed as an international application published as WO00/44364.
- II. The appeals lie from the interlocutory decision of the opposition division maintaining the patent in amended form based on auxiliary request II filed during oral proceedings on 8 December 2010.

The main request was found to contravene the requirements of Article 123(2) and (3) EPC. Auxiliary request I was considered to fulfil the requirements of Article 123 EPC but to be insufficiently disclosed. Auxiliary request II was found to meet the requirements of the EPC.

- III. The proprietor and the opponent each lodged an appeal against this decision.
- IV. With the statement setting out its grounds of appeal the appellant-patent proprietor filed a main request and auxiliary request I and refiled the auxiliary request II of the opposition proceedings.

All three requests contain the same independent claim 1. It reads:

"1. Use of a reversible p53 inhibitor in the manufacture of a medicament for reducing or eliminating p53-mediated side effects associated with a cancer therapy comprising administering a therapeutically effective dose of the reversible p53 inhibitor to a mammal in conjunction with the cancer therapy, wherein

the p53-mediated side effect is hemapoietic system damage."

- V. On 13 December 2017 oral proceedings took place in the absence of the parties, who had been duly summoned but chosen not to attend.
- VI. The appellant-opponent submitted arguments in its statement of grounds of appeal and its letter dated 11 November 2011.

Its arguments, insofar as they are relevant to the present decision, may be summarised as follows:

*Sufficiency of disclosure*

The subject-matter of claim 1 covered a broad range, claiming the use of any "reversible p53 inhibitor". The possible options for reversible p53 inhibition included not only small molecules, but antibodies, anti-sense oligonucleotides, RNAi, growth factors, etc. Further the claim covered any type of p53 inhibition, whether by way of direct interaction with p53, more generalised interaction with the cellular machinery, or indirect action via components of the signalling pathways in which p53 played a role. Guidance was provided in relation to one family of compounds including pifithrin-alpha. The data presented in the patent provided only limited information in relation to the mechanism of action of pifithrin-alpha. Consequently, the teaching was insufficient to enable the breadth of claim 1.

- VII. The appellant-patent proprietor submitted arguments in its statement of grounds of appeal and its letter dated 10 November 2011.

Its arguments, insofar as they are relevant to the present decision, may be summarised as follows:

*Admissibility of appeal*

Rule 99(2) EPC required an appellant to indicate the reasons for setting aside the decision impugned. None of the grounds of appeal relied upon by the opponent was adequately substantiated, since the opponent had made no attempt to adapt its arguments to the reasons set out in the impugned decision. Consequently the opponent's appeal was inadmissible.

*Sufficiency of disclosure*

The opponent's objections regarding sufficiency of disclosure were unsubstantiated and not based on serious doubts supported by verifiable facts. The opponent had no clear basis for contesting the breadth of the invention as claimed.

VIII. 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 auxiliary request I, both filed with the statement setting out its grounds of appeal, or, alternatively, that the opponent's appeal be rejected as inadmissible, or, alternatively, that it be dismissed.

The appellant-opponent requested that the decision under appeal be set aside, that the patent proprietor's appeal be dismissed, and that European patent No. 1143943 be revoked.

## **Reasons for the Decision**

### *1. Admissibility of the opponent's appeal*

The appellant-patent proprietor considers the appellant-opponent's statement setting out its grounds for appeal to be insufficient (see point VII above). Hence, it claims that the appeal does not comply with Rule 99(2) EPC, which requires that the statement setting out the grounds for appeal "shall indicate the reasons for setting aside the decision impugned, or the extent to which it is to be amended, and the facts and evidence on which the appeal is based".

The board finds that the appellant-opponent's statement setting out its grounds for appeal indicates in detail why it considers that the subject-matter of the claims maintained by the opposition division is insufficiently disclosed (see pages 3 to 7). On page 6, paragraph 5, the appellant-opponent explains specifically why the opposition division in its view came to a wrong conclusion in paragraphs 7.6 and 7.8 of the impugned decision. Therefore, said statement gives detailed reasons why the decision under appeal should be set aside and indicates the facts and evidence in support of the respective arguments in accordance with Rule 99(2) EPC.

The appeal is admissible.

### *2. The oral proceedings before the board took place in the absence of the parties, who had been duly summoned but chosen not to attend, as announced with letter of 10 November 2017 (appellant-patent proprietor) and*

letter dated 20 September 2017, received on 22 September 2017 (appellant-opponent). 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 - sufficiency of disclosure*

3.1 Claim 1 of the main request defines the use of a certain active agent in the manufacture of a medicament for reducing or eliminating the p53-mediated side effect of hemapoietic system damage in cancer therapy. The active agent is defined as a "reversible p53 inhibitor". The active agent is thus defined in a functional manner. Claim 1 does not define or limit the active agent by structural features.

3.2 A "reversible p53 inhibitor" exerts its activity on the p53 system of cells. The p53 system is extremely complex and allows for various different interactions. Not only is direct interaction with the p53 protein itself possible, but so too are interaction with the cellular machinery and interaction with the signalling pathways in which p53 plays a role. Some of these interactions will lead to an inhibition of p53. Some inhibitions will be reversible.

3.3 The application as filed does not provide any information as to the point within this complex system where the "reversible p53 inhibitor" interacts with the system. There is also no indication whether most, if



not all, points of interaction would lead to the same result, i.e. the reversible inhibition of p53.

The description describes tests that show that one compound, pifithrin-alpha, has the functionality of being a "reversible p53 inhibitor". A screening test for identifying p53 inhibitors is disclosed on page 43, lines 5 to 23, of the application as filed. Figure 1 illustrates the result obtained by screening a chemical library for suppression of p53-dependent transcriptional activation by using mouse Balb 3T3 cells expressing bacterial lacZ gene under the control of a p53-responsive promoter. The only member of the chemical library that is identified is pifithrin-alpha, which is the only member that gave a positive result. It is not disclosed which compounds gave negative results. A second test is needed to come to a conclusion on the "reversibility" of the p53 inhibition. Such a test is described on page 50, line 16, to page 51, line 10, using mouse embryo fibroblasts transformed with Ela+ras (line C8).

Apart from pifithrin-alpha, pifithrin-beta is also said to have shown its suitability as a reversible p53 inhibitor in the tests described above. Other than these two specific compounds, the application as filed discloses four general formulas that are said to encompass compounds having the required functionality. These general formulas are closely related to each other.

- 3.4 Considering the p53 system, its chemical and physicochemical properties and its biochemical role in cellular processes, it is concluded that an extremely large variety of compounds are possible candidates for testing. The appellant-opponent has mentioned several

classes of compounds that might be possible candidates, e.g. small molecules other than the pifithrins, antibodies, anti-sense oligonucleotides, RNAi and growth factors. The board considers that, even when looking only at the "small molecules", a plethora of compounds is encompassed. However, the application as filed provides no information as to the criteria for selecting other compounds to be tested. It is not even clear which compounds formed part of the chemical library that led to the results depicted in figure 1.

- 3.5 In sum, the skilled person has to consider on his own which classes and/or types of compounds might be involved in inhibiting the p53 system, without being given any guidance as to their chemical nature. The thus selected compounds then have to be tested as described in the application in order to determine whether they are reversible p53 inhibitors.

In view of the complex nature of the p53 system and the various points and types of interaction possible, it amounts to an undue burden to test a plethora of compounds without being provided with any indication of the criteria to be taken into consideration in selecting them.

Since the board has come to the conclusion that an undue burden is involved in finding further reversible p53 inhibitors, the subject-matter of claim 1 of the main request is not sufficiently disclosed.

4. *Auxiliary requests*

Claim 1 of auxiliary request 1 and claim 1 of auxiliary request 2 are identical to claim 1 of the main request. Therefore, the same line of argument as given under

point 3 above for claim 1 of the main request applies to these claims. The subject-matter of claims 1 of the auxiliary requests is not sufficiently disclosed.

## Order

### For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chairman:



M. Schalow

A. Lindner

Decision electronically authenticated