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Datasheet for the decision of 2 July 2015

Case Number: T 0135/11 - 3.3.02

Application Number: 97923412.7

Publication Number: 0892808

IPC: C07H21/04, C12Q1/68, C12P19/34

Language of the proceedings: EN

Title of invention:
DETECTION PROBES, KITS AND ASSAYS

Patent Proprietor:
PHRI Properties, Inc.

Opponent:
Calvo de Nó, Rodrigo

Headword:
Non-FRET probes/PHRI PROPERTIES

Relevant legal provisions:
EPC Art. 123(2)
RPBA Art. 13(1)

Keyword:
Main request - added subject-matter (yes)
Auxiliary requests - admissibility (no)

Decisions cited:

Catchword:

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Case Number: T 0135/11 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 2 July 2015

Appellant: (Opponent)	Calvo de Nó, Rodrigo Rue Champ du Roi 77 1040 Brussels (BE)
Representative:	Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Respondent: (Patent Proprietor)	PHRI Properties, Inc. 65 Bergen Street Newark, NJ 07107-3001 (US)
Representative:	Bizley, Richard Edward Avidity IP Broers Building Hauser Forum 21 J J Thomson Ave Cambridge CB3 0FA (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 5 November 2010 concerning maintenance of the European Patent No. 0892808 in amended form.**

Composition of the Board:

Chairman	U. Oswald
Members:	K. Giebeler
	L. Bühler

Summary of Facts and Submissions

I. European patent No. 0 892 808, based on European patent application No. 97923412.7, published as WO 97/39008 (hereafter referred to as "the application as filed") and entitled "Detection probes, kits and assays", was granted with 10 claims.

II. Claim 1 of the application as filed reads:

"A probe capable of hybridizing with a nucleic acid strand comprising one or two molecules from the group consisting of natural nucleotides, modified nucleotides and combinations thereof, and a non-FRET pair of labels consisting of a first fluorophore and a chromophore, said chromophore selected from the group consisting of fluorophores and quenchers, wherein interaction of the probe with a target causes the probe to change from a first conformation to a second conformation, thereby changing the distance between the labels of said label pair, and wherein in only one conformation do the labels touch sufficiently to quench the fluorescence of said first fluorophore by at least 25 percent."

III. Claim 1 as granted reads:

"A probe capable of hybridizing with a nucleic acid strand comprising one or two molecules from the group consisting of natural nucleotides, modified nucleotides and combinations thereof, and a non-FRET pair of labels, optionally two non-FRET pairs of labels, consisting of a first fluorophore and a chromophore, said chromophore selected from the group consisting of fluorophores and quenchers, wherein the non-FRET pair of labels is characterised in that, the efficiency of quenching of said first fluorophore by said

chromophore, as measured by the decrease in emission intensity of said first fluorophore when said labels are attached to oligodeoxynucleotides and separated by a FRET distance within the range of from ten to one hundred Angstroms, is less than sixty percent, and wherein interaction of the probe with a target causes the probe to change from a first conformation to a second conformation, thereby changing the distance between the labels of said label pair, and wherein in only one conformation do the labels touch sufficiently to quench the fluorescence of said first fluorophore by at least 25 percent."

IV. An opposition was filed against the granted patent on the grounds of lack of novelty and inventive step (Article 100(a) EPC), insufficiency of disclosure (Article 100(b) EPC) and added subject-matter (Article 100(c) EPC).

V. In its interlocutory decision, the opposition division decided that the claims of the main request met the requirements of the EPC.

VI. The opponent (hereafter appellant) filed an appeal against the decision of the opposition division.

VII. The proprietor (hereafter respondent) did not respond to the appeal until after the prescribed time limit had expired, a request for extension of the time limit having been refused by the then competent board. With its belatedly filed response to the appeal, the respondent submitted a new main request and seven auxiliary requests.

VIII. With letter of 1 August 2014, the respondent filed a new main request and single auxiliary request, replacing the previously filed claim requests.

IX. With letter of 4 September 2014, the appellant objected to the admittance into the proceedings of the newly filed claim requests.

X. On 14 November 2014, the board issued a communication as an annex to the summons to oral proceedings, expressing its preliminary opinion.

XI. The appellant responded to the board's communication, stating that it was withdrawing its request for oral proceedings and that it would not be represented at the oral proceedings.

XII. With letter of 24 April 2015, the respondent filed further submissions, including a new main request and ten auxiliary requests.

XIII. Claim 1 of the main request, which is identical to the main request held allowable by the opposition division, reads as follows:

"A probe capable of hybridizing with a nucleic acid strand comprising one or two molecules from the group consisting of natural nucleotides, modified nucleotides and combinations thereof, and a non-FRET pair of labels, optionally two non-FRET pairs of labels, consisting of a first fluorophore and a non-fluorescent quencher, wherein the non-FRET pair of labels is characterised in that, the efficiency of quenching of said first fluorophore by said non-fluorescent quencher, as measured by the decrease in emission intensity of said first fluorophore when said labels

are attached to oligodeoxynucleotides and separated by a FRET distance within the range of from ten to one hundred Angstroms, is less than sixty percent, and wherein interaction of the probe with a target causes the probe to change from a first conformation to a second conformation, thereby changing the distance between the labels of said label pair, and wherein in only one conformation do the labels touch sufficiently to quench the fluorescence of said first fluorophore by at least sixty percent, and at least thirty percent above the quenching efficiency expected based on spectral overlap."

XIV. Claim 1 of the first auxiliary request reads:

"A probe capable of hybridizing with a nucleic acid strand comprising one or two molecules from the group consisting of natural nucleotides, modified nucleotides and combinations thereof, and a non-FRET pair of labels, optionally two non-FRET pairs of labels, consisting of a first fluorophore and a non-fluorescent quencher, wherein the non-FRET pair of labels is characterised in that, the efficiency of quenching of said first fluorophore by said non-fluorescent quencher, as measured by the decrease in emission intensity of said first fluorophore when said labels are attached to oligodeoxynucleotides and separated by a FRET distance within the range of from ten to one hundred Angstroms, is less than sixty percent, and wherein interaction of the probe with a target causes the probe to change from a first conformation to a second conformation, thereby changing the distance between the labels of said label pair, and wherein in only one conformation do the labels touch sufficiently to quench the fluorescence of said first fluorophore by at least sixty percent and at least thirty percent

above the quenching efficiency expected based on spectral overlap, and wherein said probe is suitable for use in a multiplex assay."

XV. Claim 1 of the second and third auxiliary requests differs from claim 1 of the first auxiliary request in that the term "sixty percent" is replaced by the terms "seventy percent" and "eighty percent" respectively.

XVI. Claim 1 of the fifth auxiliary request reads:

"A multiplex assay, that includes a step of detecting that comprises contacting probes with a sample suspected to contain a target for said probes and measuring the change in fluorescence, preferably said assay further includes amplification by the PCR process and detection in real time; wherein each probe is capable of hybridizing with a target nucleic acid strand and comprises one or two molecules from the group consisting of natural nucleotides, modified nucleotides and combinations thereof, and a non-FRET pair of labels, optionally two non-FRET pairs of labels, consisting of a first fluorophore and a non-fluorescent quencher, wherein the non-FRET pair of labels is characterised in that, the efficiency of quenching of said first fluorophore by said non-fluorescent quencher, as measured by the decrease in emission intensity of said first fluorophore when said labels are attached to oligodeoxynucleotides and separated by a FRET distance within the range of from ten to one hundred Angstroms, is less than sixty percent, and wherein interaction of the probe with a target causes the probe to change from a first conformation to a second conformation, thereby changing the distance between the labels of said label pair, and wherein in only one conformation do the labels touch

sufficiently to quench the fluorescence of said first fluorophore by at least sixty percent and at least thirty percent above the quenching efficiency expected based on spectral overlap."

XVII. Claim 1 of the sixth and seventh auxiliary requests differs from claim 1 of the fifth auxiliary request in that the term "at least sixty percent" is replaced by the terms "at least seventy percent" and "at least eighty percent" respectively.

XVIII. Claim 1 of the ninth auxiliary request reads:

"A probe capable of hybridizing with a nucleic acid strand comprising one or two molecules from the group consisting of natural nucleotides, modified nucleotides and combinations thereof, and a non-FRET pair of labels, optionally two non-FRET pairs of labels, consisting of a first fluorophore and a non-fluorescent quencher, wherein the non-FRET pair of labels is characterised in that, the efficiency of quenching of said first fluorophore by said non-fluorescent quencher, as measured by the decrease in emission intensity of said first fluorophore when said labels are attached to oligodeoxynucleotides and separated by a FRET distance within the range of from ten to one hundred Angstroms, is less than sixty percent, and wherein interaction of the probe with a target causes the probe to change from a first conformation to a second conformation, thereby changing the distance between the labels of said label pair, and wherein in only one conformation do the labels touch sufficiently to provide an observed quenching efficiency of at least 90% and more preferably 95%; and wherein said probe is suitable for use in a multiplex assay that includes

amplification by the PCR process and detection in real-time."

XIX. Claim 1 of the tenth auxiliary request reads:

"A multiplex assay, that includes a step of detecting that comprises contacting at least one probe with a sample suspected to contain a target for said probe and measuring the change in fluorescence, wherein said assay further includes amplification by the PCR process and detection in real time; wherein said probe is capable of hybridizing with a target nucleic acid strand comprising one or two molecules from the group consisting of natural nucleotides, modified nucleotides and combinations thereof, and a non-FRET pair of labels, optionally two non-FRET pairs of labels, consisting of a first fluorophore and a non-fluorescent quencher, wherein the non-FRET pair of labels is characterised in that, the efficiency of quenching of said first fluorophore by said non-fluorescent quencher, as measured by the decrease in emission intensity of said first fluorophore when said labels are attached to oligodeoxynucleotides and separated by a FRET distance within the range of from ten to one hundred Angstroms, is less than sixty percent, and wherein interaction of the probe with a target causes the probe to change from a first conformation to a second conformation, thereby changing the distance between the labels of said label pair, and wherein in only one conformation do the labels touch sufficiently to provide an observed quenching efficiency of at least 90% and more preferably 95%; and wherein said probe is suitable for use in a multiplex assay that includes amplification by the PCR process and detection in real-time."

XX. Oral proceedings were held on 2 July 2015 in the absence of the duly summoned appellant. During the oral proceedings, the respondent filed an additional request, referred to as "main request A". Claim 1 of this request reads:

"A probe capable of hybridizing with a nucleic acid strand comprising one or two molecules from the group consisting of natural nucleotides, modified nucleotides and combinations thereof, and a non-FRET pair of labels, optionally two non-FRET pairs of labels, consisting of a first fluorophore and a non-fluorescent quencher, wherein the non-FRET pair of labels is characterised in that, the efficiency of quenching of said first fluorophore by said chromophore, as represented by the decrease in emission intensity of said first fluorophore when said labels are attached to oligodeoxynucleotides and separated by a FRET distance within the range of from ten to one hundred Angstroms, is less than sixty percent when indirectly measured by the procedure of Examples 1 and 2, and wherein interaction of the probe with a target causes the probe to change from a first conformation to a second conformation, thereby changing the distance between the labels of said label pair, and wherein in only one conformation do the labels touch sufficiently to quench the fluorescence of said first fluorophore by at least sixty percent and at least thirty percent above the quenching efficiency expected based on spectral overlap."

XXI. The appellant's arguments submitted in writing, insofar as they are relevant for the present decision, can be summarised as follows:

Main request - Article 123(2) EPC

Claim 1 did not comply with Article 123(2) EPC, because the definition of "non-FRET" in the claim was not disclosed in the application as filed. Said definition was arrived at by forcing together more than one statement in the application as filed, and dropping certain mandatory limitations. Moreover, said definition was not derivable from the examples of the application as filed, since none of the examples performed the experimental measurement as required by the definition in claim 1. Example 1 mentioned the experimentally measured quenching of EDANS-DABCYL, whilst explaining that this provided the baseline for calculating the expected quenching efficiency. However, the experimental measurements of claim 1 were not performed, described or even remotely implied. The examples and the description did not describe any experiments in which a fluorophore and the quencher were attached to oligodeoxyribonucleic acids and the quenching of the fluorescence of the fluorophore was measured when the labels were in the FRET range of from ten to one hundred Angstroms.

Auxiliary requests - Admissibility

The auxiliary requests should not be admitted into the proceedings because they were not filed until after the time limit to respond to the appeal had expired.

XXII. The respondent's arguments, insofar as they are relevant for the present decision, can be summarised as follows:

Main request - Article 123(2) EPC

The claims met the requirement of Article 123(2) EPC; the definition of "non-FRET" in claim 1 was directly and unambiguously derivable from page 16 of the application as filed in combination with Examples 1 and 2. The term "measured" in claim 1 referred to an indirect measurement based on the linear relationship between the spectral overlap and the degree of quenching. Example 1 of the application as filed described that the quenching efficiency was directly measured only for the reference pair EDANS-DABCYL, whereas for the other pairs of labels, an indirect measurement based on the assessment of the spectral overlap was carried out. The direct measurement for said reference pair was described in Example 2 of the application as filed, in which the quencher and the fluorophore were attached to Molecular Beacon probes via spacers and thus separated by the FRET distance. The fluorophore EDANS of said reference pair represented the "first fluorophore" referred to in claim 1. The efficiency of quenching as defined in claim 1 in the context of "non-FRET" thus corresponded effectively to the quenching efficiency expected based on spectral overlap.

Main request A - Admissibility

Main request A should be admitted into the proceedings, because it addressed the objection under Article 123(2) EPC to claim 1 of the main request. The amendments to claim 1 merely served to clarify how the skilled person would read claim 1 of the main request in the light of the description of the application as filed, which explicitly stated on page 39, line 15 to page 40, line 1, that the claims had to be read in accordance with Examples 1 and 2.

XXIII. The final requests of the parties were:

The appellant requested in writing that the decision under appeal be set aside and that the patent be revoked.

The respondent requested that the appeal be dismissed (main request) or, alternatively, that the patent be maintained in amended form on the basis of one of main request A, filed during the oral proceedings on 2 July 2015, or the first to third, fifth to seventh, or ninth to tenth auxiliary requests, all filed with letter of 24 April 2015.

XXIV. The respondent did not maintain the fourth and eighth auxiliary requests filed with letter of 24 April 2015. In the present decision, the original numbering of the remaining auxiliary requests filed with said letter is kept, i.e. the auxiliary requests have not been re-numbered.

Reasons for the Decision

1. The appeal is admissible.

2. Main request - Admissibility

In the appeal proceedings, the main request was filed for the first time after the oral proceedings had been arranged. Since, however, the main request is identical to the main request on which the opposition division based its decision, it does not change the subject of the appeal or introduce new issues.

Therefore, the board, in exercising its discretion under Article 13(1) RPBA, decides to admit the main request into the proceedings.

3. Main request - Added subject-matter (Article 123(2) EPC)

3.1 The patent in suit relates to nucleic acid hybridisation probes containing a fluorophore and a quencher, whereby the interaction of the probe with a target causes a change of the distance between the fluorophore and the quencher, thereby generating a signal. The patent in suit describes that prior art assays that employ nucleic acid hybridisation probes rely on fluorescence resonance energy transfer ("FRET"), which mechanism occurs at a distance range of from 10 to 100 Angstroms and requires the absorption spectrum of one member of the pair of labels to overlap the emission spectrum of the other member, the efficiency of FRET interaction being linearly proportional to that overlap (page 3, lines 10-25; page 4, line 46). The patent in suit describes the finding that efficient quenching can be achieved when a quenching moiety and a fluorophore are attached to nucleic acid hybridisation probes such that the fluorescing moiety and the quenching moiety are in contact or "touching", even when the rules of FRET are violated and the adsorption spectrum of the quenching moiety does not overlap the emission spectrum of the fluorescing moiety (page 4, lines 40-42; page 5, lines 13-16).

3.2 Claim 1 relates to a probe capable of hybridizing with a nucleic acid strand, said probe comprising "a non-FRET pair of labels (...) consisting of a first fluorophore and a non-fluoroscent quencher, wherein the

non-FRET pair of labels is characterised in that the efficiency of quenching of said first fluorophore by said non-fluorescent quencher, as measured by the decrease in emission intensity of said first fluorophore when said labels are attached to oligodeoxynucleotides and separated by a FRET distance within the range of from ten to one hundred Angstroms, is less than sixty percent".

3.3 The appellant submitted that this definition of a "non-FRET pair of labels" was not disclosed in the application as filed.

3.4 Article 123(2) EPC stipulates that a European patent may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed. It is the established case law of the Boards of Appeal that the content of an application comprises the disclosure directly and unambiguously derivable from it.

3.5 Example 1 of the application as filed discloses the determination of the spectral overlap between the adsorption spectrum of the quencher DABCYL coupled to a specific oligodeoxynucleotide and the emission spectrum of each of several fluorophores bound to Molecular Beacon probes. This Example furthermore describes how the expected FRET quenching efficiencies for the set of fluorophores was calculated. For this calculation, the observed quenching efficiency of the known FRET pair EDANS (fluorophore) and DABCYL (quencher) was used as a reference value. The spectral overlap of each fluorophore was divided by the spectral overlap for EDANS and multiplied by the observed quenching efficiency of EDANS. For each of the fluorophores tested, the values of the spectral overlap and of the

calculated FRET **expected quenching efficiency** are shown in Table 1.

Example 2 of the application as filed discloses the determination of the degree of quenching of candidate fluorophores by DABCYL when attached to the 5' and 3' ends of Molecular Beacon probes, respectively. The excitation and emission spectra of each molecular beacon were recorded before and after addition of the target. The percentage of observed quenching was defined as $(1-F_o/F_t)* 100$, where F_o is the intensity of emission before the addition of the target and F_t the intensity of emission after the addition of the target. Table 2 lists the **observed quenching efficiency** for each of the fluorophores tested in Example 2, as well as the expected quenching efficiency of Example 1. The observed quenching efficiency for EDANS as determined in Example 2 is the reference value used for the calculation of the expected quenching efficiency in Example 1.

3.6 Page 16, lines 1-9 of the application as filed states that "For use in an assay, a quencher (...) should have sufficient spectral overlap, as spectral overlap was determined by the procedure of Example 1, to absorb at least 60% of a fluorophore's emission by fluorescence resonance energy transfer, which we define as the minimal interaction to be considered a "FRET pair" as that term is used herein. According to that description, only EDANS of the fluorophores in Table 1 forms a FRET pair with the quencher DABCYL."

A "FRET pair" according to this definition thus has an expected quenching efficiency based on spectral overlap, as determined by the procedure of Example 1, of at least 60%.

As concerns the term "non-FRET pair", page 16, lines 13-25 of the application as filed states that "To demonstrate embodiments of probes with "touching" pairs of a fluorophore with another fluorophore or quencher, where the pairs are not FRET pairs as defined above, we prepared Molecular Beacon probes end-labeled with DABCYL at one end and one of eight different fluorophores at the other end. We tested quenching efficiency by the procedures described in Example 2. Table 2 presents the observed quenching efficiency and also the expected quenching efficiency by FRET. (...) Table 2 shows the effect on quenching that results for non-FRET pairs, which includes all fluorophores in Table 2 except EDANS".

It may be derived from this disclosure that a "non-FRET pair" is a pair of labels which is not a "FRET pair" (as defined on page 16, lines 1-9) and which, consequently, has an expected quenching efficiency based on spectral overlap, as determined by the procedure of Example 1, of less than 60%.

3.7 The question arises whether or not this definition in the application as filed of a "non-FRET pair" as having an expected quenching efficiency based on spectral overlap, as determined by the procedure of Example 1, of less than 60%, can provide a basis for the characterisation in claim 1 of a "non-FRET pair" by an efficiency of quenching of the first fluorophore by the non-fluorescent quencher, as measured by the decrease in emission intensity of said first fluorophore when said labels are attached to oligodeoxynucleotides and separated by a FRET distance within the range of from ten to one hundred Angstroms, of less than 60%.

3.8 The respondent submitted that the measurement referred to in claim 1 represented the same indirect measurement that was disclosed in Example 1 of the application as filed. In this example, the quenching efficiency was directly measured only for the reference pair EDANS-DABCYL, whereas for the other fluorophore-DABCYL pairs, the spectral overlap was assessed and the expected quenching efficiency calculated on the basis of the measurement for EDANS-DABCYL. According to the respondent, the measuring by decrease in emission intensity of "said first fluorophore" in claim 1 corresponded to the measuring with respect to the fluorophore of the reference pair EDANS-DABCYL in Example 1; the direct measurement of the quenching efficiency for the reference pair EDANS-DABCYL was described in Example 2, using Molecular Beacon probes in which the attached labels were separated by the FRET distance, which measurement corresponded to the one referred to in claim 1.

3.9 The board cannot follow this line of argument for the following reasons:

Firstly, claim 1 states that the efficiency of quenching of the first fluorophore by the non-fluorescent quencher is "measured by the decrease in emission intensity of said first fluorophore", but no such measurement is described in Example 1. This example only describes the measurement of the adsorption spectrum of the quencher and the emission spectrum of the fluorophore in order to determine the spectral overlap of the label pair, which was then used to calculate the expected quenching efficiency.
The measuring "by the decrease in emission intensity of said first fluorophore" in claim 1 cannot be understood to represent the measurement of the observed quenching

efficiency for the reference pair EDANS-DABCYL as mentioned in Example 1, because claim 1 states that the "first fluorophore" is part of the "non-FRET pair of labels", whereas, in Example 1, EDANS is part of the "FRET-pair" EDANS-DABCYL (see page 16, lines 7-9) and thus does not represent a "first fluorophore" within the meaning of claim 1.

Secondly, the measurement of the observed quenching efficiency by the procedure of Example 2, which was used for the determination of the observed quenching efficiency of the reference pair EDANS-DABCYL in Example 1, differs from the measurement referred to in claim 1. Example 2 discloses that the Molecular Beacon probes used in the experiments allowed "touching" or "contact" quenching of the label pairs (see page 16, lines 9-20), but does not disclose that the labels were separated by a FRET distance within the range of from ten to one hundred Angstroms. This is also apparent from the results of Example 2 shown in Table 2. It can be seen that the observed quenching efficiencies measured for all "non-FRET" pairs within the meaning of the application as filed (see page 16, lines 7-9) were **well above 60%** (and up to 99.10%), whereas claim 1 requires that for a non-FRET pair, the quenching efficiency of the fluorophore by the non-fluorescent quencher, as measured by the decrease in emission intensity of said first fluorophore when said labels are attached to oligodeoxynucleotides and separated by a FRET distance within the range of from ten to one hundred Angstroms, is **less than 60%.** Page 8, line 8 of the application as filed states that "the FRET range is reportedly 10-100 Å", but none of Examples 1 or 2 or any other part of the application as filed describes the determination of the quenching efficiency by measuring the decrease in emission intensity of the

fluorophore when the labels are separated by a FRET distance of said specified range.

3.10 It follows that the definition of a non-FRET pair of labels in claim 1 is not disclosed in the application as filed.

3.11 Consequently, the main request is not allowable under Article 123(2) EPC.

4. Main request A - Admissibility

4.1 Main request A was filed at the oral proceedings; it differs from the main request in that in claim 1, the word "measured" has been replaced by the word "represented", and the words "when indirectly measured by the procedure of Examples 1 and 2" have been added after the expression "is less than sixty percent".

4.2 The board has to decide on the admissibility of this request. According to the established case law of the boards of appeal, claims filed during oral proceedings must *prima facie* overcome the issue raised, without giving rise to new ones, in order to be admissible.

4.3 The board acknowledges that the main request A was filed by the respondent as an attempt to overcome the Article 123(2) EPC problem in claim 1 of the main request.

However, the board considers that the amendments in claim 1 *prima facie* do not overcome the deficiency under Article 123(2) EPC. This is because claim 1 still characterises the "non-FRET pair" of labels in relation to an efficiency of quenching which is defined by reference to a decrease in emission intensity of the

first fluorophore when said labels are separated by a FRET distance within the range of from ten to one hundred Angstroms. As set out in detail in point 3 above, the application as filed and its Examples 1 and 2 do not provide a basis for this characterisation. Therefore, the introduced reference to the procedure of Examples 1 and 2 cannot remedy the claim's deficiency under Article 123(2) EPC.

Moreover, said reference introduces a lack of clarity, contrary to Article 84 EPC, in view of the discrepancy between the characterisation of a "non-FRET" pair of labels in claim 1 on the one hand and the procedures of Examples 1 and 2 on the other. Furthermore, the introduced reference to Examples 1 and 2 gives rise to doubts as to which features and data in the Examples form part of the measurement by the procedure referred to in claim 1, resulting in a further lack of clarity. The amendments thus raise new issues under Article 84 EPC.

4.4 Since the amendments in claim 1 *prima facie* do not overcome the outstanding Article 123(2) EPC issue and raise new issues under Article 84 EPC, the board decides not to admit the main request A into the proceedings.

5. First to third, fifth to seventh, and ninth to tenth auxiliary requests - Admissibility

5.1 None of the first to third, fifth to seventh, or ninth to tenth auxiliary requests was filed within the time limit set to respond to the appeal. Pursuant to Article 13(1) RPBA, the admission of these auxiliary requests is thus at the board's discretion.

It is immediately apparent that claim 1 of each of these auxiliary requests has the same deficiency under Article 123(2) EPC as claim 1 of the main request (see point 3 above), namely that claim 1 refers to a probe comprising a "non-FRET pair of labels (...) consisting of a first fluorophore and a non-fluorescent quencher, wherein the non-FRET pair of labels is characterised in that the efficiency of quenching of said first fluorophore by said non-fluorescent quencher, as measured by the decrease in emission intensity of said first fluorophore when said labels are attached to oligodeoxynucleotides and separated by a FRET distance within the range of from ten to one hundred Angstroms, is less than sixty percent".

5.2 The respondent has neither denied that said auxiliary requests contain the same problem under Article 123(2) EPC as the main request, nor has he provided any arguments as to why the board should admit said auxiliary requests into the proceedings.

5.3 In these circumstances, the board, in exercising its discretion under Rule 13(1) RPBA, decides not to admit the first to third, fifth to seventh, and ninth to tenth auxiliary requests into the proceedings.

6. It follows from the above that there is no request on file which is both admissible and allowable.

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:

N. Maslin U. Oswald

Decision electronically authenticated