

1/2/07

Amgen's Opening Submissions

**OPENING SUBMISSIONS OF AMGEN:
For Trial On 15th January Before Mr Justice Neuberger**

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B. THE 605 PATENT		
1. Background and Contribution to the Art		
2. Roche's evidence as to inventive merit		
3. The disclosure and description of the '605 Patent		
4. Construction		
Claim 1		
Claim 26		
Claim 19		
Claim 20		
Claim 21		
VALIDITY - 605		
1. Novelty - The Legal Approach to be applied		
2. Novelty - Roche References:		
3. Novelty - TKT References:		
(1) EPO Produced From Blood Plasma and Urine		
(2) Human EPOs from Human Fused Cells		
(3) EPO produced in Human Cell Lines		
4. Sufficiency - The Legal Approach to be applied		
5. Sufficiency - the allegations		
6. Alleged lack of Enablement		
(1) lack of detail		
(2) cDNA		
(a) COS cells transformed with gDNA		
(b) CHO cells transformed with gDNA;		
(c) Human foetal liver cells		
(3) Synthetic DNA		
(4) Procaryotic not enabled		
(5) Expression in human host cells not enabled		
(6) SDS-PAGE and Average Carbohydrate Composition		
(a) SDS-PAGE background		
(b) SDS-PAGE - The objections		
(A) Which urinary EPO to use as comparator?		
(i) Different methods		
(ii) Different patients		
(iii) The 17mM fraction		
(iv) How stored		
(B) How to ascribe Mw with heterogeneous EPO		
(C) Degree of difference required		
(c) 1985/6 Papers, Amgen internal experiments and comments to the FDA		
(d) Other papers on uEPO versus rEPO		
(e) Absence of TKT/Roche experimentation		
(f) Conclusion on SDS-PAGE		
(g) Insufficiency - claim 20		
7. Breadth of claim		
(a) breadth of claim - cDNA		
(b) breadth of claim - endogenous DNA / homologous recombination		
(c) Breadth of claim - large class of sequences claimed		
8. Added Matter / Extension of Scope		

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9. Discovery as such

INFRINGEMENT - 605 - by Roche;

 Claim 26 (on claims 1 and 2).....

 Claim 27.....

 Claim 28.....

 Claim 30.....

 Claim 19.....

 Claim 20.....

 Claim 21.....

 Claim 23.....

 Claim 31.....

INFRINGEMENT - 605 - by TKT

 1. An overview of TKT's method.....

 2. TKT's method in detail.....

 3. The targeting construct.....

 4. The donor site and phase.....

 5. TKT's claimed advantages.....

 6. Infringement.....

 7. Infringement of Claim 19.....

 (1) Purposive construction.....

 (a) Does the variant affect the way the invention works?.....

 (b) Would this be obvious to the skilled reader?.....

 (c) Would strict compliance have been understood.....

 (2) Amgen's experiment comparing TKT EPO with the 30mM fraction.....

 (3) TKT criticisms of the experiment.....

 (4) TKT SDS-PAGE with 30mM fraction.....

 (5) TKT SDS-PAGE with 17mM fraction.....

 (6) Conclusion.....

 8. Infringement of claim 20.....

 9. Infringement of Claim 26.....

C. THE 678 PATENT

 1. Introduction.....

 2. The relevance of the priority question.....

 3. Technical Background.....

 4. Construction.....

 5. Priority date.....

 6. The withdrawn Roche experiment.....

 7. Priority Date

 (1) The Law.....

 (2) The Authorities.....

 8. GI cannot rely on the deposit in any event

 (1) Deposit cells not the ones analysed in the 678 patent.....

 (2) Roche's evidence fails to establish that the deposit complies with the relevant rules.....

 9. Position if Roche entitled to earlier priority.....

 10. '678 only entitled to later priority / date.....

 (1) Jacobs et al.....

 (2) Lot L07B.....

 11. Insufficiency

 12. Mere discovery

- Annex A - Identity of parties

- Annex B - procedural background

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28. The DNA sequence in this case has also been referred to as the blue-print (see the report of Dr Brenner @55 at F1/1/19 - *once you have got the 605 Patent disclosure, you have the blue print for the production of EPO*) as well as the "keys to the kingdom" by the representative of the Second Opponent [Elanex] in the Appeal before the European Patent Office.
29. In the judgment of the Federal Court of Australia in a case relating to Amgen's corresponding patent (at p.19) Hefrey J. adopted the analogy of treasure in a castle which had many gates, each with a combination lock and that the critical knowledge was the combination of the lock. Without that information it is impossible to enter the castle. Once you have that entry can be obtained by any gate (the combinations being the same). Once the castle is entered then, with reasonable time and effort, the treasure will be discovered.
30. Whether termed "a guide rope to the peak", a "blue-print", "keys to the kingdom" or "the combination for the lock", the importance of the EPO DNA and amino acid sequences are the same. Whether or not the patentee's methodology is adopted, the rest of the world is then enabled to use that information to secure expression of that which was not previously available - namely recombinant EPO - and thereby secure the therapeutic benefits which have served to transform the lives of hundreds or thousands of patients who would otherwise be severely anaemic. It can thus be seen how the Table VI data is information of general application (see further below under insufficiency).
31. In *Biogen* Lord Hoffman approved the principle that:
- "...Article 84 EPC also requires that the claims must be supported by the description, in other words, it is the definition of the invention in the claims that needs support. In the Board's judgment, this requirement reflects the general legal principle that the extent of the patent monopoly, as defined by the claims, should correspond to the technical contribution to the art in order for it to be supported, or justified⁶."*
32. Lord Hoffman also approved - at p.48 and 53 - the principle in *Genentech/Polypeptide Expression*:

⁶ Biogen at p.49

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The sequence of nucleotides which make up the exons of the EPO gene is identified, providing the basis for the production of EPO using recombinant technology whether using genomic DNA - as do Amgen, Cilag and TKT (albeit via a homologous recombination methodology) or using cDNA (Roche).

127. The Court of Appeal in Holland (upholding the First Instance Court in this action there on the merits) and the Federal Court of Australia have each independently considered the speech of Lord Hoffmann in *Biogen* and come to the conclusion that Roche's arguments regarding cDNA are to be rejected.
128. In Holland the Dutch Court of Appeal (judgment of 27 January 2000) quoted from *Biogen* at paras 11.17 and, at 13.5, held that:

In table VI of the patent the inventor has disclosed for the first time the complete and correct sequences of the coding parts (exons) of genomic DNA, besides the correct amino acid sequence of mature human EPO. On the basis of this information the skilled person knows that any alternative "means" (in this case: applying cDNA and synthetic DNA) must at any rate also include these coding sequences, if these "means" are to lead to the desired human EPO. By demonstrating the exons the inventor therefore provides the essential genetic information for obtainment of the object aimed at: the production of EPO by recombinant means. It is therefore reasonable that the inventor is permitted a generalized process claim for applying any "means" in which use is made (at least a part of) that genetic information. That in finding the alternative "means" inventions with independent merit may be involved, does not detract from the above. For these alternative "means" necessarily contain the exons disclosed in the patent, and are therefore dependent inventions". (emphasis added)

129. Likewise the Australian Federal Court considered *Biogen* at page 20 - 24 of its judgment (of 25th June 1998) and observed (at p.23) that it was a critical feature of *Biogen* that the Biogen 1 patent did not disclose the coding sequence and at page 24 held that:

"The fundamental difference which distinguishes the present case from Biogen is that in the Amgen patent the coding sequence is defined. The patent thus discloses a "principle capable of general application" and discloses a beneficial property which is common to the class. It cannot be said of it that it "discloses no principle which would enable other products [of the class] to be made".