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**Datasheet for the decision
of 8 April 2024**

Case Number: T 2214/21 - 3.3.02

Application Number: 16193088.8

Publication Number: 3147292

IPC: C07H19/06, C07H19/10,
C07H19/16, C07H19/20,
C07H21/00, C12Q1/68, G01N33/53

Language of the proceedings: EN

Title of invention:
LABELLED NUCLEOTIDES

Patent Proprietor:
Illumina Cambridge Limited

Opponent:
Hoffmann Eitle

Relevant legal provisions:
EPC 1973 Art. 76(1)
RPBA 2020 Art. 12(3), 12(5)

Keyword:

Divisional application - added subject-matter (yes)
Reply to statement of grounds of appeal - party's complete
appeal case
Discretion not to admit submission - requirements of Art.
12(3) RPBA 2020 met (no)



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Case Number: T 2214/21 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 8 April 2024

Appellant: Hoffmann Eitle
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Decision under appeal: **Interlocutory decision of the Opposition
Division of the European Patent Office posted on
11 October 2021 concerning maintenance of the
European Patent No. 3147292 in amended form.**

Composition of the Board:

Chairman M. O. Müller
Members: A. Lenzen
M. Blasi

Summary of Facts and Submissions

- I. This decision concerns the appeal filed by the opponent (appellant) against the decision of the opposition division (decision under appeal) that European patent No. 3 147 292 (patent) in amended form meets the requirements of the EPC.
- II. The patent was granted on European patent application No. 16 193 088.8, which is a second-generation divisional application. The numbers of the parent (earlier) and of the grandparent (earliest) European patent applications are 09 005 942.9 and 03 792 520.3, respectively. The earliest application had been filed as PCT application No. PCT/GB2003/003690, published as WO 2004/018493. The latter was introduced into the proceedings before the opposition division as D24.
- III. The decision under appeal is based on a main request, the claims of which were filed during the oral proceedings before the opposition division on 8 September 2021. According to this decision, the claimed subject-matter of the main request met the requirements of the EPC, *inter alia* of Article 76(1) EPC.
- IV. The respondent replied to the appeal by a letter containing solely its procedural requests, without any further explanation in relation to the substance of the case.
- V. The board summoned the parties to oral proceedings as per the corresponding requests of the parties. By letter dated 30 January 2024, the patent proprietor

(respondent) informed the board that it would not be attending the oral proceedings scheduled for 26 March 2024.

- VI. On 7 February 2024, the board issued a communication pursuant to Rule 100(2) EPC, in which it set out, *inter alia*, its preliminary negative opinion on the allowability of the amendments made in the main request. It also took a negative view on inventive step of the claimed subject-matter in the main and auxiliary requests. In so far as this conclusion concerned the auxiliary requests, it was based on the board's understanding of their claimed subject-matter. The board indicated that if this understanding was incorrect, the respondent should reply within the prescribed time limit. The board further indicated that it intended not to admit the respondent's auxiliary requests, and to reject its request for remittal.
- VII. The respondent did not file a reply to the board's communication within the prescribed time limit.
- VIII. The board then cancelled the oral proceedings.
- IX. The parties' final requests which are relevant to this decision are as follows:

The appellant requests that the decision under appeal be set aside and that the patent be revoked in its entirety. It also requests that none of the respondent's requests be admitted.

The respondent requests that the appeal be dismissed, implying that the decision under appeal be confirmed and the patent be maintained in the amended form considered allowable by the opposition division (main

request). If the main request is not allowable, the respondent requests that the case be remitted to the opposition division for further prosecution. In the alternative, the respondent requests that the patent be maintained in amended form based on one of the sets of claims of auxiliary requests 1 to 3 filed during the oral proceedings before the opposition division on 8 September 2021.

- X. Summaries of the opposition division's reasoning and the appellant's submissions - in so far as they are relevant to this decision - are contained in the reasons for the decision below.

The respondent never commented on the merits of the appeal.

Reasons for the Decision

Main request - (non-)admittance

1. The appellant requests that the main request not be admitted.

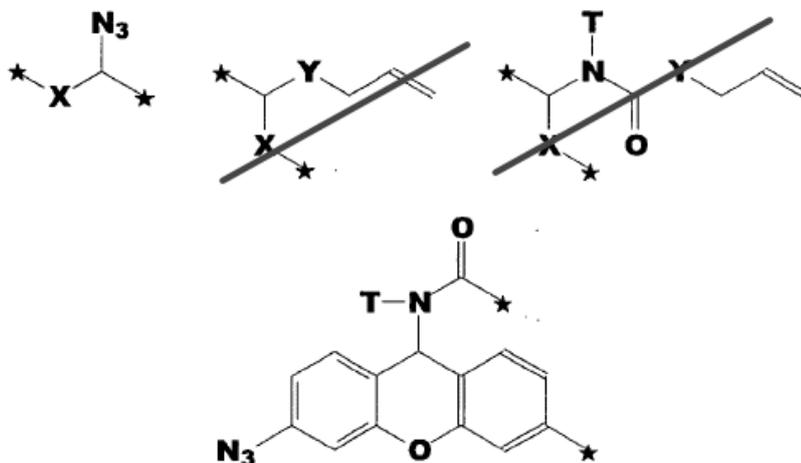
The respondent filed the claims of the main request during the oral proceedings before the opposition division on 8 September 2021 and the appellant had no objections to admittance of the main request. The opposition division examined the main request on its merits and considered it to be allowable. The decision under appeal is based on this request and it is in the proceedings. The appellant's request is therefore rejected.

Main request - amendments

2. The appellant submits that the subject-matter of claim 1 does not meet the requirements of Article 76(1) EPC in view of D24. In the absence of any indication to the contrary from the respondent, the board accepts that D24 represents the earliest application as filed.

3. Claim 1 of the main request reads as follows (showing the amendments vis-à-vis claim 1 of D24):

*"A nucleoside or nucleotide having a base attached to a detectable label via a cleavable linker, characterised in that the cleavable linker contains a moiety selected from the group comprising **consisting of:***



*(wherein X is selected from the group comprising **consisting of** O, S, NH and NQ wherein Q is a C₁₋₁₀ substituted or unsubstituted alkyl group, Y is selected from the group comprising O, S, NH and N(allyl), T is hydrogen or a C₁₋₁₀ substituted or unsubstituted alkyl group and * indicates where the*

moiety is connected to the remainder of the nucleotide or nucleoside), and wherein the nucleoside or nucleotide comprises a ribose or deoxyribose moiety with an azidomethyl protecting group attached to the 3' oxygen atom."

4. Thus, compared with claim 1 of D24, the two moieties containing an allyl group were deleted together with the definition of group Y contained in them, and the two moieties containing an azido group were retained. In addition, claim 1 of the main request now requires "*wherein the nucleoside or nucleotide comprises a ribose or deoxyribose moiety with an azidomethyl protecting group attached to the 3' oxygen atom*".

4.1 The four moieties of claim 1 of D24 are also disclosed therein on page 4, lines 10 to 25. However, neither claim 1 nor this passage discloses a preference for the two moieties recited in claim 1 of the main request.

The four moieties of claim 1 and of page 4, lines 10 to 25 of D24 are also assigned to two narrower sets of moieties, the assignment being based on whether the moiety contains an azido group or an allyl group (page 4, line 26 to page 5, line 16; page 5, line 17 to page 6, line 5; page 8, lines 10 to 14; page 11, lines 24 to 27). However, D24 discloses no preference for either of these narrower sets and therefore no preference for the set of the two azido group-containing moieties in claim 1 of the main request.

4.2 D24 discloses as possible protecting groups for the 3'-OH and 2'-OH of the ribose or deoxyribose moiety an allyl group and a group of the structure -O-Z (page 22, line 34 to page 23, line 34). One example of groups of structure -O-Z are those in which Z is -C(R')₂-N₃ (page

23, line 35 to page 24, line 2). Preferred representatives of the group $-C(R')_2-N_3$ are the azidomethyl group ($R' = H$: page 24, lines 2 to 3) and those in which R' is selected "from the structures given above and hydrogen; or in which $(R')_2$ represents an alkylidene group of formula $=C(R''')_2$, e.g. $=C(Me)_2$ " (page 24, line 24 to page 25, line 3). Therefore D24 does not disclose a preference for protecting groups containing azido groups, let alone those containing azidomethyl groups as required by claim 1 of the main request (over e.g. allyl protecting groups). D24 does not disclose either, contrary to the opposition division's view (decision under appeal, page 8, second paragraph), that the azidomethyl group is preferred among the protecting groups containing azido groups.

- 4.3 The ribose or deoxyribose sugar comprises a hydroxyl protecting group attached to the 2' or 3' oxygen atom (D24, claim 10). This does not leave any choice for deoxyribose (having a hydroxyl group only at C-3' but not at C-2') but does for ribose (having hydroxyl groups at both C-2' and C-3'). Provided that the nucleoside or nucleotide has a ribose sugar moiety, D24 discloses that protecting groups can be attached directly at the 3' position, the 2' position or both (page 22, lines 15 to 24). Therefore D24 does not disclose a preference for the 3' position of ribose as required by claim 1.
5. Against this background, the board agrees with the appellant that the following three selections need to be made from the disclosure of D24 to arrive at the subject-matter of claim 1:

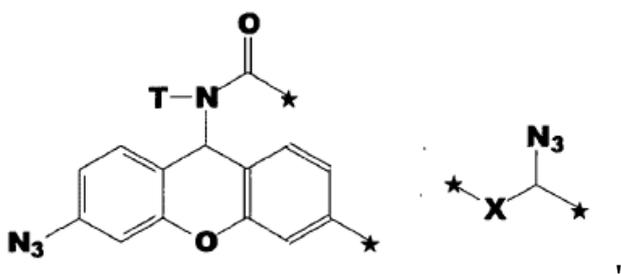
- a selection of the two azido group-containing moieties
- a selection of an O-azidomethyl protecting group
- a selection of a protecting group at the 3' position

It is established case law that such a multiple selection results in added subject-matter unless there is a pointer to the combination of selections made, e.g. in the form of preferences for the selections made. As explained above, such preferences do not exist in the present case.

6. In its decision, the opposition division relied on the following passages of D24 as pointers.

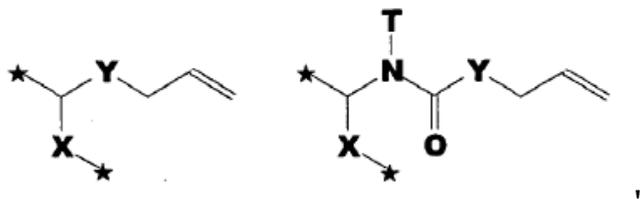
6.1 The passage on page 8, lines 10 to 14 was cited as a pointer for the selection of the two linkers comprising an azido group-containing moiety:

"Where the linkers comprise an azide-containing group the linkers may contain a moiety of the formula:



The board does not consider this convincing. The passage on page 11, lines 24 to 27 could equally be cited as a pointer in precisely the opposite direction:

"Where the linkers comprise an allyl group, these may be of the formulae:



6.2 The passage on page 25, lines 18 to 32

"The labile linker may, and preferably does, consist of functionality cleavable under identical conditions to the block. This makes the deprotection process more efficient since only a single treatment will be required to cleave both the label and the block. ... Similarly, if the linkage contains an azido moiety as discussed and claimed herein and the blocking group comprises an azido moiety, e.g. is of formula Z wherein R" is N₃ as discussed hereinbefore, both linkage and blocking group will be cleavable under identical conditions."

was cited as a pointer for the combination of the two linkers comprising an azido group-containing moiety with the azidomethyl protecting group.

However, this passage is very general and does not identify the moieties or the group mentioned in claim 1.

6.3 The passage on page 22, lines 15 to 24

"The skilled person will appreciate how to attach a suitable protecting group to the ribose ring to block interactions with the 3'-OH. The protecting group can be attached directly at the 3' position,

or can be attached at the 2' position (the protecting group being of sufficient size or charge to block interactions at the 3' position). Alternatively, the protecting group can be attached at both the 3' and 2' positions, and can be cleaved to expose the 3'OH group."

was cited as a pointer for the selection of the 3' position. The opposition division reasoned that the skilled person, knowing that azidomethyl was a small group, would have considered only the 3' position as a point of attachment for this protecting group.

The board does not consider this convincing. Even if it were accepted that the azidomethyl group is a small group, it is not clear what justifies the conclusion that its size is too small to effectively block interactions at the 3' position when it is present at the 2' position.

7. In view of the above, the subject-matter of claim 1 does not meet the requirements of Article 76(1) EPC.

Auxiliary requests 1 to 3 - admittance

8. The sets of claims of auxiliary requests 1 to 3 were filed during the oral proceedings before the opposition division on 8 September 2021.

In its reply to the statement of grounds of appeal, the respondent did not provide any explanation in relation to auxiliary requests 1 to 3, the claims of which had been submitted at the oral proceedings before the opposition division. It in particular did not explain why the amendments made in the auxiliary requests overcame any objection raised against the main request.

9. Thus, with regard to auxiliary requests 1 to 3, the respondent did not present a complete case with its reply, contrary to Article 12(3) RPBA. Therefore the board has discretion over whether or not to admit that part of the respondent's appeal case. Considering that substantiation is completely lacking and new issues would have to be assessed on appeal for the first time, the board decides, in line with the appellant's request, not to admit auxiliary requests 1 to 3 (Article 12(5) RPBA).

Request for remittal

10. Since none of the auxiliary requests is admitted, there is no auxiliary request on the basis of which the case could be remitted to the opposition division for further prosecution. Therefore the request for remittal is rejected.

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

M. O. Müller

Decision electronically authenticated