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**Datasheet for the decision
of 2 February 2024**

Case Number: T 0360/20 - 3.3.02

Application Number: 02781434.2

Publication Number: 1451351

IPC: C12Q1/68, C07H19/10, C07H19/20,
C07H21/00

Language of the proceedings: EN

Title of invention:
LABELLED NUCLEOTIDES

Patent Proprietor:
Illumina Cambridge Limited

Opponents:
Kilger, Christian
Hoffmann Eitle

Headword:

Relevant legal provisions:
EPC Art. 123(2)
RPBA 2020 Art. 12(6)

Keyword:

Amendments

Late-filed request

Decisions cited:

Catchword:



Beschwerdekammern
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Case Number: T 0360/20 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 2 February 2024

Appellant: Illumina Cambridge Limited
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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 13 December
2019 revoking European patent No. 1451351
pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman	M. O. Müller
Members:	S. Bertrand
	R. Romandini

Summary of Facts and Submissions

- I. The appeal by the patent proprietor ("appellant") lies from the opposition division's decision to revoke European patent No. 1451351.
- II. Claim 1 as granted relates to a nucleotide or nucleoside molecule having a base that is linked to a detectable label via a cleavable linker.
- III. The following documents are referred to in the present decision.
- | | |
|-----|---|
| D29 | Wikipedia Article - Disulfide |
| D30 | Brown, Duane, "Reduction of protein disulfide bonds by sodium borohydride", <i>Biochim. Biophys. Acta</i> , Vol. 44, 1960 |
- IV. The impugned decision is bound by the requirements of Article 123(2) EPC. The opposition division concluded, *inter alia*, that claims 1, 6 and 10 of each of the main request and auxiliary request 1 did not fulfil the requirements of Article 123(2) EPC.
- V. In its statement of grounds of appeal, the appellant contested the reasoning of the opposition division and submitted that, contrary to the opposition division's decision, claims 1, 6 and 10 of the main request were in compliance with Article 123(2) EPC. The appellant filed an auxiliary request.
- VI. Opponent 1 ("respondent 1") and opponent 2 ("respondent 2") filed replies to the grounds of appeal. They submitted that the claims of the main

request contained added subject-matter. They objected to admittance of the auxiliary request.

- VII. The board summoned the parties to oral proceedings, as requested by the parties, and issued a communication under Article 15(1) RPBA 2020. In the communication, the board gave as its preliminary opinion that claims 1, 6 and 10 of the main request did not fulfil the requirements of Article 123(2) EPC, and that the auxiliary request should not be admitted into the proceedings, in accordance with Article 12(6) RPBA 2020.
- VIII. With a letter dated 26 October 2023, the appellant stated that it would not attend the scheduled oral proceedings.
- IX. Oral proceedings were cancelled.
- X. The parties' requests, where relevant to the decision, were as follows.

The appellant requested:

- that the decision under appeal be set aside and the case be remitted to the opposition division for further prosecution, and
- that the auxiliary request be admitted into the proceedings.

Respondents 1 and 2 requested:

- that the appeal be dismissed, implying that the opposition division's decision to revoke the patent be upheld,
- that the auxiliary request not be admitted into the proceedings, and

- should the board decide to allow any request under Article 123(2) EPC, that the case be remitted to the opposition division for further prosecution.

XI. The appellant's case and the respondents' cases are summarised in the Reasons below.

Reasons for the Decision

Main request

1. Added subject-matter - Claim 1

1.1 Claim 1 of the main request reads as follows.

"1. A nucleotide or nucleoside molecule, having a base that is linked to a detectable label via a cleavable linker containing a disulfide linkage, wherein the molecule has a ribose or deoxyribose sugar moiety comprising a protecting group attached via the 2' or 3' oxygen atom and the cleavable linker and the protecting group are cleavable under identical conditions and wherein the linker can be cleaved by exposure to a metal or a reducing agent."

Claim 1 as filed reads as follows.

"1. A nucleotide or nucleoside molecule, having a base that is linked to a detectable label via a cleavable linker."

1.2 In its decision (point 6.1 of the Reasons), the opposition division held that the main request extended beyond the content of the application as filed, since the features of claim 1 of the main request were derived from multiple lists.

According to the reasoning of the opposition division, the following features of claim 1 of the main request were considered to be decisive as regards the assessment of added subject-matter:

- (i) a cleavable linker containing a disulfide linkage,
- (ii) the cleavable linker and the protecting group are cleavable under identical conditions, and
- (iii) the cleavable linker can be cleaved by exposure to a metal or a reducing agent.

The opposition division concluded that at least two independent selections from two lists, namely a first selection of a **disulfide linkage** from a list of several cleavable linkers and a second selection of **a metal or a reducing agent** from a list of cleaving agents, were necessary to arrive at the subject-matter of claim 1 of the main request.

In the replies to the grounds of appeal, respondents 1 and 2 applied the same reasoning, and argued that claim 1 did not therefore meet the requirements of Article 123(2) EPC.

- 1.3 The appellant submitted that the above features of claim 1 of the main request were based on the application as filed. The basis for the disulfide linkage was found on page 7, line 29 and page 13, line 15 of the application as filed. The basis for the metal or reducing agent was disclosed on page 12, line 19 of the application as filed.

1.4 The board notes the following.

The passage in the application as filed on page 7, line 29 discloses "disulfide linkers". The whole sentence including the term "disulfide linkers" on page 7, lines 28 to 33 reads: "*Fig.2 shows structures of linkers useful in the invention, including (1) **disulfide linkers** and acid labile linkers, (2) dialkoxybenzyl linkers, (3) Sieber linkers, (4) indole linkers and (5) t-butyl Sieber linkers in addition to a general definition of the linkers that may be used.*" (Emphasis added by the board.)

The whole sentence comprising the passage in the application as filed on page 13, line 15 reads: "*Suitable linkers are shown generally in Fig. 2 and include, but are not limited to, **disulfide linkers** (1), acid labile linkers (2, 3, 4 and 5; including dialkoxybenzyl linkers (e.g., 2), Sieber linkers (e.g., 3), indole linkers (e.g., 4), t-butyl Sieber linkers (e.g., 5)), electrophilically cleavable linkers, nucleophilically cleavable linkers, photocleavable linkers, cleavage under reductive conditions, oxidative conditions, cleavage via use of safety-catch linkers, and cleavage by elimination mechanisms.*" (Emphasis added by the board.)

From the above passages, a first selection from the list of linkers is thus needed to arrive at the "disulfide linkage" specified in claim 1 of the main request.

The passage on page 12, line 19 of the application as filed to which the applicant referred is part of a sentence which reads: "*The linker can be cleaved by any suitable method, including exposure to acids, bases, nucleophiles, electrophiles, radicals, **metals**, **reducing***

or oxidising **agents**, light, temperature, enzymes etc." (Emphasis added by the board.)

From this passage, a second selection from the list of cleaving agents is thus needed to arrive at the "metal" and "reducing agent" specified in claim 1 of the main request.

1.5 Following the reasoning in the case law of the boards of appeal, this combined selection of features pertaining to separate embodiments of the application as filed does not emerge directly and unambiguously, in the absence of any pointer to that particular combination, from the content of the application as filed for the person skilled in the art.

1.6 The appellant argued that the skilled person would automatically employ the agents specified in claim 1 to remove the disulfide linker specified in this claim, since these were the agents that were commonly known to result in cleavage of the disulfide bond. Here, the appellant relied on D29 and D30 as representing common general knowledge on the cleavage of disulfide bonds and disclosing cleavage by reduction and by using metals.

The board acknowledges that D29 (pages 3 and 4, "Reactions") and D30 (page 365) disclose the cleavage of disulfide bonds, *inter alia* by reduction or by using hydride agents such as sodium borohydride, both of which correspond to cleavage by a reducing agent as specified in claim 1. However, as a first point, D29 also discloses other cleavage agents, namely cleavage by contact with electrophiles or nucleophiles, see page 2, first paragraph of the section "Properties". Hence, as set out by the respondents, a disulfide linkage can be cleaved in other ways than by a metal or a reducing

agent. It cannot thus be the case that a skilled person who wanted to cleave a disulfide linkage would, on the basis of their common general knowledge, inevitably use the cleavage agents specified in claim 1 of the main request. As a second point, there is in fact nothing in D29 or D30 about the second alternative cleavage agent specified in claim 1 of the main request, i.e. a metal agent.

The board concludes that, in the absence of a pointer to combine the features "disulfide linkage" and "a metal or a reducing agent", claim 1 of the main request does not fulfil the requirements of Article 123(2) EPC. The same reasoning applies to claims 6 and 10 of the main request.

This point was made in the board's communication under Article 15(1) RPBA 2020, and was not commented on by the appellant.

Auxiliary request

2. Claims 1, 6 and 10 of the auxiliary request differ from the respective claims of the main request in that the cleaving agent is restricted to a reducing agent. In claims 1, 6, 10 of the main request, the cleaving agent can be a metal or a reducing agent.
3. Admittance of the auxiliary request
 - 3.1 Respondents 1 and 2 requested that the auxiliary request not be admitted into the proceedings.
 - 3.2 As set out above, the set of claims of the auxiliary request was filed with the statement of grounds of appeal.

- 3.3 Admittance of the auxiliary request is governed, *inter alia*, by Article 12(6) RPBA 2020. This applies to the case at hand because the statement of grounds of appeal was filed after the date of entry into force of the revised version of the Rules of Procedure of the Boards of Appeal (1 January 2020, see Articles 24 and 25 RPBA 2020).
- 3.4 Under Article 12(6), second sentence, RPBA 2020, the board shall not admit requests which should have been submitted in the proceedings leading to the decision under appeal, unless the circumstances of the appeal case justify their admittance.
- 3.5 The board acknowledges that the amendment made in the auxiliary request, i.e. the restriction of the cleaving agent to a reducing agent, represents an attempt to overcome the objection of added subject-matter in the main request, raised by respondents 1 and 2 in their replies to the statement of grounds of appeal. However, the objection, based on a selection from a plurality of lists, had already been raised in respondent 1's notice of opposition (point 6.1), respondent 2's notice of opposition (point 3.1) and the opposition division's annex to the summons to attend oral proceedings (points 4.1 and 4.2). The appellant had thus had sufficient time during the proceedings before the opposition division to respond to the objection. The auxiliary request could and should have been filed then.
- 3.6 For these reasons, the board decided not to admit the auxiliary request into the proceedings, in accordance with Article 12(6) RPBA 2020.

This point was made in the board's communication under Article 15(1) RPBA 2020, and was not disputed by the appellant.

4. Neither of the appellant's claim requests is both admissible and allowable.

Order

For these reasons it is decided that:

1. The appeal is dismissed.

The Registrar:

The Chairman:



M. Schalow

M. O. Müller

Decision electronically authenticated