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Datasheet for the decision of 4 November 2014

Case Number: T 0967/09 - 3.3.04

Application Number: 98201056.3

Publication Number: 0870508

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Language of the proceedings: EN

Title of invention:
Influenza vaccine

Patent Proprietor:
Abbott Biologicals B.V.

Opponents:
Sanofi Pasteur
GlaxoSmithKline Biologicals S.A.

Headword:
Influenza vaccines/ABBOTT BIOLOGICALS

Relevant legal provisions:
EPC Art. 83

Keyword:
Main request and auxiliary request - sufficiency of disclosure (no)

Decisions cited:
T 0182/89, T 0019/90, T 0890/02, T 0327/04

Catchword:

-

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Case Number: T 0967/09 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 4 November 2014

Appellant: (Patent Proprietor)	Abbott Biologicals B.V. C.J. van Houtenlaan 36 1381 CP Weesp (NL)
Representative:	Oser, Andreas Prüfer & Partner GbR Patentanwälte Sohnckestrasse 12 81479 München (DE)
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Representative:	Ayroles, Marie-Pauline Sanofi Pasteur Direction Propriété Intellectuelle 2, avenue Pont Pasteur 69367 Lyon cedex 07 (FR)
Respondent III: (Opponent 03)	GlaxoSmithKline Biologicals S.A. 89 Rue de l'Institut B-1330 Rixensart (BE)
Representative:	Elmhirst, Elizabeth Lucy GlaxoSmithKline Global Patents (CN925.1) 980 Great West Road Brentford, Middlesex TW8 9GS (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 13 February**

2009 revoking European patent No. 0870508 pursuant to Article 101(3)(b) EPC.

Composition of the Board:

Chairwoman	G. Alt
Members:	B. Claes
	K. Garnett

Summary of Facts and Submissions

I. The current appeal lies from the decision of the opposition division dated 18 December 2008 to revoke the European patent No. 0 870 508, having the title "*Influenza vaccine*", and which had been granted for European patent application 98201056.3.

II. Independent claims 1 and 3 as granted read:

"1. Influenza surface antigen vaccine from Influenza Viruses propagated on animal cell culture obtainable by the method of claim 3 and having a host cell DNA content equal to or less than 25 pg per dose.

3. Method for the preparation of surface antigen proteins from Influenza Viruses propagated on an animal cell culture comprising the subsequent steps of:
a. treatment of the whole virus containing fluid obtained from the cell culture with a DNA digesting enzyme, and
b. adding a cationic detergent,
followed by isolation of the surface antigen proteins."

Claim 2 was dependent on claim 1 and claims 4 to 9 were dependent on claim 3.

III. This is the second appeal originating from European patent No. 0 870 508. The patent as granted was revoked a first time by the opposition division in a decision dated 3 June 2003 for the reason that the subject-matter of claims 1 and 3 as granted (sole request) lacked an inventive step (Article 56 EPC). Subsequent appeal proceedings before this board, albeit in a different composition, resulted in the decision T 327/04 of 15 December 2005. In this decision the

board overruled the decision of the opposition division and found the subject-matter of the claims as granted to comply with the requirements of novelty (Article 54 EPC) and inventive step (Article 56 EPC). The decision then under appeal did not deal with the invoked ground for opposition under Article 100(b) EPC. The board remitted the case to the opposition division for further prosecution, in particular for the examination of the requirements of sufficiency of disclosure (Article 83 EPC).

IV. Subsequently, the opposition division revoked the patent anew by its decision dated 18 December 2008, *i.e.* the decision which is the subject of the present appeal. The opposition division held that the patent as granted (sole request) did not disclose the invention in a manner sufficiently clear and complete for it to be carried out by the person skilled in the art (Article 83 EPC). In coming to this conclusion the opposition division took into account test reports relating to the DNA measurement, the slot-blot analysis and the reproducibility of an example of the patent as filed by one of the respondents (opponent 03, document (D62), see below) during the first appeal proceedings (see decision T 327/04, *supra*, section VI).

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

D6: Brands *et al.* (1996), In "*Options for the control of influenza III*", Brown, *et al.* (Eds.), pages 683- 693.

D62: Experimental test report submitted by the appellant and dated 3 June 2004.

D75: Declaration: Statement by Dr. Alexander Pasternak dated 15 June 2009.

D76: The European Agency for the Evaluation of Medicinal Products (Human Medicines Evaluation Unit), Document CPMP/ICH/381/95 (Note for guidance on validation of analytical methods: definitions and terminology).

D77: Second declaration of Dr Benoit Champluvier dated 30 October 2009.

D78: Declaration of Dr Frédéric Schynts dated 3 November 2009

VI. With its statement of the grounds of appeal, the appellant filed two further documents (D75) and (D76), the former being a declaration.

VII. With its reply to the appeal, respondent III (opponent 03) submitted two declarations (documents (D77) and (D78), comprising a number of annexes) reporting on further experimental results when repeating example 1 of the patent in suit.

VIII. Respondent II (opponent 02) replied likewise to the appeal and submitted a number of further documents and a further declaration.

IX. In a response to the submissions of the respondents, the appellant filed three further documents and a further declaration. Subsequently, after having been summoned to oral proceedings, the appellant filed with a letter dated 6 August 2014 an auxiliary request

consisting of claims 1 to 7, being identical to claims 3 to 9 of the main request (patent as granted).

X. The oral proceedings, held on 4 November 2014, were attended by the appellant and respondent III. Respondent II was not represented at the oral proceedings, as had been previously announced in writing.

XI. The requests of the parties were:

The appellant requested that the decision under appeal be set aside and the patent be maintained as granted, alternatively on the basis of the auxiliary request filed with its letter of 6 August 2014.

The respondents requested that the appeal be dismissed.

XII. The appellant's arguments may be summarised as follows:

Main request - claim 1 - sufficiency of disclosure

It was sufficient for fulfilling the requirements of sufficiency of disclosure that a person skilled in the art was in a position to reproduce an example disclosed in the patent in suit and then to verify whether the value of the parameter obtained by such reproduction corresponded to the value of the parameter indicated in the specification of the patent in suit.

The patent specification as a whole contained sufficient information such that a skilled person, with the information provided in the patent in suit and supplemented with common general knowledge, was in a position to perform accurate measurements of the residual host cell DNA content. Moreover, many

documents on record demonstrated that a skilled person could also make accurate and reliable DNA measurements in the low picogram range without undue burden. At the relevant date of the patent in suit, slot blot (and dot blot) hybridisation was very common and widely applied by experts in the relevant field. General textbooks and practical manuals existed which provided clear and elaborate practical guidance on how to perform slot/dot blot DNA hybridisation analysis for DNA quantification.

Validation of an analytical assay was generally considered important, yet clearly understood requirement in the context of pharmaceutical preparations such as vaccines (see document (D76)).

The declaration of document (D75) demonstrated that all relevant technical knowledge was readily at the disposal of the skilled person to establish and accomplish an accurate DNA measurement. The patent did not hide any any critical know-how relevant to a quantification of residual DNA. Any allegedly missing information could be compensated by applying general technical knowledge and proceeding via proper validation, always accompanied by obvious and routine control experiments (specifically: negative controls, positive controls and optionally use of known amounts of "spiked" target DNA), all routine tests during validation being guided by known validation criteria (see document (D76)).

Claim 1 defined a ratio of residual host cell DNA relative to the vaccine dose, *i.e.* a ratio of DNA to a reference amount of influenza surface antigen (HA). This did however not mean that a single dose had to be tested and measured for residual DNA content, but that it could be measured in a multitude of dose

equivalents, suitably in the order of mg amounts of HA, and the then measured amount of DNA could be calculated to the amount of DNA per one dose. A skilled person therefore did not necessarily have to make undue efforts, in particular undue optimisation efforts, for detection of DNA close to the absolute detection limit of the analytical method.

Paragraph [0024] of the patent should be read with a mind willing to understand. The skilled person would immediately understand that the DNA probe should be a whole cell genomic probe since he would know that this provided the most adequate and precise results.

The experiments described in the declarations of documents (D77) and (D78) (a) were devoid of any "in-process" control data for the experiment, such as measuring the DNA content after each step (as in the table on page 4 of the patent in suit) (b) lacked any explicit indication that the virus incubation in the fermentor was stopped 48 hours after infection as in example 1 of the patent in suit and (c) did not indicate that the nuclease was added for another four hours of incubation. In view of these deficiencies the repeat of experiment 1 of the patent in suit as described in documents (D77) and (D78) did not establish any insufficiency of disclosure of the patent.

The slot blot hybridisation conducted to measure the host cell DNA in the product resulting from the repeat reported on in declarations (D77) and (D78) was not a "validated test" as required by the patent. The measured residual DNA values were therefore not meaningful. For example, the assay to measure the DNA described in documents (D77) and (D78) had a

sensitivity of 300 pg DNA only and was thus far too weak to have the capacity of reliably detecting a host cell DNA content of equal to or less than 25 pg. Therefore, the respondent had not convincingly shown that the claimed process could not yield a vaccine with a contaminating host cell level of equal or less than 25 pg.

Auxiliary request - claim 1

Claim construction

Claim 1 was not limited to a defined DNA content level and should not be interpreted to require a host cell DNA content of ≤ 25pg/dose. Claim 1 rather defined two particular process steps to be applied in a specific order in the course of the preparation of influenza surface antigen proteins based on an animal cell culture. The capacity of this method to achieve reduced residual host cell DNA contents, which the board in its decision T 327/04 considered to contribute to substantiating the presence of an inventive step, did not mean, either explicitly or implicitly, that the feature "≤ 25pg host cell DNA per dose" was a mandatory limitation.

Sufficiency of disclosure

It was sufficient that claim 1 defined the essential process features and their combination, which as a whole described the contribution of the claimed method over the prior art. The effect that the DNA/dose ratio could be reduced supported inventiveness but could not be turned into an argument against sufficiency of disclosure, because the 25 pg DNA was close to the detection limit.

XIII. The respondents' arguments may be summarised as follows:

Main request - claim 1 - sufficiency of disclosure

The declaration in documents (D77) and (D78) reported the results of a further experiment made in response to the impugned decision of the opposition division that "*the repetition of example 1 by Opponent III was not enough to question the sufficiency of disclosure of the patent*".

A significant amount of experimental information had to be supplemented by the declarants of document (D77) and (D78) in order to be able to carry out the experiment of Example 1, both in respect of virus/vaccine production and in respect of DNA measurement. However, where the patent gave information, it was followed. An exact following (as far as possible and complemented where appropriate with missing technical information) of the protocol given in example 1 led to a final DNA content of 25 ng per 50 µg HA as measured by slot blot technique. This was 1000 times higher than the limit given in the patent of 25 pg per 50 µg HA. The results clearly showed that not only did the example not lead to the claimed low levels of residual DNA but in fact led to levels very significantly far away from those claimed. Moreover, the further measurements by the Q-PCR method and the Treshold method rendered it likely that even the 25 ng figure was a significant underestimation.

The relevant question for assessing sufficiency of disclosure was not whether or not a specifically described example was exactly repeatable, but whether

the overall teaching of a patent in respect of a claimed embodiment could reliably lead the skilled person to put it into practice (decision T 923/92). The declarations clearly demonstrated this not to be the case.

The subject-matter of a claim might properly be defined by parameters provided that there was a clear description in the patent of the method to be used for their determination. Such a description could only be omitted where: (i) a person skilled in the art already knew which method to use, or (ii) all methods gave the same result. Thus, where slot blot hybridisation was the method to be used to measure residual host cell DNA content, a clear description of this method needed to be contained in the patent unless the skilled person already knew how to perform it or all ways of performing it gave the same result. Because it had been demonstrated that different protocols for measuring DNA amounts in a sample gave different results, it was necessary that the patent provided the skilled person with the details of the slot blot protocol used to determine this critical parameter. Furthermore, no standard protocol for slot blot existed in the art.

Validation guidelines (such as in document (D76)) provided details of how to validate, not how to hybridise. They were not hybridisation guidelines. A skilled person could not validate a protocol if he did not know what the protocol was.

For compliance with the requirement of sufficiency of disclosure the patent had to offer at least (a) a detailed hybridisation protocol and the criteria to be met for its validation and (b) a method for quantifying HA and the criteria for its validation. As none of this

important guidance was contained in the patent in suit the person skilled in the technical field of analytical sciences was not in a position to validly repeat the measurements made by the patentee.

The common general knowledge of the person skilled in the art was not sufficient to enable him set up a slot blot hybridisation protocol for quantifying residual DNA. Moreover, there was no reason why the skilled person should inevitably understand that the probe referred to in paragraph [0024] of the patent (canine DNA probe) referred exclusively to a "total genomic MDCK DNA probe". Accordingly, the skilled person was not in a position to make a reliable measurement of the residual DNA without undue burden. The subject-matter of claim 1 was therefore insufficiently described.

Auxiliary request - claim 1

Claim construction

In point 24 of the reasons for the decision in T 327/04 the board had made it clear that a critical feature of the process of claim 1 (then claim 3) was its capacity to yield a vaccine with a contaminating host cell DNA level of ≤25 pg /dose. In the decision concluding that the subject matter of claim 1 was inventive, the assumption was accordingly taken by the board that this critical feature was met.

Sufficiency of disclosure

Because the board in its earlier decision T 327/04 had decided that the claimed subject-matter involved an inventive step, it had to fail for insufficiency of disclosure.

In the context of sufficiency of disclosure in relation to the subject-matter of claim 1 of the main request it had convincingly been shown that the method of claim 1, when following the protocol of example 1 of the patent in suit, did not result in a vaccine with a contaminating host cell DNA level of ≤25 pg /dose. Therefore, the considerations on sufficiency of disclosure in relation to the subject-matter of claim 1 applied *mutatis mutandis* to the patent in suit in relation to the subject-matter of claim 1.

Reasons for the Decision

1. The appeal is admissible.

2. As none of the parties have objected to any documents, declarations or claim requests newly filed during these appeal proceedings, the board sees no reason not to admit any of them into the proceedings.

3. The sole remaining ground for opposition to be dealt with in these appeal proceedings is whether or not the patent discloses the invention as defined in the two independent claims in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art (Article 100(b) EPC).

Main request - claim 1 - sufficiency of disclosure

4. In the decision under appeal the opposition division considered two points to be of relevance for coming to its decision that the patent insufficiently disclosed the invention: (i) the (non-)reproducibility of an example of the patent in suit and (ii) the measurement of the residual host cell DNA content.

4.1 Concerning point (i), the opposition division decided in favour of the patent proprietor. Indeed, the experiments described in test reports relating to the reproducibility of an example of the patent as filed by one of the respondents (opponent 03) during the first appeal proceedings differed in a number of steps from the procedure as described in the patent. In view of the doubts about the effect of these changes to the procedure described in the example of the patent and the fact that these changes were not justified by experimental evidence or facts of general knowledge, the opposition division considered that the burden of proof for demonstrating that the invention was not reproducible had not been discharged by the opposing party.

4.2 Concerning point (ii), however, the opposition division decided in favour of the opponents and consequently revoked the patent. The opposition division derived from decision T 327/04, *supra*, the requirement that the feature "host cell DNA content ≤25 pg/dose" was relevant for both claim 1 and claim 3. Accordingly, it was of critical significance for both claims that the patent in suit sufficiently disclosed a DNA measurement method for an influenza antigen vaccine which allowed reliable detection of a host cell DNA level ≤25pg/dose. This was not the case in the patent in suit as the mere mention of a "*validated*" method in paragraph [0024] was not regarded as a sufficient disclosure.

5. During the present appeal proceedings, respondent III submitted two declarations, documents (D77) and (D78), comprising one and two annexes respectively, which report on experiments designed to repeat the experiment described in Example 1 of the patent in suit, *i.e.*

which lead to the production of "Purified Bulk MaP157" comprising less than 25 **pg** of host cell DNA per 50 µg HA as measured by slot blot hybridisation (see paragraphs [0021] to [0024] of the patent in suit). The declarant of document (D77) stated that the results of repeating Example 1 of the patent in suit demonstrated that Example 1 (see table 1 of Annex 1 to the declaration) yielded a purified bulk containing 25 **ng** for a dose of 50 µg HA, with the DNA residuals being measured by a slot blot hybridisation method, *i.e.* approximately 1000 times higher than that required by claim 1. The declarant of document (D78) confirmed the results of repeating the example, and described in Annex 2 the experimental details of the applied slot blot hybridisation method to measure the residual host DNA content. In Annex 3 the declarant presented results of residual host cell DNA measurements in the same purified bulk as used for the slot blot measurement when the DNA was measured by a Q-PCR and Treshold™ assay. The results of these measurements were a magnitude of 10 times higher than the result of the measurement by slot blot hybridisation.

6. A successful objection of lack of sufficiency of disclosure presupposes that there are serious doubts, substantiated by verifiable facts (see e.g. decision T 19/90, OJ EPO 1990, 476 and decision T 890/02, OJ EPO, 497). In order to establish insufficiency of disclosure in *inter partes* proceedings, the burden of proof is upon an opponent to establish, on the balance of probabilities, that a skilled person reading the patent, using his common general knowledge, would be unable to carry out the invention (see decision T 182/89, OJ EPO 1991, 391).

7. The board considers that the results of repeating the experiment of Example 1 of the patent in suit, as described in documents (D77) and (D78) and summarised in point 5, above, sheds at least serious doubts on the reproducibility of the invention as defined in claim 1.

8. Despite two further written submissions by the appellant, it was not until the oral proceedings that the appellant contested the experimental design and conduct of repetition of example 1 of the patent in suit as reported on in documents (D77) and (D78).

8.1 The appellant submitted in particular that (a) the experiments described in the declarations were devoid of any "in-process" control data for the experiment (*i.e.* of the measurement of the DNA content after each step as in the table on page 4 of the patent in suit), (b) there was no explicit indication in the declarations that the virus incubation in the fermentor was stopped 48 hours after infection as in example 1 of the patent in suit and (c) it was not indicated that the nuclease was added during another four hours of incubation.

8.2 The board notes in this respect first of all that declaration (D77) states that "*I have designed and overseen the second GSK experiment (see Annex 1) which was designed to compare the results obtained after a repeat of the experiment described in Example 1 of the Patent*" (point 3 of the declaration, emphasis added by the board) and that "*following Example 1 of the patent yielded a purified bulk containing 25ng for a dose of 50µg of HA with the DNA residuals measured by slot blot hybridisation*" (point 4 of the declaration, emphasis added by the board). The appellant furthermore indicated when submitting the two declarations (see

section V, above) that in order to repeat the example "*a significant amount of experimental information had to be supplemented by* [the two declarants] *in order to be able to carry out the experiment, both in respect of virus/vaccine production and in respect of DNA measurement. However, where the patent did give information, it was followed*" (Underlining by the board). In the opinion of the board, the mere fact that the declarations do not provide an explicit time indication for the virus incubation (48 hrs) and nuclease treatment (4 hrs) and do not explicitly reproduce "in-process" DNA control measurements does not bring into doubt the statement that the experiment was followed, at least to the extent of the technical detail contained in the patent. In respect of the virus incubation time, the nuclease treatment period and the "in-process" control, this technical detail is uncontestedly contained in the patent.

8.3 In this context the board also notes that in the experimental test report contained in document (D62), which the appellant had submitted during the first appeal proceedings before this board and which had been considered by the opposition division in the impugned decision, there was no explicit indication of "in-process" DNA control measurements nor any indication that the nuclease was added during another four hours of incubation in study 1.

8.4 The board notes furthermore that the alleged deficiencies highlighted by the appellant do not qualify as a criticism of the procedures followed by the declarants when repeating the experiment of example 1, but merely question the credibility of the statements of the declarants as referred to in point 8.2, above, that the example was properly

reproduced. In this respect, however, the appellant has not submitted any evidence to support its allegations of lack of credibility.

8.5 In view of the above considerations the board has no reason to doubt that the virus/vaccine production method followed by the declarants was the method as disclosed in Experiment 1 of the patent in suit in as far as it goes, supplemented where necessary with common general knowledge of the skilled person.

9. Another line of argument of the appellant related to the method for the measurement of the residual host cell DNA in the purified bulk resulting from the repetition of Example 1 of the patent as described by the declarants in document (D77) and (D78).

9.1 Paragraph [0024] of the patent, when referring to the purification method of Example 1, states that "[t]*roughout the above process the host cell DNA content of samples was analysed according to a validated test based on slot blot hybridisation using a 32 P-labelled canine DNA probe*". In this respect the appellant argued that the slot blot hybridisation conducted to measure the host cell DNA in the product resulting from the repetition reported on in declarations (D77) and (D78) was not a "*validated test*" as required by the patent. The measured residual DNA values were therefore not meaningful.

9.2 The board notes in this respect that claim 1 does not recite the measurement method to be used for establishing compliance to a residual host cell DNA content of equal or less than 25 pg per dose of vaccine. In paragraph [0024]) of the patent in suit it is merely stated that "*a validated test based on slot*

blot hybridisation" was used. Therefore, in the board's opinion, it is not obligatory that the residual host cell DNA is measured by the method used by the appellant. The board considers that any residual host cell DNA measurement method as accepted by a skilled person to comply with the conventional standards of controlled scientific experimental conduct is suitable.

9.3 The amount of residual DNA measured by the declarants in the purified bulk was measured by slot blot hybridisation and calculated to be 25 ng per dose having 50 µg of HA, *i.e.* being approximately 1000 times higher than that required by claim 1. As can be taken from the technical detail contained in Annex 2 of the declaration in document (D78), in particular the autoradiography exposure results on page 5, the actual measured result was a clearly visible slot of ca. 2 ng of MDCK DNA contained in 300 µl of purified bulk. No signal was visible on the exposure when 30 µl or 3 µl of purified bulk was added to the slot. The amount of HA present in the purified bulk of the repeat was 12 µg/ml. These calculations have not been disputed by the appellant. The declarants included in the read of the residual host cell DNA a number of control results (see the autoradiography and its legend on page 5 of annex 2), namely: (i) a number of control slots corresponding to *inter alia* 10, 3, 1 ng of MDCK DNA establishing a sensitivity curve around the measured amount (in addition control slots corresponding to 300, 100, 50 and 25 pg of MDCK DNA were added which, however, reveal no signal, hence the statement of the appellant that the sensitivity of the conducted slot blot assay was merely 300 pg of host cell DNA); (ii) a number of slots in which the same amount of purified bulk was spiked with 6 ng of genomic MDCK DNA in order to evaluate a possible inhibition due to the matrix; and (iii)

negative controls containing no MDCK genomic DNA. The board considers that the experimental design for the slot blot measurement of the residual MDCK genomic DNA in the purified bulk including the various control readings complies with the conventional standard of controlled scientific experimental conduct. Indeed, the experiment established a sensitivity curve around the value to be measured and included positive as well as negative controls.

9.4 The board notes furthermore that declaration in document (D78) did not stop short with the measurement by slot blot hybridisation (by which the residual host cell DNA in the purified bulk was measured and calculated to be 25 ng per dose, being approximately 1000 times higher than required by claim 1). In addition to this measurement, the declarant also quantified and calculated the MDCK genomic DNA content of the purified bulk sample by two further DNA quantification techniques, *i.e.* the so-called Q-PCR method and Treshold method. The results of the measurements by these methods, along with these of the quantification by means of slot blot hybridisation, are reproduced on page 8 of Annex 3 to declaration (D78) and are in fact now 10 times higher per dose of vaccine than that measured by the dot blot method. In the opinion of the board they tend to confirm the results of the slot blot hybridisation measurement, which were themselves 1000 times higher than required by claim 1.

10. On the basis of the above, the board considers that the arguments as submitted by the appellant are not convincing.

11. In summary, the board is satisfied that respondent III has substantiated, by means of verifiable facts,

serious doubts that the patent does not disclose the invention as defined in claim 1 in a manner sufficiently clear and complete for it to be carried our by the skilled person. These doubts are considered not to be convincingly rebutted by the appellant. Accordingly, the board considers that respondent III has discharged its burden of proof in this respect. The board therefore concludes that the patent, in respect of the subject-matter of claim 1, lacks sufficiency of disclosure (Article 100(b) EPC).

Auxiliary request 1 - claim 1

Claim construction

12. Sufficiency of disclosure requires that the teaching of the application (Article 83 EPC) or the patent (Article 100(b) EPC) enables the skilled person to carry out the (whole) subject-matter of a claim without undue burden. The disclosure of a patent application or patent is aimed at the skilled person. It is an accepted principle in patent law that the same skilled person with the same level of skill has to be considered when, for the same invention, the two questions of sufficiency of disclosure and inventive step are being considered (see Case Law of the Boards of Appeal of the EPO, II.C.3.1). It is also the same skilled person that has to be considered when construing the subject-matter of a claim. It accordingly follows that the construction of a particular claim should be identical for the assessment of inventive step and sufficiency of disclosure.

13. The board, in its decision T 327/04 (*supra*, see points 21 to 41 of the reasons) came to the conclusion that the subject-matter of claim 3 as granted (identical to

claim 1) involved an inventive step. In its assessment of inventive step in relation to the subject-matter of this claim, the board made a number of statements reflecting the claim construction it considered applicable.

13.1 When assessing which document represented the closest prior art, the board stated in point 24 of the reasons:

"*Two* ***critical features of the process of present claim 3 are*** *inter alia (i)* ***its capacity to yield a vaccine with a contaminating host cell DNA level ≤25 pg/dose*** *(see claim 1), (ii) the propagation of the virus on animal cells. The board observes that only document D6 simultaneously deals with features (i) and (ii) above,* [...] *the board concludes that document D6 represents the closest prior art*." (Emphasis added by the board).

13.2 The board formulated the objective problem to be solved in point 25 of the reasons:

"*The objective problem to be solved departing from the disclosure of document D6 is seen in the provision of an improved method for the preparation of influenza surface antigen proteins in order to obtain a vaccine which has reduced host-cell DNA content*."

13.3 In point 27 of the reasons the board then confirms that this problem is solved by the patent when it states:

"*The results in the Table on page 4 of the patent in suit and the additional test report D62 provided by the appellant show that the above problem has indeed been solved. Document D62 even shows that if steps (a) and (b) occur simultaneously, no advantageous effect turns*

up (see Table 1, column 3: "1000 pg DNA/mg proteins" ~ 50 pg DNA/50 µg proteins)."

13.4 When subsequently assessing the inventive step of the proposed solution the board states in point 30 of the reasons that:

"*The relevant question to be answered by the board is whether it was obvious or not to modify the process described in document D6 by adding a nuclease and a solubilisation step with a cationic detergent (with the nuclease added before the detergent)* ***in the expectation of*** *solving the problem referred to under point 26 supra and* ***obtaining the advantageous effect highlighted under point 27 supra.***" (Emphasis added by the board).

13.5 Later the board summarises its findings in point 36 of the reasons that:

"*In summary, while the use of DNA digesting enzymes for lowering the DNA content was disclosed in several documents, it was in situations which were prima facie basically different from that of the preparation of an influenza virus sub-unit vaccine. Therefore,* ***it could not be foreseen that applying the methods described in these documents would achieve a ratio ≤ 25 pg residual DNA/50 µg HA,*** *a ratio which is linked to the specific degree of "stickiness" of the residual DNA to the HA and neuraminidase glycoproteins.*" (Emphasis added by the board).

14. This board derives from the above analysis of the reasons for the decision in decision T 327/04, *supra*, that the board in the first appeal acknowledged an inventive step as regards the subject-matter of claim 1 because it represented an improvement over disclosure

of document (D6) in terms of residual DNA (*i.e.* 50 pg per dose) and that it construed the then claim 3 as pertaining to a method for the production and isolation of surface antigen proteins from Influenza Viruses, whereby the surface antigen proteins isolate as a host cell DNA content of less than ≤ 25 pg / 50 µg HA.

15. The board considers that it must accept and apply the analysis of claim 3 of the patent as granted given by the board in decision T 327/04, *supra*, when assessing inventive step also for the assessment of the requirement of sufficiency of disclosure. Indeed, deviating from this previous construction would divorce any of the findings of this board in relation to sufficiency of disclosure of the invention in this claim from these findings of the board in decision T 327/04, *supra.*

16. Accordingly, for the requirement of sufficiency of disclosure to be satisfied in relation to the subject-matter of claim 1, the patent should disclose a method which achieves a residual DNA content of less than 50 pg per dose.

17. In point 11 above the board has come to the conclusion that the patent lacks sufficiency of disclosure in relation to the subject-matter of claim 1 of the main request. The board considers that, when applying the the construction of claim 1 as referred to in point 16, above, the same considerations as for claim 1 of the main request apply *mutatis mutandis* for the subject-matter of claim 1.

18. Accordingly, the board concludes that the patent in suit does not sufficiently disclose the invention in

respect of the subject-matter of claim 1 of the present request (Article 100(b) EPC).

Conclusion

19. Since neither of the appellant's requests is allowable, the appeal must be dismissed.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

P. Cremona G. Alt

Decision electronically authenticated