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**Datasheet for the decision
of 23 September 2021**

Case Number: T 3037/19 - 3 March 2004

Application Number: 08834150.8

Publication Number: 2202245

IPC: C07K16/28, A61K39/395,
A61P43/00, C07K16/46, C12N1/15,
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C12N15/09, C12P21/02

Language of the proceedings: EN

Title of invention:
Method of modifying isoelectric point of antibody via amino
acid substitution in CDR

Patent Proprietor:
Chugai Seiyaku Kabushiki Kaisha

Opponents:
Murphy, Colm Damien
CMS Cameron McKenna Nabarro Olswang LLP

Headword:
Isoelectric point modification of antibody/CHUGAI

Relevant legal provisions:
EPC Art. 84

Keyword:

Claims - clarity (no)

Decisions cited:

T 0762/90, T 0623/91, T 0923/92, T 0525/99, T 0398/01

Catchword:

-



Beschwerdekammern

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Case Number: T 3037/19 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 23 September 2021

Appellant:

(Patent Proprietor)

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Decision under appeal:

**Decision of the Opposition Division of the
European Patent Office posted on 5 September
2019 revoking European patent No. 2202245
pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chair

B. Claes

Members:

B. Rutz

P. de Heij

Summary of Facts and Submissions

- I. The patent proprietor (appellant) lodged an appeal against the opposition division's decision to revoke European patent No. 2 202 245 (hereinafter "the patent"). The patent is entitled "*Method of modifying isoelectric point of antibody via amino acid substitution in CDR*".
- II. The opposition division found, *inter alia*, that the claims of auxiliary requests 1 to 17 (all filed on 24 May 2019) were not clear (Article 84 EPC) because the term "GENETYX" did not have a precise meaning.
- III. With the statement of grounds of appeal, the appellant filed sets of claims of a main request (identical to auxiliary request 1 subject to the decision under appeal) and of auxiliary requests 1 to 11 (identical to auxiliary requests 7 to 17 subject to the decision under appeal). The appellant also filed a new document designated D31.

Claim 1 of the main request reads:

"1. A method for controlling the plasma pharmacokinetics of an IgG antibody while retaining the antigen-binding activity of the variable region, which method comprises modifying the theoretical isoelectric point of the antibody by 1.0 or more, when determined using the gene and amino acid sequence analysis software GENETYX, by a method comprising modifying the charge of at least one exposable amino acid residue on the surface of a complementarity determining region (CDR) of the antibody, wherein the exposable amino acid residue on the surface of the CDR region is at least

one amino acid residue selected from amino acid residues at positions 31, 61, 62, 64, and 65 in the heavy chain variable region and positions 24, 27, 53, 54, and 55 in the light chain variable region according to Kabat's numbering system, wherein the charge of the amino acid residue(s) is modified by amino acid substitution."

Claim 1 of each of auxiliary requests 1 to 11 contains the feature "software GENETYX".

- IV. Both opponents (respondents) replied to the appeal and submitted additional documents (designated D32 to D34 and Annexes 1 to 3, the latter having been referred to by the appellant as D35 to D37).
- V. The board summoned the parties to oral proceedings as requested and informed them of its preliminary opinion in a communication pursuant to Article 15(1) RPBA.
- VI. Subsequently opponent 1 withdrew its opposition and ceased to be a party to the proceedings.
- VII. Oral proceedings before the board were held by videoconference. At the end of the oral proceedings, the Chair announced the board's decision.
- VIII. The following documents are cited in this decision:

D25	Declaration by Mr Taichi Kuramochi
D29	GENETYX - JP Trade Mark Registration
D30	Exhibit re opposition against EP 2 202 245 B1

D31 Declaration by Mr Shigehisa Yatsuda

D34 GENETYX[®] user manual version 15

IX. The appellant's arguments on clarity (Article 84 EPC) are summarised as follows.

The case law established that "*the question whether trade designations are allowable in the wording of a claim is a question of fact that can only be answered on a case by case basis*" (see e.g. decisions T 525/99, point 3.1, and T 762/90, point 4.1.2). Therefore, the facts (or evidence) needed to be evaluated in each individual case.

The term "GENETYX software" had a precise meaning. The use of the software allowed the theoretical isoelectric point (pI) to be reliably and consistently determined.

The GENETYX software was widely used and was considered the standard for calculating the theoretical pI. In decision T 923/92 the term "Bowes melanoma cells" was accepted based on the reasoning that the cells "*were generally available and freely exchanged in the scientific community*" and "*neither secrecy agreements nor contractual obligations among the research workers restricted the use or dissemination of the cells*" (see point 44). This was comparable to the present case, in which the standard software GENETYX was used worldwide, was freely exchanged and was always available to the public.

From the case law (e.g. decisions T 762/90, T 525/99, T 623/91 and T 923/92) it could be inferred that a reference to a trade mark in a claim could be accepted

unless the likelihood of a change to the product marketed under the trade mark was proven. The burden of proof was on the respondent.

The respondent had only provided unsubstantiated allegations and speculations, and thus had not complied with its burden of proof. There was no evidence on file that the program had ever changed, or that it could be changed without changing the trade name.

The appellant had provided evidence to the contrary. From document D34 (manual of GENETYX software) it was apparent that the algorithm by Skoog and Wichman formed the basis of the pI calculation. The software thus represented nothing more than an implementation of that algorithm which facilitated its use by the skilled person (instead of manual calculation). There was also evidence on file that the results obtained for the pI when using GENETYX had not changed over the years.

Decision T 623/91 provided guidance on the quality of evidence that might be required to allow trade marks under Article 84 EPC. The board in T 623/91 decided that the claims before it complied with Article 84 EPC in view of the evidence concerning the likelihood of a change in the chemical composition without a change to the trade mark under which it was marketed. In the present case the appellant had provided more evidence, which was also of higher quality.

Genetyx Corporation, the manufacturer of the "gene and amino acid sequence analysis software GENETYX" (see document D31) and holder of the corresponding trade mark (see document D29), had confirmed that there had been and would be no changes to how the theoretical pI is determined by the software GENETYX (specifically in

relation to the algorithm which has been known as such from a publication by Skoog and Wichman (1986); see annex to document D31).

In addition, only the particular software was marketed under the trade mark and Genetyx Corporation had confirmed that the trade mark of the software would not be changed. If there were changes to the software in the way it calculates the theoretical π , the trade mark would also be changed.

Therefore, the term GENETYX, the software GENETYX and the manufacturer of the software, Genetyx Corporation, were linked. Consequently, the software GENETYX could be clearly identified.

Decision T 398/01 mentioned that "*trademarks may be allowed exceptionally if their use is unavoidable and they are generally recognised as having a precise meaning*" (see point 2.2.3). This decision, however, did not provide any explanation of when the use of a trade mark would not be unavoidable and also did not provide an interpretation of that term.

The well-known software GENETYX provided consistent and reliable results, and was the only software used and disclosed in the patent. Therefore, incorporating the use of the software GENETYX as a reference point into the claims was "unavoidable" in this sense.

In sum, the evidence provided by the appellant was sufficient to conclude that the trade mark "GENETYX" was clear, and accordingly the claims met the requirements of Article 84 EPC.

X. The respondent's (former opponent 2's) arguments on clarity (Article 84 EPC) are summarised as follows.

The established case law (e.g. decision T 398/01, point 2.2.3) and the Guidelines for Examination in the EPO (see F-IV, 4.8) stipulated that the use of trade marks in a claim was generally not allowed and defined specific, cumulative conditions for allowing the use of trade marks in claims, as a legal exception:

- a) that the trade mark was generally recognised as having a precise meaning and
- b) that the use of the trade mark was unavoidable.

The onus was on the patent proprietor to demonstrate that this legal exception applied.

The GENETYX software was not generally recognised as having a precise meaning for determining the pI of whole IgG antibodies, but rather of peptides. It did not necessarily yield consistent results, depending on the settings used (e.g. pKa values for amino acids could be changed) and depending on how the artificial "peptide" sequence was created *in silico* (e.g. order of chains in a fused molecule).

The use of the term "GENETYX" in the claim was not "unavoidable" on the effective date of the patent in view of the statement in the patent itself: "*In the present invention, **the isoelectric point can be determined by isoelectric focusing, which is known to those skilled in the art. The theoretical isoelectric point can be determined using gene and amino acid sequence analysis software (GENETYX and the like) ...***" (see paragraph [0082] of the patent, emphasis added).

One other possibility for defining the method for determining the theoretical pI of the antibody was to define specific experimental conditions for carrying out the experimental determination of the pI by isoelectric focusing (IEF). Another possibility was to define a specific, available, reliable and universally accepted algorithm, and its specific settings, to be used for the theoretical determination of the pI. The appellant had, however, chosen not to define the method for determining the change in pI in a manner avoiding the use of the trade mark "GENETYX". Therefore, the use of the term "GENETYX" in the claims was not unavoidable, and the second condition of the legal exception defined in decision T 398/01 was not fulfilled either.

Consequently, claim 1 of each claim request did not meet the requirements of Article 84 EPC.

- XI. The appellant requested, as far as relevant to the present decision, that the decision under appeal be set aside and that the case be remitted to the opposition division for further prosecution based on the set of claims of the main request or the set of claims of any one of auxiliary requests 1 to 11, all filed during the opposition proceedings and re-submitted with the statement of grounds of appeal or, alternatively, that the patent be maintained in amended form on the basis of the set of claims of the main request or on the basis of the set of claims of any one of auxiliary requests 1 to 11.

The respondent requested that the appeal be dismissed or, alternatively, that the case be remitted to the opposition division for further prosecution if the

board were to hold that one of the sets of claims met the requirements of Article 84 EPC.

Reasons for the Decision

1. The appeal complies with Articles 106 to 108 and Rule 99 EPC and is admissible.

Main request - claim 1 - clarity (Article 84 EPC)

2. The pivotal issue in the appeal is whether or not the designation of the software with the trade mark "GENETYX" in the method of determining the modification of the theoretical isoelectric point (pI) of the IgG antibody referred to in the claim by "using the gene and amino acid sequence analysis software GENETYX" (see section IV) is clear.
3. The board agrees with the appellant that it has been established in the case law that the use of trade designations such as trade marks in a claim is not excluded under the EPC in principle and that the question of whether such a designation is allowable in a claim is a question of fact that can only be answered on a case-by-case basis (see, for example, decision T 762/90 of 29 November 1991, point 4.1.2, and decision T 525/99, point 3.1.4). Nevertheless, because Article 84 EPC prescribes that the claims must define the matter for which protection is sought and must be clear, the case law equally foresees that it at least needs to be established that the marketed product defined by a given trade designation has a precise meaning and that this meaning cannot change in the course of time in a way that would impact the definition of the claimed subject-matter (see e.g.

decision T 762/90 of 29 November 1991, point 4.1.1, and decision T 270/11, point 3.3). If these facts cannot be established, a claim for subject-matter defined by reference to such a trade designation is not clear and does not meet the requirements of Article 84 EPC.

4. The opposition division held that the term "GENETYX" had no precise meaning to the skilled person when defining the software to be used and that *"even if it is assumed that the current version and that used 11 years ago when the patent in suit was filed are similar, this does not guarantee that the program will not be modified during the term of the patent. It thus cannot be excluded that future versions of GENETYX will yield pI values significantly different from those described in the contested patent. For instance, future versions of GENETYX might, for example, include particular settings that have to be selected before running the pI calculation that were not required in the version used in the patent and in version 14.0.0 used in D25"*.

5. On appeal, the appellant has maintained that there had been no recognisable changes in the identity of the GENETYX software over a certain period of time in the past, relying on the evidence provided in document D31, *inter alia*. The appellant further argued that the burden of proof was on the respondent to demonstrate that a change in meaning of the "GENETYX software" had occurred or could occur in the future (referring to decisions T 762/90 supra, T 525/99, T 623/91 and T 923/92). In fact, the appellant held that it had provided more evidence than was considered sufficient in decision T 623/91, while the respondent had failed to show that the GENETYX software had changed over time. It noted, in addition, that the statement in

decision T 923/92 that "*Bowes melanoma cells were part of the state of the art already at the priority date. Under these circumstances the Board cannot agree to the Appellants' position that it would have been the Respondents' obligation to ensure their availability for the life-time of the patent in suit by means of a deposition under Rule 28 EPC*" (see point 44.(i)) emphasised that assumptions as to the availability of the GENETYX software by the respondent were not sufficient.

6. The board cannot conclude from the case law referred to by the appellant that the burden of proof was on the respondent to demonstrate that the GENETYX software had changed or could change over time. Although decisions T 762/90 supra and T 525/99 discuss clarity issues of the cases concerned, they do not address the question of burden of proof in this context. In decision T 623/91 the board, in balancing the evidence before it, came to the conclusion that one party's evidence was more credible. The decision, however, does not address the issue of burden of proof either. In decision T 923/92 (see points 43 and 44) the board answered the question of sufficiency of disclosure of the claimed invention in view of the contested public availability of "*Bowes melanoma cells*". The board fails to see the relevance of these passages. The established standard for sufficiency of disclosure to be denied is that "*serious doubts substantiated by verifiable facts*" are provided by the opposing party (see e.g. decision T 19/90, OJ EPO 1990, 476). This standard, however, cannot be seen to also generally apply to the question of clarity, for which the applicant or, in the case of an amended patent, the patent proprietor has to show that the claims define the matter for which protection is sought in a clear and concise manner, supported by

the description (Article 84 EPC). Moreover, decision T 923/92 is not concerned with trade marks and, for that reason too, is not applicable to the present case.

7. The respondent, based on decision T 398/01, which set out that "*[t]rademarks may be allowed exceptionally if their use is unavoidable and they are generally recognised as having a precise meaning*" (point 2.2.3), argued that the burden of proof was on the party who relied on the legal exception of a trade mark used in a claim. The onus was thus on the appellant to show that (i) the term "GENETYX" had a widely recognised precise meaning and that (ii) its use in the claim was unavoidable.
8. The board agrees with the respondent on the relevance of these criteria for the case at hand and thus evaluates the evidence provided by the appellant that these requirements are met. In addition, the board agrees with the respondent that the burden of proof is on the appellant, if only for the reason that it relies on an exception to the rule that, in general reference to a trade mark, renders the claimed subject-matter unclear.
9. The appellant has relied in particular on the declaration (document D31) by the Head of the Biotechnology Development Department of Genetyx Corporation (hereafter referred to as the Genetyx declarant) that the software GENETYX "*has been distributed since 1996 in Japan and worldwide. Since its implementation in 1996 the software calculates the theoretical pI of any given amino acid sequence by applying the algorithm of Skoog and Wichman (1986)*" (see page 1, last paragraph) and confirming that "*the algorithm for the calculation of the*

theoretical pI will not be changed in any further development of Genetyx. In fact, our users appreciate and use the software Genetyx especially because it provides reliable results, in particular for the determination of the theoretical pI of molecules, such as antibodies, which results do not change over time, e.g. if different versions of the software are used" (see page 2, third paragraph).

10. The board considers that, while the declaration by the Genetyx declarant (document D31) may provide evidence that no changes have been made to the way the GENETYX software calculates the pI since its implementation, it cannot provide sufficient evidence that no changes affecting the calculation of differences of pI by the software GENETYX would occur in the future or that the trade mark will be (exclusively) used to identify this software. There are no guarantees that the persons presently in control of Genetyx Corporation will remain in full control of the use of the software and the trade mark by the company or a possible successor in title in the future. It can only be assumed that no changes are envisaged at present.

11. In particular, the board has not been presented with evidence demonstrating that the GENETYX company or a successor in title will not change or modify the algorithm underlying the GENETYX software in the future. Future versions of the GENETYX software carrying a different version number (see document D25, referring to version 14.0.0 and document D34, representing the manual for version 15) could incorporate further features or algorithms, a practice which is very common in software development. This could also change the pI value calculation for a given molecule, in particular with regard to complex protein

molecules having several peptide chains, such as antibodies.

12. Furthermore, the board has also seen no evidence that the skilled person regarded the software as the standard application for measuring the modification of the theoretical pI. The board also cannot agree that it was common general knowledge that the software GENETYX applied, as was argued by the appellant, a particular algorithm for pI calculation, i.e. here as developed by Skoog and Wichman (see annex to document D31). The only evidence provided for a link between the software GENETYX and the algorithm is the declaration (document D31) and the software manual (see document D34 and references [2] and [21] on pages 197 and 277, respectively, pointing to the scientific article by Skoog and Wichman). Apart from the fact that this manual appears to be available only in Japanese, which already seems to indicate a rather limited local distribution, it cannot be considered to be evidence of common general knowledge to the skilled person as it represents a single company publication and not a textbook publication or a comparable resource. The declaration (document D31) also provides no additional evidence for the algorithm being commonly known as the basis for the GENETYX software.
13. For these reasons the board concludes that the term "software GENETYX" has no precise and invariable meaning and is thus not clear. For this reason alone claim 1 does not comply with the requirements of Article 84 EPC.
14. For the sake of completeness, the board notes the use of the term "GENETYX" was also not unavoidable (see point 7.), as the patent itself cites other methods of

determining a difference in pI (see paragraph [0082] of the patent). The board therefore finds that the applicant/appellant could have defined the method of determining the pI difference in another way and the use of the trade designation was indeed avoidable.

15. For this reason too, claim 1 does not comply with the requirements of Article 84 EPC.

Auxiliary requests 1 to 11 - claim 1 - clarity (Article 84 EPC)

16. Claim 1 of all the auxiliary requests contains the feature "software GENETYX". The reasoning above with regard to claim 1 of the main request thus also applies to claim 1 of all the auxiliary requests. The appellant has not submitted arguments to the contrary.
17. Auxiliary requests 1 to 11 thus lack clarity (Article 84 EPC).

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chair:



I. Aperribay

B. Claes

Decision electronically authenticated