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European Biotech Patent Law Update

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Webinar agenda

- T 2570/11 – inventive step in view of suggestion in the prior art
- T 2571/12 (cf. T 950/13) – plausibility
- T 149/15 – sufficiency of disclosure
- Update to the EPO Guidelines
- T 239/16 – priority: “the PCT co-applicants approach”

T 2570/11

- Inventive step
- New drug target
- How much of a pointer to the target can exist in the art, yet inventive step of a medical use claim be acknowledged?

T 2570/11

- EP1687026 – Method for the treatment of multiple sclerosis by inhibiting IL-17 activity
- Filed 16 November 2004
- Appeal of proprietor against decision of OD to revoke the Patent
- No respondents attended the oral proceedings

T 2570/11 – Claims

- Claim 1 – Swiss-type medical use claim:

  "The use of an inhibitor of IL-17 activity for the manufacture of a medicament for the treatment and/or prophylaxis of multiple sclerosis (MS) wherein the inhibitor is an IL-17R:Fc fusion protein or an antibody or functionally active fragment thereof which binds to IL-17 or IL-17R."

- ARs 1-5: minor amendments to definition of inhibitor and/or deletion of "prophylaxis"

T 2570/11 – Prior art

- D2:
  - Experiments based on in situ hybridisation studies of IL-17 mRNA levels in:
    a) patients with MS who were either: in clinical exacerbation or remission;
    b) patients with aseptic meningoencephalitis (AM);
    c) patients with other non-inflammatory neurological disease; and
    d) healthy individuals
  - Discloses IL-17 mRNA in blood and CSF mononuclear cells is increased in MS

T 2570/11 – Prior art

- D2:

  “Numbers of IL-17 mRNA expressing blood [mononuclear cells] were higher in patients with MS and acute aseptic meningoencephalitis (AM) compared to healthy individuals.”

  “Our results thus demonstrate increased numbers of IL-17 mRNA expressing [mononuclear cells] in MS with higher numbers in CSF than blood, and with the highest numbers in blood during clinical exacerbations”

T 2570/11 – Prior art

- D2:
  - Does not disclose therapeutic treatment of MS
  - Conclusion of D2:

    "effects of increased levels of IL-17 in MS are unknown, but an induction of the production of pro-inflammatory cytokines and chemokines may be one mechanism by which IL-17 could contribute to the inflammatory brain damage in MS"

- Patent stated that IL-17 was known to be a pro-inflammatory cytokine

T 2570/11 – Prior art

- D4:
  - Discloses anti-IL-17 antibodies
  - Antibodies disclosed in a different context – the treatment of arthritis
- Patent claim 1:

  "[…] wherein the inhibitor is an IL-17R:Fc fusion protein or an antibody or functionally active fragment thereof which binds to IL-17 or IL-17R"

T 2570/11

- Inventive step:
  - D2 is suitable as the closest prior art
  - Objective technical problem:

    “the provision of means for the treatment of MS”

- Proprietor submitted a number of arguments casting doubt on the predictive value of D2

T 2570/11 – Proprietor's arguments

- Up-regulation of IL-17 **protein** is not disclosed in D2
- D2 discloses:
  - Differences in mRNA levels, not protein levels

    > "Cytokine mRNA expression is, however, not necessarily identical to protein production"

  - For example, TNFα expression is regulated at post-transcriptional and translational levels

T 2570/11 – Proprietor's arguments

- The role of IL-17 was not understood
- Cytokine network in the context of MS is immensely complex and poorly understood
- D21 (a later published review article by authors of D2) discloses:

  > "determination of cytokine levels yield, at best, incomplete information and must be supplemented by studies of additional factors that contribute to the effects of the cytokine"

- IL-17 could not be considered a validated target

T 2570/11 – Proprietor's arguments

- Other pro-inflammatory cytokine-based treatment had failed
- Knowledge that IL-17 was a pro-inflammatory cytokine does not equate to establishing an effective treatment target
- Example:
  - TNFα was known as a pro-inflammatory cytokine which has a damaging effect in MS
  - TNFα levels known to be increased in CSF of MS patients
  - Yet, TNFα failed as a treatment for MS in two clinical trials – resulted in exacerbation of MS

T 2570/11 – Decision

- D2 establishes IL-17 as a potential drug target
- Patent lacks inventive step

T 2570/11 – Decision

- Consideration of: up-regulation of IL-17 protein is not disclosed in D2

  "On the other hand, a good correlation between mRNA and protein levels have been reported for IL-10 and TNF-α in MS."

  "In conclusion, increased numbers of IL-17 mRNA expressing MNC were observed [...]. Higher numbers of IL-17 mRNA expressing blood MNC were detected [...]. The effects of increased levels of IL-17 in MS are not known, but an induction of the production of proinflammatory cytokines and chemokines may be one mechanism by which IL-17 could contribute to the inflammatory brain damage in MS"

T 2570/11 – Decision

- Consideration of: the role of IL-17 was not understood

  “This was indeed also confirmed in document D2 in the first paragraph: "Cytokines produced by infiltrating cells as well as resident cells in the brain are currently believed to regulate immune responses in MS. The cytokine network in MS is, however, not fully elucidated." (page 103, right-hand column, lines 4 to 7). However, the board is satisfied that, despite this consideration, the skilled person would consider the disclosure in document D2 to contribute to the elucidation of the MS cytokine network rather than to merely take stock of its complexity”

T 2570/11 – Decision

- Consideration of: other pro-inflammatory cytokine-based treatment had failed

  > "As far as the failure of an anti-TNF-α therapy for MS is concerned, the board concurs with the respondents that TNF-α is not IL-17 and that failure of a MS therapy based on one validated target for treatment of MS, here TNF-α, would not prevent the skilled person from persisting and to consider testing other validated targets for the treatment of MS, here IL-17."

T 2570/11 – Decision

- Board relied on a positive interpretation of D2:

  "effects of increased levels of IL-17 in MS are unknown, but an induction of the production of proinflammatory cytokines and chemokines may be one mechanism by which IL-17 could contribute to the inflammatory brain damage in MS"

T 2570/11 – Decision

"The board is thus satisfied that the skilled person would derive from the disclosure of document D2 that it identifies a correlation between the clinical appearance of MS and the expression of interleukin-17, particularly intrathecally in CSF, but also systemically in peripheral blood of MS patients."

T 2570/11 – Decision

"Even if the document does not identify IL-17 as the causative agent of MS, the skilled person would derive from it that IL-17 plays an important role in MS and that MS was an IL-17 related disorder. The board is accordingly satisfied that document D2 identifies and validates the pro-inflammatory cytokine IL-17 (see patent in suit paragraph [0002]) as a potential drug target for therapeutic strategies in the treatment of MS."

T 2570/11 – Decision

"D2 establishes IL-17 as a potential drug target for therapeutic strategies in the treatment of MS. Accordingly, the board is satisfied that the experimental teaching in document D2 would motivate the skilled person to establish the effects of inhibiting IL-17 activity in MS in the reasonable expectation of successfully reducing adverse effects of the observed correlation between the clinical appearance of MS and the expression of IL-17."

T 2570/11 – Summary

- Board's assessment:
  - Positive interpretation of hypothesis presented in conclusions of the closest prior art
  - Means to inhibit IL-17 known in the art
  - Animal models for testing effectiveness well established

- Reasonable expectation of success?

T 2571/12

- Plausibility in the assessment of sufficiency
- Comparison with T 950/13

T 2571/12

- EP1438063 – Glutathione precursors for the treatment of neuropsychiatric disorders
- Filed 26 September 2002
- Appeal of proprietor against decision of OD to revoke the Patent

T 2571/12 – Opposition

- OD revoked Patent for lack of inventive step

- However, OD decided Patent complies with requirements of sufficiency:

  "no evidence has been provided by O to show that any neuropsychiatric disorder cannot effectively been [sic] treated using a glutathione precursor such as N-acetyl-cysteine (...) the patent in suit is considered as disclosing the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art"

T 2571/12 – Claims

- AR1 – claim 1:

  "Use of a glutathione precursor in the manufacture of a medicament for the treatment of a neuropsychiatric disorder in a mammal, wherein said glutathione precursor induces, upregulates or otherwise augments antioxidant functional activity in the brain of said mammal, wherein said neuropsychiatric disorder is depression."

T 2571/12 – Patent

- Patent:
  - Depression listed as one of a number of neuropsychiatric disorders that can be treated
  - Patent discusses underlying mechanism in relation to schizophrenia
  - However, no evidence in Patent or prior art relating to effect on depression
  - Proprietor filed post-published evidence

T 2571/12 – Decision

- Established approach to sufficiency:

> "[U]nder Article 83 EPC, unless this is already known to the skilled person at the priority date, the application must disclose the suitability of the product to be used for the claimed therapeutic application (see also T 609/02, reasons 9)"

T 2571/12 – Decision

- Board disagrees with OD's decision:

  "It is the patent that has to demonstrate the suitability of the claimed treatment for the claimed therapeutic indication. As explained, for example, in decision T 609/02 supra, a simple verbal statement that compound X may be used to treat disease Y is not enough to ensure sufficiency of disclosure: rather, it is required that the patent provides some information in the form of, for example, experimental tests, to the avail that the claimed compound has a direct effect on a metabolic mechanism specifically involved in the disease, this mechanism being either known from the prior art or demonstrated in the patent per se."

T 2571/12 – Decision

"there is no evidence at all, either in the patent or in the available prior art, that makes it plausible that glutathione precursors may have a therapeutic effect in depression."

"In fact, there is no hint that the underlying mechanism which is extensively disclosed in the patent for schizophrenia, namely reduction of glutathione levels in the central nervous system and consequent oxidative stress, is also present in depression."

T 2571/12 – Decision

"post-published evidence may be taken into account for sufficiency of disclosure, but only to back up the findings in the patent application in relation to the use of the ingredient as a pharmaceutical, and not to establish sufficiency of disclosure on its own"

T 2571/12 – Summary

- Cf. T 950/13:
  - Use of dasatinib for treatment of CML
  - Dasatinib identified as preferred compound
  - Reasoning from application that dasatinib inhibits an enzyme target and a link to CML
  - Prior art: known use of another compound (imatinib) to treat CML via a similar mechanism

T 2571/12 – Summary

- T 950/13 acknowledges data not essential:

  “The application does not contain experimental evidence for dasatinib's BRC-ABL kinase inhibitory activity. However, the disclosure of experimental results in the application is not always required to establish sufficiency, in particular if the application discloses a plausible technical concept and there are no substantiated doubts that the claimed concept can be put into practice”

T 2571/12 – Summary

- T 950/13 acknowledges technical effect plausible:
  - “the board is satisfied that the application discloses at least a plausible technical concept, namely that dasatinib based on its functional equivalence to imatinib as a BRC-ABL kinase inhibitor is suitable in the treatment of CML. There are no reasons apparent to the board as to why a skilled person would *a priori* regard this teaching as incredible or implausible.”

T 2571/12 – Summary

- No evidence in Patent or prior art
- No mechanistic disclosure relating to the claimed medical use (depression)
- No plausible technical concept

- Cannot take post-published evidence into account
- Lack of sufficiency

T 149/15

- Sufficiency of disclosure
- Unimed Pharma (Abbott) & Besins Healthcare
- Testosterone gels for treating hypogonadism
- Viscosity parameter of the gel
- Device manual

T 149/15

- EP 1 937 276 B (filing date: October 2006)
- Opposition filed
- Patent revoked
  - lack of novelty (MR and AR3)
  - Added subject-matter (AR1 and AR2)
- Appeal – sufficiency of disclosure (Art. 83 EPC / Art. 100(b) EPC)

T 149/15 – Claim 1

"1. A hydroalcoholic gel pharmaceutical composition comprising:

i. from 1.50 % to 1.70 % (w/w) testosterone;

ii. from 0.6 % to 1.2 % (w/w) isopropyl myristate;

iii. from 60 % to 80 % (w/w) of an alcohol selected from the group consisting of ethanol and isopropanol;

iv. ***a sufficient amount of a thickening agent to give the composition a viscosity in excess of 9000 cps****; and*

v. water.

T 149/15 – Arguments of the parties

- Respondent / opponent
  - Viscosity measurements sensitive to how they are carried out
  - According to D1, a repeatable viscosity test should specify nine parameters:
  - Only four specified in patent
  - No upper limit – importance of spindle

- Test temperature
- Sample container size
- Sample volume
- Viscosimeter model
- Spindle used
- Whether or not to attach the guard leg
- Test speed
- Length of time or number of spindle revolutions to record viscosity
- How sample was prepared and/or loaded into the container

T 149/15 – Arguments of the parties

- Appellant / proprietor
  - Viscosity measured using a Brookfield DVII+ viscosimeter with RV6 spindle
  - Essential parameters not in patent were clear from the general disclosure in operating manual for the viscosimeter (D1)
  - No upper limit - not an issue because viscosity of gels limited in practice

T 149/15 – Decision

- Skilled person “would turn to the operating instructions (D1) to carry out the necessary measurement”
  - No publication date, but accepted by both parties as the operating instructions at the filing date

T 149/15 – Decision

- Test temperature
- Sample container size
- Sample volume
- Viscosimeter model
- Spindle used
- Whether or not to attach the guard leg
- Test speed
- Length of time or number of spindle revolutions to record viscosity
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T 149/15 – Decision

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T 149/15 – Decision

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- Viscosimeter model
- Spindle used
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- Test speed
- Length of time or number of spindle revolutions to record viscosity
- How sample was prepared and/or loaded into the container

T 149/15 – Decision

- Cannot be compared to T 808/09
  - Only information given in application was in relation to ambient temperature
- No upper limit:
  - Pharmaceutical gels cannot have unlimited viscosity
  - Spindle useful in the range 1,000 to 2 x 10^6 cps

T 149/15 – Lessons and practice points

- Art 83 EPC continues to be a reasonably low hurdle
- Information in the application + CGK
- Only one example needed
  - Reference to a specific viscosimeter
- “Information overload” when drafting
- Consideration of opposition strategy

EPO Guidelines update – November 2018

- **Sufficiency of disclosure** – substantive examination of an opposition (D-V, 4)

  > *"The skilled person wishing to implement the claimed invention reads the claims in a technically sensible manner. An objection of insufficient disclosure of the invention is therefore not to be based on embodiments that are meaningless and not consistent with the teaching of the application as a whole (see T 521/12)."*

- Attempt to rein in arguments in Opposition proceedings?

T 239/16

Article 87 EPC - Priority right

"(1) Any person who has duly filed, in or for

(a) any State party to the Paris Convention for the Protection of Industrial Property or

(b) any Member of the World Trade Organization,

an application for a patent, a utility model or a utility certificate, **or his successor in title**, shall enjoy, for the purpose of filing a European patent application in respect of the same invention, a right of priority during a period of twelve months from the date of filing of the first application.

T 239/16

PRIORITY

US application

Inventors

A + B + C

PCT

Applicants

X + Y

Applicants (for US only)

A + B + C

T 239/16

PRIORITY

US application

Inventors

A + B + C

Transfer of priority right

?

PCT

Applicants

X + Y

Applicants (for US only)

A + B + C

T 239/16

- EP 1 591 122 B (filing date: June 2001)
- Novartis
- Zoledronic Acid (ZOMETA®)
- Five opponents – raised issue of formal entitlement to priority
- Opposition Division – priority validly claimed; claims otherwise valid
- Appeal – Preliminary Opinion of Board of Appeal; everything apart from priority
- Patent revoked for lack of inventive step
- ONLY A TREND !

T 239/16 – Priority claim

PRIORITY (US)

INVENTOR(S)

Given Name (first and middle [if any])	Family Name or Surname
Zebulun D. Peter C. Ulrich	Horowitz Richardson Trechsel

PCT

(30) Priority Data:

09/597,135	20 June 2000 (20.06.2000)	US
60/267,689	9 February 2001 (09.02.2001)	US

(71) Applicant *(for all designated States except AT, US)*: **NOVARTIS AG** [CH/CH]; Lichtstrasse 35, CH-4056 Basel (CH).

(71) Applicant *(for AT only)*: **NOVARTIS-ERFINDUNGEN VERWALTUNGSGESELLSCHAFT M.B.H.** [AT/AT]; Brunner Strasse 59, A-1230 Vienna (AT).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **HOROWITZ, Zebulun, D.** [US/US]; 83 Blackburn Road, Basking Ridge, NJ 07920 (US). **RICHARDSON, Peter, C.** [GB/US]; 4 Spring Lake Drive, Far Hills, NJ 07931 (US). **TRECHSEL, Ulrich** [CH/CH]; Grosshaus, CH-7242 Luzein (CH).

T 239/16 – Priority claim

PRIORITY (US)

INVENTOR(S)	
Given Name (first and middle [if any])	Family Name or Surname
Zebulun D. Peter C. Ulrich	Horowitz Richardson Trechsel

Transfer of priority right

?

PCT

(30) Priority Data:

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T 239/16 – Opposition proceedings

- "Dated with effect from …" = retroactive
- Standard is "balance of probabilities" not "up to the hilt"
- Email chains and mail date stamps
- Contract law
- Reasonable assumption signed in time

METHOD OF ADMINISTERING BISPHOSPHONATES

while claiming the priority of my (our) above named patent application(s) in conformity with the dispositions of the International Convention.

Dated with effect from: **02 May 2001**

1. Zebulun D. HOROWITZ
2. Peter C. RICHARDSON
3. Ulrich TRECHSEL

METHOD OF ADMINISTERING BISPHOSPHONATES

while claiming the priority of my (our) above named patent application(s) in conformity with the dispositions of the International Convention.

Dated with effect from: **02 May 2001**

1. Zebulun D. HOROWITZ
2. Peter C. RICHARDSON
3. Ulrich TRECHSEL

T 239/16 – Appeal: Opponent's arguments

- New argument:
- "The inventors could not validly transfer the priority rights"
- **T 517/14** – law of the state of the employment relationship between inventor and applicant governs
  - US law → inventors assign all rights to employer
  - CH law → legal devolution of all rights to employer
  - Inventors not able to freely dispose of priority right

T 239/16 – Appeal: Patentee's response

- Conflicting law – both EPO and national
  - **T 517/14** – Israeli employment law

  - **BGH X ZR 49/12** – Law of the state in which the application was made

  - **T 62/05 –** high bar: separate and formal assignment required, signed by both parties akin to assignment under Art. 72 EPC

T 239/16 – Request for referral to the enlarged board

- *…what constitutes "successor in title" and the standard required to prove it*.

- Referring to the law and practice in the US, the legal entitlement to the right to priority should be recognised in the event that at least one of the inventors of the earlier application is mentioned in the application claiming priority.

T 239/16 – Preliminary Opinion of the Board

- Power of the EPO to decide on legal entitlement to priority right?

> *"Nevertheless, Article 87(1) EPC 1973 can be and has been regarded as sufficient legal basis for the examination of the legal entitlement to the right of priority (see the jurisprudence cited in point 3.1 above; see also the Guidelines for Examination in the EPO, edition November 2016, F-VI, 1.3; A-III, 6.1; see however also A-III, 6.9 and 6.10)."*

T 239/16 – Preliminary Opinion of the Board

- Power of the EPO to decide on legal entitlement to priority right?

> *"Therefore, it follows from Articles 60, 61 and 138 (1)(e) EPC that questions of legal entitlement (ownership and transfer) can be considered to fall, as a matter of principle, within the sole jurisdiction of the national courts or other authorities responsible. Such considerations could also apply to the legal entitlement to the right of priority (cf. J 11/95 of 27 November 1997, point 4, last sentence)."*

T 239/16 – The "PCT co-applicants approach"

- Sitting on fence, but leaning towards…

> *"It could be argued that, because the PCT application was filed on behalf the applicants of the priority application, priority is validly claimed in the PCT application even though the application was filed by several applicants that were indicated in the request for different designated states. In other words, it could be argued that* ***the applicant(s) of the first application de facto share their right of priority with any further applicant on behalf of whom the international application claiming priority has been filed*** *(cf. T 1933/12 of 21 February 2014, point 2.4; see below points 3.5)."*

T 239/16 – The “PCT co-applicants approach”

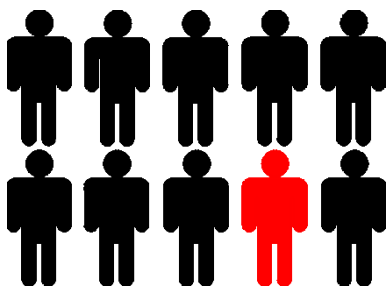
- But the inventors are applicants only for the US…

*“There are aspects suggesting that the **several applicants are to be considered as a group of joint applicants, irrespective of the designations of the states**, up until the entry of the PCT application in the national or regional phases.”*

T 239/16 – The “PCT co-applicants approach”

- Conclusion(?)

*“In other words, by the mere fact that **the applicant of the priority application is amongst the co-applicants of the subsequent applications**, the co-applicants might benefit from the claimed priority right without further ado.”*



T 239/16 – The “PCT co-applicants approach”

- Comparison with EPO direct filing:
  - If priority applicant A is one of multiple applicants for a subsequent application (A, B and C) then no issue

T 239/16 – OD cases following suit

- *Decision in EP2429574 (University Health Network; 2 Jan 2018)*

> In the case of joint applicants filing the later application, it is sufficient if one of the applicants is the applicant (or his successor in title) of the previous application. There is no need for a special transfer of the priority right to the other applicants, since the later application has been filed jointly. The same applies to the case where the previous application itself was filed by joint applicants, provided that all these applicants (or their successors in title) are amongst the joint applicants of the later European patent application (see Guidelines for examination in the EPO, edition November 2016, A-III, 6.1).
>
> In the absence of any prevailing PCT provision, the same applies in respect of an international application with designation EP in proceedings before the EPO as designated Office (Article 11(3) PCT, Article 153(2), 150(2) EPC). As

T 239/16 – OD cases following suit

- *Decision in EP2429574 (University Health Network; 2 Jan 2018)*

> The opposition division therefore concludes that under Articles 87(1), 153(2) EPC the priority right owning applicant, even if he is the applicant for certain designations of the PCT application only, can introduce the priority right into the PCT application with full effect for the PCT application as a whole. Therefore the applicants of the PCT application were formally entitled to claim priority of the previous application.

T 239/16 – OD cases following suit

Summons to Oral Proceedings:

- *EP2940044 (AbbVie; 13 July 2018)*
- *EP1737491 (AbbVie; 30 April 2018)*
- *EP2215124 (Amgen; 13 Dec 2017)*

T 239/16 – Lessons and practice points

- Merely a trend – no Board of Appeal Decisions as yet
- As long as priority and PCT share a common applicant, all is good
- Good news for patentees / US inventors
- Opponents – “broad brush approach”

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