Unified Patent Court
Einheitliches Patentgericht
Juridiction unifiée du brevet

UPC - Court of Appeal
UPC_CoA_335/2024
App_22399/2024

Order
of the Court of Appeals of the Unified Patent Court issued on
6 August 2024
concerning an application for a retrial

LEADERSHIPS

- With the choice of words "In the judgement of the court with technical expertise" in the grounds of the decision, the court expresses that it is specially equipped and qualified to assess the arguments and evidence presented in a technically complex matter. This cannot be taken to mean that the court has used the personal opinion of one or more of its judges as evidence.
- The arguments and evidence presented by the parties are assessed by the court dealing with the case and are not subject to review in the context of an application for a retrial.
- R.118.5 RoP (in Part 1 of the Rules of Procedure relating to proceedings before the Court of First Instance), which provides that the court shall in principle decide on the obligation to bear the costs of the proceedings, does not preclude the court of appeal from deciding on the apportionment of costs in summary proceedings. As follows from Art. 32(1)(c) UPCA, actions for provisional and protective measures under Art. 62 UPCA are independent actions and the decision on appeal concludes these proceedings. There is therefore a legal basis for the basic decision on costs in R.242.1 RoP.

KEYWORDS

Reopening of proceedings (R.245 RoP), basic decision on costs (R.242.1 RoP) APPLICANT (APPLICANT IN APPEAL PROCEEDINGS)

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

(hereinafter for both together and in the singular: 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 collectively and in the singular: Nanostring)
All represented by: Oliver Jan Jüngst, Attorney-at-Law, Bird & Bird, Düsseldorf, Germany

LANGUAGE OF THE PROCEDURE

German

PATENT OF DISPOSITION

EP 4108782

THE COURT AND THE DECIDING JUDGES

Second panel
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 the adoption of provisional measures) APL_576355/2023; UPC_CoA_335/2023

POINTS OF STRENGTH

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

BRIEF DESCRIPTION OF THE FACTS OF THE CASE AND THE COURSE OF THE PROCEEDINGS

1. On application by 10x, the Court of First Instance (Munich local division) ordered in the preliminary injunction proceedings by Order of 19 September 2023 that Nanostring must refrain f r o m any direct or indirect infringement of the injunction patent in the contracting member states of the UPCA.

2. Nanostring appealed against this Order. By order of 26 February 2024, the Court of Appeal (First Chamber) set aside the Court of First Instance's order, dismissed 10x's application for an interim injunction and o r d e r e d 10x to bear the costs of the proceedings as the unsuccessful party.

3. Unlike the Court of First Instance, the Court of Appeal was of the opinion that a person skilled in the art at the priority date of the patent in suit had and would consider 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 in the proceedings as D6, the Court of Appeal concluded that it w a s overwhelmingly likely that the patent in suit would be declared invalid in main proceedings for lack of inventive step.

4. On 24 April 2024, 10x filed an application to reopen the proceedings pursuant to R.245 RoP.

5. T h e President of the Court of Appeal allocated the case to the Second Panel and ordered that the judges of the court who were involved in the decision under review may not sit on the panel.

6. By Order dated 16 May 2024, Nanostring was given the opportunity t o comment on the application to reopen the proceedings. Nanostring made use of this opportunity and submitted a statement on 24 May 2024.

DOCUMENTS OF THE PARTIES

7. Essentially, 10x argues as follows:

8. With regard to the substantive decision, the Court of Appeal had 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 party submissions. This fundamentally violated the rules on the burden of proof and the taking of evidence.
    a. According to Art. 76(2) UPCA, decisions on the merits may only be based on grounds, facts and evidence which have been submitted by the parties or introduced into the proceedings by order of the court and on which the parties have had an opportunity to comment.
    b. The right to a fair trial in accordance with Art. 6 para. 1 sentence 1 ECHR includes a fair evidentiary procedure. There had been a violation of the principle of a fair trial because the court of appeal had ignored the basic procedural requirements regarding the burden of presentation and proof when reaching its decision.
    c. The argumentation with the applicants' objection that at the time of priority there was no sufficient expectation of success for the transfer of the in vitro process according to D6 into the in situ context, due to various difficulties such as "molecular crowding" or the occurrence of autofluorescence, the Court of Appeal had introduced the case with the words: "In the judgement of the court with technical expertise".
    d. This shows that the Court of Appeal relied on its own expertise and a party expert opinion. The own expertise of individual members of the panel is not evidence provided for by the Rules of Procedure.
    e. In response to the questions raised by 10x in the Reply concerning molecular displacement and the occurrence of autofluorescence in cell and tissue samples, Nanostring limited itself to the general assertion that these were completely everyday problems that were routinely solved by the skilled person and that none of the problems had been addressed or even rudimentarily solved in the patent in suit. Nanostring did not offer or submit any evidence for these claims.
    f. Evidence cannot be taken on the basis of the technical opinion of a member of the This opinion cannot be replaced by the opinion of the adjudicating body and even less so if this opinion has not even been documented in writing / has not become part of the proceedings and the parties have not had a meaningful opportunity to comment on it.
    g. In doing so, the Court of Appeal based its decision on facts which had neither been submitted by the parties nor brought into the proceedings on the Order of the court. This is a fundamental violation of Art. 76(2) UPCA.

At the same time, the Court of Appeal deviated from the basic requirements of the Rules of Procedure regarding the provision and taking of evidence when reaching its decision and disregarded the mandatory rules on the burden of presentation and proof. This also constitutes a violation of the principle of a fair trial (Art. 6 ECHR).

9. The Court of Appeal had arbitrarily made the basic costs decision.
    a. Neither the UPCA nor the Rules of Procedure contain a legal basis for a basic decision on costs in summary proceedings. The Rules of Procedure provide for a comprehensive decision on costs only in the main proceedings (R.118.5 RoP).
    b. The question of a basic decision on costs in summary proceedings w a s never raised by the court of appeal, nor discussed by the parties in the documents. Therefore, t h e r e was a violation of the principle of a fair trial (Art. 6 ECHR).

10. Nanostring essentially argues as follows:

11. There is no violation of any regulations on the burden of proof and the gathering of evidence.
    a. According to R.210.2 RoP, the taking of evidence is not required in summary proceedings and, as a rule, is not c o m p a t i b l e with the urgent nature of the proceedings.
    b. In its Order, the Court of Appeal had not only taken into account the defendants' submissions and the detailed prior art, as well as expert opinion B10, but had also relied in particular on the patent in suit itself.
    c. The questions of "molecular crowding" and the occurrence of autofluorescence raised by the applicants are not specific questions of evidence for the procedure relevant here, but a prognostic decision as to whether the in vitro procedure of D6 would also be carried out in situ with sufficient expectation of success.
    d. The Court of Appeal had examined and assessed the technical difficulties alleged by the applicants.
    e. The applicants had not substantiated the claim that the skilled person had had difficulties i n transferring the D6 procedure to in situ samples.

12. The Court of Appeal's decision on costs was not objectionable and complied with R.242.1 RoP.
    a. R.118.5 RoP does provide that a basic decision on costs must be included in the final decision following the conclusion of the main proceedings at first instance. However, this does not rule out the possibility of a decision on the allocation of costs on the merits being made in a final decision in summary proceedings.
    b. A basic decision on costs could be issued insofar as it relates to costs that have already been determined to be borne by a specific party, irrespective of the further course of the proceedings.
    c. There is a legal basis for a basic decision on costs in Rule 242.1 RoP.

REASONS FOR THE DECISION

13. The court of appeal first decides on the admissibility of the application for reopening of proceedings (R.255(a) RoP). This involves examining whether the requirements laid down in Art. 81(1) UPCA and R.245 to R.249 RoP are met.

14. Art. 81(1) UPCA makes it possible to request a retrial after a final decision if, in short, it is based on an act which qualifies as a criminal offence or on a fundamental procedural violation. These circumstances must not have been known or, in the case of a fundamental procedural violation, if known, must have been objected to during the proceedings leading to the decision or on appeal (R.248 RoP), unless such an objection could not have been raised during the proceedings before the Court of First Instance or the Court of Appeal.

15. Art. 81(1) UPCA makes it clear that a reopening of proceedings can only be granted exceptionally if the decision suffers from one of these errors and is a final decision. The reopening is thus a last resort against a decision which otherwise cannot be the subject of a review procedure in which the error could be 'remedied'.

16. The application is not admissible as the contested Order does not suffer from a fundamental procedural error. This is explained below.

17. During the proceedings, 10x denied that the professional had attempted to transfer the methods disclosed in D6 to an in situ environment. 10x argued that the skilled person had not acted with a reasonable expectation that this would be successful. In support of this argument, 10x pointed out that at the time various probes and methods for making ASMs were known, their suitability for in situ use varied, and that a skilled person would not have readily inferred from the successful use of a probe or method in vitro that that 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 the professional would be discouraged from doing so given these difficulties.

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

19. In the Order, the Court of Appeal did not follow the view of 10x. The Court of Appeal stated the following:

D6 was of interest to a person skilled in the art who, at the priority date of the patent in suit, w a s faced with the task of developing high-throughput optical multiplexing methods for detecting target molecules in a sample, as it discloses a method for detecting a plurality of amplified single molecules (ASMs) by encoding and decoding the single molecules, wherein the encoding is performed by probe-mediated generation of ring-shaped DNA and the decoding is performed by temporally sequential detection of the targeted ASMs (cf. D6, Abstract).

This is admittedly disclosed in D6 for ASMs a r r a n g e d in vitro in an array format. However, since at the priority date there was a need for multiplex analysis techniques, especially for test samples (cf. 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 (cf. also the Swedish Intellectual Property O f f i c e , PRV Consulting Report of 28 June 2023, B10, p. 5).

A suggestion or confirmation to think in this direction also resulted from the reference in D6 (p. 3, left column) that rolling-circle ASMs w e r e used in the state of the art for the readout of various genotyping assays and for the detection of proteins and protein complexes in situ with proximity ligation. That the "genotyping assays" were carried out in situ is clear 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 already describes an in situ method in its title. 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 the person skilled in the art at the priority date of the patent in suit considered the transfer of the method to an in situ environment as the next step after the successful application of an in vitro multiplex method for the detection of ASMs 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 initially carried out in vitro in "a controllable environment" (B30, p. 4, r. Sp., last para.) and, after successful implementation, was also tested in situ with positive results (B30, p. 4, l. Sp. - p.5; Abstract, Results).

Even if it is assumed with the applicants that various probes and methods for the production of ASMs were known at the time, whose suitability for an in situ application varied and that the 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, t h a t this probe or procedure w o u l d also work in an in situ context, it should be noted that this aspect d i d not prevent the authors of B30 from carrying out the detection procedure with "Turtle Probes" in situ after it had first been successfully carried out in vitro. There is no apparent reason why this would have been any different based on the detection procedure carried out in vitro with selector probes in D6.

The difference cited by the applicants in this respect, namely t h a t according to D6 the nucleic acids (analytes) were subjected to restriction digestion before the selector probes were used, whereas this w a s not necessary when using the "turtle probes" according to B30, is explained by the fact that in B30 the detection is aimed at RNA molecules, whereas the detection in D6 is aimed at genomic DNA material, which must first be prepared for hybridisation with the selector probes by restriction digestion (cf. Figure 3 A and the explanation under Figure 3). In contrast to B30, there is no reason which would have prevented the skilled person in D6 from transferring the application of the multiplex method disclosed there in vitro for the detection of nucleic acids to an in situ environment with cell or tissue samples.

The applicants' objection that there was no sufficient expectation of success from a technical point of view because they had to deal with problems such as "molecular crowding" (delimitability/distinguishability of several analytes occurring in close proximity) or "molecular crowding" was also rejected. "autofluorescence" (unpredictable interactions) in the cell or tissue sample cannot be accepted. According to the judgement of the court with technical expertise, these are problems that regularly a r i s e in connection with the in-situ detection of analytes in tissue or cell samples, but which the skilled person was able to deal with on the basis of his expertise at the time of priority and which would therefore not have prevented him from carrying out experiments in the aforementioned sense due to insufficient prospects of success (likewise the Swedish Intellectual Property O f f i c e , PRV Consulting Report, B10, p. 5). This assessment is supported by the fact that the patent in suit does not p r o v i d e any explanations on how to deal with the problems mentioned with in situ detection, such as when u s i n g immunohistochemistry methods or RNA fluorescence in situ hybridisation (FISH) (patent in suit, cf. para. 48 et seq, 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 component 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. On the contrary, it can be assumed that the skilled person was able to adjust the duration of time, taking into account other factors such as the binding affinities, the incubation conditions and the concentration of the selector probes, in such a way that the detection reagents bind sufficiently strongly to the analytes. This assessment is confirmed by the fact that even the patent in suit, which in patent claim 1 provides for incubation for a period of time s u f f i c i e n t to enable the plurality o f detection reagents t o bind to the analytes, does not provide a n y more detailed information on the specific setting. Rather, the description of the patent in suit only mentions times between 30 seconds and 48 hours or longer for contacting the samples with the detection reagents and factors that can be of importance 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 his general qualification.

20. The essence of 10x's application for a retrial is that the words "In the judgement of the court w i t h technical expertise" in the Court of Appeal's reasoning should be understood to mean t h a t the Court of Appeal used the personal opinion of one (or more) of its judges as evidence of Nanostring's submission against 10x's arguments set out above (para. 17), for which Nanostring did not provide (sufficient) supporting evidence.

21. This cannot be accepted.

22. Firstly, the opinion 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 relied not only on the submissions of 10x and Nanostring t o assess inventive step, but also on the description of the patent in suit itself and the evidence adduced by Nanostring, namely a prior art publication (B30) and party opinion B10.

24. The Order stated that B30 showed that a method which had been successfully performed in vitro had subsequently been successfully transferred to an in situ environment. The Court of Appeal held that, even a s s u m i n g that the skilled person recognised that success was not guaranteed, the difficulties raised by 10x were not so serious a s to prevent the authors o f B30 from taking this step. The Court of Appeal was not persuaded 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 use of an in vitro multiplex method for detecting ASMs, the next step would have been to consider transferring that method to an in situ environment.

25. The Court of Appeal did not follow 10x's view that there was no reasonable expectation of success from a technical point of view because the skilled person was confronted with problems. In the court's view, a skilled person was c a p a b l e o f dealing with these regularly occurring problems relating to the in situ detection of analytes in tissue or cell samples on the basis of their expertise at the priority date and, as argued by Nanostring, these problems therefore did not prevent them from carrying out tests due to an insufficient expectation of success. The Court of Appeal saw confirmation of this in the party opinion submitted by Nanostring (B10), according to which the person skilled in the art relied on by D6 knew from the publication referred to in D6 ("detection of protein and protein complexes in situ using proximity ligation" (33)), that rolling circle ASMs have previously been used to detect biological targets '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 D6.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 thus arrive at the invention according to claim 1.

26. Although the report does not expressly identify the difficulties raised by 10x, as 10x rightly a r g u e d , it is clear that the Court of Appeal inferred from the party evidence submitted by Nanostring, in particular the comments that "the skilled person knows how to adapt the methodology in [D6] for cell or tissue samples", that the expert c o n s i d e r e d that the skilled person would be able to deal with any difficulties arising f r o m adapting to an in situ environment and that these difficulties were not of such a nature that they would prevent the skilled person from e m b a r k i n g on the process.

27. The Court of Appeal found further support for its judgement in the description of the patent in suit, which contained no information on how t o deal w i t h the in situ detection issues raised by 10x.

28. I t is clear from the foregoing that the Court of Appeal did not base its reasoning on the personal opinion of one or more of its judges, but on evidence, including the patent specification, supporting Nanostring's arguments. The assessment of the arguments and evidence presented by the parties is made by the appellate court hearing the case and is not subject to review on an application for rehearing. 10x correctly did not a r g u e that the consideration of the evidence assessed and the manner in which it was assessed constituted a fundamental procedural error.

29. Unsuccessfully, 10x argues that the basic cost decision has no legal basis and that there is therefore a fundamental procedural error. As Nanostring rightly points out
R.118.5 RoP (in Part 1 of the RoP on proceedings before the Court of First Instance), according to which the court decides on the merits of the obligation t o bear the costs of the dispute, does not preclude the court of appeal from deciding on the allocation of costs in summary proceedings. As follows from Art. 32(1)(c) UPCA, actions for provisional and protective measures under Art. 62 UPCA are independent actions and these proceedings are concluded with the decision in the appeal proceedings. There is therefore a legal basis for the basic decision on costs in R.242.1 RoP.

30. A basic costs order was sought by Nanostring and 10x had the opportunity to make s u b m i s s i o n s in its defence and at the hearing, if appropriate. The fact t h a t 10x refrained from doing so did not oblige the Court of Appeal t o discuss the issue with the parties. Moreover, it does not follow from the fact that it was not discussed in the absence of a defence by 10x that 10x was not afforded a fair hearing.

31. It follows that the basic decision on costs in the contested Order is likewise not based on a fundamental procedural error.

32. It f o l l o w s from the above that the application to reopen the proceedings must be rejected as inadmissible.

ORDER

The Court of Appeal r e j e c t s the application for a retrial as inadmissible.

Issued on 6 August 2024

Rian Kalden Date: 2024.08.06 12:33:59 +02'00'

Rian Kalden, presiding judge and rapporteur

Åsa Ingeborg Simonsson Digitally signed by Åsa Ingeborg Simonsson Date: 2024.08.06 13:10:22 +02'00'

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Patricia Ursula Rombach Digitally signed by Patricia Ursula Rombach Date: 2024.08.06 16:54:04 +02'00'

Patricia Rombach, legally qualified judge