Unified Patent Court
Einheitliches Patentgericht
Juridiction unifiée du brevet

EPG - Court of Appeal
UPC_CoA_335/2024
App_22399/2024

Order
of the Court of Appeal of the Unified Patent Court issued
on 6 August 2024
concerning a request for reopening of proceedings

GUIDING PRINCIPLES

- By using the phrase "in the opinion of the technically expert court" in the grounds for its decision, the court expresses that it is particularly equipped and qualified to assess the arguments and evidence presented in a technically complex matter. This cannot be understood to mean that the court used the personal opinion of one or more of its judges as evidence.
- The assessment of the arguments and evidence presented by the parties is carried out by the court hearing the case and is not subject to review in the context of an application for a retrial.
- R.118.5 RPP (in Part 1 of the Rules of Procedure and Evidence concerning proceedings before the Court of First Instance), which provides that the court shall, as a rule, decide on the obligation to bear the costs of the proceedings, does not preclude the Court of Appeal from deciding on the allocation of costs in summary proceedings. As follows from Art. 32(1)(c) EPC, actions for interim measures and protective measures under Art. 62 EPC are independent actions, and these proceedings are concluded with the decision in the appeal proceedings. There is therefore a legal basis for the decision on costs in R.242.1 RPE.

KEYWORDS

Reopening of proceedings (R.245 Rules of Procedure), decision on costs (R.242.1 Rules of Procedure)

APPLICANT (RESPONDENT IN THE APPEAL PROCEEDINGS)

1. **10x Genomics, Inc.**, Pleasanton (CA) – US
2. **President and Fellows of Harvard College,** Cambridge (MA) – US

(hereinafter referred to collectively and in the singular as: 10x)

Both represented by: Prof. Dr. Tilman Müller-Stoy, lawyer, Bardehle Pagenberg, Munich, Germany

RESPONDENTS (APPELLANTS IN THE APPEAL PROCEEDINGS)

1. **NanoString Technologies Inc.**, Seattle (WA) – US
2. **NanoString Technologies Germany GmbH**, Munich – DE
3. **NanoString Technologies Netherlands B.V.**, Amsterdam – NL

(hereinafter referred to collectively and in the singular as:
Nanostring)

All represented by: Oliver Jan Jüngst, lawyer, Bird & Bird, Düsseldorf, Germany

LANGUAGE OF THE PROCEEDINGS

German

PROVISIONAL PATENT

EP 4108782

DECISION-MAKING BODY AND DECIDING JUDGES

Second Board of Appeal
Rian Kalden, presiding judge and rapporteur Ingeborg
Simonsson, legally qualified judge Patricia Rombach,
legally qualified judge

CONTESTED ORDER OF THE COURT OF APPEAL

□ Date: 26 February 2024
□ Order ORD_595990/2024, in the main proceedings (proceedings for interim measures)
APL_576355/2023; UPC_CoA_335/2023

ISSUES

Application for reopening of proceedings pursuant to Art. 81(1) EPGÜ in conjunction with R.245 VerfO due to fundamental procedural errors, based on a fundamental violation of the right to be heard in the proceedings (Art. 76 EPGÜ, R.247(c) VerfO) and a violation of Article 6 of the Convention for the Protection of Human Rights and Fundamental Freedoms (R.247(e) VerfO).

BRIEF DESCRIPTION OF THE FACTS AND THE COURSE OF THE PROCEEDINGS

1. At the request of 10x, the Court of First Instance (Munich Local Chamber) ordered in preliminary injunction proceedings by order of 19 September 2023 that Nanostring must refrain from any direct or indirect infringement of the injunction patent in the contracting states of the EPGÜ.

2. Nanostring appealed against this order. By order of 26 February 2024, the Court of Appeal (First Chamber) overturned the order of the Court of First Instance, dismissed 10x's application for a preliminary injunction and ordered 10x, as the unsuccessful party, to bear the costs of the proceedings.

3. Unlike the court of first instance, the Court of Appeal held that, at the priority date of the patent in suit, a person skilled in the art would have been inspired and would have considered transferring a multiplex method for detecting ASMs, which had been successfully used in vitro, to an in situ environment. Based on a publication referred to as D6 in the proceedings, the Court of Appeal concluded that it was highly probable that the contested patent would be declared invalid in main proceedings on the grounds of lack of inventive step.

4. On 24 April 2024, 10x filed a request for reopening of the proceedings pursuant to R.245 RPC.

5. The President of the Board of Appeal assigned the case to the Second Board of Appeal and ordered that the judges of the court who were involved in the decision under review should not be members of the Board.

6. By order of 16 May 2024, Nanostring was given the opportunity to comment on the application for a retrial. Nanostring availed itself of this opportunity and submitted a statement on 24 May 2024.

WRITINGS OF THE PARTIES

7. Essentially, 10x argues as follows:

8. With regard to the decision on the merits, the Court of Appeal based its decision on the expertise of individual members of the panel in a manner contrary to the rules of procedure in the case of disputed submissions by the parties. This fundamentally violated the rules on the burden of proof and the taking of evidence.
    a. According to Art. 76(2) EPGÜ, decisions on the merits may only be based on grounds, facts and evidence that have been submitted by the parties or introduced into the proceedings by order of the court and on which the parties have had the opportunity to comment.
    b. The right to a fair trial under Article 6(1) sentence 1 of the ECHR includes fair evidentiary proceedings. There was a violation of the principle of fair trial because the Court of Appeal ignored the fundamental procedural requirements regarding the burden of proof and presentation of evidence in its decision-making.
    c. The appellate court addressed the applicants' objection that, at the priority date, there was insufficient expectation of success for the transfer of the in vitro process according to D6 to the in situ context due to various difficulties, such as "molecular crowding" or the occurrence of autofluorescence, the Court of Appeal began with the words: "In the opinion of the technically expert court".
    d. This shows that the Court of Appeal relied on its own expertise and an expert opinion from one of the parties. The expertise of individual members of the panel is not a means of evidence provided for in the Rules of Procedure.
    e. In response to the questions raised by 10x in its reply regarding molecular displacement and the occurrence of autofluorescence in cell and tissue samples, Nanostring limited itself to the blanket assertion that these were completely routine problems that could be routinely solved by specialists, and that none of the problems had been addressed or even begun to be solved in the patent in question. Nanostring did not offer or present any evidence to support these claims.
    f. Evidence cannot be taken on the basis of the technical opinion of a member of the adjudication panel, and certainly not if this opinion has not even been documented in writing/become the subject of proceedings and the parties have not had a reasonable opportunity to comment on it.
    g. In doing so, the Court of Appeal based its decision on facts that neither raised by the parties nor introduced into the proceedings by order of the court. This constitutes a fundamental violation of Article 76(2) EPC.

At the same time, the Court of Appeal deviated from the fundamental requirements of the Rules of Procedure regarding the presentation and collection of evidence in its decision-making and disregarded the mandatory rules on the burden of proof and presentation of evidence. This also constitutes a violation of the principle of fair trial (Article 6 of the ECHR).

9. The Court of Appeal had made the decision on costs arbitrarily.
    a. Neither the EPGÜ nor the Rules of Procedure contained a legal basis for a decision on costs in summary proceedings. The Rules of Procedure only provided for a comprehensive decision on costs in the main proceedings (R.118.5 VerfO).
    b. The question of a basic decision on costs in summary proceedings was never addressed by the Court of Appeal, nor was it discussed by the parties in their written submissions. This constitutes a violation of the principle of fair trial (Art. 6 ECHR).

10. Nanostring essentially argues as follows:

11. There was no violation of any rules on the burden of proof and the taking of evidence.
    a. According to R.210.2 VerfO, the taking of evidence is not required in summary proceedings and is generally not compatible with the urgent nature of such proceedings.
    b. In its order, the Court of Appeal not only took into account the respondent's submissions and the detailed state of the art, as well as the expert opinion B10, but also relied in particular on the patent itself.
    c. The questions raised by the applicants concerning "molecular crowding" and the occurrence of autofluorescence are not specific questions of evidence for the procedure relevant here, but rather a prognostic decision as to whether the in vitro procedure of D6 could also be carried out in situ with sufficient expectation of success.
    d. The Court of Appeal examined and assessed the technical difficulties alleged by the applicants.
    e. The applicants had not substantiated their claim that the skilled person had encountered difficulties in transferring the method according to D6 to in situ samples.

12. The appeal court's decision on costs was not objectionable and complied with R.242.1 VerfO.
    a. R.118.5 VerfO stipulates that a decision on costs must be included in the final decision after conclusion of the main proceedings at first instance. However, this does not preclude a final decision in summary proceedings from ruling on the merits of the distribution of costs.
    b. A decision on the basis of costs may be issued insofar as it concerns costs that have already been determined to be borne by a specific party, regardless of the further course of the proceedings.
    c. There is a legal basis for a decision on costs in Rule 242.1 VerfO.

REASONS FOR THE DECISION

13. The Board of Appeal first decides on the admissibility of the request for reopening the proceedings (R.255(a) R.P.). This involves examining whether the requirements laid down in Art. 81(1) EPC and R.245 to R.249 R.P. are met.

14. Article 81(1) EPCU allows for a request to reopen proceedings after a final decision has been made if, in short, this is based on an act that qualifies as a criminal offence or on a fundamental procedural error. These circumstances must not have been known or, in the case of a fundamental procedural error, must have been raised during the proceedings leading to the decision or in the appeal proceedings (R.248 RPO), unless such an objection could not have been raised during the proceedings before the court of first instance or the appeal court.

15. Article 81(1) EPC makes it clear that a reopening of proceedings can only be granted in exceptional cases if the decision is vitiated by one of these errors and is a final decision. Reopening is therefore a last resort against a decision that cannot otherwise be subject to a review procedure in which the error could be 'rectified'.

16. The application is inadmissible because the contested order does not suffer from a fundamental procedural error. This is explained below.

17. During the proceedings, 10x disputed that the skilled person would have attempted to transfer the methods disclosed in D6 to an in situ environment. 10x argued that the skilled person would not have acted with a reasonable expectation that this would be successful. In support of this argument, 10x pointed out that at that time, various probes and methods for producing ASMs were known, whose suitability for in situ application varied, and that a skilled person would not have readily concluded from the successful application of a probe or method in vitro that this probe or method would also work in an in situ context. 10x also referred to various difficulties associated with such a transfer to an in situ environment and that, in view of these difficulties, a person skilled in the art would be deterred from doing so.

18. Nanostring contested this argument, referring, among other things, to D6, a report by its party expert Elina Staaf, who is an examiner at the Swedish Patent Office and who submitted her opinion as an expert from an institute called PRV Consulting, which is part of the Swedish Patent Office (B10), as well as to a publication belonging to the prior art with
entitled "In situ detection of non-polyadenylated RNA molecules using Turtle Probes and target primed rolling circle PRINS" (Magnus Stougaard et al.), referred to as B30 in the proceedings.

19. In its ruling, the Court of Appeal did not follow the opinion of 10x. The Court of Appeal stated the following:

For a person skilled in the art who, at the priority date of the patent in suit, was faced with the task of developing high-throughput optical multiplexing methods for detecting target molecules in a sample, D6 was of interest because it disclosed a method for detecting a plurality of amplified single molecules (ASMs) by encoding and decoding the single molecules, in which the encoding is performed by probe-mediated generation of ring-shaped DNA and the decoding is performed by temporal sequential detection of the targeted ASMs (see D6, abstract).

This is disclosed in D6 for ASMs arranged in vitro in an array format. However, since at the priority date there was a need for multiplex analysis techniques, particularly for test samples (see patent in suit, para. 2), there was reason to consider whether the encoding and decoding method disclosed in D6 could be transferred to the detection of ASMs in cell or tissue samples (see also the Swedish Intellectual Property Office, PRV Consulting Report of 28 June 2023, B10, p. 5).

A suggestion or confirmation to think in this direction also arose from the reference in D6 (p. 3, left column) that, in the prior art, rolling circle ASMs had been used for reading out various genotyping assays and for detecting proteins and protein complexes in situ using proximity ligation. The fact that the "genotyping assays" were performed in situ is evident from footnote 20 of D6, which refers to Larsson et al., "In situ genotyping individual DNA molecules by target-primed rolling-circle amplification of Padlock probes", Nat. Methods 2004, 1, 227 ff., which, as the title suggests, describes an in situ method. In addition, D6 refers to a publication on the in situ observation of protein complexes (Söderberg et al., Direct observation of individual endogenous protein complexes in situ by proximity ligation, Nat. Methods 2006, vol. 3 no. 12 [D19]).

The fact that, at the priority date of the patent in suit, the next step for the skilled person after successfully applying an in vitro multiplex method for detecting ASMs was to consider transferring the method to an in situ environment is further evidenced by B30 (Stougaard et al., "In situ detection of non-polyadenylated RNA molecules using Turtle Probes and target primed rolling circle PRINS", BMC Biotechnology 2007, 7:69). This publication describes a method for detecting non-polyadenylated RNA molecules using "a new probe format" ("Turtle Probes"), which was first performed in vitro in "a controllable environment" (B30, p. 4, right column, last paragraph) and, after successful implementation, was also tested in situ with positive results (B30, p. 4, left column – p. 5; Abstract, Results).

Even if, as the applicants assume, various probes and methods for producing ASMs were known at the time, whose suitability for in situ application varied and which would not have led the skilled person to conclude automatically from the successful application of a probe or method in vitro that this probe or method would also function in an in situ context, it should be noted that this consideration did not prevent the authors of B30 from using the detection method with "turtle probes" after it had initially been successfully tested in vitro.context, it should be noted that this consideration did not prevent the authors of B30 from performing the detection method with "turtle probes" in situ after it had initially been successfully performed in vitro. There is no apparent reason why this would have been different based on the detection method performed in vitro with selector probes in D6.

The difference cited by the applicants in this regard, namely that according to D6 the nucleic acids (analytes) were subjected to restriction digestion prior to the use of the selector probes, whereas this was not necessary when using the "turtle probes" according to B30, can be explained by the fact that in B30, detection is aimed at RNA molecules, whereas in D6, detection is aimed at genomic DNA material, which must first be prepared for hybridisation with the selector probes by restriction digestion (see, for example, Figure 3 A and the explanation under Figure 3). Unlike in B30, there is no reason why D6 would have prevented a person skilled in the art from transferring the in vitro multiplex method disclosed therein for the detection of nucleic acids to an in situ environment with cell or tissue samples.

The applicants also objected that, from a technical point of view, there was insufficient prospect of success because they were faced with problems such as "molecular crowding" (the ability to distinguish between several analytes occurring in close spatial proximity) or
The argument that the expert would have been confronted with "autofluorescence" (unpredictable interactions) in the cell or tissue sample cannot be accepted. According to the assessment of the technically competent court, these are problems that regularly arise in connection with the in situ detection of analytes in tissue or cell samples, but which the skilled person could deal with at the priority date on the basis of their expertise and which would therefore not have prevented them from carrying out experiments in the aforementioned sense due to insufficient prospects of success (see also the Swedish Intellectual Property Office, PRV Consulting Report, B10, p. 5). This assessment is supported by the fact that the patent in suit does not contain any explanations on how to deal with the aforementioned problems in in situ detection, such as when using immunohistochemistry methods or RNA fluorescence in situ hybridisation (FISH) (patent, see para. 48 ff., para. 212 ff. "Sample", para. 224 ff. "Applications of the detection reagents"; para. 234 "Immunohistochemistry"; para. 235 "In situ hybridisation", "Fluorescence in situ hybridisation").

Finally, the time factor did not give the skilled person any reason to refrain from attempting to transfer the method disclosed in D6 to the detection of analytes in cell and tissue samples. Rather, it can be assumed that, based on their expertise, the skilled person was able to adjust the duration, taking into account other factors such as binding affinities, incubation conditions and the concentration of the selector probes, in such a way that the detection reagents bind sufficiently firmly to the analytes. This assessment is confirmed by the fact that even the patent in suit, which in claim 1 provides for incubation for a period of time sufficient to allow the majority of the detection reagents to bind to the analytes, does not provide any further details on the specific setting. Rather, the description of the patent in suit merely mentions times between 30 seconds and 48 hours or longer for contacting the samples with the detection reagents and factors that may be relevant for the length of the contact times, such as binding affinities, concentrations of the probe reagents or analytes, concentrations of the detection reagents and/or the incubation conditions (patent in suit, para. 45). This suggests that the patent in suit also assumes that the skilled person is capable of correctly assessing the time component on the basis of their general qualifications.

20. 1 0x essentially justifies its application for a retrial on the grounds that the words "in the opinion of the technically competent court" in the appeal court's reasoning should be understood to mean that the appeal court used the personal opinion of one (or more) of its judges as evidence for Nanostring's submission against the arguments of 10x set out above (para. 17), for which Nanostring had not provided (sufficient) supporting evidence.

21. This cannot be accepted.

22. Firstly, this view is based on an obviously incorrect understanding of the quoted sentence. With this choice of words, the Court of Appeal expressed that it was particularly equipped and qualified to assess the arguments and evidence presented in a technically complex matter.

23. Secondly, it is clear from the order that the Court of Appeal based its assessment of inventive step not only on the submissions of 10x and Nanostring, but also on the description of the contested patent itself and on the evidence submitted by Nanostring, namely a publication from the prior art (B30) and the party expert opinion B10.

24. The order states that B30 shows that a method that was successfully carried out in vitro was subsequently successfully transferred to an in situ environment. The Court of Appeal accepted that, even assuming that the skilled person would recognise that success was not guaranteed, the difficulties raised by 10x were not so serious as to prevent the authors of B30 from taking this step. The Court of Appeal was not convinced by 10x's argument that the differences between B30 and D6 would have led to a different result. On this basis, the Court of Appeal concluded that for a skilled person starting from D6, which discloses the successful application of an in vitro multiplex method for detecting ASMs, the next step would have been to consider transferring this method to an in situ environment.

25. The Court of Appeal did not agree with 10x's view that, from a technical point of view, there was no reasonable expectation of success because the skilled person would have encountered problems. In the court's view, an expert would have been able to overcome these regularly occurring problems in connection with the in situ detection of analytes in tissue or cell samples on the basis of their expertise at the priority date, and, as Nanostring argued, these problems would therefore not have prevented them from performing tests due to insufficient expectation of success. The Court of Appeal found confirmation of this in the expert opinion submitted by Nanostring (B10), according to which the skilled person starting from D6 would have known from the publication cited in D6 ("detection of protein and protein complexes in situ using proximity ligation" (33) that rolling circle ASMs had previously been used for the detection of biological target structures 'in situ', and that "the skilled person knows how to adapt the methodology in [D6] for cell or tissue samples, whereby the reagents can freely reach their in situ analytes, e.g. by following the instructions in reference 33 in [D6]". The skilled person would therefore use the method in

[D6] in a cell or tissue and thereby arrive at the invention according to claim 1.

26. Although the report does not explicitly mention the difficulties raised by 10x, as 10x rightly points out, it is clear that the Court of Appeal concluded from the expert opinion submitted by Nanostring, in particular the statement that "the skilled person knows how to adapt the methodology in [D6] for cell or tissue samples," that the expert was of the opinion that the skilled person would be able to deal with any difficulties arising from the adaptation to an in situ environment and that these difficulties were not such as to deter the skilled person from undertaking the process.

27. The Court of Appeal found further support for its assessment in the description of the patent in suit, which contained no information on how to deal with the problems addressed by 10x in in situ detection.

28. It is clear from the foregoing that the Court of Appeal did not base its reasons on the personal opinion of one or more of its judges, but on evidence, including the patent description, supporting Nanostring's submissions. The assessment of the arguments and evidence presented by the parties is made by the appeal court hearing the case and is not reviewed in the context of a motion for reconsideration. 10x has rightly not argued that the consideration of the evidence assessed and the manner in which it was evaluated constitute a fundamental procedural error.

29. 10x unsuccessfully argues that the decision on costs has no legal basis and therefore constitutes a fundamental procedural error. As Nanostring rightly points out,
R.118.5 of the Rules of Procedure (in Part 1 of the Rules of Procedure before the Court of First Instance), according to which the Court decides on the merits of the obligation to bear the costs of the proceedings, does not preclude the Court of Appeal from deciding on the allocation of costs in summary proceedings. As is clear from Art. 32(1)(c) EPGÜ, actions for interim measures and protective measures pursuant to Art. 62 EPGÜ are independent actions and these proceedings are concluded with the decision in the appeal proceedings. There is therefore a legal basis for the decision on costs in R.242.1 VerfO.

30. Nanostring requested a preliminary ruling on costs, and 10x had the opportunity to comment on this in its response to the appeal and in the oral hearing. The fact that 10x refrained from doing so did not oblige the Court of Appeal to discuss the issue with the parties. Furthermore, the fact that this was not discussed due to the lack of a response from 10x does not mean that 10x did not receive a fair hearing.

31. It follows that the decision on costs in the contested order is also not based on a fundamental procedural error.

32. It follows from the foregoing that the application for a retrial must be dismissed as inadmissible.

ORDER

The Court of Appeal dismisses the application for a retrial as inadmissible.

Issued on 6 August 2024

Rian Kalden

Date: 06.08.2024 12:33:59 +02'00

Rian Kalden, Presiding Judge and Rapporteur

Åsa Ingeborg Simonsson

Digitally signed by Åsa Ingeborg Simonsson Date: 06.08.2024 13:10:22

Ingeborg Simonsson, legally qualified judge

Patricia Ursula Rombach

Digitally signed by Patricia Ursula Rombach Date: 06.08.2024 16:54:04

Patricia Rombach, legally qualified judge