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Datasheet for the decision of 23 November 2021

Case Number: T 2255/18 - 3.3.08

Application Number: 14168420.9

Publication Number: 2781604

IPC: C12Q1/689

Language of the proceedings: EN

Title of invention:
Sequences for detection and identification of methicillin-resistant Staphylococcus aureus

Patent Proprietor:
Geneohm Sciences Canada, Inc.

Opponent:
Beckman Coulter, Inc.

Headword:
Detection methicillin-resistant Staphylococcus aureus/GENEOHM SCIENCES CANADA

Relevant legal provisions:
EPC Art. 54, 56, 76(1), 83, 84, 123(3)
RPBA Art. 12(4)
RPBA 2020 Art. 12(2)

Keyword:
Main request - requirements of the EPC met (yes)
Admission of new documentary evidence (yes)

Decisions cited:
T 0190/99, T 2002/13, T 1146/15

Catchword:

Europäisches Patentamt
European Patent Office
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Beschwerdekammern

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Case Number: T 2255/18 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 23 November 2021

Appellant I: (Patent Proprietor)	Geneohm Sciences Canada, Inc. 2555 Boul. du Parc Technologique Québec, QC G1P 4S5 (CA)
Representative:	Jaenichen, H-R.; Schlörb, C. Vossius & Partner Patentanwälte Rechtsanwälte mbB Siebertstrasse 3 81675 München (DE)
Appellant II: (Opponent)	Beckman Coulter, Inc. 250 S. Kraemer Boulevard Brea, CA 92821 (US)
Representative:	Spencer, M.; Legg, J. Boult Wade Tennant LLP Salisbury Square House 8 Salisbury Square London EC4Y 8AP (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 5 July 2018 concerning maintenance of the European Patent No. 2781604 in amended form.**

Composition of the Board:

Chairman	B. Stolz
Members:	P. Julià
	D. Rogers

Summary of Facts and Submissions

I. European patent no. 2 781 604 is based on European patent application no. 14 168 420.9, a divisional application of the earlier European patent applications nos. 10 181 533.0, 09 174 581.0, and 02 740 158.7 (published as EP 2 322 663, EP 2 236 621, and EP 1 397 510, respectively), the later application being originally filed under the PCT and published as International patent application WO 02/099034 (hereinafter, "the parent application"). The patent was granted with 8 claims.

II. An opposition was filed on the grounds set forth in Articles 100(a), 100(b) and 100(c) EPC. The opposition division considered the main request to contravene Article 76(1) EPC (Article 100(c) EPC) and auxiliary request 1 to fulfil the requirements of the EPC.

III. Appeals were lodged by both the patent proprietor and the opponent (appellants I and II, respectively). With the statement setting out their respective grounds of appeal, appellant I filed a main request and auxiliary requests 1 to 8 and appellant II filed new documentary evidence (documents (51) to (60)).

IV. The parties replied to their respective statements of grounds of appeal. Appellant II filed new documentary evidence (document (61)).

V. The board summoned the parties to oral proceedings. In a communication pursuant to Article 17 of the Rules of Procedure of the Boards of Appeal (RPBA 2020), they were informed of the board's provisional opinion on the issues of the appeal.

VI. Both appellants replied to the board's communication.

VII. Oral proceedings were held on 23 November 2021. At these proceedings, appellant I withdrew the main request and made former auxiliary request 1 its new main request; former auxiliary requests 2 to 8 were renumbered as auxiliary requests 1 to 7, respectively.

VIII. The claims of the main request (former auxiliary request 1) read as follows:

"1. The nucleic acid of SEQ ID NO: 165 or 166, or the complement of said nucleic acid.

2. An oligonucleotide of the nucleic acid of claim 1, which is specific for MREJ type vii MRSA, wherein said oligonucleotide is suitable for specifically detecting MREJ type vii MRSA and wherein said oligonucleotide hybridizes with the SCC*mec* element right extremity of the nucleic acid of claim 1.

3. A pair of primers that hybridize with the nucleic acid of claim 1, comprising

(a) a first primer specific for MREJ type vii, wherein said first primer hybridizes with the SCC*mec* element right extremity of the MREJ type vii sequence of the nucleic acid of claim 1, and

(b) a second primer which hybridizes with a chromosomal sequence of *S. aureus* adjoining said SCC*mec* element right extremity of the MREJ type vii nucleic acid of claim 1,

wherein said primers of a) and b) enable the specific generation of an amplicon(s) which comprises sequences from both the SCC*mec* element right extremity and chromosomal DNA adjoining said right extremity of said MREJ type vii MRSA strains,

and wherein said pair of primers is suitable for specifically detecting MREJ type vii MRSA."

IX. The following abbreviations are used in this decision:

MRSA : methicillin-resistant *Staphylococcus aureus*;

MSSA : methicillin-sensitive *Staphylococcus aureus*;

SCC*mec* : staphylococcal cassette chromosome *mec*;

MREJ : *mec* right extremity junction;

wherein *mec* stands for the methicillin-resistance *mecA* gene complex.

X. The following documents are cited in this decision:

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

(2) : US 6 156 507 (publication date: 5 December 2000);

(3) : T. Ito *et al.*, Antimicrobial Agents and Chemotherapy, May 2001, Vol. 45, No. 5, pages 1323 to 1336;

(4) : K. Hiramatsu *et al.*, J. Infect. Chemother., 1996, Vol. 2, pages 117 to 129;

(6) : A.E. Simor *et al.*, Can. J. Infect. Dis., September/October 1999, Vol. 10, No. 5, pages 333 to 336;

(7) : D.C. Oliveira *et al.*, Microbial Drug Resistance, December 2001, Vol. 7, No. 4, pages 349 to 361;

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

(38): WO-A2-2007/044873 (publication date: 19 April 2007);

(51): Alignment of MREJ type vii MRSA sequence SEQ ID NO: 165 and non-MRSA *S. lugdunensis* strain C_33;

(53): GenBank accession number AY267375, CMRSA-1/ ID-61880 MREJ nucleotide sequence from document (9);

(54): Alignment of sequence AY267375 from document (9) with MREJ type vii MRSA sequence SEQ ID NO: 166;

(55): A.E. Simor *et al.*, Journal of Infectious Diseases, 2002, Vol. 186, pages 652 to 660;

(57): Alignment of MREJ type iii (SEQ ID NO: 104) and MREJ type vii (SEQ ID 165) sequences;

(58): G. Arakere *et al.*, FEMS Microbiol. Lett., 2009, Vol. 292, pages 141 to 148;

(59): Comparison of the nucleotide sequence of MRSA strain V14 (deposit under accession number AB425427) with nucleotide sequence of SEQ ID NO: 165.

XI. The arguments of appellant I, insofar as relevant to the present decision, may be summarised as follows:

Admission of new documentary evidence

Granted claim 3 and claims 4-5 were directed to an oligonucleotide and to a pair of primers, respectively, and both products were required to be suitable for specifically detecting MREJ type vii MRSA. These claims were extensively discussed at first instance and thus, appellant II had ample opportunities to file documents (51) and (53) to (59) at first instance. All these documents were late-filed, they could have been filed earlier in the proceedings, and they were neither prior art nor *prima facie* relevant; document (56) was not even related to a nucleic acid sequence of a MREJ type vii.

Main request
Article 84 EPC

The terms "MREJ type vii" and "specifically detecting MREJ type vii MRSA" were present in the granted claims and thus, they were not open to an objection under Article 84 EPC. The claims were read by a skilled person with a mind willing to understand and using the common general knowledge. Claim 2 required the claimed oligonucleotide to be specific for MREJ type vii MRSA, suitable for specifically detecting MREJ type vii MRSA, and to hybridise with the SCC*mec* element right extremity of the nucleic acid of claim 1. Figure 4 of the patent showed an alignment of the SCC*mec* integration site and the nucleic acid sequences of the MREJ types i to ix, whereby the skilled person was made aware of those sequences that were specific for MREJ

type vii. Whilst nucleic acid sequences close to the SCC*mec* integration site were very similar in all MREJ types and thus, not suitable for providing any specificity, this was not the case for more distant polymorphic regions.

The oligonucleotide of claim 2 was the primer providing MREJ type specificity and used with a second primer to generate an amplicon as defined in claim 3. Claim 3 required the claimed pair of primers to hybridise with the nucleic acid of claim 1 and the second primer with a chromosomal sequence of *S. aureus* as defined in part (b) of claim 3; hence, the second primer did not extend or go beyond the nucleic acid of claim 1. The reference in claim 3 to several amplicons indicated that multiple copies of a single amplicon were generated; this was in line with the purpose of an amplification and detection method, namely to generate as many amplicon copies as possible so as to have a good detection. No unclarity thus arose from the term amplicon in plural.

Article 76(1) EPC

The objection arising from a two-fold specificity of the oligonucleotide of claim 2, namely for MREJ type vii and for MRSA, was based on a misreading of the feature "specific for MREJ type vii MRSA". There was a basis in the parent application for an oligonucleotide specific for MREJ type vii. Basis was also present for the claimed oligonucleotide and pair of primers, regardless of the method in which they were used. This use was not limited in the parent application to typing methods, let alone to typing methods with at least four MREJ types. The second primer in claim 3 was limited by the feature requiring the claimed pair of primers to be

suitable for specifically detecting MREJ type vii MRSA; such (second) primers had a basis in the parent application.

Article 123(3) EPC

Claim 2 read as granted claim 3 with additional features requiring the claimed oligonucleotide to be specific for MREJ type vii MRSA and to hybridise with the SCC*mec* element right extremity of the nucleic acid of claim 1. These features were further restrictions of the claim; hence, there was no extension of the scope of protection. The features introduced into claim 3, in particular the hybridisation of the second primer with a chromosomal sequence of *S. aureus*, did not extend the scope of protection *vis-à-vis* granted claim 4 because the claimed pair of primers, first and second, was still required to hybridise with the nucleic acid of claim 1.

Article 83 EPC

Claim 2 was not directed to an oligonucleotide having a two-fold specificity, for MREJ type vii and for MRSA. A skilled person knew that two primers were always necessary for having both specificities, as taught also in the parent application, wherein Figure 2 showed that two-fold specificity was achieved only with two primers. Claim 2 was directed to the first primer, the primer providing the MREJ type vii specificity.

Article 83 EPC required enablement and sufficiency of disclosure at the relevant date. According to the parent application, no sequences with significant homology to the MREJ type vii sequences (SEQ ID NO: 165 and 166) were retrieved in a BLAST search at the

relevant date (page 33, lines 20 to 22). MSSA and MRSA strains that were unknown at the relevant date, were not prior art and hence, they had no bearing on enablement. The parent application provided the tools and information for a skilled person to handle new MSSA and MRSA strains, selecting primers specific for MREJ type vii and identifying false positives. The skilled person knew how to distinguish MRSA strains from MSSA strains. The *orfX* sequence of the MSSA strain *S. lugdunensis* shown in document (51) was different from that of the MRSA strains of the MREJ type vii disclosed in the parent application. These strains could be distinguished by designing appropriate second primers in line with the teachings of the parent application.

In the parent application, sequence SEQ ID NO: 98 was disclosed as specific for MREJ type iii, not MREJ type vii. This sequence was shown in document (57) to have two mismatches when compared with sequence SEQ ID NO: 165 of MREJ type vii; hence, these sequences were different and generated different amplicons. The pair of primers SEQ ID NO: 64 and 98 did not fall within the scope of claim 3 because the sequence SEQ ID NO: 98 was not specific for MREJ type vii. Figure 4 of the parent application showed that sequences of the different MREJ types near or close to the integration (junction) site had a high degree of identity. Thus, a skilled person would not have selected primers within this region but far away from it, namely in polymorphic regions where more differences were present; with the information shown in Figure 4 and sequences SEQ ID NO: 165 and 166, such a selection was a routine task and required no undue burden from the skilled person.

The subject-matter of claims 2 and 3 was defined by structural (nucleic acid of claim 1) and functional features; the oligonucleotide of claim 2 and the first primer of claim 3 were required to be specific for MREJ type vii and suitable for specifically detecting MREJ type vii MRSA. If these requirements were not fulfilled, the oligonucleotide/primer did not fall within scope of these claims. In this sense, claims 2 and 3 were self-contained. The fact that certain primers could bind to more than one MREJ type was not an indication that the claimed subject-matter could not be worked; a skilled person could always chose another primer based on the nucleic acid sequences disclosed in the parent application.

Article 54 EPC

Neither document (1) nor document (2) anticipated claims 2 or 3 of the main request. None of these documents disclosed the nucleic acid of SEQ ID NO: 165 or 166. This sequence was necessary for obtaining an oligonucleotide as defined in claim 2, i.e. specific for MREJ type vii and suitable for specifically detecting MREJ type vii, and for designing a pair of primers with a first primer as defined in part (a) of claim 3.

Article 56 EPC

Document (1) provided neither a motivation for a skilled person to screen further MRSA strains nor a reasonable expectation of finding new MREJ types, let alone the MREJ type vii. The three MRSA strains isolated in Japan, UK and Germany were identified in document (1) as representative examples of worldwide epidemic MRSA strains. Positive results were obtained

in all tests performed and all MRSA strains isolated in 18 countries were identified using the method disclosed in document (1). Nor did document (3) provide such a motivation and expectation of success. Although the MREJ type of the MRSA strain 85/5328 was not indicated in Table 1 of document (3), no reasons were given and no further information could be derived therefrom, let alone the presence of a new MREJ type different from the known MREJ types i, ii and iii. The MRSA strain 85/5328 was also identified as being non-typable in Figure 4 of document (4) and it was suggested that the right junction point could have been spontaneously deleted from that strain. Although the MREJ non-typable nature of the MRSA strain 85/5328 was known since 1996, neither document (1) nor document (3), the latter published in 2001, referred to a possible presence of a new MREJ type. This was so because there was no reason to expect from the disclosures of any of documents (1) and (3), that new MREJ types could be present in other MRSA strains, let alone the MREJ type vii of sequence SEQ ID NO: 165 or 166.

Starting therefrom, the objective technical problem was the provision of oligonucleotides and primers for improved detection of MRSA strains. This problem was solved by the subject-matter of the main request which was however not obvious for the skilled person, neither from any of documents (1) or (3) alone nor when in combination with document (7) or any other prior art.

Document (7) was concerned with the overall structure and variability of the SCC*mec* element. Extensive alterations and variability in the studied SCC*mec* elements was shown to be present in regions far away from the right junction. There was no reference in this document to the polymorphic sequences from the SCC*mec*

extremity at the right junction, nor to any specific MREJ type. On the contrary, document (7) referred to a conserved segment (dcs) close to the right junction and, although it was stated that some MRSA strains had an insertion between the end of dcs and *orfX* (page 355, left-hand column, third paragraph; page 356, Table 3), no further information was provided and there was no characterisation of said region, in particular not for strains BK793 and HDG2. Post-published document (38) was not prior art and could not be used for drawing any conclusions on document (7). Hindsight knowledge of the patent was required for considering the disclosure of document (7) to make a skilled person aware of the presence of new MREJ types different from those disclosed in documents (1) and (3).

Likewise, documents (9) and (53) to (55) were post-published and not prior art. Even if strain CMRSA-1 had been publicly available in 1999 (document (6)), there was no indication in any of documents (1) and (3) that could have led a skilled person to this strain. Nor could be reasonably expected that this strain could provide a new MREJ type, let alone the MREJ type vii. Hindsight knowledge of the patent was required for combining these documents in order to arrive at the claimed subject-matter. Furthermore, document (9) disclosed a large list of MRSA strains; whilst strain EMRSA I was indicated in Table 1 of this document to be isolated from Germany, a strain with the same designation was isolated from Canada according to footnote (c) of Table 3 of the patent. Thus, the actual source of the MREJ type vii of sequence SEQ ID NO: 166 was ambiguous.

XII. The arguments of appellant II, insofar as relevant to the present decision, may be summarised as follows:

Admission of new documentary evidence

The main request in appeal was filed, as auxiliary request 1, at the end of the oral proceedings at first instance; it was also only at the end of these proceedings that the requirements of Article 83 EPC were considered. The filing of documents (51) and (56) to (59) was in direct reaction to the reasons given by the opposition division under this article in the decision under appeal. Documents (53) to (55) were filed in appeal because the public availability of the CMRSA-1 strain had not been challenged prior to the oral proceedings at first instance.

Main request
Article 84 EPC

The oligonucleotide of claim 2 was required to be "specific for MREJ type vii MRSA", i.e. a two-fold specificity: for MREJ type vii and for MRSA. The patent taught that two primers were always necessary for MREJ specific detection of a MRSA strain; thus, it was not clear how to achieve a two-fold specificity by a single oligonucleotide. The alignment of the MREJ type vii sequence SEQ ID NO: 165 and the sequence of the MSSA *S. lugdunensis* strain *C_33* in document (51) showed that the preferred primers disclosed in the patent as specific for MREJ type vii (SEQ ID NO: 112 and 113) were not specific for MRSA; the latter specificity was provided by a second primer that was specific for the *orfX* chromosomal sequence of MRSA strains (SEQ ID NO: 71). Moreover, the term "specific for MREJ type vii" was not defined in the claim (such as by

reference to a SEQ ID NO), thereby introducing further unclarity.

A lack of clarity in claim 3 arose from the term "adjoining" in the definition of the second primer because there was no constraint to the location of the sequence with which this primer hybridised. Yet, the claim also required the pair of primers to hybridise with the nucleic acid of claim 1 which was in conflict with the above definition. Claim 3 was also ambiguous because it was not clear how a pair of primers could generate more than one amplicon of a single target sequence and what was meant by its specific generation.

Article 76(1) EPC

Claim 2 required the oligonucleotide to have two specificities, for MREJ type vii and for MRSA. However, according to the parent application, these two specificities could only be achieved by using two primers. There was no basis in the parent application for a single oligonucleotide having both specificities. The feature "specific for MREJ type vii" was disclosed in the parent application only in the context of typing methods; oligonucleotides and pairs of primers with specificities such as those defined in claims 2 and 3 were only disclosed in typing methods. There was no basis in the parent application for the claimed oligonucleotides and pair of primers other than when used in methods of typing. Moreover, the typing methods disclosed in the parent application involved the use of at least four MREJ types together, at the same time.

The second primer in claim 3 was not constrained to hybridise with the *orfX* chromosomal sequence of *S. aureus*; it could hybridise partly with a sequence

within the nucleic acid sequence of claim 1 and partly with another sequence outside this sequence. There was no basis in the parent application for such a primer. Moreover, since the *orfX* sequence of MSSA strains had about 80% sequence identity with the *orfX* sequences of MRSA strains (document (51)), the second primer of claim 3 was so broadly defined that it covered (second) primers hybridising with MSSA strains. These primers had no basis in the parent application.

Article 123(3) EPC

Whilst the granted claims required the claimed oligonucleotide to be a fragment of the nucleic acid of claim 1, the oligonucleotide of claim 2 was defined as hybridising with the SCC*mec* element right extremity of the nucleic acid of claim 1 and thus, implying that the sequence was not identical to that of the nucleic acid of claim 1. Although the pair of primers of claim 3 was required to hybridise with the nucleic acid of claim 1, the second primer was defined as hybridising with a chromosomal sequence of *S. aureus* adjoining the SCC*mec* element right extremity of the MREJ type vii nucleic acid of claim 1, without being limited or constrained to the *orfX* chromosomal sequence of *S. aureus*.

Article 83 EPC

Claim 2 required the claimed oligonucleotide to have two specificities, for MREJ type vii and for MRSA. However, according to the disclosure of the parent application, two primers were necessary for achieving both specificities. The parent application failed to provide sufficient information on how to achieve a single oligonucleotide with both specificities.

Document (51) showed the alignment of the MREJ type vii SEQ ID NO: 165 with the sequence of a MSSA strain (*S. lugdunensis* strain *C_33*), indicating the binding sites for the first and second primers (SEQ ID NO: 112, 113, and SEQ ID NO: 71, respectively). This MSSA strain contained an SCC*mec* right extremity sequence identical to sequence SEQ ID NO: 165, including the biding site for the first primer, the primer specific for MREJ type vii (SEQ ID NO: 112, 113). Thus, this first primer could not provide MRSA specificity; a second primer was necessary for MRSA specificity. A single oligonucleotide, such as that of claim 2, could not be specific for both, MREJ type vii and MRSA.

The second primer as defined in part (b) of claim 3 was not required to be specific for MRSA *versus* MSSA strains and thus, the detection method produced false positives. The requirement that the second primer had to hybridise with a chromosomal sequence of *S. aureus* was not enough for distinguishing MRSA from MSSA strains. Several second primers disclosed in the parent application were not specific for MRSA *versus* MSSA strains, such as sequence SEQ ID NO: 71. The nucleic acid of the MSSA strain shown in document (51) would have been also amplified and detected when using sequences SEQ ID NO: 112, 113 and 114 as a first primer (specific for MREJ type vii) and sequence SEQ ID NO: 71 as a second primer (*orfX* chromosomal sequence).

A large number of first primers disclosed in the parent application as specific for a determined MREJ type were actually not specific for said MREJ type. In view of the high identity among the sequences shown in Figure 4 of the parent application, MREJ type vii specificity was not possible to achieve; the sequences of the MREJ types iii and vii were largely identical. Document (57)

showed an alignment of sequences SEQ ID NO: 104 (MREJ type iii, Table 10 of parent application) and SEQ ID NO: 165, wherein sequence SEQ ID NO: 98 - disclosed as a first primer specific for MREJ type iii (Table 5 of parent application) - was largely identical to the sequence of the MREJ type vii. The pair of primers of sequences SEQ ID NO: 98 and SEQ ID NO: 64, when used as first and second primer, resulted in amplification and detection of both MREJ type iii and type vii.

Document (58) stated that the SCC*mec* element of MREJ type iii of MRSA strain V4 (deposit number AB425427) was highly homologous to the SCC*mec* element of the *S. aureus* strain CCRI-9583; this latter strain was one of the MRSA strains used in the parent application for isolating sequences SEQ ID NO: 165 and 166 of the MREJ type vii (Table 4; MRSA strains SE1-1 (CCRI-9583) and ID-61880 (CCRI-9589)). Document (59) showed an alignment of the sequence of the MRSA strain V14 with sequence SEQ ID NO: 165 of MRSA strain CCRI-9583, wherein the sequences corresponding to primers SEQ ID NO: 64 (*orfX*, second primer) and SEQ ID NO: 112, 113 and 114 (first primers specific for MREJ type vii; Example 7 of parent application) were identical in both the V14 and the CCRI-9583 strain.

Therefore, it was incorrect to conclude that primers specific for the MREJ type vii could be prepared by following routine design procedures, as concluded by the opposition division in the decision under appeal.

Article 54 EPC

No objections were raised under this article if the oligonucleotide of claim 2 and the first primer of claim 3 were each specific for a MREJ type vii sequence

defined by the nucleic acid of SEQ ID NO: 165 or 166; i.e. not cross-reacting with any other MREJ type sequence. To the extent that these claims were construed differently, so that MREJ type vii specificity was achieved by the amplicon(s) (by virtue of their sequence or length) rather than the primers themselves, an objection for lack of novelty was raised based on documents (1)/(2).

Article 56 EPC

The skilled person, as defined in decision T 2002/13, was familiar with the prior art disclosing the MREJ types i, ii and iii, in particular documents (1) and (3); the latter document cited in the patent under the heading "Background of the invention". Any of these documents could be taken as closest prior art.

The method disclosed in document (1) was generally applicable and had been applied to characterise MRSA strains isolated in Japan, UK and Germany. These three MRSA strains defined the three known MREJ types i, ii and iii and were said to be representative examples of epidemic MRSA strains isolated in various countries worldwide; the screening of 28 epidemic MRSA strains in 18 countries was reported. Although document (1) disclosed the application of this method to these three types of MRSA strains, this method - with design of appropriate primers, screening and determination of MREJ sequences - was general and not limited thereto (page 5, lines 23 to 27 and lines 48 to 52). The teachings of examples 1 to 3 were general and reference was made to the structures of the *mec* region DNAs as being diverse and the necessity of designing appropriate primers - based on the disclosed concept

and method - for determining epidemic MRSA strains spread over the world (page 10, lines 39 to 42).

Document (3) was the prior art most contemporaneous to the patent and thus, the most updated understanding of the disclosure of document (1). Document (3) reported the screening of 38 MRSA strains isolated worldwide and the MREJ types of these strains were shown in Table 1. Except for the MRSA strain 85/5328, all strains were from the MREJ types i, ii or iii. The fact that the MRSA strain 85/5328 MRSA could not be typed informed the skilled person of the presence of other MREJ types. The importance of exploring staphylococcal genomes of more MRSA strains and finding more diversified members of SCC*mec* was stated in the conclusion of document (3) (page 1335, right hand column, last paragraph).

Starting therefrom, the objective technical problem was the provision of oligonucleotides and appropriate primers for identifying and determining further MREJ types of MRSA strains. This problem was solved by the subject-matter of the main request.

For a skilled person, it was obvious from either document (1) or document (3) to screen more MRSA strains and expect to find new MREJ types as predicted in document (3). Indeed, based on the teachings of the latter document, document (7) reported the design of appropriate primers and the presence of structural variability in the *mecA* downstream region of various SCC*mec* types of MRSA strains (Table 3), such as for the MRSA strains BK793 (identified as MREJ type xv in Table 8 of document (38)) and HDG2 (identified as MREJ type iv). These expectations were confirmed in post-published document (9), wherein the method described in documents (3) and (7) was used to routinely screen a

large number of MRSA strains available worldwide and to identify the new MREJ types iv, v and vii (Tables 1, 4 and 5 of document (9)). The MREJ type vii was obtained from the MRSA strains CMRSA-1 and CCRI-9583 (GenBank accession numbers AY267375 and AY267384, respectively). The MRSA strain CMRSA-1 was identified as a Canadian epidemic strain with reference to document (55). Document (55) reported the characterisation of MRSA found in Canadian hospitals and, with reference to document (6) of these appeal proceedings, stated that the strain CMRSA-I was the most abundant epidemic Canadian strain. Document (6) showed that the strain CMRSA-1 was already publicly available in 1999 upon request and that this strain was commonly referred to as the "Ontario epidemic strain".

The MRSA strains CMRSA-1 and CCRI-9583 were the strains used for isolating the MREJ type vii in the patent. As indicated in Table 4 of the patent, the sequences SEQ ID NOs: 165 and 166 were obtained from the MRSA strains SE1-1 (CCRI-9583) and ID-61880 (CCRI-9589), and the origin of these strains was indicated in Table 3 to be Ontario, Canada. Although the MRSA strain ID-61880 (CCRI-9589) was identified as the Canadian clone EMRSA-1 in the footnote (c) of Table 3 of the patent, this designation was an obvious typographical error because it corresponded to the Canadian CMRSA-1 strain, as correctly indicated on page 47, lines 6 to 8 of the parent application. Evidence was on file showing that the MRSA strain CMRSA-1 (CCRI-9589) was publicly available at the relevant date (document (6)) and that the MREJ sequence of this strain (GenBank AY267375) and that of SEQ ID NO: 166 were identical (document (54)).

XIII. Appellant I (patent proprietor) requested to maintain the patent upon the basis of the main request (former auxiliary request 1) or, alternatively, upon the basis of auxiliary requests 2 to 8, all requests filed with the statement of grounds of appeal.

XIV. Appellant II (opponent) requested to set aside the decision under appeal and to revoke the patent.

Reasons for the Decision

Admission of new documentary evidence

1. Documents (51) to (61) were filed by appellant II in appeal proceedings and thus represent new documentary evidence.

2. Article 12(2) RPBA 2020 states that, in view of the primary object of the appeal proceedings to review the decision under appeal in a judicial manner, a party's appeal case shall be directed to, *inter alia*, evidence on which the decision under appeal was based. Since documents (51) to (61) were filed before the date of entry into force of the RPBA 2020, Article 12(4) RPBA 2007 applies to the present case for the purpose of establishing admittance (Article 25(2) RPBA 2020). According to Article 12(4) RPBA 2007, the board may hold inadmissible evidence which should have been presented in the first instance proceedings.

3. For the board to reach a decision on the appellant I's main request, it is first necessary to decide on the admission of documents (51) and (53) to (59) into the appeal proceedings.

3.1 The filing of document (51) and documents (56) to (59) by appellant II is in direct response to the opposition division's discussion - in the decision under appeal and in the context of Articles 76(1), 83 and 84 EPC - of the feature "suitable for specifically detecting MREJ type vii MRSA". This feature is present in claims 2 and 3 of the main request and is highly relevant for assessing whether or not the main request fulfils the requirements of these articles.

Document (51) shows the alignment of the nucleic acid sequence SEQ ID NO: 165 of claim 1 of the main request with the nucleic acid sequence of *S. lugdunensis* strain C_33. Whilst document (58) provides the (EMBL)/ GenBank accession number of the sequence of the MRSA strain V14, document (59) shows this sequence and an alignment with sequence SEQ ID NO: 165.

Whilst none of the sequences shown in the alignment of document (56) is one of the nucleic acid sequences cited in the main request, document (57) shows the alignment of the nucleic acid sequence SEQ ID NO: 165 (MREJ type vii) of claim 1 of the main request with the nucleic acid sequence SEQ ID NO: 104 (MREJ type iii) disclosed in the parent application.

3.2 The filing of documents (53) to (55) by appellant II is in direct response to reasons given in the decision under appeal and in the context of Article 56 EPC, as well as to the considerations made on the public availability of the MRSA strain CMRSA-1 and the MREJ sequence of this strain at the relevant date.

Documents (53) to (55) are cited under Article 56 EPC and are concerned with the MRSA strain CMRSA-1. This MRSA strain was disclosed in document (6) and cited in

document (9); the latter document providing the MREJ sequence of this strain by reference to the GenBank accession number. Documents (53) and (54) show the nucleic acid sequence deposited in GenBank and its alignment with sequence SEQ ID NO: 166 (MREJ type vii) of claim 1 the main request.

4. The board, in the exercise of its discretion, decides to admit documents (51), (53) to (55) and (57) to (59) into the appeal proceedings, but not document (56).

Main request

5. The main request is the auxiliary request 1 filed with appellant I's statement of grounds of appeal and upheld by the opposition division. Thus, it already forms part of the appeal proceedings.

Article 84 EPC

6. According to the established case law, the claims are read by a skilled person with a mind willing to understand and taking into account the common general knowledge (cf. T 190/99 of 6 March 2001; see "Case Law of the Boards of Appeal of the EPO", 9th edition 2019, II.A.6.1, 307). In the present case, the skilled person is defined in decision T 2002/13, namely a person skilled in amplification techniques, and familiar with MSRA in general and the detection and identification of MREJ types in particular (cf. T 2002/13 of 17 May 2013, point 4 of the Reasons).

7. Hence, the skilled person is aware that MRSA specificity and MREJ type specificity can only be achieved by using two primers; a first primer providing the specificity for a determined MREJ type, and a

second primer providing the specificity for MRSA. This is part of the skilled person's common general knowledge as shown by all prior art on file and that cited in the patent under the heading "Background of the invention", in particular document (4) concerned with MREJ types i, ii and iii. Thus, the feature in claim 2 defining the oligonucleotide as "specific for MREJ type vii MRSA" is read by the skilled person as requiring said oligonucleotide to be specific for the MREJ type vii of a MRSA strain. Neither is this feature ambiguous nor does it give rise to any unclarity in the properties defining the claimed oligonucleotide.

8. The meaning of the term "specific" in the feature "specific for MREJ type vii" is also clear and not open to interpretation for a skilled person as defined above. This term is understood by the skilled person as requiring the primer to bind to, or hybridise with, the MREJ type vii sequence but not with the sequence of other MREJ types, such as those of the MREJ types i to vi and viii to x. This is in line with the description and examples of the patent, such as Example 7, wherein reference is made to primers specific for MREJ type iii (SEQ ID NO: 67), MREJ type iv (SEQ ID NO: 79), MREJ type v (SEQ ID NO: 80) and a primer specific for *orfX* (SEQ ID NO: 64); the relevance of the latter is disclosed on page 24, lines 10 to 14 of the parent application (see also page 36, lines 4 to 12).

9. The alignment shown in document (51), in particular the location of the MREJ type vii sequences (SEQ ID NO: 112 and 113) and the MRSA *orfX* sequence (SEQ ID NO: 71), confirms the disclosure of the patent and the skilled person's common general knowledge on the relevance of using two primers for attaining a two-fold specificity: a first primer providing the MREJ type vii specificity

by hybridising with the SCC*mec* element right extremity of the MREJ type vii nucleic acid of claim 1, and a second primer providing the MRSA specificity by hybridising with the *orfX* chromosomal sequence of *S. aureus* adjoining said SCC*mec* element right extremity. The relevance of MSRA specificity is also disclosed in the patent with reference to sequence SEQ ID NO: 71 and other sequences targeting the *orfX* gene, wherein from all these sequences "only one (SEQ ID: 64) was found to be specific for MRSA" (cf. page 24, lines 10 to 14 of the parent application).

10. No ambiguity arises from the term "adjoining" in the definition of the second primer in part (b) of claim 3. This is so because in the preamble of this claim, the pair of primers is required to hybridise with the nucleic acid of claim 1. Both, the first and second primer, must hybridise with the nucleic acid of claim 1; the sequence of the second primer cannot extend or go beyond the nucleic acid of claim 1. For this reason, the term "adjoining" in claim 3 is neither ambiguous nor open to interpretation; the second primer is constrained to a sequence hybridising with the nucleic acid of claim 1 (SEQ ID NO: 165 or 166), a sequence which, as shown in document (51), contains the *orfx* chromosomal sequence of *S. aureus* and does not go beyond that sequence.

11. Claim 3 is directed to "a pair of primers" that "enable the specific generation of an amplicon(s)", wherein the term "amplicon" is used in plural. As stated above, the skilled person as defined in decision T 2002/13 (*supra*) is familiar with amplification techniques using primers and thus, s(he) knows that a pair of primers comprising a first primer specific for MREJ type vii and a second primer as defined in part (b) of claim 3 generates an

amplicon that comprises the sequence specific for the MREJ type vii. In line with the purpose of an amplification, this pair of primers is expected to amplify - to generate as many copies as possible of - this amplicon, so as to allow the specific detection of MREJ type vii MRSA required in claim 3.

12. The term "specific generation" in claim 3 cannot be read in isolation but must be read in the context of claim 3 which defines the first primer as "specific" for MREJ type vii and requires the pair of primers to be suitable for "specifically" detecting MREJ type vii MRSA. The terms "specific" and "specifically" in the claim are understood by the skilled person as having the same meaning as that explained in point 8 above. The "specific generation of an amplicon(s)" is linked to the specificity of the pair of primers which is defined in parts (a) and (b) of claim 3; no ambiguity arises from this term. The same reasoning applies to the term "specifically detecting MREJ type vii MSRA" in claims 2 and 3 of the main request (see decision T 1146/15 of 22 November 2021, points 12 to 16 of the Reasons).

13. Thus, the main request fulfils the requirements of Article 84 EPC.

Article 76(1) EPC

14. As stated under Article 84 EPC, the feature "specific for MREJ type vii MRSA" in claim 2 requires the claimed oligonucleotide to be specific for MREJ type vii of a MRSA strain and not, as argued by appellant II, to have a two-fold specificity, namely for MREJ type vii and for MRSA. It is known in the art that such a two-fold specificity can only be achieved with a pair of

primers. Appellant II's objection based on this feature requires to misread the claim and to disregard the common general knowledge of a skilled person as defined in decision T 2002/13 (*supra*).

15. There are several references in the parent application to primers specific for a determined MREJ type, in particular, to primers specific for MREJ type vii (cf. *inter alia*, page 15, lines 12 and 13; page 36, lines 4 to 8). Claim 12 of the parent application is directed to a method for typing a MREJ of a MRSA strain which comprises the reproduction of the method of claims 1 to 11 with primers specific for a determined MREJ type. Dependent claims 2 to 22 of the parent application refer to primers for the detection of, *inter alia*, MREJ type vii, including the nucleic acid sequences SEQ ID NO: 112 and 113 (cf. *inter alia*, claims 6 and 7); these sequences are derived from the nucleic acid sequences SEQ ID NO: 165 and 166 as shown in Table 5 and described in Example 7 of the parent application (cf. page 52, lines 16 to 20). In the parent application, the nucleic acid sequences SEQ ID NO: 165 and 166 are identified as sequences of the MREJ type vii and claimed as such in claim 13 of the parent application. Claim 14 of the parent application is directed to an oligonucleotide which hybridises with the nucleic acid of claim 13 and with one or more MREJ of the types referred to in that claim. Likewise, claim 17 of the parent application is directed to a composition of matter comprising primers defined as in claim 13. Neither the nucleic acids of claim 13 nor the oligonucleotides and primers of claims 14 and 17 are linked to, or associated with, any particular method; these specific primers are disclosed - and claimed - in the parent application as such, regardless of the particular method in which they are used and of the

number of specific primers used for carrying out these methods.

16. Claims 1 to 3 of the main request are product-claims directed to a nucleic acid (claim 1), oligonucleotide and a pair of primers (claims 2 and 3, respectively). All these products, in particular the oligonucleotide of claim 2, are directly derivable from the parent application as stated in point 15 above. Although the term "specific generation" in claim 3 is not disclosed *verbatim* in the parent application, it is nevertheless directly and unambiguously derivable therefrom. The use of a primer with a determined MREJ type specificity, in particular the MREJ type vii specificity, as directly taught in the parent application, results in the specific generation of an amplicon(s). The same reasoning applies to the term "specifically detecting MREJ type vii MRSA" in claims 2 and 3 (see decision T 1146/15 of 22 November 2021, points 12 to 16 of the Reasons).

17. As stated under Article 84 EPC, the second primer defined in part (b) of claim 3 is not broadly defined but constrained by the requirement to hybridise with the chromosomal sequence of *S. aureus* within the nucleic acid of claim 1 (SEQ ID NO: 165 or 166). The preamble of claim 3 further requires the pair of primers, i.e. both first and second primers, to hybridise with the nucleic acid of claim 1, thereby excluding sequences which hybridise with sequences beyond those of the nucleic acid of claim 1. Therefore, the term "adjoining" in the definition of the second primer in claim 3 is structurally limited by the nucleic acid sequence of claim 1.

18. Moreover, the definition of the second primer is further constrained in claim 3 by the requirement of being "suitable for specifically detecting MREJ type vii MRSA", wherein MRSA specificity is provided by said second primer. This feature excludes all pairs of primers not suitable for specifically detecting MREJ type vii MRSA; thereby excluding second primers not specific for MRSA, such as the sequence SEQ ID NO: 71 shown in document (51) (see page 24, lines 10 to 14 of the parent application). Second primers, and pairs of primers comprising these second primers, as defined in claim 3 are directly and unambiguously derivable from the parent application.

19. It follows from these considerations that the main request complies with Article 76(1) EPC.

Article 123(3) EPC

20. Claim 1 of the main request reads as granted claim 1 and is directed to the nucleic acid of SEQ ID NO: 165 or 166 or the complement of said nucleic acid. Whilst granted claim 2 is directed to a "fragment of the nucleic acid of claim 1", claim 2 of the main request is directed to an "oligonucleotide of the nucleic acid of claim 1" and then other features characterising the claimed oligonucleotide are defined. However, this first requirement defines the oligonucleotide of claim 2 of the main request as a fragment of the nucleic acid of claim 1 and thus, as in the granted claims. The additional feature in claim 2 of the main request, not present in the granted claims, requires the claimed oligonucleotide to hybridise with the SCC*mec* element right extremity of the nucleic acid of claim 1. This feature only limits the scope of the claim to those fragments that fulfil this additional

requirement and further brings the wording of the claim in line with that of claim 3. Thus, claim 2 does not go beyond the scope of the granted claims and therefore, does not extend the scope of the protection granted.

21. Whilst the "pair of primers that hybridise with the nucleic acid of claim 1 or 2" in granted claim 4 is only characterised by the feature "wherein said pair of primers is suitable for specifically detecting MREJ type vii MRSA", the pair of primers of claim 3 of the main request is further defined by structural features of the first and second primers (parts (a) and (b) of claim 3, respectively) and by a functional feature, namely that said primers "enable the specific generation of an amplicon(s)" which is further defined in the claim. As stated under Articles 84 and 76(1) EPC (*supra*), the second primer is constrained by both structural and functional features and, as a result thereof, the scope of claim 3 of the main request is, if at all, narrower than that of granted claim 4.

22. The main request complies thus with Article 123(3) EPC.

Article 83 EPC

23. As stated under Article 84 EPC, the oligonucleotide of claim 2 does not have two specificities, it is specific only for MREJ type vii. This, as stated also under Articles 84 and 76(1) EPC, is in line with the common general knowledge of a skilled person defined as in decision T 2002/13 (*supra*) and with the information provided by document (51).

24. As stated also under Articles 76(1) and 84 EPC, the second primer is defined in claim 3 by a structural (hybridizes with a chromosomal sequence of *S. aureus*

adjoining ... nucleic acid of claim 1) and a functional feature; the latter requires the primer to be specific for MRSA. In line therewith, the parent application discloses the selection of sequence SEQ ID NO: 64 as optimal second primer and provides a reason for this selection, namely because it "was found to be specific for MRSA based on testing with a variety of MRSA, MSSA, MRCNS and MSCNS strains (Table 12)" (cf. page 24, lines 10 to 14) (wherein MRCNS: methicillin-resistant coagulase-negative staphylococci; MSCNS: methicillin-sensitive coagulase-negative staphylococci). Although the sequence SEQ ID NO: 71 shown in document (51) fulfils the structural requirement of part (b) of claim 3, it does not fulfil the functional requirement of this claim.

25. As also shown in document (51), there are stretches of the *orfX* chromosomal sequence within the sequence SEQ ID NO: 165 significantly different from the *orfX* chromosomal sequence of *S. lugdunensis* (MSSA) strain C_33, which can be thus selected as appropriate second primers with MRSA specificity. It is also known to a skilled person that the accuracy of such a selection improves when increasing the number of MRSA, MSSA, MRCNS and MSCNS strains available for testing or screening. The disclosure of the parent application provides thus guidance and clear instructions for the skilled person to select a second primer with the structural and functional features defined in claim 3.

26. The same guidance and instructions apply also to the selection of the first primer defined in claim 3. Figure 4 of the parent application provides an alignment of the sequences of MREJ types i to ix. This alignment allows a skilled person to select those sequences specific for the MREJ type vii as required in

part (a) of claim 3. This alignment shows that, at the SCC*mec* integration site, the sequences of all MREJ types are very similar, if not identical. Thus, it is not a region where sequences specific for a determined MREJ type are present. Indeed, sequence SEQ ID NO: 98 is located close to the SCC*mec* integration site (first 27 nucleotides in Figure 4) and, although this sequence is disclosed in Table 5 and in the description of the parent application as specific for MREJ type iii (cf. *inter alia*, page 23, line 24), this sequence is not actually specific for MREJ type iii because, as shown in Figure 4, it has a high homology with the corresponding sequences of other MREJ types, including MREJ type vii. The alignment in document (57) shows the presence of only two mismatches (out of 28 nucleotides) between sequence SEQ ID NO: 98 and the corresponding sequence of MREJ type vii.

27. Although sequence SEQ ID NO: 98 is identified as a primer specific for MREJ type iii, this primer is not used in any of the examples of the parent application, wherein sequence SEQ ID NO: 67 is used as the primer specific for MREJ type iii. Nor is sequence SEQ ID NO: 98 identified in the parent application as a primer specific for MREJ type vii. The erroneous information on the MREJ type specificity of sequence SEQ ID NO: 98 neither invalidates nor renders inappropriate the guidance and instructions derivable from the disclosure and teachings of the parent application by a skilled person defined as in decision T 2002/13 (*supra*). The sequence SEQ ID NO: 165 of claim 1 has 1282 bases and is much longer than the fragment of 483 bases shown in document (57); this fragment is located near the SCC*mec* integration site and, contrary to sequence SEQ ID NO: 165, does not comprise MREJ sequences with high heterogeneity. In fact, these polymorphic sequences are

the MREJ sequences selected as first primers specific for MREJ type vii as exemplified by sequences SEQ ID NO: 112 and 113 (cf. Example 7 on page 52, lines 16 to 20); the location of these sequences with respect to the SCC*mec* integration site is shown in document (59).

28. Document (59) provides an alignment of the first 893 bases of sequence SEQ ID NO: 165 with the sequence of *S. aureus* strain V14 (GenBank accession number AB425427.1), a MRSA strain described in post-published document (58) (GenBank accession number on page 143, right-hand column, fourth paragraph). Document (59) shows these sequences to be 99% identical, with only four differences located within the *orfX* chromosomal sequence; the sequences of the SCC*mec* integration site and the right extremity junction (MREJ) are identical. Although document (58) identifies the SCC*mec* element carried by strain V14 as a type-III SCC*mec* element, it clearly states that it is a novel type-III SCC*mec* variant, a new variant of a type-III SCC*mec* cassette, and a unique SCC*mec* element (cf. *inter alia*, page 142, paragraph bridging left and right-hand columns).

29. Document (58) states that the SCC*mec* element carried by strain V14 contains a 422 bp sequence which is highly homologous to that identified in strain CCRI-9583, and further states that the "422 bp nucleotide sequence downstream of *orfX* was found to be identical to that carried by CCRI-9583 (GenBank accession no. AY267384)" (cf. page 141, abstract; page 144, right-hand column, last paragraph). As shown in Tables 3 and 4 of the parent application, strain CCRI-9583 is the MRSA strain from which sequence SEQ ID NO: 165 was obtained, a sequence identified in Table 4 and in the description of the parent application as a MREJ type vii. Thus, the presence of the 422 bp sequence in strain V14 informs

the skilled person that, according to the disclosure and teaching of the parent application, the MREJ type of strain V14 is, to all effects, a MREJ type vii. Although most MRSA strains have the same SCC*mec* type and associated MREJ type, this is not always the case (cf. page 1332, left-hand column, lines 2 to 7 of document (3); page 1881, Table 4 of document (9)). Therefore, the novel, new or unique type-III SCC*mec* variant identified in document (58) is associated with a MREJ type vii.

30. It follows from these considerations that the parent application provides sufficient information for a skilled person to achieve an oligonucleotide as defined in claim 2 and to select a pair of primers as defined in claim 3. Thus, the requirements of Article 83 EPC are fulfilled.

Priority

31. The findings of the opposition division as regards the non-entitlement of the main request to the claimed priority have not been contested in appeal. The priority document (CA 2,348,042; 4 June 2001) neither discloses a MREJ type vii MRSA strain nor the nucleic acid of SEQ ID NO: 165 or 166 (cf. page 16, point 8 of the decision under appeal).

Article 54 EPC

32. Documents (1) and (2), with K. Hiramatsu *et al*. as inventors, are cited under Article 54 EPC; document (2) is also cited as prior art in the parent application (cf. *inter alia*, page 4, line 6; page 5, line 2). None of these documents discloses the nucleic acid of SEQ ID NO: 165 or 166 nor a MREJ type vii MRSA strain. Thus,

they do not anticipate the subject-matter of claim 1 of the main request.

33. The objection for lack of novelty of claims 2 and 3 of the main request is raised only if the feature "specific for MREJ type vii" characterising the oligonucleotide of claim 2 and the first primer in part (a) of claim 3, is understood or interpreted as not excluding oligonucleotides and first primers cross-reacting or hybridising with other MREJ types such as those disclosed in documents (1) and/or (2). Since, as stated under Articles 84 and 76(1) EPC (*supra*), this interpretation is not in line with the reading of these claims by the skilled person (cf. *inter alia*, point 8 above), the objection for lack of novelty is not relevant. This is also in line with the findings of the opposition division as regards novelty (cf. page 17, point 9.3 of the decision under appeal).

34. Thus, the main request fulfils the requirements of Article 54 EPC.

Article 56 EPC

35. The opposition division considered that both, documents (1) and (3), could be used as closest prior art. Both documents are cited by the appellants in the appeal proceedings as appropriate closest prior art. Two of the five inventors cited in document (1) are authors of document (3); document (1) was filed in February 1997 and document (3) was published in May 2001, the latter document follows the teachings, and uses the method and products, disclosed in the former document. As an aside, documents (1) and (2) are based on the same International patent application (WO 97/31125); document (2) is cited in the patent and,

together with document (3), acknowledged as relevant prior art.

36. This prior art is described in the patent under the heading "Background of the invention" and summarised by the opposition division in the decision under appeal as disclosing "sequences, primers and oligonucleotides of MREJ types i, ii and iii"; wherein the technical difference between this prior art and the claimed subject-matter was identified as "the sequence of a different MREJ type, MREJ type vii ... as well as oligonucleotides and primer pairs derived from said sequences, which are specific for said new MREJ type" (cf. page 21, point 10.3 of the decision under appeal). The appellants addressed this prior art in their submissions in appeal and there is agreement on its relevance.

37. Starting therefrom, the objective technical problem may be formulated in the terms used by the opposition division, namely "the provision of nucleic acid sequences for the detection of a new (further) MREJ type MRSA strain". It is not contested that this problem is solved by the claimed subject-matter (cf. paragraph bridging pages 21 and 22, and first full paragraph on page 22 of the decision under appeal).

38. It is thus to be assessed whether this solution was obvious to the skilled person in light of the prior art and whether there was a reasonable expectation of success (cf. "Case Law", *supra*, I.D.2, 176, and I.D.7, 200).

39. The three MRSA strains used for the determination of the sequences disclosed in document (1) are identified as "representative examples of epidemic strains

isolated in various countries of the world" (cf. page 4, lines 28 to 35). Document (1) acknowledges that "[t]here are at least three types of *mec* DNAs in MRSA strains" (cf. page 5, line 25) and that "the structures of *mec* region DNAs are however diverse. It is therefore necessary to adequately perform designing of effective primers based on the concept and procedures disclosed in the present invention after determination of the structure and nucleotide sequence of each *mec* with respect to epidemic MRSA strains spread over the world" (cf. page 10, lines 39 to 42). Likewise, document (3) concludes that "[a]t least three distinct members make up the [SCC*mec*] family ... Exploration of staphylococcal genomes of more strains will find more diversified members of SCC*mec* ..." (cf. page 1335, right-hand column, first full paragraph). There is thus a clear motivation in this prior art for a skilled person to look for, and characterise, more SCC*mec* members of MRSA strains and, in doing so, identify and characterise the MREJ types of these SCC*mec* members; remains thus to assess the skilled person's expectation of success.

40. Document (1) reports studies carried out with "28 epidemic MRSA strains in 18 countries, including Japan, of the world" and states that "positive results were obtained in **all** the tests" (emphasis by the board) (cf. page 6, lines 30 to 33). The primers based on the disclosed nucleotide sequences of the "*mec* region DNAs makes it possible to detect and identify **all** the MRSAs in various countries of the world" (emphasis by the board) (cf. page 16, lines 3 to 8); the 24 epidemic MRSA strains from 14 countries used in these studies are shown in Table 5 of document (1). Document (3) discloses the results of the studies carried out four years later using 38 epidemic MRSA strains isolated in

20 countries, including the MRSA strains: NCTC 10442, N315 and 85/3907, identified in document (1) as "representative examples of epidemic strains", and which have the MREJ types i, ii and iii, respectively (cf. page 4, lines 28 to 35 of document (1); page 1324, Table 1 of document (3)).

41. According to document (3), MREJ typing is a quick SCC*mec* typing method that takes advantage of the polymorphism among the three types of SCC*mec* in the right extremity. The location of the mR2 and mN16 primers - within the structures of the three types of SCC*mec* elements - used for MREJ typing is shown in Figure 1 of document (3) (cf. page 1331, left-hand column to page 1332, line 2 of the left-hand column). Except for the MRSA strain 85/5328, all other MRSA strains shown in Table 1 of document (3) have one of the three MREJ types of the three representative epidemic MRSA strains of document (1) and, although most strains have the same SCC*mec* type (I to II) and associated MREJ type (i to iii), this is not always the case (strain 93/H44 with a SCCmec type III and an associated MREJ type i) (cf. page 1332, left-hand column, lines 2 to 7 of document (3)).

42. These results are in line with those reported in document (4), a document published in 1996 which explains the advantages of MREJ typing (cf. page 122, left-hand column, first paragraph) and already identifies the MRSA strain 85/5328 as non-MREJ typable (cf. page 124, Figure 4). However, whilst document (3) provides no explanation as to why this MRSA strain is not MREJ typable, document (4) refers to a spontaneous deletion of "the right junction point" as a possible reason for this strain not being MREJ typable (cf. page 124, last sentence in the footnote of Figure 4).

Thus, document (4) neither hints at, nor provides any expectation of the existence of a MREJ type different from the three MREJ types known from documents (1)/(3). Rather, document (4) informs the skilled person of the presence of MRSA strains with no MREJ type at all. Although the MRSA strain 85/5328 was available for at least five years (1996 - 2001) to the inventors/authors of documents (1)/(3), the skilled persons with a large - if not the largest - technical experience in the relevant field, the information in document (3) on the MREJ type of the MRSA strain 85/5328 is no better than that provided in document (4), notwithstanding the explicit indication in document (3) to look for and characterise further SCC*mec* members.

43. Document (7) reports on studies which, as in document (3), concern the structural variability of the SCC*mec* in general. However, contrary to document (3), document (7) does not provide any information on MREJ typing, let alone on any specific MREJ type. Figure 1 shows the basic structures of the SCC*mec* types I, II and III described in document (3) as well as that of the SCC*mec* type IV and SCC*mec* types IA and IIIA variants; the chromosomal right junction (RJ) of all these SCC*mec* elements is adjacent to the *orfX* gene. There is however no information on the MREJ types of any of these SCC*mec* variants or the SCC*mec* type IV. Reference is also made to the detection of SCC*mec* type I and III variants and, as regards type III variants, document (7) states that "[t]he downstream vicinity of *mec*A showed variations in several strains belonging to this genetic background" (cf. page 355, left-hand column, fourth paragraph). However, there is again no information as to whether these variations extend to the vicinity of the chromosomal right junction, within the sequence of the right junction,

and/or further to the *orfX* gene. Table 3 provides more information on these SCC*mec* type III variants but there is neither an explicit reference to, nor detailed information on, the sequence of the chromosomal right junction. In the absence of this information, this disclosure cannot have any effect on the skilled person's expectations.

44. Likewise, document (7), as regards the SCC*mec* type I variants, refers to the MRSA strain BK793 as having "an insertion of at least 8 kb ... identified during the hybridization screening between the end of *dcs* and *orfX*. I-PCR and sequencing of the flanking regions of these insertions showed no homology to any sequences available in databanks" (cf. page 355, left-hand column, third paragraph). However, there is no information on the localization of the 8 kb insertion and/or whether this insertion results in a modification of the sequence of the chromosomal right junction and in a new MREJ type. On page 352, it is stated that "[i]solates in which variability was found were selected for further characterization by l-PCR or cloning followed by nucleotide sequencing" (cf. sentence bridging left and right-hand columns on page 352); the protocol for long-range PCR (l-PCR) is given on the same page (cf. page 352, left-hand column, second paragraph). It is common general knowledge that long-range PCR amplifies large DNA fragments (more than 5 kb) and thus, the localization of the insertion in the MRSA strain BK793 is not directly derivable from the information disclosed in document (7), not even from Table 3 which refers only to a *dcs*::insertion but without any further indication.

45. Although SCC*mec* types are usually the same as the associated MREJ types, this is not always the case as

shown in document (3). Thus, it could not be assumed that the new SCC*mec* type IV and SCC*mec* variants disclosed in document (7) would necessarily contain a MREJ type variant of the known MREJ types i, ii or iii or a completely new MREJ type, let alone the MREJ type vii (see also Table 4 of document (9), wherein several SCC*mec* types and associated MREJ types of MRSA strains are indicated). Leaving aside the question whether or not it would be obvious for a skilled person to follow the guidance of document (7) and characterise the new SCC*mec* type and type variants - identifying thereby the associated MREJ types (cf. page 352, paragraph bridging left and right-hand column), the disclosure of document (7), as regards the expectations of the skilled person, does not go far beyond that of document (3).

46. It is only in document (9) that a new MREJ, namely MREJ type iv, is identified in the MRSA strain HDG2 (cf. page 1882, left-hand column, first paragraph), a MRSA strain identified in document (7) as having a SCC*mec* type IIIB variant structure (cf. page 356, last line in Table 3 of document (7)). Indeed, document (9) states that, based on the concept and method described in documents (3) and (4), new MREJ types iv, v and vii were identified and characterised in 15 out of the 206 MRSA strains studied (cf. page 1882, left-hand column, first paragraph; see page 1881, Table 4). These results were obtained by developing a multiplex PCR assay with the design of a set of specific primers to the various SCC*mec* right extremity sequences and a primer specific to *S. aureus orfX* (cf. page 1876, left-hand column, sixth paragraph under the heading "Primers and probes"; and page 1882, left-hand column, first paragraph). However, document (9) is a post-published document and thus, not relevant for assessing the expectations of

the skilled person at the relevant date. These expectations must be derived from the prior art availab le at the relevant date and thus, in the present case, from the prior art documents (3), (4) and (7). As seen from the considerations above, the skilled person could not have derived any reasonable expectations of success from any of these prior art documents.

47. In fact, with reference to post-published documents (9) and (55) and to the prior art document (6), the objection of lack of inventive step relies not only on the alleged skilled person's expectations of success but also on the availability at the relevant date of the MRSA strain from which the claimed MREJ type vii (SEQ ID NO: 166) was isolated. The board however is not convinced by this argument either.

47.1 Document (9) informs the reader that the MRSA strains CMRSA-1 and CCRI-9583 have a SCC*mec* type II structure and an associated MREJ type vii (cf. page 1881, Table 4), and that the MREJ sequences of these strains have the GenBank accession numbers AY267375 and AY267384 (cf. page 1878, left-hand column). The MREJ sequence of the MRSA strain CMRSA-1 is identical to sequence SEQ ID NO: 166 (see document (54)). Indeed, Table 4 of the parent application shows that sequences SEQ ID NO: 165 and 166 were isolated from the MRSA strains CCRI-9583 and CCRI-9589, and the MRSA strain CCRI-9589 is identified on page 47, lines 6 and 7 of the parent application as "the highly epidemic MRSA Canadian clone CMRSA1". Table 3 of the parent application refers to these MRSA strains and in the footnote (c) identifies the MRSA strain CCRI-9589 with "Canadian clone EMRSA1" which, in light of the above reference in the description of the parent application, is understood to be the MRSA strain CMRSA-1.

47.2 The MRSA strain CMRSA-1 is identified as a Canadian epidemic MRSA in Table 1 of document (9) with reference to the bibliographic reference 47, document (55) in these proceedings (cf. page 1878, left-hand column, first paragraph; page 1877, Table 1, right-hand column, last paragraph, of document (9)). In document (55), the MRSA strain CMRSA-1 is also identified as the most prevalent clonal type in Canadian hospitals and it is stated that this strain, together with three other MRSA strains (CMRSA-2 to CMRSA-4), was previously described in bibliographic reference 24, document (6) in these proceedings (cf. page 652, abstract; page 654, left-hand column, first paragraph, of document (55)).

47.3 Document (6) was published in 1999 and refers to the MRSA strain CMRSA-1 as the "Ontario epidemic strain" because it was the "most widely found in the province of Ontario", although it was also sporadically isolated in other Canadian provinces and in the United States and European countries (cf. paragraph bridging pages 334 and 335). Document (6) states that the MRSA strains CMRSA-1 to CMRSA-4 were available upon request (cf. page 334, right-hand column, second paragraph). Thus, the MRSA strain CMRSA-1 (CCRI-9589) with a MREJ type vii sequence identical to sequence SEQ ID NO: 166 was available to a skilled person at the relevant date.

47.4 The skilled person could thus have taken the MRSA strain CMRSA-1, identified and isolated the SCC*mec* structure and associated MREJ sequence and characterise thereby the MREJ type of this strain, namely the MREJ type vii of sequence SEQ ID NO:166. However, according to the established case law, the relevant question is not whether it **could** have been done but whether it **would** have been done (cf. "Case Law", *supra*, I.D.5,

197). Thus, in the present case, the question is whether the skilled person would have selected the MRSA strain CMRSA-1 from among all other epidemic MRSA strains available worldwide, thereby disregarding all other MRSA strains for which the SCC*mec* structure had already been fully or partially characterised but not the associated MREJ sequence, such as those described in the prior documents (3) and (4) and, in particular in document (7), and whether the skilled person would have further developed an appropriate multiplex PCR assay and designed suitable specific primers such as those disclosed in document (9). In the absence of any hint or suggestion in the prior art, in particular in the closest prior art documents (1)/(3), that would have led the skilled person to the MRSA strain CMRSA-1, the board considers that the above question can only be answered in the negative. In the absence of such a hint or suggestion, hindsight knowledge of the patent was required for arriving at the claimed subject-matter.

48. Thus, the board sees no reason to deviate from the findings of the opposition division as regards Article 56 EPC and therefore, the main request fulfils the requirements of this article.

Order

For these reasons it is decided that:

The appeals are dismissed.

The Registrar: The Chairman:

L. Malécot-Grob B. Stolz

Decision electronically authenticated