Enablement in Claims to Therapeutic Treatment

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35 U.S.C. § 112, 1st Paragraph

- Specification must teach how to make and use the invention
- Is the experimentation needed to practice the invention undue or unreasonable?

Therapeutic Treatment

- **Inquiry may involve**
  - **How to use the claimed invention**
  - **How to make the claimed invention**
- **Method claims reciting therapeutic treatment**
- **Composition or compound claims reciting intended therapeutic use**

35 U.S.C. § 112, 1st Paragraph

- The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art

- However, even in unpredictable arts, a disclosure of every operable species is not required

35 U.S.C. § 112, 1st Paragraph

- In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)
- Examiner is the fact finder
- All evidence must be weighed by the examiner
- No per se rules
- Case-by-case analysis

35 U.S.C. § 112, 1st Paragraph

- The examiner has the initial burden to establish a reasonable basis to question the enablement provided for the either the full scope or a part thereof of the claimed invention
- There must be a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support

35 U.S.C. § 112, 1st Paragraph

- References should be supplied if possible to support a prima facie case of lack of enablement, but are not always required
- Specific technical reasons are always required

State of the Art

- Whether or not experimentation is routine depends on what is well-known in the art at the time of filing
- Enablement analysis is performed based on the state of the art combined with any evidence presented in the specification

State of the Art

- **An applicant may omit from the disclosure any routine technology that is well known at the time of application**

Therapeutic Methods/Uses

- **Is there any unpredictability in the scope of the claimed therapeutic method and has this unpredictability been resolved by evidence presented in the specification?**

In re Gardner, 427 F.2d 786, 166 USPQ 138 (C.C.P.A. 1970)

- Claim to a pharmaceutical composition comprising 2-aminomethyl-1,3-benzodioxole compounds having antidepressant activity
- "In effect, by [claiming therapeutic activity, applicants] are claiming in terms of use. It behooves them, therefore, to disclose how to use, as section 112 ordains . . . ."

In re Gardner, 427 F.2d 786, 166 USPQ 138 (C.C.P.A. 1970)

- **Specification lacked the disclosure of**
  - **the recipient of the composition**
  - **the proper dosage**
  - **any working examples**
  - **an animal model**

In re Gardner, 427 F.2d 786, 166 USPQ 138 (C.C.P.A. 1970)

- **Appellants, relying on an affidavit, argue**
  - **efficacy in a rat model correlated to antidepressant activity in man**
  - **that the proper dosage would have been within the skill of a pharmacologist**

Highlights and Guidance

- The lack of direction provided by the inventor and the lack of working examples appeared to be the factors weighed most heavily by the court
- The enablement of compositions reciting activity or intended use must be considered

In re Jolles, 628 F.2d 1322, 206 USPQ 885 (C.C.P.A. 1980)

- Methods of treating acute myeloblastic leukemia in humans comprising administration of naphthacene derivatives
- Pharmaceutical compositions for treatment of acute myeloblastic leukemia comprising naphthacene derivatives

In re Jolles, 628 F.2d 1322, 206 USPQ 885 (C.C.P.A. 1980)

- **Specification**
  - Claimed derivatives had a close structural relation to daunorubicin and doxorubicin
- **Two declarations**
  - Clinical treatment of human patients with acute myeloblastic leukemia
  - Mouse tests on sarcoma tumors and leukemia of eight structurally similar compounds, one of which was the same as tested clinically

In re Jolles, 628 F.2d 1322, 206 USPQ 885 (C.C.P.A. 1980)

- **The Examiner**
  - Alleged that there was no utility and therefore no enablement
  - Provided no documentary evidence
- **The Board**
  - Affirmed the Examiner
  - Provided no documentary evidence

In re Jolles, 628 F.2d 1322, 206 USPQ 885 (C.C.P.A. 1980)

- **The Court**
  - **noted that neither the solicitor nor the examiner provided support for the assertion regarding "incredible utility"**
  - **held that Board erred by failing to give sufficient weight to the similarity of the remaining claimed derivatives to the allowed derivative**
  - **This similarity combined with the close structural relationship to known anti-neoplastic agents would have enabled the method/use**

Highlights and Guidance

- **The state of the prior art, the amount of direction provided by the inventor as well as the declaration evidence outweighed the Examiner's unsupported allegations**
- **A finding of lack of enablement must be based on evidence**

In re Bundy, 642 F.2d 430, 209 USPQ 48 (C.C.P.A. 1981)

- **Claims to prostaglandin E analogs**
- **Specification disclosed**
  - **biological activities of natural PGEs**
  - **therapeutic uses relying on the biological activities**
  - **unexpected increase in analogs' biological activity**
  - **no working examples**

In re Bundy, 642 F.2d 430, 209 USPQ 48 (C.C.P.A. 1981)

- **Examiner found a lack of enablement citing a reference stating that "small changes in prostaglandin structure could alter potency or induce diametrically opposed pharmacological effects"**

In re Bundy, 642 F.2d 430, 209 USPQ 48 (C.C.P.A. 1981)

- **Court held that**
  - **The evidence of change in pharmacologic activity was related to PGF, not PGE**
  - **The discussion of PGE related only to a matter of degree of potency**
  - **The result in Gardener was distinguished due to claims to compounds without recitation of use**

Highlights and Guidance

- **Claims to compounds or compositions that do not recite an intended use need only one enabled use**
- **Evidence of unpredictability must be sufficiently related to the claimed invention**

Glaxo v. Teva, 2004 WL 1875017 (D. Del. 2004)

- Glaxo patents with claims to a method of treatment for the relief of nausea and vomiting comprising the administration of ondansetron
- As one of the defenses to an action for infringement, Teva asserted lack of enablement of a priority document

Glaxo v. Teva, 2004 WL 1875017 (D. Del. 2004)

- Teva argued the absence of working examples in the priority document
- The priority document
  - Identifies ondansetron specifically
  - Teaches its use as anti-emetic
  - Provides a dosage range
  - Provides routes of administration

Glaxo v. Teva, 2004 WL 1875017 (D. Del. 2004)

- **Court finds**
  - **no requirement in the law for working examples**
  - **priority document clear on its face**
  - **Teva bore the burden of providing clear and convincing evidence of lack of enablement and failed to do so**

Highlights and Guidance

- **Lack of working examples alone is insufficient to support a finding of lack of enablement**
- **The absence of working examples may be probative where the evidence indicates unpredictability that may need to be resolved by exemplary evidence**

Rasmussen v. SmithKline, 413 F.3d 1318, 75 USPQ2d 1297 (Fed. Cir. 2005)

- Interference appeal
- Rasmussen lost interference to SmithKline
- Claims to methods of treating prostate cancer by administration of a 5aR-inhibiting compound, specifically finasteride

Rasmussen v. SmithKline, 413 F.3d 1318, 75 USPQ2d 1297 (Fed. Cir. 2005)

- **The Board held that Rasmussen's priority document failed to enable the claimed invention in view of**
  - **The state of the art**
  - **The lack of data to demonstrate the effects of finasteride in treating prostate cancer**

Rasmussen v. SmithKline, 413 F.3d 1318, 75 USPQ2d 1297 (Fed. Cir. 2005)

- On appeal, Rasmussen argues that
  - The Board's findings regarding lack of a showing of efficacy are not relevant to a finding of lack of enablement, but pertains only to utility
  - The enablement requirement of Section 112 does not mandate a showing of utility and if it does, the requirement mandates only a showing that it is "not implausible" that the invention will work for its intended purpose

Rasmussen v. SmithKline, 413 F.3d 1318, 75 USPQ2d 1297 (Fed. Cir. 2005)

- **The court disagrees, holding**
  - **Failure to disclose "how to use" may support a rejection under 35 USC 112, 1st paragraph**
  - **"[I]t is proper for the examiner to ask for substantiating evidence unless one with ordinary skill in the art would accept the allegations as obviously correct."**

Highlights and Guidance

- **The unpredictability in the state of the art and the level of skill was unresolved by the Appellant**
- **Evidence of unpredictability in the art in the absence of data that resolves the unpredictability is often the basis for a conclusion of lack of enablement**

Impax v. Aventis, 496 F.Supp.2d 428 (D. Del. 2007)

- Claims to method of treating ALS by administering riluzole
- Impax asserted invalidity based on prior art anticipation of Aventis patent
- Aventis argued asserted prior art was not enabling

Impax v. Aventis, 392 F.Supp.2d 428 (D. Del. 2007)

- **Aventis asserted that the patent**
  - **discloses thousands of formula I compounds and numerous diseases, yielding thousands of possible combinations**
  - **provides no direction or guidance to arrive at the claimed invention of using riluzole to treat ALS**
  - **does not disclose any working examples of the claimed invention**

Impax v. Aventis, 392 F.Supp.2d 428 (D. Del. 2007)

- **Impax asserted that the patent**
  - **includes riluzole as a formula I compound**
  - **suggests that formula I compounds may be used to treat ALS**
  - **provides some dosage information**

Impax v. Aventis, 392 F.Supp.2d 428 (D. Del. 2007)

- **Impax directs the Court to information contained in the patent to suggest that undue experimentation would not be required**
  - **In human therapy, the compounds according to the invention are especially useful in the treatment and prevention of convulsive phenomena, schizophrenic disorders, and in particular the deficiency forms of schizophrenia, sleep disorders, phenomena linked to cerebral ischaemia and also neurological conditions in which glutamate may be implicated, such as Alzehimer's disease, Huntington's chorea, amyotrophic lateral sclerosis and olivopontocerebellar atrophy**

Impax v. Aventis, 392 F.Supp.2d 428 (D. Del. 2007)

- **The District Court finds**
  - **"the compounds of the claimed invention are associated with the treatment of at least 8 different diseases, and there is nothing in the patent which would lead one to recognize that any specific compound, let alone riluzole, would be used to treat any specific disease, let alone ALS."**
  - **that the mere mention of riluzole was insufficient to put one skilled in the art in the possession of the claimed invention as is required to support a conclusion of enablement**

Highlights and Guidance

- **Specification detailing extensive lists of conditions to be treated and compounds to be used, yielding large numbers of possible combinations may suggest lack of enablement of claim to specific combination in the absence of working examples and if evidence of unpredictability exists in the prior art**

Pharmaceutical Resources v. Roxane Laboratories, Inc., 2007 WL 3151692 (Fed. Cir. 2007)

- Non-precedential Fed. Cir. opinion affirming the District Court finding that Par's patents were invalid for lack of enablement
- Claims to oral pharmaceutical composition of megestrol acetate, choices of specific alcohols and a surfactant

Pharmaceutical Resources v. Roxane Laboratories, Inc., 2007 WL 3151692 (Fed. Cir. 2007)

- Claim language did not limit type or amount of surfactant
- Specification stated that invention was not limited to particular surfactants
- Par asserted that broadest reasonable interpretation of claim did not limit type or amount of surfactant

Pharmaceutical Resources v. Roxane Laboratories, Inc., 2007 WL 3151692 (Fed. Cir. 2007)

- Par stressed unpredictability in formulation based on type and amount of surfactant during prosecution of patents
- Par's expert testified to unpredictability of formulation with surfactants during previous trial with another litigant

Pharmaceutical Resources v. Roxane Laboratories, Inc., 2007 WL 3151692 (Fed. Cir. 2007)

- The court held the claims lacked enablement based, in part, on evidence of unpredictability provided previously by Par
- The court also considered the breadth of the claims, the presence of working examples and unsupported conclusions in declarations

Highlights and Guidance

- **Evidence of unpredictability presented to support a conclusion of nonobviousness may be then appropriate to support a finding of lack of enablement for at least a portion of the scope of the claim**

Review

- **Enablement analysis of therapeutic treatment claims begins with the claims by determining breadth of the claims with regard to**
  - **The condition to be treated**
  - **The compound/composition administered**

Review

- **Enablement analysis of therapeutic treatment claims continues with determination of the presence of any unpredictability within the state of the art with regard to**
  - **The condition to be treated**
  - **The compound/composition administered**

Review

- **Enablement analysis of therapeutic treatment claims finishes with the specification by evaluation of**
  - **The presence or absence of working examples**
  - **The evaluation of any other evidence of record, e.g. declarations**

Review

- **Evidence of unpredictability or predictability may occur in the**
  - **Etiology of the condition/disease**
  - **Number/type of other accepted treatments**
  - **The presence or absence of art-recognized animal models**
  - **Manner of formulation and/or delivery**

Highlights and Guidance

- **The Examiner is the fact finder and must provide the evidence**
- **The Examiner must weigh the evidence and provide the rationale**
- **No per se rules!**

Highlights and Guidance

- Consider claim construction
- Consider the evidence
- No per se rules!

Thank You!

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