Actavis v Lilly/Icos

The Supreme Court looks at obviousness

Tom Mitcheson QC

THREE NEW SQUARE

INTELLECTUAL PROPERTY

Claim 10 of Lilly/Icos Patent

- "Use of a unit dose containing 1 to 5mg of a compound having the structure [of tadalafil] for the manufacture of a medicament for administration **up to a maximum total dose of 5mg of said compound per day** in a method of treating sexual dysfunction in a patient in need thereof".
- Dose of 5mg per day led to reduced side effects and enabled regular daily dosing (not "on demand")

Birss J - §§342-344

- Clinical programme has many routine and obvious steps in it.
- Prior art (Daugan patent) disclosed 50 mg tablet: 25mg/day dose obvious.
- But 5mg daily dose **not obvious** taking into account the following factors:

Birss J

- Skilled team highly motivated to investigate tadalafil.
- The programme would involve very substantial resources of time, money and people but it would be pursued.
- 5mg would not be chosen as the first test of efficacy at Phase IIa nor for first dose ranging study

Birss J

- Team would not have anticipated **daily dosing** as something to be studied from the outset.
- But once half-life discovered it is likely that daily dosing would be included.
- By the time the idea of investigating lower doses presents itself, team would have established safe, tolerable and effective doses of tadalafil at 25mg on demand and 10 mg daily. Then the impetus to investigate lower doses **would be reduced but not eliminated**.

Birss J

- Overall the team would embark **on the project** with a reasonable expectation of success in establishing tadalafil as safe, tolerable and effective.
- However, efficacy at 5mg tadalafil was **not shown to be predictable or worth considering**.
- The team would know that in principle there would be a minimum effective dose for tadalafil but would also know that its definition depends on a **value judgment**.

Birss J

- As for dose ranging studies, the team would conduct them hoping for a dose response.
- Following discovery of a plateau starting at 25 mg or 10mg, there would **very likely** be a subsequent dose ranging study including 5 mg.
- The team would include 5 mg in this study hoping to see a dose response but would have **no reasonable expectation** that 5mg would produce a clinically relevant effect at all nor one with minimal side effects.

Birss J

- The path to a 5 mg dose requires the discovery of new information such as the half life. That information would **inevitably be found** in any clinical programme.
- The path includes an important result which is **unexpected** even if it is not actually surprising, i.e. the plateau in the dose response from 10 to 100 mg.
- There is also a **surprising result**: the existence of a useful effect with reduced side effects.

Kitchin LJ

- *The judge has lost sight of the fact that, on his own findings, the claimed invention **lies at the end of the familiar path through the routine pre-clinical and clinical trials' process**. The skilled but non-inventive team **would** embark on that process **with a reasonable expectation of success** and in the course of it they would carry out Phase IIb dose ranging studies with the aim of finding out, among other things, the dose response relationship. **It is very likely that in so doing they would test a dose of 5mg tadalafil per day** and, if they did so, they would find that it is safe and efficacious. At that point they would have arrived at the claimed invention.*

Kitchin LJ – Evidence at trial

- "Q: We know we are on the top plateau for efficacy and we know that going lower will reduce the side effects. It is really a **no brainer**, is it not doctor?
- A: To go to a lower dose?
- Q: Yes.
- A: **Yes. In this patient population, yes.**"

Kitchin LJ – Evidence at trial

- "Q: . . . As I understand your evidence, you think Dr Pullman [one of the two inventors] did something inventive. Yes?
- A: Yes.
- Q: Exactly what was that?
- A: **Thinking that a lower dose will need to be tested before the results came out - before the results of the 10-100 came out.**
- Q: Oh, so you mean thinking to test lower before you saw that LVBG study? A: Yes.
- **Q: Right, because I think you accept that once they came out you would have gone lower anyway. Yes?**
- **A: Yes, based on the report, yes."**

Supreme Court – the Arguments

- Lilly – CA had not applied s.3 PA/Article 56 EPC and asked "what was obvious to the skilled person at the priority date".
- Lilly – CA also failed to give effect to EPO's approach of finding invention where there was an unexpected technical effect (here efficacy with reduced side effects).
- Actavis – CA correct. Routine work cannot be patentable.

Supreme Court – Lord Hodge

- Competing approaches in the UK (*Windsurfing)* and EPO (problem and solution):

  > *While both approaches focus on the inventive concept put forward in the claims,* ***neither approach should be applied in a mechanistic way****. Both are glosses on the text of section 3 of the 1977 Act and article 56 of the EPC and neither require a literalist approach to the wording of the claim in identifying the inventive concept.*

- 10 relevant factors

1. Obvious to Try

- It is relevant to consider whether at the priority date something was “obvious to try” - whether it was obvious to undertake a specific piece of research which had a reasonable or fair prospect of success
- But there is no requirement that it is manifest that a test ought to work; that would impose a straightjacket which would preclude a finding of obviousness in a case where the results of an entirely routine test are unpredictable

2. Routine Work

- Routine nature of the research and any established practice of following such research through to a particular point may be a relevant consideration which is weighed against the consideration that the claimed process or product was not obvious to try at the outset of a research programme

3. Burden/Cost

- Burden and cost of the research programme is relevant. But the weight to be attached to this factor will vary depending on the particular circumstances.
- Patent protection not the only reward – referred to the data exclusivity regime which may confer ten years of exclusive marketing protection against competition from generic manufacturers

4. Value Judgments

- The necessity for and the nature of the value judgments which the skilled team would have in the course of a testing programme are relevant considerations as both the trial judge and the Court of Appeal held
- [But with different conclusions…]

5. Number of Paths

- The existence of alternative or multiple paths of research will often be an indicator that the invention contained in the claim or claims was not obvious.
- If the notional skilled person is faced with only one avenue of research, a “one way street”, it is more likely that the result of his or her research is obvious than if he or she were faced with a multiplicity of different avenues.
- But it is necessary to bear in mind the possibility that more than one avenue of research may be obvious

6. Motive

- The motive of the skilled person is a relevant consideration. The notional skilled person is not assumed to undertake technical trials for the sake of doing so but rather because he or she has some end in mind.
- It is not sufficient that a skilled person *could* undertake a particular trial; one may wish to ask whether in the circumstances he or she *would* be motivated to do so

7. Surprising Result

- The fact that the results of research which the inventor actually carried out are unexpected or surprising is a relevant consideration as it may point to an inventive step
- Suggests that a test was not obvious to try
- Or the absence of a known target of the research which would make it less likely that the skilled person would conduct a test

8. Step by Step

- One must not use hindsight, which includes knowledge of the invention.
- Obvious danger of a step by step analysis is that the combination of steps to arrive at the invention is ascertained by hindsight knowledge of successful invention.
- Where the pattern of the research programme which the notional skilled person would undertake can clearly be foreseen, it may be legitimate to take a step by step analysis

9. Bonus Effect

- It is necessary to consider whether a feature of a claimed invention is an added benefit in a context in which the claimed innovation is obvious for another purpose

10. Nature of Invention

- Here a dosage patent with a Swiss-form claim and an EPC 2000 claim. The possibility that a dosage patent with such claims may be valid has been recognized both by the EPO and in the United Kingdom courts.

Role of the Appellate Court

- *South Cone*, *Biogen*, *In Re B*
- In the absence of a legal error by the trial judge - which might be asking the wrong question, failing to take account of relevant matters, or taking into account irrelevant matters - CA justified in differing from a trial judge's assessment of obviousness if the appellate court were to reach the view that the judge's conclusion was outside the bounds within which reasonable disagreement is possible.
- It must be satisfied that the trial judge was wrong

Was the CA correct to interfere?

- Birss J, without relying on hindsight, held that it was "very likely" that the skilled team would research further by testing doses of 10mg and 5mg.
- Dr Saoud accepted that the decision to test the lower doses, including the 5mg dose, was "a no brainer".
- In short, the skilled team, having embarked on the Phase IIb tests, **would have continued their search for a dose response relationship**, because the purpose of the Phase IIb study had not been fulfilled.

Was the CA correct to interfere?

- This **undermined several of the factors** which Birss J relied on for non-obviousness.
- The fact that a 5mg dose was so much lower than the prior art 50mg dose **is neither here nor there**.
- The lack of an expectation of efficacy at a 5mg dose is a factor of **little weight** if, as was found, the skilled team **would be very likely to study such a dose** in the search for a dose response relationship.
- For the same reason the fact that the effectiveness of tadalafil at a dose of 5mg was a **surprise can carry little, if any, weight**.

Was the CA correct to interfere?

- The finding that there was an important **value judgment** to be made when the therapeutic plateau was identified at the same time as a marketable dose can **bear little weight** when there is a finding, which is not tainted by hindsight, that the skilled team **would continue their tests**.
- I consider that the Court of Appeal was entitled to treat the judge's **failure to appreciate the logical consequences of the finding** (that it was very likely that the skilled team would continue the testing) as an **error of principle** which allowed an appellate court to carry out its own evaluation.
- New ground of appeal – failure to appreciate logical consequences of a factual finding…?

Analysis of facts

- The completion of the Phase IIb dose ranging studies led to the asserted invention.
- Reduced side effects was a bonus – “an added benefit which does not prevent the identification of 5mg as the appropriate dose from being obvious”.
- Did not matter that 5mg dose was not predictable in advance - *Conor* not authority for the proposition that, in all circumstances, obviousness must be assessed by reference to the precise wording of the claim

Analysis of facts

- Once a day made no difference.
- The judge correctly treated the daily dosing regime as obvious because it was the result of the inevitable discovery of the half-life of tadalafil in Phase 1 of the tests.
- Claim not confined to the daily dosing regime but also covered on demand use of the drug subject to a maximum total dose of 5mg per day.
- The inventive concept by which a patentee seeks to justify his or her monopoly must apply to all embodiments falling within the claims which are said to have independent validity.

Foreign Judgments

- “I do not find the judgments particularly helpful”.
- While consistency of approach between the domestic courts of the signatory states to the EPC on matters of principle is desirable, we are not bound by the judgments of other national courts and it is possible that national courts applying the same law may come to different conclusions for various reasons
- Evidence may differ & even when the same, each court’s findings of fact based on that evidence may not be the same

UK v EPO

- No-one has ever suggested that the problem-and-solution approach is the only way to go about considering obviousness.
- No formula should distract the court from the statutory question.
- *I am not persuaded that the problem-and-solution approach would* necessarily *give a different answer from that of the Court of Appeal*.
- Absence of expectation of effectiveness at 5mg does not militate against the conclusion that the team would have investigated that dose in the course of implementing the prior art.

But no effect on Selection Patents

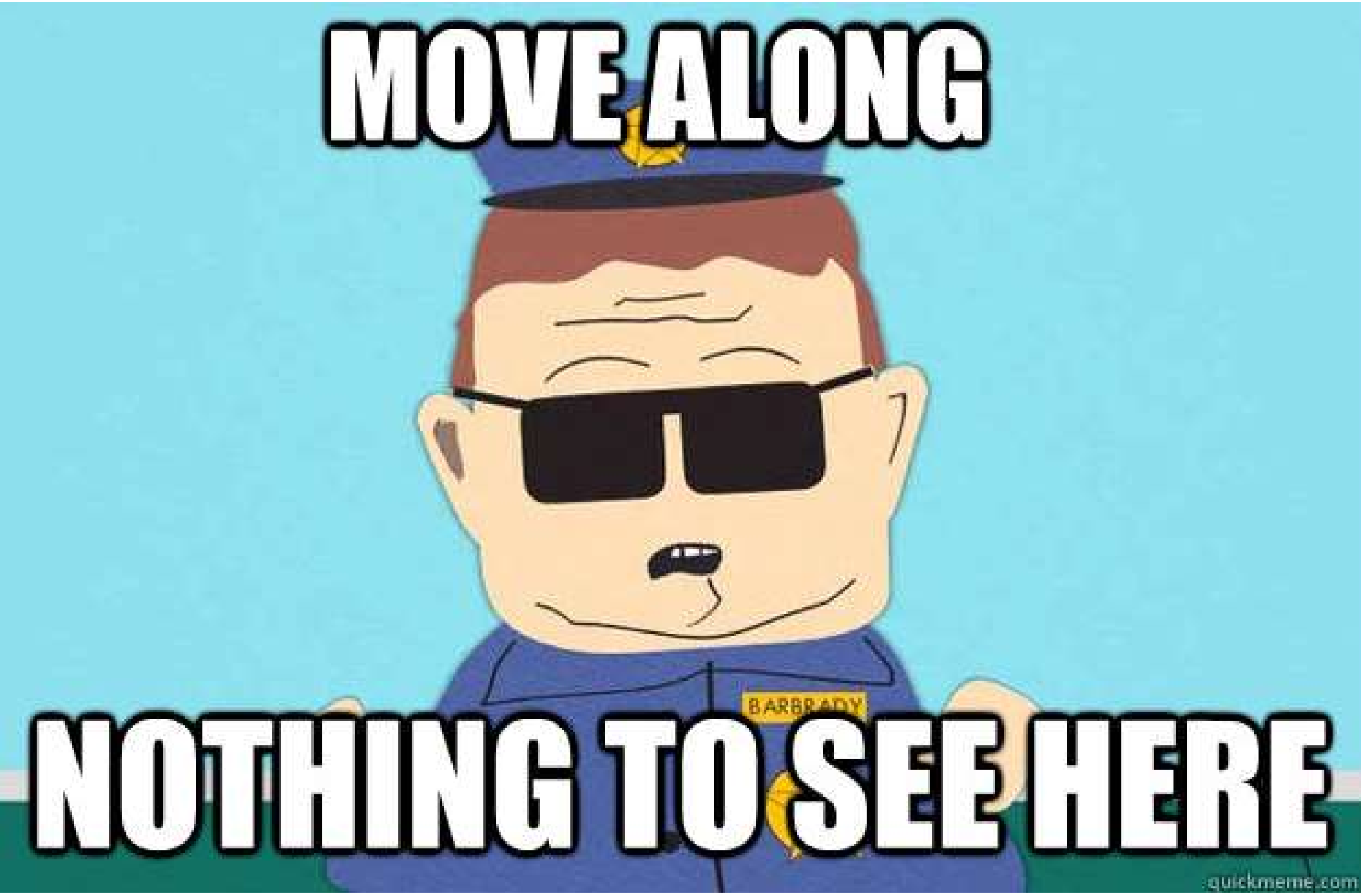
- This judgment does not militate against selection patents or improvement patents.
- Patentable if the selection is not arbitrary and is justified by a hitherto unknown technical effect.
- The use of **well-known research tests** of itself does not render such selections and improvements obvious.

Yet G2/08 at §6

- Is a different technical teaching reflected in the claimed definition of the dosing regime?
- In G2/08 it was reduced side effects…
- Previous case-law was said to continue to apply
  - *Furthermore, if the distinguishing feature of a claim seeking patent protection for a known medicament to be used for a different treatment of the same illness is a dosage regime and is something else than a mere selection from a prior broader disclosure,* ***a new technical effect caused by said feature*** *shall be considered when examining inventive step under Art 56 EPC*

T91/98 – Mrs Kinkeldy

- Claimed doses 3-250x lower than prior art & inhibited replication of the mouse retrovirus while being little toxic to mouse cells.
- Unexpected & advantageous result that effective at such low concentrations.
  - The Respondents argued that it only required **routine work** to find out which unit dose would be appropriate. This may well be, **yet it does not affect inventive step**, which, as was just mentioned, **is not due to finding out the relevant dose is but to the fact that this dose is substantially lower** than that which had been found effective against the mouse retrovirus.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