

**Internal distribution code:**

- (A) [ - ] Publication in OJ
- (B) [ - ] To Chairmen and Members
- (C) [ - ] To Chairmen
- (D) [ X ] No distribution

**Datasheet for the decision  
of 13 August 2020**

**Case Number:** T 2472/17 - 3.3.01

**Application Number:** 12730009.3

**Publication Number:** 2705363

**IPC:** G01N33/50, G01N33/574

**Language of the proceedings:** EN

**Title of invention:**

DEVICE AND METHOD FOR NON-INVASIVE COLLECTION OF COLORECTAL  
MUCOCELLULAR LAYER AND DISEASE DETECTION

**Applicant:**

Diagnodus Limited

**Headword:**

Non-invasive collection of colorectal mucocellular layer/  
DIAGNODUS

**Relevant legal provisions:**

EPC Art. 123(2), 56

**Keyword:**

Amendments - allowable (yes)  
Inventive step - (yes)



**Beschwerdekammern**  
**Boards of Appeal**  
**Chambres de recours**

Boards of Appeal of the  
European Patent Office  
Richard-Reitzner-Allee 8  
85540 Haar  
GERMANY  
Tel. +49 (0)89 2399-0  
Fax +49 (0)89 2399-4465

Case Number: T 2472/17 - 3.3.01

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.01**  
**of 13 August 2020**

**Appellant:** Diagnodus Limited  
(Applicant) Building 502 Babraham Research Campus  
Babraham, Cambridgeshire CB22 3AT (GB)

**Representative:** Martin, Philip John  
Marks & Clerk LLP  
62-68 Hills Road  
Cambridge  
CB2 1LA (GB)

**Decision under appeal:** **Decision of the Examining Division of the  
European Patent Office posted on 25 April 2017  
refusing European patent application No.  
12730009.3 pursuant to Article 97(2) EPC.**

**Composition of the Board:**

**Chairman** A. Lindner  
**Members:** M. Pregetter  
P. de Heij

## **Summary of Facts and Submissions**

- I. The appeal lies from the decision of the examining division to refuse European patent application 12730009.3.
- II. The following documents, cited during the examination and appeal proceedings, are referred to below:
  - (2) WO2006/039405
  - (7) A. Loktionov, *Int. J. Cancer*, 2007, 120, 2281-2289
- III. The examining division refused the application for non-compliance with the requirements of Article 123(2) EPC of the single claim filed during oral proceedings before the examining division.
- IV. The appellant (applicant) lodged an appeal against this decision. Together with the statement of grounds of appeal, it re-submitted the claim underlying the decision under appeal as its main request and submitted auxiliary requests 1 to 13. It also requested that the board consider inventive step of the main and the auxiliary requests.
- V. On 26 March 2020, the board issued a communication pursuant to Article 15(1) RPBA 2020.
- VI. By letter dated 3 June 2020, the appellant withdrew its main request and auxiliary requests 1 to 8. Former auxiliary request 9 was indicated to represent the new main request, the sole claim of which reads as follows:

"1. A non-invasive method for collecting a sample of intestinal or bowel cells or cell fragments the method consisting of:

(a) taking a swab of mucocellular layer material which originates from said bowel or intestine and is excreted during defaecation, from the surface of the anal area in the vicinity of the exterior opening of the anal canal, wherein said swab is taken following defaecation before cleaning the area, and

(b) placing said swab of mucocellular layer material into a medium for sample storage or lysis;"

VII. The oral proceedings were cancelled.

VIII. The appellant's arguments, in so far as they are relevant to the present decision, may be summarised as follows.

#### Amendments

Claim 1 of the main request could be directly and unambiguously derived from page 13, lines 1 to 14, of the application as filed.

#### Inventive step

Document (2) was the closest prior art, as identified by the examining division. It disclosed the obtaining of a sample by biopsy or by taking a swab of rectal cells. The difference between the subject-matter of claim 1 of the main request and the disclosure of document (2) was thus the non-invasive technique. Additionally, no method of collecting a sample of intestinal or bowel cells by taking a swab of especially mucocellular layer material from the surface of the anal area in the vicinity of the exterior

opening of the anal canal was disclosed. Furthermore, neither document (2) nor document (7) taught a method consisting only of taking a swab of the surface of the anal area and placing the swab into a medium for sample storage or lysis. The technical problem was thus the provision of a non-invasive method that required no processing of the sample to obtain the collected cells other than the steps recited in the claim.

Document (7), referring to stool samples, which were the samples obtained by the usual non-invasive sampling method at that time, indicated that no significant amounts of exfoliated cells could be obtained for reliable cytological assessment or intracellular biomarker identification. Consequently, the subject-matter of claim 1 was inventive over a combination of documents (2) and (7).

- IX. The appellant's final requests were, as understood by the board, that the decision under appeal be set aside and that a patent be granted on the basis of claim 1 of the main request, filed with the statement setting out the grounds of appeal as auxiliary request 9, or, alternatively, that a patent be granted on the basis of any of auxiliary requests 1 to 4, filed as auxiliary requests 10 to 13 with the statement setting out the grounds of appeal.

### **Reasons for the Decision**

1. The appeal is admissible.
2. *Amendments*
  - 2.1 The subject-matter of claim 1 of the main request can be derived from the combination of claims 1 to 3

(selecting one of the two options of dependent claim 2) with the passage on page 1, lines 6 to 9, of the application as filed which discloses that a sample of colorectal mucocellular layer is excreted during the natural act of defaecation.

A similar disclosure can be found on page 13, lines 1 to 14, requiring, however, that the swab be taken within 5 minutes of defaecation.

2.2 Claim 1 defines a "method for collecting a sample" "consisting of" steps (a) and (b). The limitation to a method consisting of merely these two steps is justified in view of the following passages of the application as filed.

Page 13 describes a "first" aspect of the invention, which is a "non-invasive method for collecting a sample". Swabbing and placing the swab in a storage medium or a lysis medium are the only two process steps described for this "first" aspect (page 13, lines 1 to 18). The disclosure on page 13 then turns to a "further" aspect, which is a method for diagnosing bowel disease (page 13, line 20). Further aspects can be found on page 14, lines 25, to page 15, line 2. Still further embodiments relate to a device for collecting a sample. On page 20 of the description, details of the method of sampling are given (page 20, lines 12 to 26). These details provide specifications on how to carry out steps (a) and (b) of claim 1 of the main request. No additional process steps going beyond steps (a) and (b) are disclosed. The same applies to the explanation of the method for collecting the sample of page 30, lines 8, to page 31, line 26. Example 1, the only example of the application, does not give any details of the sampling method. Finally, neither the

"clauses" on pages 40 to 45 nor the claims as filed indicate any further process steps.

The application as filed discloses further method steps which are, however, irrelevant for assessment for compliance with the requirements of Article 123(2) EPC of claim 1 of the main request since they relate to the discussion of background art (e.g. page 3, line 11, to page 7, line 30) or methods for diagnosing, screening or monitoring, i.e. methods that involve the analysis of sampled markers.

- 2.3 The subject-matter of claim 1 of the main request can thus be directly and unambiguously derived from the application as filed. The requirements of Article 123(2) EPC are fulfilled.

3. *Novelty*

The search report has not identified any documents relevant for the assessment of novelty. Nor does the board have any objection in view of the documents on file.

4. *Inventive step*

- 4.1 The application relates to the provision of a method for collecting a sample of colorectal mucocellular layer for detecting diagnostically informative disease biomarkers (page 1, lines 6 to 9). Analysing the mucocellular layer containing exfoliated cells, cell fragments and biomolecules reflecting the state of the colorectal mucosa may be crucial in detecting colorectal cancer (page 8, lines 2 to 10).

To this end, a non-invasive method for collecting a

sample of intestinal or bowel cells or cell fragments comprising taking a swab of mucocellular layer material originating from the bowel or intestine from the surface of the anal area in the vicinity of the exterior opening of the anal canal, with this swab being taken following defaecation, is taught (page 13, lines 1 to 7).

4.2 Document (2) is the closest prior art.

It discloses a kit for use in the early detection of colorectal cancer (claim 14). A container for receiving a sample containing rectal mucosal cells obtained through a non-invasive procedure is defined. However, document (2) does not describe, neither in claim 14 nor anywhere else, the obtaining of rectal mucosal cells through a non-invasive procedure. The skilled person would thus have come away with no guidance on how to carry out such a non-invasive procedure.

The description of document (2), when discussing Figure 6, describes a system comprising a swab and a container (page 24, lines 11, to page 25, line 10). The shaft of the swab is made of a material with sufficient mechanical strength for effectively swabbing the rectal area (page 24, lines 21 to 23). On page 24, lines 32 to 35, it is mentioned that the swabbing is done "as a minimally invasive sampling technique".

It is thus not clear whether exclusively an invasive (or "minimally invasive") sampling technique or also a non-invasive sampling technique is used in document (2). However, a non-invasive sampling technique for obtaining rectal mucosal cells is not detailed. In particular, the area of the body that would be swabbed when carrying out a non-invasive



sampling technique is not disclosed. Furthermore, no indication on when to swab is given.

- 4.3 The subject-matter of claim 1 of the main request thus differs from the disclosure of document (2) in the area (the surface of the anal area in the vicinity of the exterior opening of the anal canal) swabbed and in the time (following defaecation before cleaning the area) of the swabbing.

No conclusion on whether an effect is linked to these two differences has been reached.

The problem can be seen as an alternative method for collecting a sample of intestinal or bowel cells or cell fragments.

The problem has been solved. Example 1 and the results depicted in Figures 5 to 7 show that a sample comprising colonocytes can be obtained by the claimed method.

As there is neither a document on file that teaches to swab the defined area at the defined time nor a document that discloses that intestinal (or bowel cells/cell fragments) or mucocellular layer material stemming from the rectum can be found on the outer surface of the anal area after defaecation, the skilled person would not have been led by the prior art to perform the claimed method. Consequently, the claimed subject-matter is a non-obvious alternative.

- 4.4 The subject-matter of claim 1 of the main request involves an inventive step (Article 56 EPC).

## Order

### For these reasons it is decided that:

The decision under appeal is set aside.

The case is remitted to the examining division with the order to grant a patent with the following claim and a description to be adapted thereto:

Claim 1 of the main request, filed with the statement setting out the grounds of appeal on 5 September 2017 as auxiliary request 9.

The Registrar:

The Chairman:



G. Nachtigall

A. Lindner

Decision electronically authenticated