Examination Matters – webinar series in the medical field

Experimental data: Impact on patentability in medical applications
Presenting today

The presenter(s)

Elsie Cielen
- Examiner Search/Examination/Opposition
- Expert Patent Procedures Management
- Sector HBC – 2nd Medical Applications
- PhD Chemistry, KU Leuven, BE

Britta Kley
- Litigator for an international law firm, 2001-2004
- Lawyer at the EPO since 2004
- Lawyer in Directorate Patent Law since 2012
- Doctorate Degree in Law, University of Trier, DE
Experimental data: Impact on patentability in medical applications

Objectives

- Understanding under which conditions an objection of insufficiency of disclosure or lack of inventive step can be overcome by submitting post-published evidence

- Becoming aware of the impact enhanced publication requirements for clinical trail data may have on further medical use claims

- Gaining awareness of the role of clinical trials as prior art in relation to novelty and inventive step, and the importance of the presence of experimental data in the application as filed
Experimental data: Impact on patentability in medical applications

Agenda

- Experimental data and sufficiency of disclosure / inventive step
  - Background
  - Practical case
  - Conclusion

- Clinical trials and novelty / inventive step
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  - Publication requirements for clinical trial data
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Experimental data and sufficiency of disclosure / inventive step

Article 56 vs Article 83

Claimed invention lacks reproducibility (non-working examples):

- If the technical **effect** expressed in the claim is not achieved: **Art. 83**
  Technical effect is part of the proposed solution, hence it cannot be part of the problem

- If the **effect** is not expressed in the claim but is **part of the problem** to be solved: **Art. 56**
Can insufficiency of disclosure or lack of inventive step be solved by submitting post-published evidence?
Experimental data and sufficiency of disclosure / inventive step

Late filed evidence: of avail

Later filed examples or new effects may be taken into account in support of patentability, e.g.:

▪ an **additional example**, as evidence that the invention can be applied, on the basis of the information in the application as filed, over the whole field claimed

▪ a **new effect** in support of inventive step, provided that it is implied by or at least related to an effect disclosed in the application as filed
Experimental data and sufficiency of disclosure / inventive step

Late filed evidence of no avail: T 609/02

Claim

Use of a steroid hormone which fails to promote transcriptional activation of glucocorticoid receptor- or retinoic acid receptor- responsive genes, for the preparation of a pharmaceutical for the treatment of AP-1 stimulated tumour formation, arthritis, asthma, allergies and rashes, said hormone being identified by the method according to the previous claims
Experimental data and sufficiency of disclosure / inventive step

Late filed evidence of no avail: T 609/02 (2)

- Second medical use claim: therapeutic effect is functional technical feature of the claim
- Unless known at priority date, application must disclose suitability of the product for the claimed therapy
- Simple verbal statement in application is not enough
- For sufficient disclosure of a therapeutic application, results in clinical trials/animals not always necessary
Experimental data and sufficiency of disclosure / inventive step

Late filed evidence of no avail: T 609/02 (3)

- Patent must provide information, e.g. tests, to show that claimed compound has direct effect on mechanism involved in the disease, this mechanism being known from prior art or demonstrated in patent.

- Showing pharmaceutical effect in vitro sufficient if for skilled person this effect directly and unambiguously reflects therapeutic application, i.e. if there is a "clear and accepted established relationship" between shown physiological activities and disease.

Art. 83 EPC
Experimental data and sufficiency of disclosure / inventive step

Late filed evidence of no avail: T 609/02 (4)

- Once this evidence is available from application, post-published evidence may be taken into account,
  - but only to back-up findings in the patent application in relation to the use of the ingredient as a pharmaceutical,
  - not to establish sufficiency of disclosure on their own\(^1\)
Experimental data and sufficiency of disclosure / inventive step

Late filed evidence of no avail: T 609/02 (4)

- Once this evidence is available from application, post-published evidence may be taken into account,
  - but only to back-up findings in the patent application in relation to the use of the ingredient as a pharmaceutical,
  - not to establish sufficiency of disclosure on their own¹

- **T 801/06**: r. 28: claimed therapeutic effect may be proven by any kind of data, as long as they clearly and unambiguously reflect the therapeutic effect

¹ Case Law of the Boards of Appeal of the EPO, 8th edition 2016, section II.C.6.2
Experimental data and sufficiency of disclosure / inventive step

Late filed evidence of no avail: T 1329/04

Claim

A polynucleotide encoding a polypeptide having GDF-9 activity selected from the group consisting of:
(a) a polynucleotide having the nucleic acid sequence of SEQ ID NO:3;
(b) a polynucleotide encoding a polypeptide having the amino acid sequence of SEQ ID NO:4;
...

Art. 56 EPC
Experimental data and sufficiency of disclosure / inventive step

Late filed evidence of no avail: T 1329/04 (2)

- The definition of an invention as being a contribution to the art requires that it is at least made *plausible* by the disclosure in the application that its teaching solves indeed the problem it purports to solve.

- Supplementary *post-published evidence* may in the proper circumstances also be taken into consideration,

**BUT**

it may *not* serve as the *sole basis* to establish that the application solves indeed the problem it purports to solve.
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Experimental data and sufficiency of disclosure / inventive step

Case 1 (1)

Claim

A compound of formula (1) for use in the treatment of a CNS disorder associated with the dopamine D2 receptor, which is bipolar disorder.
### Experimental data and sufficiency of disclosure / inventive step

#### Case 1 (1)

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- "The potent D2 receptor antagonist in the present invention is useful for various disorders of the CNS associated with the dopamine D2 receptor that induces bipolar disorders." |
Experimental data and sufficiency of disclosure / inventive step

**Case 1 (1)**

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Disclosure
- data show that compound is D2 receptor antagonist
- "The potent D2 receptor antagonist in the present invention is useful for various disorders of the CNS associated with the dopamine D2 receptor that induces bipolar disorders."

Do you think that the information in the application is sufficient?
→ ☑ yes  □ no
**Experimental data and sufficiency of disclosure / inventive step**

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Experimental data and sufficiency of disclosure / inventive step

Case 1 (2)

D6, D7 and D8 (in time) show direct relationship between D2 antagonism and the suitability for the treatment of bipolar disorders

- D6 is a patent application
- D7 is a postgraduate medicine special report
- D8 is an article published in a scientific journal
### Case 1 (2)

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Do you think that these documents can be used in support of the statement in the description?

→ yes  no
Experimental data and sufficiency of disclosure / inventive step

Case 1 (2)

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Do you think that these documents can be used in support of the statement in the description?

→ ☑ yes  ☐ no

→ Documents cannot support the description. They do not represent common general knowledge, because the field is not so new that common general knowledge is solely reflected in patent documents and scientific articles (GL, G-VII, 3.1).
Experimental data and sufficiency of disclosure / inventive step

Case 1 (3)

Post-published evidence

Additional data provided in several documents and in a letter by the Proprietor with conclusive evidence
Experimental data and sufficiency of disclosure / inventive step

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Additional data provided in several documents and in a letter by the Proprietor with conclusive evidence

Can the applicant’s post-published evidence be taken into account?
Experimental data and sufficiency of disclosure / inventive step

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<td><strong>Post-published evidence</strong></td>
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Can the applicant’s post-published evidence be taken into account?

→ ☑ yes  ❌ no
Experimental data and sufficiency of disclosure / inventive step

Case 1 (3)

Post-published evidence

Additional data provided in several documents and in a letter by the Proprietor with conclusive evidence

Can the applicant’s post-published evidence be taken into account?

→ ☑ yes  ❌ no

Post-published evidence cannot be taken into account.

- The application as filed does not disclose the suitability of a compound of formula (1) for the treatment of bipolar disorder, and there is no common general knowledge to provide the missing link.
- In such a case, post-published evidence cannot cure the deficiency of disclosure of the patent.
Experimental data and sufficiency of disclosure / inventive step

Aspects relevant for Art. 83 assessment

▪ to what extent does the original application reveal the suitability of compounds for the claimed therapeutic use?

▪ to what extent can the skilled person supplement this disclosure with its common general knowledge?

▪ to what extent are pre-published documents to be considered as common general knowledge?, and

▪ can any alleged deficiency of the disclosure of the patent / application be cured by post-published evidence?
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## Experimental data and sufficiency of disclosure / inventive step

### Conclusion: post-published evidence

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# Experimental data and sufficiency of disclosure / inventive step

## Conclusion: post-published evidence

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- Each case has to be judged on its own merits, depending on the specific circumstances of the case
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## Clinical trials and novelty / inventive step

### Clinical trial phases

<table>
<thead>
<tr>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Testing of drug for dose-ranging</td>
<td>- Testing of drug on patients to assess efficacy and side effects</td>
<td>- Testing of drug on patients to assess efficacy, effectiveness and safety</td>
</tr>
<tr>
<td>- 20-100 healthy volunteers</td>
<td>- 100–300 patients with specific diseases</td>
<td>- 300–3 000 patients with specific diseases</td>
</tr>
<tr>
<td>- determines whether drug is safe to check for efficacy</td>
<td>- determines whether drug can have any efficacy; at this point, the drug is not presumed to have any therapeutic effect</td>
<td>- determines a drug's therapeutic effect; at this point, the drug is presumed to have some effect</td>
</tr>
<tr>
<td>- no efficacy studied</td>
<td></td>
<td></td>
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Clinical trials and novelty / inventive step

Clinical trials: T 158/96

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<tr>
<td>Prior art</td>
<td>Sertraline is undergoing phase II clinical trials</td>
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</table>
Clinical trials and novelty / inventive step

Clinical trials: T 158/96 (2)

Same therapeutic effect shown in the prior art?

- no prediction of therapeutic activity (no +/- results)
  - many drugs fail to proceed to phase III
  - OCD is complex
  - no consensus how to study OCD (heterogeneous populations)
  - no animal model for OCD
  - no reliable preclinical evaluation of utility of sertraline in OCD
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- the case was remitted to the first instance
"The information in a citation that a medicament is undergoing a clinical phase evaluation for a specific therapeutic application is not prejudicial to the novelty of a claim directed to the same therapeutic application of the same medicament if such information is plausibly contradicted by the circumstances and if the content of said citation does not allow any conclusion to be drawn with regard to the actual existence of a therapeutic effect or any pharmacological effect which directly and unambiguously underlies the claimed therapeutic application"
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Clinical trials and novelty / inventive step

Legal Framework

- European Medicines Agency policy on publication of clinical data for medicinal products for human use
  
  *applicable as from 1 January 2015*

  
  *expected to apply as from 2020.*
# Clinical trials and novelty / inventive step

## Legal Framework

<table>
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<tr>
<th>Medicinal products covered</th>
<th>Clinical data publication policy</th>
<th>Clinical Trial Regulation</th>
</tr>
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<tbody>
<tr>
<td>Centrally authorised products only</td>
<td>All investigational medicinal products</td>
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<table>
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<th>Clinical studies covered</th>
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<th>Clinical trials conducted in and outside the EU</th>
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<th>Documents published</th>
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<th>All clinical trial-related information (e.g. protocol, decision on trail conduct, summary of trial results, study reports, etc.)</th>
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| Publication from | October 2016 | Expected in 2020 |
Clinical trials and novelty / inventive step

Legal Framework

- Patent application I
- Pre-clinical development
- Patent application II
- Clinical trials
- Patent application III
- Marketing authorisation
- Patent application IV

Prior art for appl. I
Prior art for application II
Prior art for application III
Disclosure of clinical trial reports
Clinical trials and novelty / inventive step

CCI can remain unpublished upon request

- **Art. 81(4)(a) Regulation (EU) No. 536/2014:**
  All data submitted shall be publicly accessible unless confidentiality is justified to protect commercially confidential information (CCI), if there is no overriding public interest in disclosure.

- **Sec. 4.2.2 EMA policy on publication:**
  Information contained in clinical reports should not be considered CCI. However, the EMA acknowledges that in limited circumstances clinical reports can contain CCI.
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Clinical trials and novelty / inventive step

Case 2 (1)

Claim 1  Medicament comprising a combination of compound X and compound Y for use in treating cancer.
Clinical trials and novelty / inventive step

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<th>Claim 1</th>
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| Prior art | ▪ D1: Compound X and Y are each effective for breast cancer in monotherapy  
▪ D2: Phase I clinical trial of X and Y against cancer ongoing at the filing date; no data |
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Is D2 prejudicial to the novelty of claim 1?
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Is D2 prejudicial to the novelty of claim 1?  
→ yes yes  
→ no
Clinical trials and novelty / inventive step

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Claim 1

Medicament comprising a combination of compound X and compound Y for use in treating cancer.

Prior art

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Is D2 prejudicial to the novelty of claim 1?
→ yes  no
→ Not prejudicial.
The knowledge that clinical trials were on-going does not anticipate the claimed matter, because the results of said trials were not yet available.
Clinical trials and novelty / inventive step

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Do you find the opponent’s argument that since the two mono-therapies were known to be effective from D1, the combination was also inevitably effective, convincing?
Clinical trials and novelty / inventive step

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- [x] yes
- [x] no
Clinical trials and novelty / inventive step

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→ ☑ yes  ☐ no
→ Not convincing.

There is no evidence in the prior art that the combination is safe; the interaction between the drugs may result in toxicity.
Clinical trials and novelty / inventive step

Case 2 (2)

Example 1:
= results of a phase I study
MTD (maximum tolerated dose) of X in combination with Y
at this dose, the combination treatment is safe
dose finding study found partial response in some patients
Clinical trials and novelty / inventive step

Case 2 (2)

Disclosure

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Clinical trials and novelty / inventive step

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- D1
- D2

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In view of the data in the application, the problem is the provision of a safe and effective combination for treating cancer. Is the solution obvious?
- yes
- no

→ Obvious according to the BoA in the "real" case T2506/12.
Clinical trials and novelty / inventive step

**Case 2 (3)**

- The 2 drugs were known as **effective** in **mono-therapy** for the same cancer types.

- No evidence on file that there was no "reasonable expectation of success".

- D2 proved that pharmaceutical researchers considered the expectation of success of the combination treatment **sufficient** to justify a clinical trial.

- Such trials were not initiated based on a general "try and see attitude", but on the base of existing favourable results, for ethical and economic reasons. They were **not** a mere "screening exercise".
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## Clinical trials and novelty / inventive step

### Conclusion: Clinical trials

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<th>Inventive step</th>
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| **Ongoing clinical trial is not prejudicial to the novelty if:**  
  ▪ information is plausibly contradicted by the circumstances, and  
  ▪ no conclusion can be drawn about actual existence of effect  
| **If the prior art provides no technical evidence that the combination treatment is safe, an "effective treatment" is not disclosed in the prior art**  
| **If prior art discloses effectiveness of each drug individually, and that clinical trials are ongoing,**  
  in the absence of evidence to the contrary,  
  there is reasonable expectation that the combination treatment will be successful |
**Clinical trials and novelty / inventive step**

### Conclusion: Clinical trials

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- Each case has to be judged on its own merits, depending on the specific circumstances of the case
Clinical trials and novelty / inventive step

**Cited decisions**

- Landmark decisions:
  - T 609/02, T 1329/04, T 158/96

- Other decisions:
  - T 801/06

- Decisions underlying practical cases:
  - T 2059/13, T 2506/12 (see also T 0239/16)
Experimental data: Impact on patentability in medical applications

Agenda

✓ Experimental data and sufficiency of disclosure / inventive step
  - Background
  - Practical case
  - Conclusion

✓ Clinical trials and novelty / inventive step
  - Background
  - Publication requirements for clinical trial data
  - Practical case
  - Conclusion

▪ Questions
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<tr>
<td>now</td>
<td>via chat to &quot;All participants&quot;</td>
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<tr>
<td>later</td>
<td>via mail ➔ <a href="mailto:academy@epo.org">academy@epo.org</a></td>
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