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Case Number: T 2002/13 - 3.3.08

Application Number: 06825875.5

Publication Number: 1934613

IPC: C12Q1/68, G01N33/569, C07H21/04

Language of the proceedings: EN

Title of invention:
SEQUENCES FOR DETECTION AND IDENTIFICATION OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) OF MREJ TYPE XI

Patent Proprietor:
Becton Dickinson Infusion Therapy Systems Inc.

Opponents:
Beckman Coulter, Inc.
König Szynka Tilmann von Renesse - Patentanwälte Partnerschaft mbB

Headword:
Methicillin resistant Staphylococcus/BECTON DICKINSON

Relevant legal provisions:
EPC Art. 123(2), 123(3)

Keyword:
Main request,auxiliary requests 1 and 2 - added subject-matter (yes)
Auxiliary request 3 - broadening of scope of protection (yes)
Auxiliary requests 4 and 5 - admission into proceedings (yes)
Auxiliary requests 4 and 5 - fulfil requirements EPC (no)

Decisions cited:
G 0002/10, T 0190/99

Catchword:

Europäisches Patentamt
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Case Number: T 2002/13 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 17 May 2017

Appellant: (Patent Proprietor)	Becton Dickinson Infusion Therapy Systems Inc. 1 Becton Drive Franklin Lakes, NJ 07417-1880 (US)
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Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 2 August 2013 revoking European patent No. 1934613 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairwoman	M. R. Vega Laso
Members:	P. Julià
	D. Rogers

Summary of Facts and Submissions

I. European patent No. 1 934 613 with the title "Sequences for detection and identification of methicillin-resistant Staphylococcus aureus (MRSA) of MREJ type xi" was granted on European patent application No. 06 825 875.5, filed as international patent application under the PCT and published as WO 2007/044873 (hereinafter "the patent application"). The patent was granted with 21 claims. Claim 1 as granted read as follows:

"1. A method to detect the presence or absence of an MREJ type xi methicillin-resistant *Staphylococcus aureus* (MRSA) strain characterised as having within the right extremity of SCCmec the sequence of SEQ ID NOs 17, 18 or 19 comprising:

contacting a sample to be analyzed for the presence or absence of said MRSA strain, said MRSA strain including a *Staphylococcal* cassette chromosome mec (SSCC*mec*) element containing a *mecA* gene inserted into chromosomal DNA, thereby generating a polymorphic right extremity junction (MREJ) type xi sequence that comprises sequences from both the SCC*mec* element right extremity and chromosomal DNA adjoining said right extremity, with a first primer and a second primer, wherein said first and second primers are at least 10 nucleotides in length, and wherein said first primer hybridizes with said SCC*mec* element right extremity of an MREJ type xi sequence selected from the group consisting of SEQ ID NOs: 17, 18 and 19 and complements thereof, and wherein said second primer hybridizes with a chromosomal sequence of *S. aureus* to specifically

generate an amplicon if such MRSA strain is present in said sample; and
detecting the presence or absence of said amplicon."

II. Two oppositions to the grant of the patent were filed relying on the grounds for opposition under Article 100(a) EPC in conjunction with Articles 54 and 56 EPC, and Articles 100(b) and 100(c) EPC.

III. In a decision under Article 101(3)(b) EPC posted on 2 August 2013, an opposition division of the European Patent Office found that the amendments introduced into the claims according to the main request, auxiliary requests 1 to 4, and auxiliary request 6 contravened Article 123(2) EPC, and that the subject-matter claimed in auxiliary requests 5 and 7 did not fulfil the requirements of Article 56 EPC. Accordingly, the opposition division revoked the patent.

IV. The patent proprietor (appellant) lodged an appeal and filed together with the statement setting out its grounds of appeal six sets of claims as new main request and auxiliary requests 1 to 5.

V. Both opponent 01 and opponent 02 (respondents I and II, respectively) replied to the statement of grounds of appeal.

VI. The board summoned the parties to oral proceedings. In a communication under Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) attached to the summons, the board expressed a provisional, non-binding opinion on some of the issues to be discussed at the oral proceedings.

VII. In reply thereto, the appellant and respondent I filed further substantive submissions. Respondent II, without making any substantive submissions, informed the board that it would attend the scheduled oral proceedings.

VIII. Oral proceedings were held on 17 May 2017.

IX. Claim 1 of the main request is identical to claim 1 as granted, except for the deletion of all references to the sequences of SEQ ID NOs: 18 and 19.

X. Claim 1 of auxiliary request 1 is identical to claim 1 of the main request, except for the deletion of the wording "*within the right extremity of SCCmec*" in the preamble of the claim.

XI. Claim 1 of auxiliary request 2 reads as claim 1 of the main request, except for the presence of the wording "*generation of SCCmec right extremity junction sequence data by*" after the preamble of the claim, and the replacement of the wording "*... and wherein said first primer hybridizes with said SCCmec element right extremity of an MREJ type xi sequence selected from the group consisting of SEQ ID NOs: 17 and complements thereof, and wherein said second primer hybridizes with a chromosomal sequence of S. aureus ...*" by the wording "*... and wherein each of said first and second primer hybridizes with said sequence of SEQ ID NO: 17 or complements thereof ...*" in the characterizing part of the claim.

XII. Claim 1 of auxiliary request 3 combines the amendment as in the preamble of claim 1 of auxiliary request 1 with the amendments introduced into the characterizing part of claim 1 of auxiliary request 2.

XIII. The preamble of claim 1 of auxiliary requests 4 and 5 is identical to the preamble of the main request and auxiliary request 1, respectively. In both auxiliary requests, the characterizing part of claim 1 reads as in auxiliary request 2, except for the deletion of the wording "*generation of SCCmec right extremity junction sequence data by*".

XIV. The following documents are referred to in this decision:

(2): A. Huletsky *et al.*, J. Clin. Microbiol., May 2004, Vol. 42, No. 5, pages 1875 to 1884;

(8): EP-A2-0 887 424 (publication date: 30 December 1998);

(34): Communication under Rule 71(3) EPC issued by the examining division on 12 August 2010;

(35): T. Ito *et al.*, Antimicrobial Agents and Chemotherapy, June 1999, Vol. 43, No. 6, pages 1449 to 1458.

XV. The submissions made by the appellant concerning issues relevant to this decision, were essentially as follows:

Main request and auxiliary requests 2 and 4
Article 123(2) EPC

The feature "*having within the right extremity of SCCmec the sequence of SEQ ID NOs 17*" in the preamble of claim 1 did not offend against Article 123(2) EPC.

According to the case law (see decision T 190/99 of 6 March 2001), the claims were addressed to a skilled

person and had to be read with a mind willing to understand and a constructive approach. In the present case, the notional skilled person was a Ph.D. molecular biologist familiar with PCR and the prior art on methicillin-resistant *S. aureus* (MRSA) and the *mec* right extremity junction (MREJ) assay, *inter alia* documents (2) and (8). Figure 1 of document (2) and Figure 7 of document (8) showed schematic representations of a MREJ and a MRSA identification method, respectively.

Claim 1 was directed to the detection method of the MREJ type xi MRSA disclosed in the patent application. A skilled person would read the claim having in mind the common general knowledge and, in particular, documents (2) and (8). He/she would understand that the sequence of SEQ ID NO: 17 was not within the right extremity of a *Staphylococcus* cassette chromosome *mec* (SCC*mec*), but was a MREJ type xi sequence as stated in the characterizing part of the claim. Indeed, the wording "*the sequence of SEQ ID NOs 17*" stood for a specific nucleic acid sequence which the skilled person would immediately identify as a MREJ sequence because it included the sequence from the polymorphic right extremity of SCC*mec* and the *orf*X chromosomal sequence of *S. aureus*, as clearly shown for the MREJ type xi sequence depicted in Figure 3 of the patent application. Thus, a skilled person would immediately identify the objected feature in claim 1 as erroneous and read it in a correct manner.

In the communication under Rule 71(3) EPC (document (34)), the examining division had cited paragraph [0082] of the patent application as a basis for the objected feature. Even though the opposition division acknowledged that this paragraph provided a literal

basis, it considered that, in the light of the disclosure of the patent application, a skilled person would not regard this paragraph as a basis because the sequence of SEQ ID NO: 17 was a MREJ type xi sequence and could thus not be within the right extremity of a SCC*mec* (see point 4.2.6.2 of the decision under appeal). If a skilled person interpreted paragraph [0082] in a manner consistent with the remainder of the patent application, he/she would apply the same interpretation to the feature in claim 1 because it was reproduced *verbatim* from this paragraph. Indeed, the claim made technical sense only if this interpretation was applied because the skilled person was instructed to select the first and second primers from the SCC*mec* element right extremity of an MREJ type xi and from a chromosomal sequence of *S. aureus*, respectively.

The wording "*the sequence of SEQ ID NO: 17*" ,(emphasis added), could not be equated to "*the sequence SEQ ID NO: 17*". Whilst the latter meant the complete sequence SEQ ID NO: 17, the former meant only a fragment of this sequence, namely the fragment of the sequence SEQ ID NO: 17 "*within the right extremity of a SCCmec*", as stated in claim 1.

Main request and auxiliary request 1
Article 123(2) EPC

The feature *"wherein said second primer hybridizes with a chromosomal sequence of S. aureus"* in the characterizing part of claim 1 did not contravene Article 123(2) EPC.

Claim 1 did not define the second primer as hybridizing with any arbitrary chromosomal sequence of *S. aureus* because this primer was further required to be able,

together with the first primer, to "*specifically generate an amplicon if such* [MREJ type xi] *MRSA strain was present in said sample*". The length of a MREJ (~ 1 kb) was defined in paragraph [0009], and Table 11 of the patent application showed the length of the generated amplicons (longest 1.2 - 1.4 kb). Longer amplicons were not manageable and made no technical sense. The (hybridization) location of the second primer was not limited to the *orfX* portion of the *S. aureus* chromosome but included any chromosome sequence of *S. aureus* that allowed the generation of the amplicon cited in claim 1. The second primer was thus functionally defined and, accordingly, limited thereto.

The MREJ sequences were described in paragraph [0009] of the patent application as comprising "*sequences from the SCCmec right extremity as well as bacterial chromosomal DNA to the right of the SCCmec integration site*", without any length limitation. Paragraph [0034] referred to a chromosomal DNA adjacent to the right SCC*mec* integration site in general, and Figures 2 and 3 showed that these sequences went beyond the *orfX* sequence of *S. aureus*. Paragraph [0050] referred to primers/probes suitable for detection of MRSA of MREJ types xi to xx, which were selected within the DNA sequences from proprietary fragments or from selected database. Paragraph [0052] stated that sequences other than those explicitly disclosed in the patent application were also contemplated, such as sequences selected from public databases which were suitable for amplification of MREJ type xi and for diagnostic purposes. All these (primer/probe) sequences were only functionally limited. The (second) primers of claim 1 were thus clearly disclosed in the patent application.

Moreover, the patent application disclosed a second primer having the sequence of SEQ ID NO: 44 (see paragraph [0016]). Figure 2 showed that this sequence hybridized partially with the *orfX* sequence and partially with other, non-*orfX* chromosomal sequence of *S. aureus*. It was apparent also from Figure 3 of document (35) that the sequence of SEQ ID NO: 44 hybridized only partially with the *orfX* sequence and extended far beyond it. Thus, the patent application provided a basis for a second primer as defined in claim 1.

Auxiliary request 3
Article 123(3) EPC

The features "*detect the presence or absence of an MERJ type xi MRSA*" and "*specifically generate an amplicon if such MRSA strain was present in said sample*" were functional features characterizing the method of claim 1 of both the granted claims and auxiliary request 3. These features required the first and second primers to hybridize with MRSA sequences for MREJ amplification. According to the patent application, MERJ included sequences from the right extremity of SCC*mec* and from the *S. aureus* chromosomal sequence adjacent to the right site of the SCC*mec* integration site, i.e. the *orf*X sequence of *S. aureus* (see, *inter alia*, paragraph [0034]).

In the method defined in claim 1 as granted, a first primer hybridized with the SCC*mec* element right extremity of the sequence of SEQ ID NO: 17 and a second primer with a chromosomal sequence of *S. aureus*. This chromosomal sequence was not arbitrary, but was limited to those sequences that fulfilled the functional requirement of "*specifically generate an amplicon if*

such MRSA strain was present in said sample". In claim 1 of auxiliary request 3, both the first and second primers hybridized with the sequence of SEQ ID NO: 17. In order to fulfil the functional requirement, the first primer had to hybridize with the SCC*mec* element right extremity present within the sequence of SEQ ID NO: 17, and the second primer with the *orf*X chromosomal sequence of *S. aureus* present within the sequence of SEQ ID NO: 17. Thus, the primer pair had to hybridize with these two regions of the sequence of SEQ ID NO: 17 in order to generate an MREJ amplicon that could detect whether the MREJ type xi was present in a sample.

Whilst the second primer was defined in granted claim 1 as hybridizing with a *S. aureus* chromosomal sequence, the second primer was defined in claim 1 of auxiliary request 3 as hybridizing with the portion of the *orf*X chromosomal sequence of *S. aureus* present within the sequence of SEQ ID NO: 17. The population of primers making up the primers in claim 1 of auxiliary request 3 was thus narrowed in comparison to the population of primers defined in granted claim 1. Therefore, the scope of claim 1 of auxiliary request 3 was narrower than the scope of claim 1 as granted.

XVI. The respondents' submissions, insofar as they are relevant to the present decision, may be summarized as follows:

Main request and auxiliary requests 2 and 4
Article 123(2) EPC

The feature "*having within the right extremity of SCCmec the sequence of SEQ ID NOs 17*" in the preamble of claim 1 offended against Article 123(2) EPC.

According to the case law, a claim had to be clear by itself. To read a claim with a mind willing to understand did not mean to ignore the wording of the claim and read it in a way other than as worded. In the light of the prior art on MREJ and the disclosure of the patent application, the objected feature was technically incorrect. The sequence of SEQ ID NO: 17 was defined in the patent application as a MREJ sequence made up of a SCC*mec* right extremity sequence and the *orfX* chromosomal sequence of *S. aureus*, this last sequence not being within the SCC*mec* cassette. There was no basis in the patent application for a MREJ type xi MRSA strain characterized by having the sequence of SEQ ID NO: 17 within the right extremity of SCC*mec*.

Paragraph [0082] related to experiments performed to characterize MREJ sequences and not to methods of detecting MRSA strains of a particular MREJ type. Paragraph [0081] stated that the sequence of SEQ ID NO: 17 had a portion of the *orfX* sequence and the sequence within the SCC*mec* right extremity that differed from the MREJ types i to x sequences known in the prior art. In this context, paragraph [0082] stated that the sequences within the SCC*mec* right extremity of three MRSA strains were nearly identical and the reference to SEQ ID NO: 17, within parentheses, was a simple way to link the MREJ sequence to the specific MRSA strain CCRI-12157. Neither of paragraphs [0081] and [0082] disclosed a MREJ type xi MRSA strain having the sequence of SEQ ID NO: 17 within the right extremity of SCC*mec*.

There was no basis in the patent application for interpreting the wordings "*the sequence of SEQ ID*

NO: 17" ,(emphasis added), and "*the sequence SEQ ID NO: 17*" differently.

Main request and auxiliary request 1
Article 123(2) EPC

The feature *"wherein said second primer hybridizes with a chromosomal sequence of S. aureus"* in the characterizing part of claim 1 contravened Article 123(2) EPC.

The patent application disclosed specific MREJ sequences and detection methods relying on primer pairs hybridizing with these MREJ sequences. Primers that did not hybridize with the MREJ sequences were not disclosed as being part of the invention. However, claim 1 did not require the second primer to hybridize with a MREJ sequence, but merely with a *S. aureus* chromosomal sequence so that an amplicon was generated. Claim 1 did not require the amplicon to be specific for a MREJ type xi sequence and it did not functionally limit the second primer in any manner. Thus, claim 1 comprised detection methods in which the second primer did not hybridize with the MREJ type xi sequence. There was no basis in the patent application for these embodiments.

According to paragraph [0048] of the patent application, the disclosed MREJ sequences enabled a skilled person to design primers/probes for detection of MRSA strains having the specific MREJ types disclosed in the patent application. It was stated in paragraph [0050] that the design of these primers could be based on sequences of certain sources, but they were all designed to hybridize with the disclosed MREJ sequences. Paragraph [0052] did not provide a basis for

selecting the second primer from any (arbitrary) *S. aureus* chromosomal region, but only from the MREJ sequences disclosed in the patent application.

As shown in Figure 3 of document (35), a primer with the sequence of SEQ ID NO: 44 hybridized with the *orfX* sequence from *S. aureus* and overlapped with the cR2 primer, which was described as located in *orfX* (see page 1454, left-hand column of document (35)). The primer of sequence SEQ ID NO: 44 was disclosed in the patent application as a (annealing/sequencing) primer that annealed to the 5' end of *orfX* (see paragraph [0070]) and was used to generate amplification products for sequencing purposes. The sequencing strategy disclosed in Example 2 and Figure 1 of the patent application was not specific for the method of the invention, but rather related to the generation of MREJ sequence data from which the MRSA/MREJ detection methods were developed. Even if it was assumed that the primer of sequence SEQ ID NO: 44 did not hybridize with the *orfX* sequence but extended beyond it, a generalization based on this sole primer was not allowable.

Auxiliary request 3
Article 123(3) EPC

Claim 1 as granted required the generation of an amplicon using two primers. The first primer hybridized with the SCC*mec* element right extremity of an MREJ type xi sequence of SEQ ID NO: 17, and the second primer hybridized with a *S. aureus* chromosomal sequence. The first and second primers defined in claim 1 of auxiliary request 3 were each required to hybridize with the sequence of SEQ ID NO: 17 so as to specifically generate an amplicon. Although the

definition of the primers in auxiliary request 3 was narrower than in the claims as granted, it included the possibility that both, the first and second primer, hybridized with the SCC*mec* element right extremity sequence or across the SCC*mec* junction/integration site. Neither of these possibilities was contemplated in the granted claims. Thus, the scope of claim 1 of auxiliary request 3 was broader than the scope of claim 1 as granted.

XVII. The appellant (patent proprietor) requested to set aside the decision under appeal and to maintain the patent upon the basis of the claims of the main request, or alternatively, upon the basis of the claims of one of auxiliary requests 1 to 5, all filed under cover of the statement of grounds of appeal dated 11 December 2013.

XVIII. Respondents I and II (opponents 01 and 02, respectively) requested to dismiss the appeal.

Reasons for the Decision

The patent application and the related technical field

1. The highly conserved *mecA* gene, which encodes a ß-lactam-resistant penicillin binding protein (PBP) with ß-lactam-resistant transpeptidase activity, is present in methicillin-resistant *Staphylococcus aureus* (MRSA) strains, but absent from methicillin-sensitive *S. aureus* (MSSA) strains (cf. paragraph [0004] of the patent application). The *mecA* gene is carried by a mobile genetic element, named staphylococcal cassette chromosome *mec* (SCC*mec*), which integrates at a specific site in the chromosome of the MSSA strains, namely at

the 3' end of an open reading frame *orfX* encoding a putative 159-amino acid polypeptide (cf. paragraph [0005]). The nucleotide sequences at the right extremity of the SSC*mec* sequences are polymorphic. The *mec* right extremity junction (MREJ), which has a length of ~ 1 kb, includes sequences from the polymorphic SCC*mec* right extremity as well as from the bacterial chromosomal DNA to the right of the SCC*mec* integration site, i.e. the *orfX* open reading frame (cf. paragraphs [0006] to [0009]). MREJ types i to x had been characterized in the prior art. The patent application discloses the nucleic acid sequences of MREJ types xi to xx as well as methods for detecting and quantifying these MREJ types. The patent as granted relates to embodiments which concern the sequence of SEQ ID NO: 17, 18 or 19, a MREJ type xi nucleic acid sequence.

Main request and auxiliary requests 1 to 3

2. The main request and auxiliary requests 1 to 3 filed with the statement of grounds of appeal are identical to auxiliary request I and auxiliary requests III to V underlying the decision under appeal, respectively. These requests were considered by the opposition division and a decision was taken thereupon. Hence, they are part of the present proceedings.

Main request
Article 123(2) EPC

The feature "having within the right extremity of SCCmec the sequence of SEQ ID NOs 17" in the preamble of claim 1

3. In the decision under appeal, the opposition division found that the feature "*having within the right extremity of SCCmec the sequence of SEQ ID NOs 17*" did

not have a basis in the patent application (cf. point 4.2.6.2 of the decision). The board shares the view of the opposition division on this issue.

4. In line with the established case law of the Boards of Appeal, the claims must be read with a mind willing to understand and make technical sense of them, ruling out thereby illogical or technically meaningless interpretations (cf., *inter alia*, T 190/99 of 6 March 2001). The claims are directed to a person skilled in the art, who in the present case is a person skilled in amplification (polymerase chain reaction, PCR) techniques and familiar with MRSA in general, and the detection and identification of MREJ types in particular.

5. The "*sequence of SEQ ID NO: 17*" referred to in claim 1 stands for a specific nucleic acid sequence which is identified as a MREJ sequence - indeed, a MREJ type xi sequence - because it has the polymorphic *mec* right extremity of the SCC*mec* sequence and a fragment of the *orfX* chromosomal sequence of *S. aureus* (see the nucleic acid sequence "*mrej_xi*" shown in Figure 3 of the patent application). Thus, the sequence of SEQ ID NO: 17 cannot be within the right extremity of SCC*mec* but it actually includes part of the SCC*mec* sequence. The contested feature in claim 1 is therefore not ambiguous or open to interpretation but technically inaccurate or plainly wrong. This has not been disputed by the appellant who acknowledges that a skilled person would immediately recognize the feature of claim 1 as erroneous.

6. However, even if, as the appellant contends, the skilled person immediately recognizes the feature in claim 1 as being technically inaccurate or erroneous,

this does not allow him/her to disregard it, since the feature is part of the claim and defines the claimed subject-matter - even though erroneously. The case law on which the appellant relied, namely T 190/99 (*supra*), rules out illogical or technically meaningless interpretations of an otherwise technically meaningful feature of a claim. However, the case law does not allow the reader to disregard an illogical or technically inaccurate feature of a claim and hence to interpret such a feature in a correct manner. Thus, if a claim includes contradictory features, such as the contested feature in the preamble of claim 1 and the feature referring to SEQ ID NO: 17 as an MREJ type xi sequence in the characterizing part of claim 1 (cf. point IX supra), this contradiction cannot be resolved by merely disregarding the technically inaccurate feature and considering only the convenient technically meaningful feature. All the less so when assessing the compliance of these two features with Article 123(2) EPC. In the board's view, any other approach would provide an unwarranted advantage to the patentee/appellant. Hence, the case law on which the appellant relied does not support its case.

7. For the purpose of Article 123(2) EPC, the relevant question is whether the illogical or technically inaccurate feature fulfils the same criterion that has also to be fulfilled by a logical or technically meaningful feature, namely whether it is directly and unambiguously derivable from the patent application. This is, according to the established case law, the "gold standard" for assessing the compliance with Article 123(2) EPC (cf. G 2/10, OJ 2012, page 376, point 4.3 of the Reasons for the Decision).

8. In the decision under appeal, the opposition division considered that the passage in paragraph [0082] of the patent application, when read within the whole disclosure of Example 3, did not provide a basis for the feature "*having within the right extremity of SCCmec the sequence of SEQ ID NOs 17*" (cf. point 4.2.6.2 of the decision under appeal). The board shares the view of the opposition division.

9. At the beginning of Example 3 of the patent application, it is stated in paragraph [0081] that "[t]*he sequences obtained for 15 of the 17 strains non-amplifiable by the MRSA-specific primers detecting MREJ types i to x previously described were compared to the sequences available from public databases. In all cases except MRSA strain CCRI-12845, the orfX portion of the MREJ sequence had an identity close to 100% to publicly available sequences for orfX ... While the orfX portion of most* ***MREJ*** *fragments (****SEQ ID NOs.: 15-20****, 25-26, 39-42, 55-56) shared nearly 100% identity with publicly available S. aureus orfX sequences, with the exception of strain CCRI-12845, the DNA sequence within the right extremity of SCCmec itself was shown to be different from those of MREJ types i, ii, iii, iv, v, vi, vii, viii, ix, and x ... Thus, ten different novel* ***MREJ*** *sequence types are reported herein: MREJ types xi to xx.*" (emphasis by the board). This disclosure characterizes the sequence of SEQ ID NO: 17 as a MREJ sequence (the novel MREJ type xi sequence) which has two different parts (subsequences), namely a first part which is the sequence found within the polymorphic right extremity of SCC*mec*, and a second part which is a sequence having a 100% identity with publicly available *S. aureus orfX* sequences. Indeed, the second sentence of paragraph [0082] confirms that the sequence of SEQ ID NO: 17 is a MREJ sequence ("[t]*hese new sequences*

were designated as ***MREJ*** *type xi (****SEQ ID NOs.: 17****-19)";* emphasis by the board).

10. In the first sentence of paragraph [0082], on which the appellant relied as the literal basis for the contested feature in claim 1, it is stated that "[t]*he sequences* ***within*** *the right extremity of SCCmec obtained from strains CCRI-12157, CCRI-12198, and CCRI-12199 (****SEQ ID NOs.: 17****, 18, and 19) were nearly identical to each other, ...* " (emphasis by the board). Contrary to appellant's view, this sentence does not provide a literal basis of the feature in claim 1 because it does not reproduce *verbatim* the wording of the contested feature in claim 1. After defining the sequence of SEQ ID NO: 17 as a MREJ sequence in paragraph [0081] and, indeed, as a MREJ type xi sequence according to the second sentence of paragraph [0082], the first sentence in paragraph [0082] can only be understood as referring to one part (subsequence) of said MREJ type xi sequence of the sequence of SEQ ID NO: 17, namely the polymorphic *mec* right extremity of SSC*mec*, whilst the complete MREJ type xi sequence of the sequence of SEQ ID NO: 17 is found within the specific strain CCRI-12157. Contrary to appellant's argument, the board does not see any ambiguity in the first sentence of paragraph [0082] and if, arguably, there were any, then it is certainly not reproduced *verbatim* in the feature of claim 1, a feature which is, in itself, clear and unambiguous but, as acknowledged by all parties, technically inaccurate.

11. The appellant further argued that the meaning of the wording "*sequence of SEQ ID NO: 17*" (underlining by the board) as in claim 1 differs from that of "*sequence SEQ ID NO: 17*", because the former refers only to a part of the nucleic acid sequence listed in SEQ ID NO: 17,

namely the part (subsequence) within the right extremity of SCC*mec* (cf. point XV *supra*).

The board is not aware of any general convention widely accepted in the particular technical field under consideration corroborating appellant's interpretation and there is no evidence on file to support such a convention. In any case, appellant's interpretation is not directly and unambiguously derivable from the patent application itself. On the contrary, references in the patent application using the wording "*the sequence of SEQ ID NO*" in the context of probes or oligonucleotides, such as in paragraph [0028] and claims 48, 49 and 53 of the patent application, concern full-length or complete sequences and not fragments, parts or subsequences thereof.

12. For these reasons, Article 123(2) EPC is contravened.

The feature "wherein said second primer hybridizes with a chromosomal sequence of S. aureus" in the characterizing part of claim 1

13. In the decision under appeal (cf. point 2.1.4), the opposition division found that the feature "*wherein said second primer hybridizes with a chromosomal sequence of S. aureus*" did not have a basis in the patent application. The board shares the view of the opposition division on this issue.

14. In claim 1, the first primer is defined as hybridizing "*with said SSCmec element right extremity of an MREJ type xi sequence selected from the group consisting of SEQ ID NOs: 17 and complements thereof*", and the second primer as hybridizing "*with a chromosomal sequence of S. aureus*" (cf. point IX *supra*). Whilst hybridization

of the first primer is specified to be within the MREJ type xi sequence, in principle the second primer may hybridize with any region of the *S. aureus* chromosomal sequence. However, as the appellant argued (cf. point XV *supra*), the region where the second primer hybridizes is not arbitrary because claim 1 further requires that an amplicon is specifically generated if such MRSA strain is present in said sample, a functional feature characterizing thus the second primer (cf. points IX *supra*).

15. Leaving aside the possible interpretations of this functional feature put forward by the respondents during the opposition and appeal proceedings (particularly regarding the term "*specifically*"), it is worth noting that claim 1 does not specify any length or length range for the specifically generated amplicon. It is known in the nucleic acid amplification field that the length of an amplicon depends on many variables and design preferences and, for standard purposes, it may be between about 100 bp and about 1000-1500 bp. Indeed, this is the length range of the amplicons generated for MREJ types xi to xx as disclosed in Table 11 of the patent application. According to document (35), the *orfX* gene of *S. aureus* putatively encodes a 159 amino acid polypeptide and has a length of less than about 700 nucleotides (cf. page 1450, right-hand column second paragraph, and page 1455, Figure 3 of document (35)). Thus, with an amplicon of 1500 bp in length and a first primer hybridizing adjacent to the SSC*mec* insertion site, the second primer may well hybridize with a *S. aureus* chromosomal sequence far beyond the *orfX* chromosomal sequence of *S. aureus* shown schematically in Figure 1 of the patent application. Therefore, the functional feature characterizing the second primer in claim 1

allows this primer to hybridize with chromosomal sequences of *S. aureus* outside the *orfX* sequence. The decisive question is thus whether such an embodiment is directly and unambiguously derivable from the patent application.

16. There is a first reference to "*bacterial chromosomal DNA*" in paragraph [0009] of the patent application but this reference is clearly directed only to the part (subsequence) of the *S. aureus* chromosomal sequence within the MREJ sequence. In the same sentence, the MREJ sequence is defined as being of "*approximately 1 kilobase*" in length and thus, although the length of the bacterial chromosomal DNA is not explicitly indicated, this chromosomal DNA is clearly limited to the DNA directly adjacent to the SCC*mec* insertion site and present within the MREJ sequence, i.e. the *orfX* sequence of *S. aureus*. This is in line with the disclosure in paragraph [0034], wherein the reference to "*chromosomal DNA adjacent to the right SCCmec integration site*" is also limited to the chromosomal sequence within the MREJ sequence (cf. page 11, lines 5-7 of the patent application). Indeed, immediately thereafter reference is made in the same paragraph to the use of "*the novel MREJ sequences*" disclosed in the patent application as "*parental sequences from which primers and/or probes useful in the detection and identification of MRSA ... are derived*" (cf. page 11, lines 7-12 of the patent). It is in the light of this disclosure that the selection of DNA sequences "*from proprietary, or from selected database sequences*" referred to in paragraph [0050] must be understood. An understanding supported by the disclosure in paragraph [0052], wherein all references to the design of sequences and/or selection of public database sequences are also explicitly linked to the novel MREJ sequences

disclosed in the patent application and therefore, not extending beyond the *orfX* sequence comprised within said MREJ sequences.

17. As a basis for a second primer hybridizing with a *S. aureus* chromosomal sequence different from the *orfX* sequence, the appellant referred to the primer of the sequence of SEQ ID NO: 44 (cf. point XV *supra*). The board cannot accept appellant's argument. The primer of sequence of SEQ ID NO: 44 is located within the *orfX* sequence of *S. aureus* and does not extend beyond this sequence. The sequence of SEQ ID NO: 44 is found at positions 1382 to 1404 in the (NCTC8325) sequence of Figure 3 of document (35), starting 14 nt 5'-upstream of the predicted start codon of the *orfX* gene. The primer of SEQ ID NO: 44 overlaps with the cR2 primer described in document (35) as being "*located in orfX*" (cf. page 1454, left-hand column first two lines, and page 1455, Figure 3 of document (35)). Indeed, in the patent application, the primer of sequence of SEQ ID: 44 is disclosed as annealing to the 5' end of *orfX* and used in an isolation/sequencing strategy of the MREJ types xi to xx disclosed in Example 2 of the patent application (cf. page 23, paragraphs [0070], [0072], and Figures 1 and 2 of the patent application). Moreover, as stated by the respondents (cf. point XVI *supra*), the disclosure in the patent application of a single primer with a specific sequence and a particular hybridization location, such as the sequence of SEQ ID NO: 44, cannot be considered to be a basis for a broad generalization of the second primer to hybridize with any possible *S. aureus* chromosomal sequence.

18. Also for these reasons, claim 1 contravenes Article 123(2) EPC.

Conclusion

19. The appellant's request to maintain the patent on the basis of claims 1 to 21 according to the main request cannot be granted.

Auxiliary requests 1 and 2
Article 123(2) EPC

20. Claim 1 of auxiliary request 1 includes the feature "*wherein said second primer hybridizes with a chromosomal sequence of S. aureus*" in the characterizing part of the claim (cf. point X *supra*). This feature contravenes Article 123(2) EPC for the same reasons as given for the main request (cf. points 13 to 18 *supra*).

21. Claim 1 of auxiliary request 2 includes the feature "*having within the right extremity of SCCmec the sequence of SEQ ID NOs 17*" in the preamble of the claim (cf. point XI *supra*). This feature offends against Article 123(2) EPC for the same reasons as given for the main request (cf. points 3 to 12 *supra*).

22. Thus, the patent cannot be maintained on the basis of either request.

Auxiliary request 3
Article 123(3) EPC

The feature "wherein each of said first and second primer hybridizes with said sequence of SEQ ID NO: 17 of complements thereof"

23. In the decision under appeal (cf. page 6, first paragraph), the opposition division found that the

feature "*wherein each of said first and second primer hybridizes with said sequence of SEQ ID NO: 17 of complements thereof*" did not extend the scope of protection as compared to the granted claims. The board does not agree with the opposition division on this issue.

24. Claim 1 as granted defines a first primer hybridizing "*with said SSCmec element right extremity of an MREJ type xi sequence selected from the group consisting of SEQ ID NOs: 17* [...] *and complements thereof*" and a second primer that "*hybridizes with a chromosomal sequence of S. aureus to specifically generate an amplicon if such MRSA strain is present in said sample*" (cf. point I *supra*). The sequence of both the first and second primer may be located closely or immediately adjacent to the SCC*mec* insertion site defining the MREJ type xi of sequence of SEQ ID NO: 17 but, whilst the first primer must necessarily hybridize with a sequence within the SCC*mec* element right extremity of said MREJ type xi, the second primer may hybridize with any *S. aureus* chromosomal sequence, not necessarily within the MREJ type xi of sequence of SEQ ID NO: 17. All possible combinations of first and second primers fulfilling these conditions form the population of primer pairs that can be used in the method according to claim 1 as granted.

25. Amended claim 1 of auxiliary request 3 defines the first and second primers by the feature that "*each of said first and second primer hybridizes with said sequence of SEQ ID NO: 17*", and further requires that they "*specifically generate an amplicon if such MRSA strain is present in said sample*" (cf. point XII *supra*). Thus, even though the first primer is not explicitly required to hybridize with the SCC*mec*

element right extremity of the MREJ type xi of sequence of SEQ ID NO: 17, a detection of the MRSA strain in the sample implicitly requires that at least one of the primers, if not both of them, must necessarily hybridize with sequences located within the polymorphic right extremity of the SCC*mec* because it is this specific polymorphic sequence which characterizes the MREJ type xi MRSA strain and allows its detection (cf. paragraphs [0007], [0012] and [0034], and claim 1 of the patent application).

26. The second primer in the method of claim 1 of auxiliary request 3 does not hybridize with any chromosomal sequence of *S. aureus* - as in claim 1 as granted, but only with the MREJ type xi sequence of SEQ ID NO: 17. Although this definition of the second primer is narrower than the definition of the second primer found in claim 1 as granted, the second primer as defined in claim 1 of auxiliary request 3 may now hybridize not only with the *orfX* sequence closely or immediately adjacent to the SCC*mec* insertion site defining the MREJ type xi sequence of SEQ ID NO: 17, but it may also hybridize with the insertion site itself, as well as with the SCC*mec* right extremity as far as this second primer, together with an appropriate first primer, specifically generate an amplicon if an MREJ type xi MRSA strain is present in the sample. A method using such combinations of first and second primers does not fall within the scope of granted claim 1. Since in the amended claim 1 the protection conferred by claim 1 as granted has been extended, the amendment is not allowable under Article 123(3) EPC.

27. Thus, the appellant's request to maintain the patent on the basis of claims 1 and 2 according to auxiliary request 3 fails.

Auxiliary requests 4 and 5

28. The sets of claims according to auxiliary requests 4 and 5 were not before the opposition division and were first filed during the appeal proceedings. They were filed by the appellant at the earliest stage of the appeal proceedings, namely together with the statement setting out its grounds of appeal (cf. point IV *supra*), and, purportedly, are intended to overcome the adverse findings on Article 123(2) EPC in the decision under appeal. The board, exercising its discretion under Article 12(4) RPBA, decides to admit them into the appeal proceedings.

Articles 123(2) and (3) EPC

29. Claim 1 of auxiliary request 4 includes the feature "*having within the right extremity of SCCmec the sequence of SEQ ID NO: 17*" in the preamble of the claim, and the feature "*wherein each of said first and second primer hybridizes with said sequence of SEQ ID NO: 17 or complements thereof*" in the characterizing part of the claim. For the same reasons as given for the main request (cf. points 3 to 12 *supra*), the first feature contravenes Article 123(2) EPC. Moreover, the second feature offends against Article 123(3) EPC for the same reasons as given for auxiliary request 3 (cf. points 23 to 27 *supra*).

30. Claim 1 of auxiliary request 5 includes the feature "*wherein each of said first and second primer hybridizes with said sequence of SEQ ID NO: 17 or complements thereof*" in the characterizing part of the claim. This feature contravenes Article 123(3) EPC for

the same reasons as given for auxiliary request 3 (cf. points 23 to 27 *supra*).

31. Thus, the patent cannot be maintained on the basis of either request.

Final conclusion

32. It the absence of any allowable request, the patent cannot be maintained.

Order

For these reasons it is decided that:

The appeal is dismissed

The Registrar: The Chairwoman:

A. Wolinski M. R. Vega Laso

Decision electronically authenticated