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Case Nos: A3/2015/3602
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A3/2016/0017

IN THE COURT OF APPEAL (CIVIL DIVISION)
ON APPEAL FROM THE HIGH COURT OF JUSTICE
CHANCERY DIVISION
PATENTS COURT
The Hon Mr Justice Arnold
[2015] EWHC 2548 (Pat)

Royal Courts of Justice
Strand, London, WC2A 2LL

Date: 13/10/2016

Before:

LORD JUSTICE PATTEN
LORD JUSTICE KITCHIN
and
LORD JUSTICE FLOYD

- -

Between:

WARNER-LAMBERT COMPANY LLC	**Appellant**
- and -	
(1) GENERICS (UK) LIMITED (trading as MYLAN)	
(2) ACTAVIS GROUP PTC EHF	
(3) ACTAVIS UK LIMITED	
(4) CADUCEUS PHARMA LIMITED	**Respondents**
THE SECRETARY OF STATE FOR HEALTH	**Intervener**

- -

Richard Miller QC, Tom Mitcheson QC, Miles Copeland and Tim Austen instructed by **Allen & Overy LLP** for **Warner-Lambert**
Michael Bloch QC, Richard Meade QC and Kathryn Pickard (instructed by **Taylor Wessing LLP**) for **Mylan**
Richard Meade QC, Adrian Speck QC and Isabel Jamal (instructed by **Powell Gilbert LLP**) for **Actavis**
Michael Silverleaf QC and Richard Davis instructed by the **Government Legal Department** for the **Secretary of State**

Hearing dates: 23-26 May 2016

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Approved Judgment

Lord Justice Floyd:

Introduction

1. In the various appeals which are before the court, three main questions arise. Firstly, did Arnold J correctly hold certain claims of the patent in suit invalid for insufficiency; and, if so, should he have held more claims invalid on that ground? Secondly, was he correct in holding the patentee's application to amend claim 3 of the patent, made after judgment on the issue of invalidity, to be an abuse of the process of the court? Thirdly, if there were any valid claims which were the subject of the allegation of infringement, was the judge correct to hold that there was no infringement of the (Swiss-form, second medical use) claims in the patent?

2. Warner-Lambert Company LLC ("Warner-Lambert") is the proprietor of European Patent (UK) No. 0 934 061. Although the title of the specification is "Isobutyl GABA and its derivatives for the treatment of pain", the derivative of interest is called pregabalin, to which the Swiss-form, second medical use claims are limited. Warner-Lambert markets pregabalin under its trade mark Lyrica for the treatment of neuropathic pain, as well as for its previously known indications of general anxiety disorder ("GAD") and epilepsy. It does so through Pfizer Ltd ("Pfizer"). Lyrica is one of the Pfizer Group's most successful products. Global sales of Lyrica amounted to approximately $4.6 billion in 2013 with UK sales in the same year amounting to approximately $310 million. Not surprisingly, this is a market of considerable interest to generic pharmaceutical manufacturers both for the existing medical indications and the new. I will refer to Warner-Lambert and Pfizer as "Warner-Lambert", without attempting to distinguish between them.

Procedural history

3. Generics (UK) Ltd, trading as Mylan, and Actavis Group PTC EHF ("Mylan" and "Actavis PTC") commenced separate claims for revocation of the patent on 24 June and 12 September 2014 respectively, relying on the grounds of lack of inventive step and insufficiency. On 8 December 2014 Warner-Lambert commenced a claim for infringement of the patent against Actavis PTC, Actavis UK Ltd and Caduceus Pharma Ltd. I will refer to all the Actavis companies and Caduceus as "Actavis".

4. Warner-Lambert applied for an interim injunction to restrain the sales of Actavis' generic pregabalin product, which was branded Lecaent. That application came before Arnold J, who dismissed it in a judgment dated 21 January 2015, see [2015] EWHC 72 (Pat). He did so on the twin grounds that Warner-Lambert had no arguable case of infringement, and that, in any event, the balance of justice favoured refusal of the injunction. Actavis then made an application to strike out Warner-Lambert's claim for infringement. That application also came before Arnold J, who struck out the claim for infringement insofar as it was made under section 60(2) of the Patents Act 1977 ("the Act"). Notwithstanding his earlier conclusion that Warner-Lambert had no arguable case of infringement, he allowed Warner-Lambert's infringement claim made under section 60(1)(c) of the Act to proceed to trial: see his two judgments, [2015] EWHC 223 (Pat) and [2015] EWHC 249 (Pat). In so doing, Arnold J recognised that the correct scope to be afforded to Swiss-form second medical use claims was a developing area of patent law. On 28 May 2015 this court dismissed Warner-Lambert's appeal against the refusal of the interim injunction but

allowed an appeal against the striking out of the claim under section 60(2) of the Act: see [2015] EWCA Civ 556 ("*Warner-Lambert CoA*"). In so doing the court held that, on its view of the law and contrary to that applied by Arnold J, Warner-Lambert's infringement case under both subsections of the Act was arguable: see Floyd LJ at [133] and [140].

5. The actions themselves then came to trial, again before Arnold J, in June and July 2015. By then Actavis had retaliated with a counterclaim for groundless threats of patent infringement. Arnold J handed down his judgment ("the main judgment") on 10 September 2015: see [2015] EWHC 2548 (Pat). In the main judgment Arnold J held that:

   i) none of the claims of the patent lacked inventive step over any of the prior art relied on by Mylan and Actavis;

   ii) each of claims 1, 3, 4, 6, 13 and 14 of the patent was invalid on the ground of insufficiency;

   iii) even if claims 1 and 3 had been valid, Actavis would not have infringed those claims pursuant to section 60(1)(c) or section 60(2) of the Act;

   iv) in consequence, and as a result of certain letters sent out by Warner-Lambert, Pfizer was liable for making groundless threats of patent infringement proceedings.

6. The judge gave both Mylan and Actavis on the one hand and Warner-Lambert on the other permission to appeal against his decision on the issue of insufficiency, Mylan and Actavis contending that the judge should have made more extensive findings of insufficiency. The judge also gave Warner-Lambert permission to appeal in respect of his decision relating to infringement under section 60(1)(c), but not his decision under section 60(2). Floyd LJ later granted Warner-Lambert permission to appeal on the latter sub-section as well.

7. On 1 October 2015 Warner-Lambert made a conditional application to amend the patent. Insofar as these amendments consisted of deletion of entire invalid claims, they were uncontroversial. One amendment, however, sought to rewrite claim 3, the claim to the use of pregabalin to treat neuropathic pain, to add the words "caused by injury or infection of peripheral sensory nerves". By the addition of these words Warner-Lambert sought to limit the scope of the claim to *peripheral* neuropathic pain, and thus to exclude from its scope parts of the claim, in particular *central* neuropathic pain, that were found to be vulnerable to the insufficiency attack. This amendment was opposed by Mylan and Actavis. The judge directed that the question of whether that part of the application to amend was an abuse of the process of the court should be tried as a preliminary issue. In a further judgment ("the abuse judgment") given on 25 November 2015, [2015] EWHC 3370 (Pat), Arnold J decided that issue in favour of Mylan and Actavis without deciding the merits of the amendment application.

Technical background

8. There is a certain amount of technical background to be traversed before the issues can be addressed. The judge dealt with the background in paragraphs 37 to 82 of his

judgment. Not all of that material is relevant to the issues which remain live on appeal. What follows is a highly abbreviated summary, based on that section of the judgment.

The nervous system

9. The nervous system comprises two main parts: the central nervous system and the peripheral nervous system. The central nervous system comprises the brain and spinal cord. The peripheral nervous system comprises the nerves outside those structures. The nervous system includes cells called neurons which transmit information through electrical and chemical signals.

Types of pain

10. At the priority date in 1996 pain was classified into a number of different types, although not all neuroscientists and clinicians would necessarily categorise pain types in precisely the same way.

    i) *Nociceptive pain* occurs where stimuli such as heat, extreme cold, intense mechanical pressure and chemicals stimulate fibres known as nociceptors. The nociceptors then transmit impulses via the spinal cord to the brain where they are perceived as pain. Nociceptive pain has a bio-protective function in that it alerts the brain to the presence of the noxious stimulus so that appropriate avoidance measures can be taken. This type of pain resolves with treatment of the underlying cause.

    ii) *Inflammatory pain* is a type of nociceptive pain. The body's response to an injury involves the release of chemical mediators which increase the sensitivity of nociceptors, causing pain both at the site of injury and in the surrounding area.

    iii) *Neuropathic pain* is caused by damage to the nervous system itself. One definition of neuropathic pain is "pain initiated or caused by a primary lesion or dysfunction of the nervous system". The lesion or dysfunction can occur either in the peripheral nervous system or the central nervous system. Unlike nociceptive pain, neuropathic pain does not necessarily subside when the noxious stimulus is removed. A wide range of diseases may cause neuropathic pain by their effect on the nervous system. Two of the most common causes of neuropathic pain are diabetes and herpes, which can give rise to diabetic (peripheral) neuropathy ("DPN") and post-herpetic neuralgia ("PHN"), both examples of neuropathic pain.

    iv) *Peripheral neuropathic pain* is the type of neuropathic pain where the lesion or dysfunction is in the peripheral nervous system.

    v) *Central neuropathic pain*, sometimes called *central pain*, is neuropathic pain where the lesion or dysfunction is in the central nervous system.

    vi) *Idiopathic pain* is pain of unknown origin.

Hyperalgesia and allodynia

11. The term "hyperalgesia" describes the increased response to a stimulus that is normally painful. Primary hyperalgesia occurs at the site of injury, whereas secondary hyperalgesia is pain experienced in areas surrounding the injured site. The related term "allodynia" is used to describe pain that is experienced in response to stimuli that would *not* normally be expected to cause pain (e.g. light touch).

Sensitisation

12. Sensitisation describes the process by which neurons display increased activity with a lower threshold to stimulation. Such sensitisation can occur both at the periphery and centrally.

13. Central sensitisation can be induced by, for example, repeated noxious heat stimuli, tissue injury, tissue inflammation, injury to a nerve or ectopic activity in an injured nerve. It was first discovered as a response in the spinal cord to a barrage of activity in C-fibre nociceptors that detect noxious stimuli and connect the peripheral nervous system to the central nervous system. These stimuli in nociceptor sensory fibres trigger an increase in synaptic strength of neurons in the dorsal horn of the spinal cord. This has been described as an increase in "gain" in the dorsal horn. Pharmacological treatment may reduce the gain.

Animal models

14. A number of animal models are used in testing new drugs for the treatment of pain. The following are of relevance to the issues which we have to decide:

    i) *The rat paw formalin test*. Formalin is injected into a rat's paw. This causes the rat to lick and bite its paw because of the pain. The rat's behaviour is then monitored in two phases, the first lasting about 10 minutes and the second lasting about 45 minutes during which the rat's physical behaviour in tending or biting the wound is monitored.

    ii) *The carrageenan test.* Carrageenin is injected into the paw of a rat and tests are carried out to determine the extent of thermal or mechanical hyperalgesia.

    iii) *The post-operative pain model*. The rat's paw is incised, but the nerve is not damaged. The wound is closed by suture. After 24 hours the rat is assessed for mechanical hyperalgesia and tactile allodynia.

The patent in suit

15. The specification begins at [0001] by stating that the invention:

> "is the use of [pregabalin] in pain therapy, as the compound exhibits analgesic/antihyperalgesic action."

16. In [0002] the authors explain that the compound of the invention is a known agent useful in "antiseizure therapy for central nervous system disorders" of which examples are given. Epilepsy is the first example. The invention is then summarised in [0003] as follows:

> "The instant invention is a method of using a compound identified below in the treatment of pain, especially for treatment of chronic pain disorders. Such disorders include, but are not limited to, inflammatory pain, postoperative pain, osteoarthritis, pain associated with metastatic cancer, trigeminal neuralgia, acute herpetic and postherpetic neuralgia, diabetic neuropathy, causalgia, brachial plexus avulsion, occipital neuralgia, reflex sympathetic dystrophy, fibromyalgia, gout, phantom limb pain, burn pain, and other forms of neuralgic, neuropathic, and idiopathic pain syndromes."

17. The identified compound is pregabalin or a pharmaceutically acceptable salt thereof. Under the heading "Detailed description" at [0006] the specification makes another statement of what the invention is:

> "The instant invention is a method of using [pregabalin] or a pharmaceutically acceptable salt thereof as an analgesic in the treatment of pain as listed above. Pain such as inflammatory pain, neuropathic pain, cancer pain, postoperative pain, and idiopathic pain which is pain of unknown origin, for example, phantom limb pain are included especially. *Neuropathic pain is caused by injury or infection of peripheral sensory nerves*. It includes, but is not limited to pain from peripheral nerve trauma, herpes virus infection, diabetes mellitus, causalgia, plexus avulsion, neuroma, limb amputation, and vasculitis. Neuropathic pain is also caused by nerve damage from chronic alcoholism, human immunodeficiency virus infection, hypothyroidism, uremia, or vitamin deficiencies. *Neuropathic pain includes, but is not limited to pain caused by nerve injury such as, for example, the pain diabetics suffer from*." (emphasis supplied).

18. The italicised references to neuropathic pain were a particular focus of the arguments on construction to which I will have to come.

19. The specification then describes the results from four animal tests. These are the rat paw formalin test, the carrageenin induced mechanical and thermal hyperalgesia tests, and the post-operative pain test.

20. According to the specification at [0017], the rat paw formalin test showed that the administration of pregabalin dose-dependently blocked the licking/biting behaviour during the *late phase* of the formalin response. However, pregabalin did not affect the *early phase* at any of the doses tested.

21. The results from the carrageenin-induced mechanical and thermal hyperalgesia tests are said at [0019] and [0021] to show that pregabalin dose-dependently antagonised the hyperalgesia, but it is common ground that the tests do not distinguish between primary and secondary hyperalgesia.

22. The specification states at [0021] that "These data show that gabapentin and [pregabalin] are effective in the treatment of inflammatory pain." The parties

disagreed over whether this sentence was referring to all the animal data up to that point, or only the carrageenin tests. Mylan and Actavis contended that it was the former, and Warner-Lambert the latter. If Mylan and Actavis were right, the sentence might suggest that the patentee was not prepared to make a prediction based on all the animal models going beyond the effectiveness of pregabalin for the treatment of inflammatory pain. In the end, not much turned on this debate.

23. At [0022] and [0023] the specification refers to two assays, described in papers referred to as "Bennett" and "Kim", which are animal models of peripheral neuropathic pain. No test results in accordance with these assays are, however, recorded.

The claims

24. The important claims are claims 1 and 3. Claim 1 is in the following terms:

> "Use of [pregabalin] or a pharmaceutically acceptable salt thereof for the preparation of a pharmaceutical composition for treating pain."

25. Claim 3 is to the use according to claim 1, wherein the pain is neuropathic pain. Claim 2, inflammatory pain, is not alleged to be infringed. Lyrica is not licensed for the treatment of inflammatory pain. The remaining claims are to more specific categories of pain: cancer (claim 4); post-operative (claim 5); phantom limb (claim 6); burn (claim 7); gout (claim 8); osteoarthritic (claim 9); trigeminal neuralgia (claim 10); acute and post-herpetic (claim 11); causalgia (claim 12); idiopathic (claim 13); and fibromyalgia (claim 14).

The skilled addressee

26. It was common ground before the judge, and remains so before us, that the patent was directed to a team consisting of a neuroscientist and a clinician. The clinician would be a specialist in the treatment of pain, and the patent would be of particular interest to neurologists and anaesthetists. The judge held that, on the issue of plausibility in the light of the animal model results reported in the patent, the neuroscientist would inevitably take the lead.

Insufficiency

27. On this appeal the main battle ground was the judge's finding of insufficiency. The judge's conclusions on obviousness were not the subject of the appeal.

The law

28. The statutory ground on which the court may revoke a patent for "insufficiency" is contained in section 72(1)(c) of the Act. It is that:

> "the specification of the patent does not disclose the invention clearly enough and completely enough for it to be performed by a person skilled in the art."

29. Insufficiency may be deployed as an attack on validity not only where the directions in the specification are inadequate to enable the skilled person to perform the invention at all (i.e. to produce something falling within a claim), but also where a claim is excessively broad having regard to the patentee's contribution to the art. In *Regeneron Pharmaceuticals Inc. and another v Genentech Inc.* [2013] EWCA Civ 93; [2013] RPC 28, at paragraphs 100 and 101, Kitchin LJ set out the principles which apply to such an objection of insufficiency:

> "100. It must therefore be possible to make a reasonable prediction the invention will work with substantially everything falling within the scope of the claim or, put another way, the assertion that the invention will work across the scope of the claim must be plausible or credible. The products and methods within the claim are then tied together by a unifying characteristic or a common principle. If it is possible to make such a prediction then it cannot be said the claim is insufficient simply because the patentee has not demonstrated the invention works in every case.
>
> 101. On the other hand, if it is not possible to make such a prediction or if it is shown the prediction is wrong and the invention does not work with substantially all the products or methods falling within the scope of the claim then the scope of the monopoly will exceed the technical contribution the patentee has made to the art and the claim will be insufficient. It may also be invalid for obviousness, there being no invention in simply providing a class of products or methods which have no technically useful properties or purpose."

30. In the present case it is necessary to examine a little further what is meant by the requirement that the specification should make the invention plausible or credible. The requirement originated in the jurisprudence of the Boards of Appeal of the European Patent Office. Similar requirements arise in that jurisprudence in several contexts. For example, it must be plausible that an invention has industrial applicability if it is not to fall foul of the requirement under Article 57 of the European Patent Convention. It also arises in the context of lack of inventive step under Article 56, when applying the line of jurisprudence beginning with the decision of the Technical Board of Appeal of the EPO ("TBA") in T 0939/92 *Agrevo/Triazole herbicides.*

31. In T 0609/02 *Salk Institute for Biological Studies* the TBA was faced in opposition proceedings with a claim to the use of a steroid hormone which "fails to promote transcriptional activation of" a particular group of receptor genes which was "for the preparation of a pharmaceutical for the treatment of AP-1 stimulated tumor formation, arthritis, asthma, allergies and rashes". The patentee argued that the skilled person would be able to find out by testing which steroid hormones both failed to activate the receptors and disrupted AP-1 stimulation of AP-1 responsive genes. Later published material showed that the claims were "reproducible" and led to the identification of compounds which would be appropriate for use. The Board found that the patent specification provided no evidence at all relating to the invention claimed. No hormone was identified having the dual property of disrupting AP-1 stimulated

transcription and failing to promote hormone regulated transcription. Furthermore no data of any kind was identified indicating that such a hormone, if it were identified, could have an impact on any of the identified diseases.

32. The Board rejected the patentee's submission that the later published data could be admitted to show sufficiency. At paragraph 8 the Board said:

> "Sufficiency of disclosure must be satisfied at the effective date of the patent, ie on the basis of the information in the patent application together with the common general knowledge then available to the skilled person. Acknowledging sufficiency of disclosure on the basis of relevant technical information produced only after this date would lead to granting a patent for a technical teaching which was made at a date later than the effective date of the patent. The general principle that the extent of monopoly conferred by a patent should correspond to, and be justified by, the technical contribution to the art, has to be kept in mind…".

33. The Board went on to explain that, where a claim was in the so-called "Swiss" form (the use of a compound in the manufacture of a medicine for use in therapy), the specification ought to disclose the suitability of the product to be manufactured for the claimed therapeutic application. However, the patent system recognised the intrinsic difficulties that this requirement would place in the way of the patenting of pharmaceuticals if interpreted as requiring evidence of tests in humans or animals. The Board continued at paragraph 9:

> "Yet, this does not mean that a simple verbal statement in a patent specification that compound X may be used to treat disease Y is enough to ensure sufficiency of disclosure in relation to a claim to a pharmaceutical. 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. Showing a pharmaceutical effect in vitro may be sufficient if for the skilled person this observed effect directly and unambiguously reflects such a therapeutic application… or,…, if there is a "clear and accepted established relationship" between the shown physiological activities and the disease… Once this evidence is available from the patent application, then post-published (so-called) expert evidence (if any) may be taken into account, 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 their own."

34. The patentee submitted that there was no purpose in requiring *in vitro* tests, as these would not themselves be predictive of *in vivo* efficacy. The Board acknowledged this, but pointed out that an *in vitro* test would at least establish that the necessary

components ("protagonists") for the test were available, and could establish a definite link between the ingredient and the mechanism allegedly involved in the disease state. It concluded at paragraph 10:

> "The presence of a cause/effect relationship is, thus, made plausible. For how incomplete the data might be, they nonetheless go one step further towards disclosing the invention without leaving an undue burden to the reader."

35. The Board went on to reject the claim in the case before it, because no such hormone had been identified, and there was "not a shred" of evidence that switching off AP-1 activation of transcription would not affect the overall metabolism in such a way that would make it unsuitable as a medicament. There was also no evidence that switching off the transcription of all AP-1 responsive genes in a way which would produce relief from the claimed diseases. In fact, as it said at paragraph 11:

> "Otherwise stated, the subject-matter of claim 6, is limitless and untried downstream developments in relation to yet to be demonstrated molecular mechanisms. In the board's judgment, it amounts to no more than an invitation to set up further research programs for which no guidance is forthcoming."

36. As to the post-published material, the Board considered that it indicated that it took a few years of research work possibly involving an inventive step and, therefore, undue burden, to put the claimed subject matter into practice.

37. In T 1329/04 *Johns Hopkins University School of Medicine* the claim under consideration was to a polynucleotide encoding a polypeptide having GDF-9 activity selected from a list. When addressing inventive step the TBA considered that the problem to be solved was identifying a new member of a super-family known as TGF-β. Whether or not that problem was plausibly solved by the claimed invention depended on whether or not it was plausible that GDF-9 was a further member of that super-family. The TBA pointed to important structural differences between GDF-9 and the super-family, leading to the conclusion that GDF-9 could not be clearly and unambiguously identified as a member of that family. This itself would not have been fatal if it had been demonstrated that GDF-9 in fact played a role similar to members of the super-family. Yet there was, as the board emphasised, "no evidence at all in that respect". The TBA concluded (see paragraph 11) that:

> "there is not enough evidence in the application to make at least plausible that a solution was found to the problem which was purportedly solved."

38. As to the post-published evidence, at paragraph 12 the TBA said:

> "This cannot be regarded as supportive of an evidence which would have been given in the application as filed since there was not any. The said post-published documents are indeed the first disclosure going beyond speculation. For this reason, the post-published evidence may not be considered at all. Indeed, to do otherwise would imply that the recognition of the claimed

> subject-matter as a solution to a particular problem could vary as time went by. Here, for example, had the issue been examined before the publication date of the earliest relevant post-published document, GDF-9 would not have been seen as a plausible solution to the problem of finding a new member of the TGF-β superfamily and inventive step would have had to be denied whereas, when examined thereafter, GDF-9 would have to be acknowledged as one such member. This approach would be in contradiction with the principle that inventive step, as all other criteria for patentability, must be ascertained as from the effective date of the patent. The definition of an invention as being a contribution to the art, i.e. as solving a technical problem and not merely putting forward one, requires that it is at least made plausible by the disclosure in the application that its teaching solves indeed the problem that it purports to solve. Therefore, even if supplementary post-published evidence may in the proper circumstances also be taken into consideration, it may not serve as the sole basis to establish that the application solves indeed the problem it purports to solve."

39. One can draw the following conclusions from these cases:

i) A mere assertion that compound X is suitable for treating disease Y is not sufficient without any more to render the invention plausible: *Salk* [9];

ii) The disclosure of the patent specification does not have to be definitely predictive of the efficacy of the invention: *in vitro* tests which may well not be reproducible in humans or animals may suffice: *Salk* [10], [11];

iii) An example of adequate support to amount to a plausible disclosure would be experimental tests, showing that the claimed compound has a direct effect on a metabolic mechanism specifically involved in the disease: *Salk* [9];

iv) Later published data are not admissible if they alone render the invention plausible: *Salk* [9], *Johns Hopkins* [12];

v) Ultimately the purpose of the requirement of sufficiency is to place the reader in possession of the invention without imposing undue burden on him by way of further investigation or research: *Salk* [10].

40. It is true that some passages in *Salk* appear to go further, and if taken literally might be thought to impose a higher threshold before an invention can be regarded as plausible. For example in paragraph 9 the Board gave the example of a pharmaceutical effect established *in vitro* which it considered might be sufficient if the observed effect directly and unambiguously reflects the therapeutic application, or if there is a clear and accepted established relationship between showing the physiological activity and the disease. These are, however, no more than examples of ways in which a specification may give adequate data to render an invention plausible. They are not to be read as prescriptive.

41. In *Human Genome Sciences Inc v Eli Lilly & Co* [2011] UKSC 51; [2012] RPC 6 the Supreme Court was dealing with a case in which a structure-activity relationship between a claimed compound and a group of compounds known to have a particular activity was said to render it plausible that the new compound was capable of industrial application under Article 57 of the European Patent Convention. Summarising the jurisprudence of the EPO, Lord Neuberger PSC said at paragraph 107:

> "The general principles are:
>
> …
>
> (iii) A merely "speculative" use will not suffice, so "a vague and speculative indication of possible objectives that might or might not be achievable" will not do (T 0870/04, para.21; T 0898/05, paras.6 and 21);
>
> (iv) The patent and common general knowledge must enable the skilled person "to reproduce" or "exploit" the claimed invention without "undue burden", or having to carry out "a research programme" (T 0604/04, para.22; T0898/05, para.6);
>
> Where a patent discloses a new protein and its encoding gene:
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> (v) The patent, when taken with common general knowledge, must demonstrate "a real as opposed to a purely theoretical possibility of exploitation" (T 0604/04, para. 15; T 0898/05, paras.6, 22 and 31);
>
> (vi) Merely identifying the structure of a protein, without attributing to it a "clear role", or "suggest [ing]" any "practical use" for it, or suggesting "a vague and speculative indication of possible objectives that might be achieved", is not enough (T0870/04, paras.6-7, 11 and 21; T 0898/05, paras. 7,10 and 31);
>
> (vii) The absence of any experimental or wet lab evidence of activity of the claimed protein is not fatal (T 0898/05, paras. 21 and 31; T 1452/06, para.5);
>
> (viii) A "plausible" or "reasonably credible" claimed use, or an educated guess", can suffice (T 1329/04, paras.6 and 11; T 0640/04, para.6; T 0898/05, paras.8, 21, 27, and 31; T 1452/06, para.6; T 1165/06 para.25);
>
> (ix) Such plausibility can be assisted by being confirmed by "later evidence", although later evidence on its own will not do (T 1329/04, para.12; T 0898/05, para.24; T 1452/06, para.6; T 1165/06, para.25);

> (x) the requirements of a plausible and specific possibility of exploitation can be at the biochemical, the cellular or the biological level (T0898/05, paras. 29-30)."

42. These observations are obviously not all directly applicable to the objection of insufficiency, made as they are in the context of industrial applicability, where all that is necessary is that invention should be "made or used in any kind of industry". However there are common principles underlying the two objections, in particular the requirement to place the invention or its industrial application in the hands of the skilled reader without undue burden. In paragraph 134 of his judgment, Lord Neuberger described the two objections as having "a close connection, indeed overlap".

43. Lord Hope, in paragraphs 149 to 154 explained why the Court of Appeal in that case had adopted too exacting a standard. He was content to accept Jacob LJ's comment, at paragraph 111 of his judgment ([2010] RPC 14) that the word "plausibly" implies that "there must be some real reason for supposing that the statement is true". Lord Hope considered that the Court of Appeal, in various passages, had been looking for a description that showed that a particular use for the product had actually been demonstrated rather than that the product had plausibly been shown to be "usable": see paragraph 151.

44. One can detect a similar approach to the question of whether an invention is shown to be plausible in the context of obviousness. In *Conor Medsystems Inc v Angiotech Pharmaceuticals Inc* [2008] UKHL 49; [2008] RPC 28 the claimed invention was a taxol-coated stent said to be suitable for preventing complications ("restenosis") associated with the insertion of the stent. The trial judge (Pumfrey J) had approached the issue of obviousness on the basis that the specification went no further than proposing that taxol was worth experimenting on and did not establish whether it would be safe or prevent restenosis. On that basis the claimed stent was obvious. After explaining *Agrevo* and *Johns Hopkins* as cases where "there was nothing in the description to justify the assertion that all the compounds in the class would have herbicidal properties" and "where the specification contained no more than speculation about whether GDF-9 activity might be useful", Lord Hoffman said at [36]:

> "These cases are in my opinion far from the facts of this case. The specification did claim that a taxol coated stent would prevent restenosis and Conor did not suggest that the claim was not plausible. That would have been inconsistent with the evidence of its experts that taxol was just the thing to try."

45. That passage indicates that it may be difficult to sustain the argument that an invention is not plausible in the face of evidence that the specification would render it obvious to try. At [37] Lord Hoffmann described the requirement of plausibility as a threshold test, although of course that expression does not tell one anything about the height of the threshold.

46. The EPO and domestic cases do, however, indicate that the requirement of plausibility is a low, threshold test. It is designed to prohibit speculative claiming, which would otherwise allow the armchair inventor a monopoly over a field of endeavour to which

he has made no contribution. It is not designed to prohibit patents for good faith predictions which have some, albeit manifestly incomplete, basis. Such claims may turn out to be insufficient nonetheless if the prediction turns out to be untrue. A patent which accurately predicts that an invention will work is, however, not likely to be revoked on the ground that the prediction was based on the slimmest of evidence. Thus, the claims will easily be seen not to be speculative where the inventor provides a reasonably credible theory as to why the invention will or might work. The same is true where the data in the specification is such that the reader is encouraged to try the invention.

47. We heard argument as to whether the invention is only to be treated as plausible if the reader of the specification would be encouraged to try the invention with a reasonable prospect of success, thereby bringing the test for plausibility into line with that sometimes used in the context of obviousness. I do not accept that there is any reason to align the tests in this way. A test designed to prevent speculative claiming need go no further than requiring the patentee to show that the claim is not speculative: the specification does not need to provide the reader with any greater degree of confidence in the patentee's prediction than that.

The insufficiency issue and how it arose

48. The way in which the issues in relation to insufficiency developed is of some relevance to the question of amendment and abuse of process. It is convenient to deal with it here, however.

49. The plea of insufficiency relied on by Mylan and Activis is set out in full at paragraph 40 of the abuse judgment. Stripped to its essentials it was alleged that the animal model results which were reported in the patent did not make it plausible that pregabalin would be effective in treating any type of pain as referred to in paragraph [0003], or as claimed in any claim, other than those for which the animal tests provided a plausible model. The plea also contained an allegation that it would require undue effort on the part of the skilled person to identify whether the compound of claim 1 was in fact effective in treating any (and if so which) types of pain referred to in paragraph [0003] or as claimed in any claim, other than those for which the animal tests provided a plausible model. It was the former aspect of the plea, and not the latter, which ultimately succeeded before the judge.

50. This pleading did not of course make it clear which specific types of pain Mylan and Actavis claimed were, and which types were not, rendered plausible by the animal model. It left it open to Mylan and Actavis to identify any type of pain and assert that its treatment by pregabalin was not plausible. Warner-Lambert chose not to ask for further information about the Mylan and Actavis case, however.

51. On 12 December 2014 Mylan and Actavis served a statement of the matters which they contended to be common general knowledge and on 27 January 2015 Warner-Lambert served a reply statement which took the form of an amended version of the Mylan and Actavis statement. The Mylan and Actavis statement asserted that it was common general knowledge that neuropathic pain included pain caused by damage in the central nervous system. Warner-Lambert's response was to restrict neuropathic pain to pain which is caused by damage to peripheral nerves. The Warner-Lambert version also included a section on central sensitisation. Mylan and Actavis accepted

that it was apparent to them from this statement that central sensitisation was to be the basis on which Warner-Lambert would seek to rebut the allegation of insufficiency. They asserted, and the judge accepted, that it was not apparent to them precisely how Warner-Lambert would seek to do so before they received Warner-Lambert's evidence in chief.

52. The parties exchanged evidence in chief on 17 April 2015. It was common ground that the main focus of the insufficiency attack in the Mylan and Actavis evidence in chief was the distinction between neuropathic pain and inflammatory pain. Thus, the case advanced in the evidence of Professor Wood was primarily that central sensitisation was only recognised as a minor feature of inflammatory pain, and not of neuropathic pain at all, and therefore that the data in the patent only supported claims to those pain types which were inflammatory in nature. Neither of the Mylan and Actavis experts distinguished between peripheral neuropathic pain and central neuropathic pain when commenting on the plausibility of the claims in question in their evidence in chief. There were, however, explanatory passages in Dr Scadding's report where he distinguished between peripheral and central neuropathic pain. In particular, he included as Appendix 1 to his report a classification of causes of neuropathic pain, dividing the conditions into five groups. One of the groups was headed "Peripheral Nerve", but others were plainly related to the central nervous system, including "Spinal Cord", "Brain Stem" and "Brain".

53. The case presented in the evidence of Professor Woolf for Warner-Lambert was that the three animal models were models of central sensitisation and, as such, were appropriate models of any pain types which included central sensitisation as a component. This included all the claimed pain types.

54. Evidence before the judge on the abuse of process application showed that the advisers to Mylan and Actavis first appreciated the importance of showing that there were types of pain with no central sensitisation component on receipt of this evidence in chief.

55. Evidence in reply was exchanged on 22 May 2015. It continued to be the primary case of Mylan and Actavis that the data presented in the patent did not make the treatment of neuropathic pain of any kind plausible. However, in paragraph 7.4 of his second report, Dr Scadding stated:

> "As for neuropathic pain caused by lesions in the central nervous system, it would not occur to the Skilled Clinician that these possessed a central sensitisation component. For example ischaemic and haemorrhagic stroke are relatively common causes of central pain, as is multiple sclerosis (MS). MS typically affects the spinal cord in multiple sites (although it frequently also affects the brain stem, cerebellum, and cerebral hemispheres). *Other types of neuropathic pain where the primary cause is a lesion in the central nervous system and which the Skilled Clinician would not expect to possess a central sensitisation component are listed in Appendix 1 to my First Report under the headings Spinal Cord, Brain Stem, and Brain*." (emphasis supplied).

56. The judge thought that this passage was adequate to put Warner-Lambert on notice that the answer put forward by Mylan and Actavis to Warner-Lambert's sufficiency case - that central sensitisation was a unifying principle or characteristic - did not assist where the claims in question covered pain with no central sensitisation component. Warner-Lambert, however, adduced evidence on the application that it did not appreciate the significance of that evidence. The judge appears to have accepted that evidence.

57. Skeleton arguments for the trial were exchanged on 22 June 2015. The distinction between peripheral and central neuropathic pain was clearly raised by Mylan and Actavis as part of their argument on the insufficiency of claim 3. Thus, for example, they said that:

> "… important types of neuropathic pain such as pain from stroke and multiple sclerosis had no relationship to central sensitisation, since they do not involve any peripheral damage. So the claim is still too broad."

58. When the case was opened, counsel for Actavis drew attention orally to this point. Counsel for Warner-Lambert took no objection to the point being run at that stage, and did not suggest that he was taken by surprise by it.

59. During his cross-examination, Professor Wood volunteered the fact that there were types of pain such as thalamic pain after a stroke where there was no peripheral nervous system involvement at all. He went on to confirm, however, that most types of neuropathic pain involved the peripheral nervous system.

60. Dr Scadding was not cross-examined about paragraph 7.4 of his second report. Instead, it was suggested to him, based on the passage in the patent at [0006], that the use of the term neuropathic pain in the patent was limited to peripheral neuropathic pain. The cross-examination in question is set out at paragraphs 109 and 110 below. This interpretation of the term was later also espoused by Professor Woolf.

61. At this stage, therefore, it is clear that Warner-Lambert and its advisers were aware of the potential problem for the sufficiency of the patent if the claims extended to central neuropathic pain. It would be fair to add that Mylan and Actavis and their advisers must also have been aware at this stage that one of Warner-Lambert's answers to this potential problem was to contend, as a matter of construction, that the monopoly of claim 3 was limited to peripheral neuropathic pain.

62. A further potential answer to the problem that the claims extended to central neuropathic pain (which has no central sensitisation component) was to argue that the unifying characteristic which justified that breadth of claim was that the pain types were all characterised by hyperalgesia and/or allodynia, that is to say, independently of whether there was a central sensitisation component. It is convenient to explain how this potential argument emerged by reference to the decision of the judge on this issue, to which I now turn.

The decision of Arnold J on the issue of insufficiency

63. The judge addressed the issues of construction which arose and which were relevant to the issue of insufficiency at paragraphs 243 to 252 and 257 to 261 of his judgment. These were: the meaning of "pain" in claim 1 and the meaning of "neuropathic pain" in claim 3.

64. The judge rejected (at paragraph 251) Warner-Lambert's contention that "pain" in claim 1 was restricted to types of pain characterised by hyperalgesia and/or allodynia and having a central sensitisation component. Pain meant any type of pain. The judge gave four reasons for rejecting this construction:

    i) There was no mention of central sensitisation anywhere in the patent, or indeed any suggestion that there was a common mechanism or other link between the disparate kinds of pain listed in [0003].

    ii) The list included at least two types of pain which did not have a central sensitisation component, namely fibromyalgia and idiopathic pain. Phantom limb pain would not be regarded as having a central sensitisation component either.

    iii) The references to "neuropathic pain" in the patent would not be understood to be confined to peripheral neuropathic pain, and hence as excluding central neuropathic pain.

    iv) The evidence of Professor Clauw, Professor Wood and Dr Scadding was consistently to the effect that the patent would not be read as being limited to central sensitisation.

65. The judge also rejected the alternative argument advanced by Warner-Lambert in its closing submissions that claim 1 was limited to any type of pain characterised by hyperalgesia and/or allodynia (i.e. without a requirement for the central sensitisation component). In the judge's view the argument had been advanced too late, and had not been explored with any of the witnesses. It also suffered from many of the defects of Warner-Lambert's primary construction.

66. Accordingly the judge accepted Mylan and Actavis's contention that "pain" would be interpreted in accordance with the definition of pain approved by the International Association for the Study of Pain ("IASP") in its classification of chronic pain:

> "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage".

67. The judge also rejected Warner-Lambert's argument that "neuropathic pain" in claim 3 was limited to peripheral neuropathic pain. Although the judge said it was striking that this argument was not foreshadowed in Warner-Lambert's evidence or skeleton argument, he did not suggest that this argument was not fully open to Warner-Lambert. He was right to do so given that it had been put to Dr Scadding in cross-examination. As explained above, the argument was advanced in order to exclude central neuropathic pain, and thus insulate the claim against the potential success of

the allegation of insufficiency based on excessive claim breadth. Here, the judge relied on the IASP definition of neuropathic pain:

> "Pain initiated or caused by a primary lesion or dysfunction in the nervous system.
>
> *Note*: see also Neurogenic Pain and Central Pain. Peripheral neuropathic pain occurs when the lesion or dysfunction affects the peripheral nervous system. Central pain may be retained as the term when the lesion or dysfunction affects the central nervous system."

68. As the judge observed subsequently in the abuse judgment, through no fault of his own, he had misquoted this definition in paragraph 50 of the main judgment by building into the definition a distinction between the central and peripheral nervous system. However, the distinction between peripheral neuropathic pain and central pain is made in the Note which follows immediately from the definition, so the judge concluded that the error was not material.

69. The judge's further reasons for rejecting Warner-Lambert's construction of claim 3 were in summary the following:

i) The expression "neuropathic pain" appeared to be used quite generally in the specification and there was no reference to peripheral neuropathic pain, still less any indication that central neuropathic pain was not intended to be included.

ii) The only basis for the construction was the sentence in paragraph [0006] which stated that neuropathic pain "is caused by injury or infection of peripheral sensory nerves". This was a correct statement whichever construction was adopted. Furthermore the final sentence of the paragraph, which stated that neuropathic pain "includes, but is not limited to pain caused by nerve injury such as, for example [DPN]" was clearly non-limiting language.

iii) The patent contained specific subsidiary claims to phantom limb pain and fibromyalgia pain which the judge concluded (see below) were regarded as ones involving central neuropathic pain.

70. Much of Warner-Lambert's remaining answer to the insufficiency case depended on showing that the skilled person would, based on his common general knowledge, understand the patent to be disclosing a principle of wide application. Thus, as the patent specification itself did not expressly state what this principle was, it was necessary for Warner-Lambert to establish that the skilled person would be able to make the necessary inferences in the light of his or her common general knowledge. The judge summarised Warner-Lambert's case in relation to the common general knowledge as follows.

> "(i) central sensitisation was recognised to be a common mechanism in many pain states;

> ii) it was known that central sensitisation was a component in both neuropathic pain and inflammatory pain; and
>
> iii) it was recognised that there was a causal link between central sensitisation and hyperalgesia and allodynia."

71. These propositions were disputed, at least to some extent, by Mylan and Actavis. The judge concluded that the concept of central sensitisation was a well-known concept on which there was a substantial body of work by July 1996 (paragraph 180). It was generally understood that central sensitisation *contributed* to peripheral neuropathic pain. Warner-Lambert did not contend that it was common general knowledge that central sensitisation was *causative* of peripheral neuropathic pain.

72. Professor Woolf's textbook, The Textbook of Pain, had described central sensitisation in terms of a number of "modes". In mode 3, the dorsal horn in the spinal cord can become sensitised following peripheral tissue injury, peripheral inflammation and damage to the peripheral and central nervous systems. Mode 4 was described as the reorganised state, which was qualitatively quite different to the earlier modes and was one in which cells die, axon terminals degenerate or atrophy, and the structural contact between cells at the synapses may be considerably modified. The Woolf textbook explained:

> "This mode represents true pathology and its contribution to neuropathic and central pain disorders is only just beginning to become apparent."

73. The judge held that, considering the evidence as a whole, it had not been shown that mode 4, the reorganised state, was part of the common general knowledge of the neuroscientist or the clinician.

74. It was common ground that central sensitisation was a common mechanism in peripheral neuropathic and inflammatory pain. Nevertheless, the pharmacology of these pain states was different, in that drugs that were effective for treating inflammatory pain did not affect neuropathic pain. Non-steroidal anti-inflammatory drugs, NSAIDs, were an example of this.

75. Subject to certain exceptions relied on by Professor Woolf, there was no evidence that central sensitisation contributed to central pain states. The theory of central sensitisation required repetitive C-fibre barrage from a damaged peripheral nerve, and many central pain conditions had nothing to do with damage to peripheral nerves. Professor Woolf's main exception was phantom limb pain. The judge did not accept that it was common general knowledge that phantom limb pain had a central sensitisation component.

76. The judge also considered what was known about fibromyalgia. Here the judge preferred the evidence of Professor Clauw to that of Dr Scadding, that fibromyalgia was considered to be a form of neuropathic pain in 1996, but one in which there was unlikely to be a component of central sensitisation in the absence of any peripheral damage or inflammation which was causative of the pain.

77. The judge next considered the link between central sensitisation, neuropathic pain and secondary hyperalgesia and allodynia. Warner-Lambert contended that it was common general knowledge that central sensitisation resulted in secondary hyperalgesia and allodynia. The judge concluded at paragraph 205 that it was common general knowledge that:

> "(i) neuropathic pain was characterised by secondary hyperalgesia and allodynia in the sense that these symptoms were present in the large majority of patients, but a significant minority did not display these symptoms.
>
> (ii) secondary hyperalgesia and allodynia involved central augmentation. In some cases this would be central sensitisation, but not in all cases."

78. As to the rat paw formalin test, the judge reached three important conclusions. Firstly, it was common ground by the end of the trial that the second phase of the test had a central sensitisation component. Secondly, the judge concluded that it was not common general knowledge that central sensitisation played the dominant role in the second phase of the test. Thirdly, the judge concluded that it was not common general knowledge that the rat paw formalin test was predictive of efficacy in treating neuropathic pain.

79. The judge commenced his consideration of the sufficiency of claim 3 by noting that it needed to be divided into central neuropathic pain and peripheral neuropathic pain. In the light of his finding that it was common general knowledge that central sensitisation was not thought to have a role in central neuropathic pain, the judge concluded that it was not possible for Warner-Lambert to rely on central sensitisation as a unifying principle covering both central and peripheral neuropathic pain. The judge then noted and rejected the alternative argument advanced by Warner-Lambert, that a unifying characteristic or principle which embraced central neuropathic pain was the presence of hyperalgesia and/or allodynia. The judge said that this alternative argument was not open to Warner-Lambert as it was not pleaded, was not advanced in Warner-Lambert's evidence or opening skeleton argument, was not put to Dr Scadding or Professor Wood, was not supported by Professor Woolf, and was first suggested by Professor Clauw (who gave evidence last) in cross-examination. Quite apart from that, the evidence as a whole did not support the proposition. The only expert who espoused it was Professor Clauw, and then only late in the day. Further, it was difficult to reconcile with the fact that NSAIDs were known to be effective for the treatment of inflammatory pain, but not neuropathic pain.

80. Although Warner-Lambert had sought to rely on the fact that pregabalin in the form of Lyrica had subsequently been authorised for central neuropathic pain, that later work could not justify a claim that was speculative when it was made.

81. The judge then turned to peripheral neuropathic pain. At paragraph 351 he said:

> "… I consider that the evidence is finely balanced. In addition to the general points made above, Warner-Lambert's case suffers from the problem that it has not been established that it was common general knowledge that the rat paw formalin test

> was predictive of efficacy for neuropathic pain. Moreover, as discussed above, Prof Woolf accepted that the carrageenin and post-operative pain models did not assist in this regard. Nevertheless, I have concluded on balance that, given that plausibility is a relatively low threshold, the data contained in the specification, when read with the common general knowledge, just make it plausible that pregabalin would be effective to treat peripheral neuropathic pain. This is because the common general knowledge as to (i) the involvement of central sensitisation (at least as an amplifying mechanism) in both inflammatory pain and peripheral neuropathic pain and (ii) the role played by central sensitisation in the rat paw formalin test would have suggested to the skilled team that it was possible that a drug which was effective for inflammatory pain, in particular as modelled by the second phase of the formalin test, would also be effective in peripheral neuropathic pain, although this would not necessarily be the case. This conclusion is supported by the evidence not only of Prof Woolf, but also of Dr Scadding and Prof Wood in cross-examination. Dr Scadding said that, when he read the Patent, he thought that it "could be the case" that pregabalin would be effective for (peripheral) neuropathic pain, although a demonstration of that was missing. Prof Wood more or less accepted that it was a credible suggestion, although he made it clear that he would want to test it experimentally."

82. Despite this favourable finding for Warner-Lambert, it was not enough to save claim 3, which also covered central neuropathic pain, and as there was at that stage no application to amend it to limit it to peripheral neuropathic pain, it was invalid.

83. Claim 4 was restricted to cancer pain. As cancer pain could be either peripheral or central depending on the location of the tumour, that claim was invalid as well. Claim 6 was to phantom limb pain. Based on his finding that phantom limb pain was regarded as a form of central neuropathic pain, and had not been established to have a central sensitisation component, that claim was invalid as well. Claim 14 was to fibromyalgia pain. It was not plausible that pregabalin would be effective in treating fibromyalgia. Whether or not it was regarded as a type of neuropathic pain, it was not common general knowledge that it had a central sensitisation component. It was therefore invalid.

84. On the other hand claims 10 (trigeminal neuralgia pain), 11 (PHN) and 12 (causalgia) were valid as they were forms of peripheral neuropathic pain, and did not therefore suffer from the central pain problem which invalidated the other claims.

85. It followed that claim 1 was also invalid, as it extended to all types of pain. There was no basis for saying that it was plausible that pregabalin would be effective for all types of pain.

The arguments on the appeals

86. Mr Mitcheson QC, who argued the insufficiency case on behalf of Warner-Lambert, had a number of criticisms of the judge's findings about the common general knowledge, which I must deal with below. He went on to make three main points. Firstly, he maintained the arguments which the judge had rejected about the construction of claims 1 and 3. If Warner-Lambert was correct on those issues, the claims were plausible substantially across their breadth. Secondly, he submitted that the claims were plausible substantially across their breadth even on the construction arrived at by the judge. Thirdly he submitted that the claims were plausible because pregabalin was shown to be anti-hyperalgesic.

87. Mr Meade QC, who argued this part of the case for Mylan and Actavis, submitted that the judge was right on the issues of construction, and right on that construction to reject the suggestion that the claims were plausible substantially across their breadth. He also submitted that the judge had been wrong to find that the claims which were limited to types of peripheral neuropathic pain, claims 10, 11 and 12, were plausible.

Discussion

Common general knowledge

88. It is first necessary to address Mr Mitcheson's challenges to the judge's findings about the common general knowledge.

89. Mr Mitcheson first made a challenge to the judge's division of neuropathic pain into peripheral and central neuropathic pain when considering central sensitisation. He submitted that this was not a distinction that would be drawn in the common general knowledge, the common general knowledge perception being that central sensitisation contributed to neuropathic pain generally. The papers relied on by the judge in support of the proposition that central sensitisation contributed to peripheral neuropathic pain in fact made no distinction between peripheral and central neuropathic pain. Moreover in the passages of evidence relied on by the judge as showing a link, based on central sensitisation, between inflammatory and peripheral neuropathic pain, the witnesses did not themselves make a distinction between peripheral and central neuropathic pain, but referred to neuropathic pain generally.

90. Mr Mitcheson also pointed to a passage from Professor Woolf's Textbook of Pain describing mode 3 which suggested that "the sensitisation of the dorsal horn can occur following peripheral tissue injury, peripheral inflammation and damage to the peripheral and central nervous systems". This indicated, he submitted, that central sensitisation may indeed be involved when there is damage to the central nervous system, i.e. in central neuropathic pain states.

91. I do not accept these submissions. Firstly, the judge's principal reason for the division of neuropathic pain into peripheral and central neuropathic pain for these purposes flowed from the common general knowledge understanding of central sensitisation, which involved damage to a peripheral nerve to provide the repetitive C-fibre barrage required. In most central pain states there was no such damage to the peripheral nerves. The skilled person would therefore understand, as part of the common general knowledge, that the distinction made by the judge was a real one.

Secondly, I do not see how this conclusion can be affected by the passage from the textbook by Woolf. Although the judge did find that mode 3 was part of the common general knowledge, he made no specific finding about the short extract relied on. Thirdly, there was, in any event, ample evidence to show that the skilled person would not expect central pain to possess a central sensitisation component. Dr Scadding had produced an appendix to his first report which showed a large number of pain conditions caused by a lesion in the central nervous system, such as ischaemic and haemorrhagic stroke, which the skilled person would not expect to possess a central sensitisation component. These were put to Professor Woolf, who accepted their generality, whilst making his reservation about phantom limb pain.

92. Next, Mr Mitcheson attacked the judge's finding that it was not common general knowledge that phantom limb pain (referred to in claim 6) had a central sensitisation component. The evidence on this topic was as follows:

i) Professor Woolf had said that phantom limb pain "almost certainly" had a central sensitisation component.

ii) Professor Wood had accepted that the following passage in a paper by Vaccarino and Chorney was reflective of the common general knowledge:

> "Peripheral tissue and nerve damage often leads to pathological pain syndromes such as phantom limb pain, spontaneous pain, hyperalgesia and allodynia. There is good evidence that the pain that develops after peripheral nerve or tissue damage is related to long-lasting changes in central nervous system function produced by the injury (i.e. central sensitisation)".

iii) Phantom limb pain is the result of amputation. In the classification produced as an appendix to his report, Dr Scadding had indicated that phantom limb pain was a central pain with no central sensitisation component, whereas amputation pain was peripheral.

93. The difficulty which arises is that there is undoubtedly peripheral nerve damage when a limb is amputated, which would give rise to immediate pain with a central sensitisation component. Later, when phantom limb pain is experienced, there is no longer any C-fibre barrage, but the cause of the phantom limb pain may still be tied back to the initial nerve damage, which may have caused permanent changes in the central nervous system.

94. Notwithstanding what Professor Wood accepted in cross-examination, the judge was justified in finding that it was not common general knowledge that phantom limb pain possessed a central sensitisation component. He had Dr Scadding's unchallenged evidence that he did not regard it in that way. He had expressed reservations about Professor Woolf's evidence in general, which in any event did not go as far as saying that it was common general knowledge that phantom limb pain possessed a central sensitisation component. He might have added that the fact that the patent in suit categorised phantom limb pain as idiopathic, i.e. of unknown origin, added force to that conclusion.

95. Mr Mitcheson also attacked the judge's finding that fibromyalgia was considered to be a type of neuropathic pain without a central sensitisation component. There are two parts to this point. The first part of the point is whether it is correct, as a matter of common general knowledge, to categorise fibromyalgia as neuropathic pain at all. The significant points were as follows:

i) Dr Scadding gave evidence in his first report that fibromyalgia was not considered to be a neuropathic pain type in 1996. However Dr Scadding had said that he would defer to Professor Clauw when it came to fibromyalgia.

ii) Professor Wood had classified fibromyalgia as an "unknown" pain type i.e. idiopathic. He had said in his first report:

> "The cause of fibromyalgia pain was at the priority date (as it is today) unknown".

iii) Prof Woolf had included a sentence in his first report which appeared to distinguish between neuropathic pain and pain in fibromyalgia.

iv) Fibromyalgia is not mentioned anywhere in the chapter in the Textbook of Pain dealing with neuropathic pain.

v) Professor Clauw had said that fibromyalgia was encompassed within the IASP definition of neuropathic pain. This was because the definition extended to "dysfunction" of the nervous system, and not only to "lesions".

vi) Other passages in Professor Clauw's evidence referred to the fact that, historically, fibromyalgia had been labelled "idiopathic" by clinicians; and dealt separately with fibromyalgia as a condition in contrast to established neuropathic pain conditions such as PHN and DPN.

vii) In paragraph 195 of the judgment, the judge says that Professor Clauw "*also explained in cross-examination that the same drugs were used to treat fibromyalgia as other forms of neuropathic pain*". In fact what Professor Clauw said did not carry the necessary implication that fibromyalgia was a type of neuropathic pain:

> "Q. But the mechanisms that produce the symptoms of fibromyalgia were still speculative; is that right?
>
> A. The precise mechanisms were speculative but again the drugs, for example, that we used to treat fibromyalgia in 1996 are exactly the same drugs that were being used to treat neuropathic pain."

96. In order to be classified as neuropathic pain, it would need to be established that fibromyalgia was caused by a lesion or dysfunction of the central nervous system. Neither Dr Scadding, the Mylan and Actavis neurological expert, nor Professor Wood, their expert neuroscientist, was prepared so to classify it. Dr Scadding said that, in the absence of peripheral involvement "thoughts then turn" to the central nervous system but that there was confusion at the time as to the pathogenesis.

Professor Wood's refusal to classify fibromyalgia as neuropathic pain included a table which did, in clear contrast, classify other conditions as neuropathic.

97. Mr Meade deals with this by saying that Professor Clauw was "*the witness who really knew about fibromyalgia*", and that Dr Scadding, as the judge pointed out, was prepared to defer to Professor Clauw in relation to fibromyalgia as it lay within his special expertise.

98. However Professor Clauw's evidence, whilst explaining that the breadth of the IASP definition allowed the conclusion that fibromyalgia was a neuropathic pain condition, did not go so far as to say that it would routinely be so regarded at the priority date. He made the point in this way in paragraph 25 of his first report:

> "Many of the pain conditions that our group has studied (e.g. fibromyalgia ...) were previously labelled "idiopathic" by clinicians because there was no clear pathology in the tissues that seemed likely responsible for causing these pain states. Now these conditions are more or less acknowledged by clinicians to be diseases of the central nervous system (CNS) …"

99. In paragraph 44 of his first report Professor Clauw said:

> "By the Priority Date, research had shown that the underlying etiologies of neuropathic pains, including postherpetic neuralgia, diabetic peripheral neuropathy, and post-operative pain, as well as conditions such as fibromyalgia, may have some relation to central augmentation/sensitization."

100. This passage appears to make a distinction between the exemplified neuropathic pains and fibromyalgia. Thus, even if Dr Scadding's evidence is to be wholly ignored on the footing that he deferred to Professor Clauw, I do not consider that Professor Clauw's evidence established that fibromyalgia was regarded as a form of neuropathic pain. I think the judge's conclusion on this issue was unsupported by the evidence.

101. The second aspect of the point is whether it was common general knowledge that fibromyalgia possessed a central sensitisation component. The judge held that it was not. I was not persuaded that there was any basis for this court to depart from the judge on that question.

Construction

102. Mr Mitcheson submitted that the judge should not have construed the word "pain" in claim 1 by reference to the IASP definition, but ought to have taken account of the rest of the specification of the patent, which acted as its own dictionary. He submitted that paragraph [0006], by its reference to "pain as listed above", specifically limited the invention to the pain types listed in paragraph [0003], and the judge had ignored the effect of what he contended was a limitation. The pain types listed in [0003] were all characterised by hyperalgesia and allodynia. The judge had failed to give proper consideration to the different understanding of the clinician from that of the neuroscientist. The clinician would be more interested in symptoms than the theory of

central sensitisation which was the province of the neuroscientist. He submitted that the skilled reader would understand the patentee to be limiting the claim to the types of pain condition listed in paragraph [0003], and any other type of pain characterised by hyperalgesia and allodynia. That understanding was reinforced by the reference in paragraph [0001] to the fact that the compound exhibited antihyperalgesic action.

103. The argument advanced by Warner-Lambert on construction is, in essence, the second of the two arguments advanced at the trial, and which the judge held not to be open to them, but nevertheless considered to be incorrect for many of the same reasons as he rejected their primary argument. The primary argument, which sought to limit the scope of claim 1 to pain conditions having a central sensitisation component, could not survive a finding that the conditions specifically listed included ones where there was no common general knowledge understanding as to their origin.

104. I also reject the secondary argument for the following reasons. Firstly, although it is often said that a specification can act as its own dictionary, not every use in the specification of a term found in the claim will be understood by the reader to be a definition. On no basis can paragraph [0006] or [0003] or the two paragraphs read together be taken to be a definition of what the patentee means by the term "pain". They are statements exemplifying the broadest statement of invention, namely that pregabalin is suitable for the treatment of pain.

105. Secondly, although the reference back in paragraph [0006] to "*pain as listed above*" is undoubtedly to paragraph [0003], paragraph [0003] does not contain a closed list of chronic pain disorders. The disorders "*include, but are not limited to*" the listed conditions.

106. Thirdly the reference in paragraph [0001] to the fact that pregabalin is "antihyperalgesic" is a slim foundation on which to assert that "pain" would not have its ordinary, broad meaning, particularly as it is mentioned in the same breath that it also has analgesic action.

107. In short if the patentee had intended to limit the claims to the pain conditions listed in paragraph [0003] or to pain characterised by hyperalgesia or allodynia, he could easily have done so. I reject this construction argument.

108. Mr Mitcheson is on rather firmer ground with his argument about the scope of claim 3. There was some evidence of a usage of the term "neuropathic pain" to mean "peripheral neuropathic pain". Whether the term "neuropathic pain" would be understood to include central neuropathic pain is therefore dependent on the context in which it is used. Accordingly, the skilled reader could certainly regard the sentence in paragraph [0006] that "neuropathic pain is caused by injury or infection of peripheral sensory nerves" as a possible pointer in the direction that the patentee was using the term to mean peripheral neuropathic pain. The final sentence of paragraph [0006] did not necessarily detract from that proposition, when it states that "neuropathic pain includes but is not limited to pain caused by nerve injury such as, for example, the pain diabetics suffer from". The first quoted sentence includes infection, whilst the second does not.

109. Mr Mitcheson also relied on a passage of cross-examination of Dr Scadding based on the first of the two sentences in paragraph [0006] of the specification:

> "Q. … Then there follows a reference to neuropathic pain, and what the patent says is: "neuropathic pain is caused by injury or infection of peripheral sensory nerves." Do you see that?
>
> A. Yes.
>
> Q. In fact, you would understand that as a reference to peripheral neuropathic pain?
>
> A. Yes.
>
> Q. This reflects the discussion we were having earlier. There was some uncertainty about what neuropathic pain means as a matter of common general knowledge at the priority date, but the patent here defines what it means by "neuropathic pain"?
>
> A. Yes.
>
> Q. And whilst some might suggest that the patent should really have used the term "peripheral neuropathic pain", instead of "neuropathic pain", it is pretty clear what is meant by the term as a result of paragraph [0006]?
>
> A. Yes."

110. The earlier discussion referred to in that passage of cross-examination went like this:

> "Q. … Do you accept that there was some confusion about the terminology in the early '90s?
>
> A. Yes, there was. So, one always would have to look at the context to see what was being meant?
>
> A. Precisely.
>
> Q. So, for example, when an author used the term "neuropathic pain", whether or not he or she meant to include central pain would have to be looked at in context?
>
> A. Yes, although by then people were using the broader terminology of "neuropathic pain" to include central pain.
>
> Q. But there might be instances where they were not?
>
> A. Exactly, and one would have to look very carefully, as you point out, at the context in which it was being used."

111. Prof Woolf's evidence was that the term "neuropathic pain", rightly or wrongly, was commonly used at the priority date to mean peripheral neuropathic pain.

112. Mr Mitcheson submitted that the judge had been wrong to rely on the existence of the subsidiary claims to phantom limb pain and fibromyalgia as contraindications. As to

the former, phantom limb pain was stated to be "*idiopathic pain which is pain of unknown origin*" at page 3 lines 50-52 of the specification. It was therefore outside the scope of claim 3, even on the basis that it extended to all forms of neuropathic pain. For reasons explained above, the judge had been wrong to say that it was common general knowledge that fibromyalgia was a form of neuropathic pain: it too was pain of unknown origin so far as the common general knowledge was concerned, and the patent did not contradict that view.

113. Mr Meade submitted that although a clinician might refer to someone with a peripheral neuropathic pain condition as having "neuropathic pain", there was no usage of neuropathic pain so as to exclude central pain. He supported the judge's reliance on phantom limb pain and fibromyalgia. Warner-Lambert's construction had the odd effect that these conditions, as well as recognised central neuropathic pain conditions such as stroke pain and multiple sclerosis pain, were included in claim 1 but not in claim 3, albeit that the latter two were nowhere mentioned in the patent. Further he relied on the mention of "vitamin deficiencies" as an example of something the patent describes as neuropathic pain, but which can be either central or peripheral depending on the particular vitamin deficiency.

114. I approach the question of construction on the footing that the skilled reader would not understand the patentee to regard either phantom limb pain or fibromyalgia as neuropathic pain. Nevertheless, I do not think that the skilled reader would think that the patentee intended to exclude central neuropathic pain from claim 3. The skilled person would observe that the patentee was making very broad claims as to the efficacy of pregabalin for treating pain of all kinds. Although there was a usage of omitting the word "peripheral", there was, as Mr Meade submits, no usage of the term so as to mean that central neuropathic pain is excluded. Given the breadth of the claims that the patentee is making for pregabalin in general, and in paragraphs [0003] and [0006], it seems to me unlikely that the reader would interpret neuropathic pain restrictively.

115. Despite Mr Mitcheson's skilful cross-examination of Dr Scadding, the construction of the claims is ultimately a matter for the court and not for the expert. His evidence that there was a wide and narrow usage of the term "neuropathic pain" was of course relevant and admissible, but the question of whether the context justified adoption of the narrow construction in claim 3 was not one on which the witness' opinion could be determinative.

116. I conclude that the judge was right to hold that neuropathic pain in claim 3 did not exclude central neuropathic pain.

117. I would add that I arrive at the same conclusion even taking into account the judge's conclusions (to which I will have to come) that the claims to peripheral and central neuropathic pain were plausible and implausible respectively. I would think that, in a clear case, where there are two possible meanings of a term, it might be legitimate to adopt the narrower meaning if there were common general knowledge reasons for saying that the wider meaning led to the claim extending to implausible embodiments. In the present case it is not realistic to suppose that the skilled reader would conclude from a comparative evaluation of plausibility that neuropathic pain was confined to the peripheral kind.

Sufficiency of claim 3

118. Mr Mitcheson placed particular reliance on the following passage in the cross-examination of Dr Scadding:

> "Q. I think you accept that the reader of the patent would be interested in the suggestion that pregabalin could be used to treat chronic pain?
>
> A. Yes.
>
> Q. The experiments demonstrate the effect of pregabalin and gabapentin to reduce hyperalgesia and allodynia in rat models?
>
> A. Yes.
>
> Q. As we discussed this morning, you would be aware that hyperalgesia and allodynia were common symptoms both in neuropathic pain and in inflammatory pain?
>
> A. Yes.
>
> Q. So it is a credible claim, is it not, Doctor, that pregabalin can be used to treat all the pain conditions set out in paragraph [0003]?
>
> A. It is credible, but my first reaction, my Lord, if I may say, when I saw the patent was that these claims for neuropathic pain were based on two animal models which I certainly regarded as being models of inflammatory pain... But that was my first reaction. I thought, well, the thing that is-- this could be the case, what is missing here is demonstration that these drugs are effective or not effective in an established model of neuropathic pain.
>
> Q. Can I suggest that the skilled clinician would also recognise that the maintenance of all the conditions referred to in paragraph [003] was contributed to by central sensitisation?
>
> A. Yes, to some extent…
>
> Q. The recognition of the central sensitisation component is further basis for thinking that the claim that pregabalin can be used to treat the pain conditions set out is credible?
>
> A. It is credible, but, as I've said, the skilled clinician would not be able to interpret these in the way that we have been discussing here over the last three days; and I believe it is the case, when I read this through -- but there is not mention of central sensitisation within this document. So there is no pointer that that is what the interpretation of how these results should be interpreted. Again, I find that odd.

> Q. As we discussed this morning, Doctor, you recognise that central sensitisation contributed to both inflammatory pain types and neuropathic pain types at the priority dates?
>
> A. Yes.
>
> Q. And I think that you heard the evidence from Prof Wood yesterday, when he accepted that central sensitisation also played a role in the formalin test?
>
> A. Yes. I do not deny that at all.
>
> Q. So, on that basis, these claims are supported by the data in the patent?
>
> A. Yes."

119. Mr Mitcheson draws attention to the fact that in those answers Dr Scadding did not seek to distinguish between central and peripheral neuropathic pain. Dr Scadding went on to accept that, even if he was not convinced by the patent that pregabalin would be effective to treat pain in humans, there was sufficient data in the patent to motivate him to move ahead and provide confirmatory data if he wished. The Bennett and Kim tests would have been relatively straightforward things to ask the neuroscientist to do. Dr Scadding accepted that those tests would further confirm the claims in the patent that pregabalin was effective to treat neuropathic pain. Again, in his answers, Dr Scadding did not differentiate between central and peripheral neuropathic pain.

120. Apart from reliance on this evidence, Mr Mitcheson's answer to the insufficiency attack based on central neuropathic pain relied essentially on the following points. Firstly he submitted that the judge had been wrong to "parse" claim 3 into central and peripheral neuropathic pain, a process he described as "salami slicing". The claim should have been approached at a more general level. This was an illegitimate process which was unfair to patentees, and ignored the fact that there were no concrete definitions of the categories of pain at the time. Secondly, even if it was right to split up the claim in this way, central pain was not a significant part of the genus covered by either claim 1 or claim 3 and the claim was enabled substantially across its scope. This was supported by the evidence of the experts who did not distinguish between central and peripheral neuropathic pain when challenged on the plausibility of the claims. Thirdly, the claims were in fact sufficient because the skilled person would be motivated to do the Bennett and Kim tests, which he could do without undue burden. If that was done he would discover that it was effective. Fourthly, the claims were at least partially supported on the judge's findings concerning peripheral neuropathic pain, and, to the extent that the *Johns Hopkins* principles applied, it was legitimate to look at later evidence which showed that pregabalin was in fact effective to treat all the types of pain. Fifthly, the judge had failed to look at the claims from the perspective of the clinician. The judge had focussed on the evidence of the neuroscientist. Had he focused on the evidence of the clinicians he would have seen a unifying principle of hyperalgesia and allodynia.

121. I reject these submissions. I would accept for present purposes that there may be cases where an insufficiency attack focuses on a contrived or artificial part of the claim, and where, as a consequence, the attack does not undermine the validity of the claim as a matter of substance. The present case is, however, a long way from such a case. The skilled person would know from the common general knowledge definition of neuropathic pain that it divided naturally into these two parts. So to divide the claim is therefore neither unrealistic nor unfair. Further, once it is accepted that claim 3 extends to central neuropathic pain, there is a significant part of the claim which, although perhaps representing a minority of conditions, nevertheless covers some important ones, such as stroke and multiple sclerosis. I can see no basis on which one could say that, as a matter of substance, one can ignore that part of the claim when considering whether it is plausible.

122. I do not accept that the later evidence principle derived from *Johns Hopkins* can come to the rescue of the claim if there is in fact no data in the patent from which one can make predictions about central neuropathic pain. Later evidence may be deployed to make good a claim where there is some basis for it in the patent. We were not shown any case where the principle had been deployed to make good a prediction for which there was no basis.

123. I do not accept that the judge lost sight of the evidence of clinicians. The argument that the unifying principle could be seen from the fact that all the conditions are characterised by hyperalgesia and allodynia (without reference to central sensitisation) was not made part of Warner-Lambert's case at a sufficiently early stage. The suggestion that the symptoms alone were a sufficient unifying characteristic needed to be put fairly to the Mylan and Actavis witnesses if it was to be put forward as an independent unifying characteristic. Mr Mitcheson relied on two passages of evidence to suggest that it had been.

124. Firstly, Mr Mitcheson relied on the first part of the evidence of Dr Scadding which I have set out above concerning hyperalgesia and allodynia, where Dr Scadding accepted that it was a credible claim that pregabalin could treat all the pain types set out in paragraph [0003] of the specification, albeit that it had not been demonstrated in any established model of neuropathic pain. However, Dr Scadding gave these answers after he had accepted that neuropathic pain was limited to peripheral neuropathic pain. The cross-examination then went on to suggest that, in addition to the symptoms, central sensitisation was "a further reason" for the credibility of the claim. I do not think that Dr Scadding had an opportunity of dealing with a case that hyperalgesia and allodynia alone rendered plausible a claim to central neuropathic pain.

125. Secondly Mr Mitcheson relied on a passage of cross-examination of Professor Wood, albeit that Professor Wood was a neuroscience expert and not a clinician. Professor Wood's reaction was that one could "hope and speculate" that a drug which was having an effect on one type of pain characterised by hyperalgesia and allodynia would have an effect on other such pain states. He pointed out that there were multiple mechanisms contributing to hyperalgesia and allodynia, so one could not draw that conclusion. It was a possibility, but one could not be reasonably sure that it was necessarily true. It was only after having made these qualifications that he accepted that it was a credible suggestion.

126. I would therefore not interfere with either of the judge's reasons for rejecting the symptoms alone as a unifying characteristic. It seems to me that they were not fully raised as part of Warner-Lambert's case, and the evidence as a whole did not support them.

127. Mr Mitcheson's most attractive point was based on the evidence of Dr Scadding which I have set out above and Dr Scadding's acceptance that the skilled person would be encouraged by the data in the patent to ask the neuroscientist to test pregabalin for neuropathic pain. I think the answer to the point must be that Dr Scadding could not have given that evidence if asked to focus on central neuropathic pain. The passage of cross-examination relied on comes immediately after Mr Mitcheson had secured Dr Scadding's agreement to the fact that the patent was restricting itself to peripheral neuropathic pain, and it is likely that Dr Scadding did not have central neuropathic pain in mind. Moreover the tests which would be carried out were the Bennett and Kim tests, neither of which is a test for central neuropathic pain. Thus the testing which Dr Scadding envisaged could not sensibly render plausible the claim that pregabalin was effective for central neuropathic pain.

128. I would therefore reject Warner-Lambert's challenge to the judge's finding that claim 3 was not plausible across its breadth.

129. I turn therefore to Mylan and Actavis' challenge to the Judge's finding that the patent did make a plausible claim that pregabalin was effective to treat peripheral neuropathic pain. Their case is that the patent simply made no plausible claim to the treatment of neuropathic pain at all. Mr Meade contends that the judge overlooked passages in the *Salk* case which require a higher standard for plausibility. Further, in paragraph 351 the judge had applied a much looser test, namely whether it was possible that pregabalin would have the desired effect. This placed the bar too low. He further submitted that the judge's finding that the rat paw formalin test was not predictive of efficacy in treatment of neuropathic pain was fatal to a finding that the claim to neuropathic pain was plausible.

130. I reject both these submissions. As I have explained, I do not accept that those passages in *Salk* lay down a general principle. The test represents a very low threshold.

131. The judge's use of the word "possible" in paragraph 351 must be taken in context. He correctly directed himself that the threshold test of whether something is plausible is a low one. He placed reliance on the evidence of Dr Scadding, as well as that of Professor Wood. Neither witness was saying that the suggestion was merely a possible one in the sense that it was not impossible. Dr Scadding in particular, in the passages I have cited, placed express reliance on the observations in the patent.

132. I do not think that the judge's finding that the rat paw formalin test was not predictive of efficacy was fatal to the claim to neuropathic pain being plausible. The patent clearly demonstrated that pregabalin was likely to be effective in the treatment of inflammatory pain. The skilled reader would recognise inflammatory pain had a central sensitisation component as an amplifying mechanism. The skilled reader would also know that peripheral neuropathic pain had a central sensitisation component as well. There was, accordingly, a sufficient unifying principle between the two types of pain to justify a claim which included peripheral neuropathic pain.

The results presented would therefore suggest to the skilled person that pregabalin might be effective for peripheral neuropathic pain. The test results would not have enabled a firm prediction of efficacy to be made. I have no difficulty, however, with the judge's ultimate conclusion that a claim to efficacy for peripheral neuropathic pain was plausible.

133. I think this conclusion is fortified by the fact that it was established through the evidence that the skilled team would be encouraged by the data in the patent to carry out simple tests (which are themselves identified in the patent) to confirm the suitability of pregabalin for peripheral neuropathic pain. I would have thought, on the basis of that evidence (as I think the judge did) that the specification had thereby made a contribution to the art which would justify a claim to peripheral neuropathic pain. Mr Meade sought to counter this suggestion by reference to the requirement in the context of obviousness for a reasonable prospect of success, but I have already explained why I do not think that the tests in these two different contexts are aligned.

134. I would therefore reject the challenge to this aspect of the judge's reasoning as well.

Abuse of process

135. In the light of the conclusions thus far, it is necessary to consider whether the judge was correct to deny Warner-Lambert the opportunity to amend claim 3, by the addition of the words I have indicated, so as to limit the claim to the subject matter which the judge held was both inventive and rendered plausible by the patent.

The law

136. Section 75 of the Act governs the amendment of patents in infringement or revocation proceedings:

> "(1) In any proceedings before the court or the comptroller in which the validity of a patent is put in issue the court or, as the case may be, the comptroller may, subject to section 76 below, allow the proprietor of the patent to amend the specification of the patent in such manner, and subject to such terms as to advertising the proposed amendment and as to costs, expenses or otherwise, as the court or comptroller thinks fit.
>
> (2) A person may give notice to the court or the comptroller of his opposition to an amendment proposed by the proprietor of the patent under this section, and if he does so the court or the comptroller shall notify the proprietor and consider the opposition in deciding whether the amendment or any amendment should be allowed.
>
> (3) An amendment of a specification of a patent under this section shall have effect and be deemed always to have had effect from the grant of the patent…"

137. Section 63 deals with the case where a patent is found to be partially valid. The section provides that the court may grant relief subject to conditions, one of which

will normally be that the patent must be amended to the court's satisfaction. The limits of the meaning of the term "partially valid" have not been fully explored. However, in *Hallen v Brabantia* [1990] FSR 134, this court held that a claim was partially valid where, by virtue of the cascade of claim dependencies, it could be construed as a number of discrete claims. The meaning of "partially valid" may, of course, be wider. Section 125(2) of the Act makes it clear that a claim may contain more than one invention. At page 140 Aldous J (as he then was) said:

> "Therefore under section 125 you look to a claim to see what the invention is (or inventions are) and thereafter when considering validity under section 72(1)(a) ascertain whether that invention is (or those inventions are) patentable. If one of those inventions is a patentable invention then the patent is partially valid."

138. An application to amend under section 75 may be determined in advance of the trial of an infringement or revocation action, but the more usual modern practice is for it to be heard at the same time. The patentee may make the application conditionally on a finding that the claims in question are found invalid, or unconditionally, in which case he will not seek to defend the validity of the unamended claims and overall success is critically dependent on obtaining the amendments.

139. Mylan and Actavis' case of abuse of process is founded on the principle that the court may regard it as abusive for a party to seek to raise in a second set of proceedings matters which it should have raised in earlier proceedings between that party and the same adversary. The authorities on this rule were reviewed by Lord Bingham in *Johnson v Gore Wood & Co* [2002] 2 AC 1, where he concluded at [31]:

> "But *Henderson v Henderson* abuse of process, as now understood, although separate and distinct from cause of action estoppel and issue estoppel, has much in common with them. The underlying public interest is the same: that there should be finality in litigation and that a party should not be twice vexed in the same matter. This public interest is reinforced by the current emphasis on efficiency and economy in the conduct of litigation, in the interests of the parties and the public as a whole. The bringing of a claim or the raising of a defence in later proceedings may, without more, amount to abuse if the court is satisfied (the onus being on the party alleging abuse) that the claim or defence should have been raised in the earlier proceedings if it was to be raised at all. I would not accept that it is necessary, before abuse may be found, to identify any additional element such as a collateral attack on a previous decision or some dishonesty, but where those elements are present the later proceedings will be much more obviously abusive, and there will rarely be a finding of abuse unless the later proceeding involves what the court regards as unjust harassment of a party. It is, however, wrong to hold that because a matter could have been raised in earlier proceedings it should have been, so as to render the raising of it in later proceedings necessarily abusive. That is to adopt too dogmatic

> an approach to what should in my opinion be a broad, merits-based judgment which takes account of the public and private interests involved and also takes account of all the facts of the case, focusing attention on the crucial question whether, in all the circumstances, a party is misusing or abusing the process of the court by seeking to raise before it the issue which could have been raised before. As one cannot comprehensively list all possible forms of abuse, so one cannot formulate any hard and fast rule to determine whether, on given facts, abuse is to be found or not. Thus while I would accept that lack of funds would not ordinarily excuse a failure to raise in earlier proceedings an issue which could and should have been raised then, I would not regard it as necessarily irrelevant, particularly if it appears that the lack of funds has been caused by the party against whom it is sought to claim. While the result may often be the same, it is in my view preferable to ask whether in all the circumstances a party's conduct is an abuse than to ask whether the conduct is an abuse and then, if it is, to ask whether the abuse is excused or justified by special circumstances. Properly applied, and whatever the legitimacy of its descent, the rule has in my view a valuable part to play in protecting the interests of justice."

140. Lord Millett added at 59-60:

> "It is one thing to refuse to allow a party to relitigate a question which has already been decided; it is quite another to deny him the opportunity of litigating for the first time a question which has not previously been adjudicated upon. This latter (though not the former) is prima facie a denial of the citizen's right of access to the court conferred by the common law and guaranteed by article 6 of the Convention for the Protection of Human Rights and Fundamental Freedoms (1953). While, therefore, the doctrine of res judicata in all its branches may properly be regarded as a rule of substantive law, applicable in all save exceptional circumstances, the doctrine now under consideration can be no more than a procedural rule based on the need to protect the process of the court from abuse and the defendant from oppression. In *Brisbane City Council for AG for Queensland* [1979] AC 411, 425 Lord Wilberforce, giving the advice of the Judicial Committee of the Privy Council, explained that the true basis of the rule in *Henderson v Henderson* 3 Hare 100 is abuse of process and observed that it 'ought only to be applied when the facts are such as to amount to an abuse: otherwise there is a danger of a party being shut out from bringing forward a genuine subject of litigation'. There is, therefore, only one question to be considered in the present case: whether it was oppressive or otherwise an abuse of the process of the court for Mr Johnson to bring his own proceedings against the firm when he could have brought them

> as part of or at the same time as the company's action. This question must be determined as at the time when Mr Johnson brought the present proceedings and in the light of everything that had then happened. There is, of course, no doubt that Mr Johnson could have brought his action as part of or at the same time as the company's action. But it does not at all follow that he should have done so or that his failure to do so renders the present action oppressive to the firm or an abuse of the process of the court. As May LJ observed in *Manson v Vooght* [1999] BPIR 376, 387, it may in a particular case be sensible to advance claims separately. In so far as the so-called rule in *Henderson v Henderson* suggests that there is a presumption against the bringing of successive actions, I consider that it is a distortion of the true position. The burden should always rest upon the defendant to establish that it is oppressive or an abuse of process for him to be subjected to the second action".

141. The application of this rule in the context of a patentee who seeks to make amendments to claims of a patent after judgment on the issue of validity has been considered by this court in a number of cases, most recently in *Nokia GmbH v IPCom GmbH* [2011] EWCA Civ 6, [201l] FSR 15, a case which is subsequent to the decision of the House of Lords in *Johnson v Gore-Wood*. In his judgment in that case Jacob LJ drew extensively on his earlier judgment in *Nikken Kosakusho Works v Pioneer Trading Co* [2005] EWCA Civ 906, [2006] FSR 4. He said:

> "97. In *Nikken*, the patentee once the court had found his patent to be invalid applied to amend by a re-writing amendment of the same general sort as is sought here. The trial judge refused this in the exercise of his discretion and because he found the amendment unallowable. This court upheld his decision on discretion and did not need to consider the second point.
>
> 98. All three members of the Court gave judgments. I said at [8] after having pointed out that s.75(1) of the Patents Act 1977 says the Court "may allow the proprietor of the patent to amend":
>
> > There are different situations in which the exercise of the discretion to allow amendment of a patent may be sought: (a) before a trial; (b) after trial, at which certain claims have been held valid but other claims held invalid, the patentee simply wishing to delete the invalid claims (I would include here also the case where the patentee wishes to re-write the claims so as to exclude various dependencies as in *Hallen v Brabantia* [1990] FSR 134. There the patentee is in effect continuing to claim which he had claimed before but in a much smaller way); and (c) after a trial in which all claims have been held invalid but the patentee wishes to insert what he hopes are validating amendments.

99. I would only add that classes (a) and possibly (b) are really cases of a partially valid patent, a situation which the Act recognises in s.63. This provides that the court may grant relief in such a case. It will usually (probably invariably) only do so on terms that the patent is amended to cut out the invalid claims. Mr Alexander in his skeleton argument half suggested that the present case was one of a partially invalid patent. Not so. Floyd J held all the claims invalid. This is a class (c) type.

100. I described the position for such a type in *Nikken*:

> [11] Class (c) involves something different, a proposed claim which was not under attack and could not have been under attack prior to trial. If the court is to allow such a claim to be propounded after trial, there is almost bound to be a further battle which would arise in the proposed amendment proceedings. That battle will be over whether or not the proposed amended claim is valid. I say "almost bound" because I can just conceive a case where the point was covered by the main litigation in some way or other.

I should have added that a further battle may also arise about the allowability of the amendments. In this case if IPCom were allowed to apply for the amendments, there would indeed be battles both about allowability (and clarity) and validity.

101. In *Nikken* I then went on to say that an exercise of discretion to allow two trials would be improper for three reasons which I can summarise here:

> (a) It would breach the general procedural rule laid down as long ago as 1843 in *Henderson v Henderson* (1843) 3 Hare 100, that a party should normally not be allowed to advance in a second proceeding matter he could have advanced in the first.
>
> (b) That rule had been applied in patent cases by this Court in *Windsurfing v Tabur Marine* [1985] RPC 59 and Aldous J in *Lubrizol v Esso* [1998] RPC 727. I said Aldous J had epitomised the position when he said, at p.790:
>
> > I believe it is a fundamental principle of patent litigation that a party must bring before the court the issues that he seeks to have resolved, so as to enable the court to conclude the litigation between the parties.
>
> (c) The general court rules were "dead against" allowing amendment proceedings requiring a second trial after a first trial had determined the patent was invalid. I put it this way:

> [19] … The whole code is governed by the overriding objective contained in Part 1.1.1. 1.1.2 specifies some examples of cases of dealing with a case justly. 2(b) is "saving expense". Plainly a second trial would cause increased expense. 2(d) is ensuring that it is "dealt with expeditiously and fairly". Having two bites of the cherry is doing neither of those things.
>
> [20] The rules descend into more detail. Under the court's duty to manage cases, 1.4 requires the court actively to manage cases and 1.4.2 says that active case management includes "identifying the issues at an early stage and dealing with as many aspects of the case as it can on the same occasion".

102. Moreover I considered that a case involving the validity of a patent concerned not merely the private rights of the parties but also the public interest and the court was "particularly entitled to have regard to that".

103. I also said that:

> [25] In the real world patentees, faced with a real problem about the construction of their claims, ought to face up to them early and decide whether they need an amendment or might need an amendment. That is one of the purposes of the rule, to make people face up to their cases at an early stage, not at a late stage.

That of course also applies to the validity of the claims.

104. Both Laws LJ and Waller LJ delivered short, but emphatic concurring judgments. Laws LJ said:

> [33] I agree. I wish only to underline my firm support for the view, which is a major and emphatic theme of my Lord, Jacob LJ's judgment, that the result of this appeal is driven by the principle of the general law given by *Henderson* and clothed with renewed vigour by the overriding objective of the CPR, that in any given litigation the parties are required to bring forward their whole case. It provides [the report says "provokes"] certainty and [the report says "of"] economy and minimises expense, and it applies as powerfully in this area of the law as any other.

And Waller LJ:

> [34] In one sense the question is whether there should be some special rule in patent cases. In any other litigation it would be unfair to allow a party to amend his case post judgment so as to allow an opportunity to succeed after a

> further trial, however small. The question is whether there is something special about patent litigation. The authorities do not support the proposition that there is something special. Indeed, those authorities cited both by the judge and by my Lord go to the opposite effect. Those are reinforced, as I would see it, by the new CPR. I am relieved to find the position to be so."

142. Jacob LJ then went on to consider whether what the court said in *Nikken* should be relaxed or watered down. He first rejected the contention that it was inconsistent with *Johnson v Gore-Wood*. He accepted entirely that the true test was one of abuse of process – procedural fairness - and that the burden lies on the party objecting to the second action to show this. He continued:

> "However where a party fails to advance a case he could have advanced much earlier and does so without any real justification, he is abusing the process and the other party is therefore entitled to object. It is not normally procedurally fair to subject the other side to successive cases when you could readily have put them all in one go."

143. Jacob LJ also considered an argument based on Art. 138 of European Patent Convention 2000, which provides:

> "(1) Subject to Art. 139 a European patent may be revoked with effect for a Contracting State only on the grounds that [the grounds are specified].
>
> (2) If the grounds for revocation affect the European patent only in part, the patent shall be limited by a corresponding amendment of the claims and revoked in part.
>
> (3) In proceedings before the competent court or authority relating to the validity of the European patent, the proprietor of the patent shall have the right to limit the patent by amending the claims. The patent as thus limited shall form the basis of the proceedings."

144. The argument was that this provision drew no distinction between *Nikken* type (a), (b) or (c) amendments and thus created a right to make an amendment of any type, subject to cases where the patentee's conduct was really culpable or amendment would cause unjust oppression. The argument was rejected because the main purpose of Art. 138 was to ensure that national authorities had an amendment procedure. Prior to the amendment of the Treaty, the laws of some countries did not allow patent amendment post-grant at all. Art. 138 was not intended to govern national rules of procedure concerning patent amendment, still less to require national courts to conduct them in a manner which national law regarded as an abuse of process. Moreover, the Article does not apply to a case where the grounds of revocation affect the European patent as a whole. The provision is only about a case where the grounds of revocation affect the patent in part. In any event the Article was not intended to override national procedural rules as to procedural fairness. I reached similar

conclusions about the impact of the central amendment procedure on national amendment proceedings in *Zipher Ltd v Markem Systems Ltd* [2008] EWHC 1379; [2009] FSR 1 at paragraph 220.

145. In *Nikken*, Jacob LJ also rejected an argument that the second trial would be short:

> "16. Applying that here, plainly there would be a second trial, the very thing that Oliver LJ is saying ought not to happen. Mr Baldwin's only answer is that the second trial would be a little one. That will not do."

146. From these authorities it can be seen that the correct classification of the amendment is a vital first step in the assessment. The reason that *Nikken* type (c) rewriting amendments are particularly unlikely to be allowed after a trial is that they create new issues which are, in the normal run of a case, unlikely to have been decided at trial. The evidence on the issue of validity will not have been directed to the feature or features sought to be introduced for the first time by amendment because it was never made clear, either by the existing claims (e.g. as in *Hallen*) or any application to amend, that the patentee would be seeking to assert or defend a monopoly of that scope. In addition, issues about allowability of rewriting amendments are much more likely to arise.

147. The court's power to dismiss or strike out an action as an abuse of process is only discretionary in a limited sense. The first task is to determine whether the conduct complained of is or is not an abuse. If it is an abuse, it would only be in rare circumstances that the claim would not be struck out: per Lloyd LJ in *Stuart v Goldberg Linde* [2008] 1 WLR 823 at [24]. The decision as to whether the conduct complained of is an abuse is one which involves the evaluation of a number of factors, and an appellate court will be reluctant to intervene where the decision rests upon such an exercise. It will generally only interfere where the judge has taken into account immaterial factors, omitted to take account of material factors, erred in principle or come to a conclusion that is impermissible or not open to him: see *Aldi Stores Ltd v WFP Group plc and others* [2008] EWCA Civ 1260; [2008] 1 WLR 748, per Thomas LJ at [16].

The judge's reasoning

148. The judge concluded that the proposed amendments raised arguable issues as to their clarity and scope. He further concluded that, at trial, the only target which Mylan and Actavis were concerned with in their insufficiency case was claim 3, it not having been contended by Warner-Lambert prior to trial that claim 3 was restricted to peripheral neuropathic pain. For that purpose, it was enough to show that the claim extended to a class of pain for which it was not plausible that pregabalin would be effective, and they chose for this purpose central neuropathic pain. In order to invalidate the claim it was not necessary for them to target peripheral neuropathic claim. The effect of the amendment application was to make essential that previously unnecessary task.

149. Moreover, Mylan and Actavis had adduced evidence that their initial investigations suggested that trigeminal neuralgia pain, the subject of claim 10, was an example of neuropathic pain caused by injury or infection to peripheral sensory nerves but which

would not have been thought to have a central sensitisation component. Other types of pain falling into this category were also being investigated.

150. The judge did not consider that a second trial would be necessary on the issue of infringement because Warner-Lambert had offered an undertaking not to bring any further claim for infringement of claim 3 as proposed to be amended in respect of Lecaent based on the same facts as were considered at the trial in July 2015.

151. Next the judge considered whether Warner-Lambert themselves were the victims of procedural unfairness, because of the late stage at which the insufficiency point concerning central neuropathic pain was clearly articulated. He considered the various stages at which Warner-Lambert could have picked up the significance of the point. He concluded:

> "141. … even if Warner-Lambert could be forgiven for not having spotted the point before, I consider that Mylan and Actavis made their case crystal clear in their skeleton argument exchanged a week before trial. Warner-Lambert did not complain at that stage that it had been taken by surprise. Nor did Warner-Lambert launch a conditional application to amend claim 3. Instead, Warner-Lambert chose to stand its ground and fight on claim 3 as it stood. During the trial, Warner-Lambert elected to try and deal with the problem primarily by advancing a narrow construction of claim 3."

152. The judge also took into account two further points which he considered to be of minor significance in favour of Mylan and Actavis. The first was the impact in terms of delay which the amendment application might have on the final resolution of the dispute between the parties. He recognised, however, that it could not be assumed that this would necessarily be the case, as a second trial could possibly take place on an expedited basis, and catch up with the appeal if the appeal was not expedited.

153. The second minor point was the wider public interest. Both sides had made an appeal to the wider public interest as supporting their respective positions. Mylan and Actavis relied on the public interest in the expeditious revocation of invalid monopolies, particularly given the widespread interest of generic suppliers in the pregabalin market. Warner-Lambert relied on the public interest in rewarding inventors, and thereby incentivising research into inventions which benefit the public, particularly in the pharmaceutical field. Warner-Lambert relied on the main judgment as establishing that a claim limited to peripheral neuropathic pain was both inventive and sufficiently disclosed. Third parties were not bound by the judgment in these proceedings and could bring their own claims for revocation.

154. The judge dealt with these arguments in the following way:

> "147. I entirely accept that a key purpose of the patent system is to incentivise research for the benefit of the public, and nowhere more so than in the pharmaceutical field. On the other hand, another key purpose of the patent system is to ensure that monopolies are properly justified, and in particular that the scope of the patentee's monopoly reflects his technical

> contribution to the art. One way in which the latter purpose is achieved is by allowing any party to challenge the validity of a patent for the benefit of all the patentee's actual and potential competitors. In my view the principles on post-trial validating amendments which have been developed by the courts take account of these competing considerations. They do so in a way which favours finality, consistently with the general policy of the courts concerning litigation. While it is true that parties like Sandoz could bring their own claims for revocation, they would have to start from scratch with the delay which that would entail. Thus I consider that the public interest is another minor factor in favour of Mylan and Actavis' argument on abuse of process."

155. The judge expressed his conclusion on this abuse of process at paragraph 148 of the abuse judgment:

> "148. Applying the broad merits-based test articulated by Lord Bingham in *Johnson v Gore Wood*, I consider that the application to amend claim 3 is an abuse of process because it could and should have been made prior to trial. Warner-Lambert not only had ample opportunity to make a conditional application to amend prior to trial, but also ought to have appreciated, for the reasons explained above, that it needed to do so if it wished to contend a claim limited in that manner would be independently valid. If the amendment application was allowed to proceed, it could not be determined fairly without a second trial on validity. Furthermore, there is a risk that such a second trial would delay the overall resolution of the dispute. Accordingly, in my view, the amendment application amounts to unjust harassment of Mylan and Actavis. It would also be contrary to the interests of other generic suppliers of pregabalin. It is true that the consequence (subject to the outcome of the appeals) will be that claim 3 is invalid and must be deleted, but that consequence is attributable to Warner-Lambert electing to defend the insufficiency attack on claim 3 in the way in which it did, which proved unsuccessful (subject to the outcome of the appeals), and not making a conditional application to amend before trial. As the cases show, Warner-Lambert is not the first patentee to have made that mistake."

Submissions

156. Mr Miller QC, who argued this part of the appeal for Warner-Lambert, submitted that the effect of the amendment was simply to excise from the claim the part which the judge had held to be invalid. The judge had in effect made a finding that claim 3 was partially valid, which gave rise to a prima facie right to amend. This was the sort of case which Jacob LJ had recognised as conceivable in paragraph 11 of *Nikken*, namely a case "where the point was covered by the main litigation in some way or other." He also submitted that the inability to amend claim 3 did not simply affect

Warner-Lambert's position as against Actavis, but affected its ability to enforce an amended claim against third parties (save to the extent that some classes of peripheral neuropathic pain are covered by sub-claims). This was a factor to which the judge had failed to accord weight.

157. The principal point which he made, however, is that the judge was in error to hold that a second trial on any relevant issue of validity was required. The issues of clarity and added matter were not relevant, because there had not thus far been any inquiry into the clarity of an amended claim 3, or whether it added matter. Mylan and Actavis were not being twice vexed on these issues which would have had to be decided at whatever stage the amendment was applied for. In any event these were very small issues unlikely to involve any or any significant evidence. So far as sufficiency was concerned, there could not be a second trial, because the judge had already decided the issue of the validity of claim 3 as limited to peripheral neuropathic pain.

158. Accordingly, Mr Miller challenged head-on the judge's conclusion that, with an amended claim, it would be necessary for the first time for Mylan and Actavis to win on insufficiency in relation to peripheral neuropathic pain, when it was not necessary before. Mylan and Actavis had given peripheral neuropathic pain their best shot. The judge had made a finding in paragraph 351 of the main judgment that the data contained in the specification when read with the common general knowledge made it plausible that pregabalin would be effective to treat peripheral neuropathic pain. There was no suggestion that the judge was not entitled to make such a finding, (except to the extent that the finding was the subject of the Mylan and Actavis cross-appeal which is before us). Mr Miller went as far as to say it would be an abuse of process for Mylan and Actavis to seek to attack the sufficiency of a claim to peripheral neuropathic pain. Accordingly the judge had taken into account a factor which he ought not to have taken into account, namely an ability on the part of Mylan and Actavis to raise arguments in a second trial on validity which would themselves be an abuse of the process of the court.

159. Mr Miller next submitted that the judge had been wrong to say that the authorities established that the length of the second trial was not an important factor. The length of a second trial was always a material factor, particularly in the assessment of whether a party is truly being subjected to unjust harassment. In *Nikken* Jacob LJ was not laying down any general principle that the length of any subsequent trial could never be relevant.

160. Mr Miller next dealt with the judge's conclusion that Warner-Lambert had not itself been the subject of procedural unfairness by the way in which Mylan and Actavis had raised the insufficiency point on which they succeeded at trial. He submits that the pleadings did not put Warner-Lambert on notice of that attack. If the attack had been pleaded in plain language, Warner-Lambert would have been able, had they wished, to frame an amendment to deal with it. Moreover it was no answer to point to the absence of a request by Warner-Lambert for clarification of the pleading, given that Mylan and Actavis had not conceived of the attack until they received Warner-Lambert's evidence. Mr Miller also relied heavily on Warner-Lambert's evidence, which the judge appeared to have accepted, that they did not see the significance of the point about central neuropathic pain on receipt of the reply evidence.

161. Mr Miller recognised that, by the time the trial was under way, Warner-Lambert's team had appreciated the significance of central neuropathic pain to the insufficiency attack and decided to argue that claim 3 was limited to peripheral neuropathic pain. He points out that although it is easy with hindsight to be critical of Warner-Lambert's team, a great deal of frenetic activity occurs at a trial, and the fact that they did not launch a last minute application to amend should not be held too heavily against them. This was not a case of Warner-Lambert having the opportunity all through the proceedings of defending themselves against this attack: the way in which the issues developed meant that it was only at a relatively late stage that a strategy could be developed for dealing with the point.

162. Finally Mr Miller submitted that the judge should not have attached weight to the two minor points, delay in resolving the dispute and the interests of other generic suppliers. As to the former point, on the basis that it was not an abuse, the second trial could have taken place very swiftly and caught up with this appeal in the same way that the appeal on this preliminary issue has done. The interests of other generic suppliers were simply not relevant. Abuse of process was concerned with whether Mylan and Actavis were being "vexed twice", not with the interests of third parties. There was no question of harassment of third parties who had chosen to sit back and wait for the outcome of the present litigation, without joining issue with Warner-Lambert. Third parties had no right to expect that the litigation might resolve any issue as far as they were concerned, given that it might settle before trial. Moreover, independent third parties would not be bound by the outcome if any claims were held valid, and could subject the claims of the patent to fresh, or even the same attack.

163. Mr Bloch QC, who argued this part of the appeal for Mylan and Actavis, supported the judgment of Arnold J. He stressed that the judge was conducting an evaluation of factors. Not only was the judge's overall evaluation entitled to respect in this court, but so also was his assessment of the various factors which go into that assessment, such as when parties should have appreciated points, the likely course of any further trial and whether there was a risk of delay.

164. When Warner-Lambert appreciated, or should have appreciated, that it had an amendment to make it should have drawn the matter to the attention of the court promptly so as not to appropriate to itself the case management implications of it making an amendment. It was wrong to postpone the decision as to whether it should make an amendment until after trial, when it had lost.

165. Mr Bloch submitted that Warner-Lambert should have made the application to amend following the receipt of the common general knowledge statement from Mylan and Actavis to which they then responded. If that was wrong, there were a number of further stages, which the judge summarises, at which they should have done so. At the very latest they should have done so when they read the second report of Dr Scadding.

166. Mr Bloch submitted that it was beyond belief that Warner-Lambert had not considered their fall-back position in relation to claim 3 at the stage of the common general knowledge statement. The original statement proffered by Mylan and Actavis referred to both central and peripheral neuropathic pain but had no section on central sensitisation. Warner-Lambert's response had been to exclude reference to central neuropathic pain and add a section on central sensitisation. He infers that the strategy

was to argue that the unifying principle justifying the breadth of claim was central sensitisation and that central neuropathic pain was an obstacle to the success of that strategy.

167. Mr Bloch also relied on the cross-examination of Dr Scadding which he submitted showed that Warner-Lambert had seen how the words of paragraph [0006] of the patent could be used to found an argument on construction of claim 3. If it was possible to see how those words could found a construction argument, Warner-Lambert must have seen how they could found an amendment.

168. Mr Bloch submitted that the conduct of Warner-Lambert needed to be analysed objectively because abuse was concerned with what the court expected of parties. If a party fails to pick up obvious warning signs of a point against them, the court is entitled to take an adverse view. The judge was entitled to find that Warner-Lambert were not victims of unfairness.

169. Turning to the substance of the further trial, Mr Bloch pointed out that the amendment sought did not use the term "peripheral neuropathic pain" because that term did not appear in the patent. Rather it sought to limit the claim to pain arising from a particular cause, namely damage to the peripheral nervous system. That claim would be insufficient if there was a type of neuropathic pain falling within the cause limitation in respect of which it was common general knowledge that it did not have a central sensitisation component. Although the judge had made findings that the invention was plausible in relation to peripheral neuropathic pain there were key findings that were missing. Thus there was no finding that peripheral neuropathic pain was co-extensive with the cause limitation. There is no finding as to where "caused" in the proposed limitation was a reference to the initial cause or the immediate cause or both.

170. Mr Bloch submitted that Warner-Lambert had endeavoured to meet these arguments by referring to Dr Scadding's acceptance that the patent was using the term neuropathic pain to mean pain caused by damage to the peripheral nervous system. But the judge had not accepted that evidence. In summary there were open issues as to clarity and sufficiency which Mylan and Actavis ought to be permitted to explore at a further trial if Warner-Lambert is permitted to apply to amend.

171. Mr Bloch supported the point accepted by the judge that, with a claim which extended (at least on the Mylan and Actavis construction) to central neuropathic pain, it was not necessary to hone the insufficiency attack show a lack of plausibility of peripheral neuropathic pain. Although arguments had been run in relation to peripheral neuropathic pain, it had not been necessary to focus on them when no limitation by way of amendment had been framed.

172. The judge had been entitled to take the public interest in finality into account. He did not ignore the fact that Warner-Lambert were deprived of the opportunity of framing a claim to a valuable invention. What the judge had done was to say that the balance came down in this particular case in favour of finality.

Discussion

173. Given the clarity and emphatic nature of the guidance given in the earlier decisions of this court, which the judge clearly directed himself by reference to, and given the close analysis which the judge has given to the various factors which are in play, and their overall evaluation, Mr Miller plainly faces an uphill task in asking this court to allow the appeal on this point. Understandably, a large number of points have been debated in the written arguments and at the hearing of the appeal, but in the end there are only two which make this case even a potential candidate for allowing post-judgment amendment. These are (a) the fact that the subject matter of the proposed amended claim is or may be already the subject of a finding in the main judgment, and (b) the extent to which the procedural history hampered Warner-Lambert from formulating the amendment earlier.

174. The first point concerns the correct categorisation of the amendment sought. The reason why the jurisprudence views with hostility the rewriting of claims after judgment is that, in contrast to the case where the claim existed in some form in the unamended patent, the party attacking the patent has not had a proper opportunity during the trial to address that claim. A further trial is thus rendered necessary in order to avoid procedural unfairness to that party, and it is the imposition of that further trial which is regarded as undue harassment. The special feature of the amendment sought in the present case is that, whilst it undoubtedly involves some rewriting, it is intended to give effect to the construction of claim 3 for which Warner-Lambert argued at trial. Construction is the central issue in almost all patent cases. Issues such as obviousness, insufficiency and infringement have to be approached on the basis of all the constructions which are in play. Once Mylan and Actavis knew Warner-Lambert's construction of claim 3, they plainly had an opportunity to attack the sufficiency of the claim on that construction. Moreover it was an opportunity of which they availed themselves. Their contention was that the invention was not plausible for any type of neuropathic pain: they did not in any way limit their attack to central pain. For example it was and remains their case that claims 10, 11 and 12, which are limited to specific types of peripheral neuropathic pain, were insufficient.

175. In terms of the opportunity which was afforded to Mylan and Actavis to contend that the patent was not enabled for peripheral neuropathic pain, I have difficulty in distinguishing this case from a notional one in which claim 3A was to neuropathic pain generally, and claim 3B was to peripheral neuropathic pain. So far as I can see, Mylan and Actavis would still have run their case against neuropathic pain generally, which would if accepted have invalidated both claims, coupled with their alternative case based on central neuropathic pain, which would only have touched claim 3A.

176. It is tempting, therefore, to think that it is not the absence of an application to amend which is at the root of the alleged unfairness to Mylan and Actavis: if they have a complaint about the issue of sufficiency it has to be based on the fact that the construction advanced by Warner-Lambert was raised very late. After all, the judge cannot have regarded it as procedurally unfair for Warner-Lambert to run their construction argument. Mylan and Actavis did not suggest it was not open to Warner-Lambert. The judge ruled on it and ruled on the sufficiency of a claim so construed.

177. I confess that I was at one point attracted to this analysis. In the end, however, I have concluded that it is incorrect. The categorisation of the amendment, and the extent to

which a monopoly of that scope was considered at the trial is not the sole question for consideration. Mr Miller's argument, by focusing only on the nature of the amendment, ignores the true nature of the abuse. The amendment gives Warner-Lambert an alternative route to a successful outcome, which is not dependent on winning the construction argument. Although they would have to overcome the clarity and added matter objections, the amendment, if allowed, renders the construction issue moot. It is not fair to Mylan and Actavis to treat a trial in which only the construction issue is in play as equivalent to one in which an amendment is in play as well. Mylan and Actavis may have taken the view that their position on the construction argument was very strong, and there was no need to focus their firepower on the narrow construction. That view may (I do not say would) have changed if they had known that Warner-Lambert conditionally intended to seek amendment in the event that they failed on construction. That modified view could have caused them to refocus their attack, with a consequence for the evidence which they would have sought to adduce.

178. Considerations of this kind involve a degree of speculation. I would be inclined however to eschew too deep an enquiry into whether anything would have been done differently, and further evidence needed. The court adopts a similar approach in the case of new points raised on appeal, when it is suggested that further evidence might have been adduced at the trial had the point been properly raised there. In *Crane t/a Interdigital Satellite Services v Sky-in-home and another* [2008] EWCA Civ 978 at paragraph 21 Arden LJ said:

> "…in my judgment the court has to be satisfied that [the respondent] will not be at risk of prejudice if the new point is allowed because it might have adduced other evidence at trial, or otherwise conduct the case differently. It should consider for itself, as best it can, what factual issues are likely to be raised by the new case. Moreover, in circumstances such as the present, where there has been no disclosure relative to the new way in which the appellant seeks to put his case and virtually no opportunity to consider the matter, I do not consider that the court can reasonably expect the party against whom the amendment is sought to be made to be specific about the evidence he would have adduced had the point been raised earlier. If there is any area of doubt, the benefit of it must be given to the party against whom the amendment is sought. It is the party who should have raised the point at trial who should bear any risk of prejudice."

179. In addition, I do not accept that Warner-Lambert are entitled to place on one side the issues relating to allowability of the amendments, on the basis that they would have arisen anyway. It is clear that they may necessitate expert evidence, and would much more conveniently have been dealt with in a single trial.

180. I think, therefore, that the amendment sought here involves an abuse of process, unless Warner-Lambert can show that they had a good reason for not raising it at trial.

181. If it could be said that, by reason of the late emergence of the central neuropathic pain point, Warner-Lambert had a good reason for not raising the conditional amendment

at the first trial, then it would be hard to describe their subsequent attempt to raise it as an abuse of the process of the court.

182. Both sides can be said to have kept their cards fairly close to their chest: Mylan and Actavis only unleashed their central neuropathic pain point in a single paragraph of a reply expert report. Warner-Lambert were slow in appreciating its significance. Ultimately, however, I do not think the procedural history matters. What was plainly necessary was for Warner-Lambert to indicate, no later than the commencement of the trial, that in the event of an adverse finding on the sufficiency of claim 3, it would seek to amend. They plainly could have done so. If they had done so it would have been necessary for the court to decide how to case manage the situation which then arose. There would have been a range of options open, but the court is in the highest degree unlikely to have countenanced the possibility of a second trial raising issues of sufficiency and requiring the same witnesses to be recalled.

183. I therefore do not consider that there is any basis for this court to interfere with the judge's evaluation on the issue of abuse of process.

Infringement

184. For the purposes of its claim of infringement Warner-Lambert relied on claims 1 and 3. These claims are invalid, and the judge's ruling that Warner-Lambert should not be permitted to apply in these proceedings for a validating amendment of claim 3 stands. It follows that the infringement claim fails.

185. This court has already examined the proper interpretation of Swiss-form, second medical use claims in the interim injunction proceedings in the present case, see *Warner-Lambert CoA*. The court was invited by both parties at that stage to decide the issue of law so that the parties knew where they stood for the purposes of the trial. Arnold J, however, permitted the parties to make submissions on the issue, on the ground that this court's decision was not necessary for the decision which the court ultimately reached. In the main judgment, he expressed forceful reservations about the conclusion which had been reached in *Warner-Lambert CoA.* In the end, however, he loyally decided to follow this court's decision on the legal issues which arose.

186. I entirely accept that the analysis of the proper interpretation of Swiss-form second medical indication claims in *Warner-Lambert CoA* was not necessary for the decision, and is therefore *obiter* as a statement of law for the purposes of proceedings between other parties. Mr Miller contends that it was not open to the judge to hear fresh argument on the point *in the present case* in the absence of a conflicting decision of higher authority. I can see some technical force in that submission. Nevertheless, in view of the judge's obviously profound reservations about the law, it would not be right to leave this case without considering the principal arguments, even though they are no longer necessary for this decision. A full review of the judge's conclusions on infringement, including those on indirect infringement, is no longer justified.

187. The issue which this aspect of the case raises is, and remains, one of great difficulty. The law is struggling on the one hand to give the patentee a proper reward for his contribution to the art by elucidating the new use for the drug, whilst at the same time not excluding the competing manufacturer from making and marketing the drug for its known purpose. The issue is complicated by the interaction with the law relating to,

and the practices of the market in, prescription medicines. The solution adopted by this court in *Warner-Lambert CoA* was an attempt to strike the right balance by not placing insuperable obstacles in the path of the patentee, whilst at the same time recognising in very clear terms that the remedies available for infringement will have to be moulded so as to achieve fair and proportionate relief tailored to the very special circumstances of this type of case.

188. I propose therefore to deal with four matters. Firstly, it is right that I should take a further look at the law on the construction of second medical use claims in Swiss form in the light of Arnold J's reservations and the further developments in the law of other states and the EPO. Secondly, I propose to deal with the arguments addressed to us by the intervener, the Secretary of State for Health, who was not called upon in *Warner-Lambert CoA*, and who has served a respondent's notice on the issue of the proper interpretation of Swiss-form claims. Thirdly, I propose to address Warner-Lambert's complaint that the judge failed correctly to apply the law as stated in *Warner-Lambert CoA*. Fourthly, I will say something about indirect infringement.

Swiss-form claims

189. The interpretation of Swiss form claims is a matter which has been considered in a number of member states of the EPC. At paragraph 74 onwards of *Warner-Lambert CoA* I referred to a number of decisions in those other states, concluding that a uniform approach had not yet emerged.

190. As to Germany, I reviewed the decision of the German Federal Court of Justice in *Carvedilol II* (decision of 14 March 2013); the decision of the Landgericht Düsseldorf in *Chronic Hepatitis C Treatment* (decision of 19 December 2006); the decision of the Oberlandesgericht Düsseldorf in *Cistus* (decision of 31 January 2013); and the decision of the Landgericht Hamburg in *Warner-Lambert Company LLC v Aliud Pharma GmbH*. At paragraph 81 I said:

> "81. It would therefore appear from these cases that what the German courts look for in these circumstances is some outward manifestation in the manufacture itself (which may include the packaging, but not advertising) which can be specifically attributed to the new use. But it may be that the desire to avoid "sophistry" and an investigation into the facts involving the drawing of inferences as to what the manufacturer's knowledge or intention may have been, has resulted in the introduction of a rule which may be narrower than is legally necessary. If a manufacturer is actively inducing, for example by advertising, the use of his product for the patented indication, it is difficult to see, on any basis, why the manufacture is not "for" the patented indication"

191. The "only packaging will do" approach has obvious advantages of practicality, but I remain very clearly of the view that it does not provide adequate protection for the patentee. I did not understand Mr Speck, who argued this part of the case for Actavis, to contend that we should rigidly follow the approach of the German courts. These matters arise as a matter of interpretation of the word "for". The parties are agreed that the word imports a mental element. Packaging may be a means of demonstrating

the necessary mental element, whatever that is, but it cannot possibly be the only means of doing so.

192. A somewhat wider approach appears to be adopted in Spain, where what is looked for is an express authorisation for the new indication or some other act of encouragement of the use for that indication. Thus in *Wyeth v Arafarma and Qualtec* Case 539/07, the Madrid Court of Appeal considered that it was necessary to show that:

> "… the defendants have marketed their [drug] by having applied for and received the administrative approval for the same for the new patented therapeutic indication *or had performed another procedure directed at strengthening the use of the same for that new indication*." (emphasis supplied)

193. Much more recently, in France, by a decision of the Tribunal de Grande Instance dated 26 October 2015 in *Warner-Lambert and others v Sandoz and others* Case 15/58725 (Judge Marie-Christine Courboulay) the court, in summary proceedings, held that Warner-Lambert's claim for infringement was not sufficiently established. Sandoz had a skinny label product and had sent an information email to doctors and pharmacists prior to launch stating that the product was not indicated for neuropathic pain because it considered that the efforts made to prevent the prescription of the drug for the patented indication were adequate. There was a complaint that Sandoz had not also communicated with the health authorities. The evidence showed that Sandoz had obtained a larger share of the market than was represented by non-pain use. It is clear from the judgment (at page 5 of the translation) that the court considered that Sandoz had positive obligations if it were to market the drug under its own marketing authorisations for the non-pain indications. At page 7 the court said:

> "Thus it can be found that Sandoz has only marketed the indications for which they have received a marketing authorisation, has included a leaflet that only refers to the two indications epilepsy and GAD, has largely informed physicians and pharmacists at the time of the launch of [its generic pregabalin] through the email sent at the beginning of October.
>
> Regarding the messages to be sent to the health authorities, it appears that Pfizer has done it to alert them of their rights and of the need to protect such rights so that it was irrelevant for Sandoz itself to send a letter.
>
> It should be further noted that Sandoz has agreed to send a more explicit message to physicians and pharmacists in the city and in hospitals to describe how to prescribe or dispense [its generic pregabalin] in order to avoid infringement of the patentee's rights.
>
> Therefore, there is no active infringement on the basis of direct infringement."

194. The court went on to consider an advertisement in a pharmacists' publication in which Sandoz referred the value of the potential market which could only be correct if it

included the market for pain. Reliance on this advertisement was rejected on the basis that "infringement shall not be assessed subjectively but only objectively".

195. It appears, therefore, that in France the court does not take the "only packaging will do" approach but looks to what the generic manufacturer has done to prevent use for the patented indication. That approach involves a recognition that the manufacturer does not escape liability where he does not encourage the new use, but comes under a responsibility to show that he has taken steps to discourage it. Such an approach necessarily involves an evaluation of whether the generic manufacturer has done enough.

196. As an aside, I would mention the Danish case of *Warner-Lambert Company LLC and another v Krka d.d. and another*, a decision of the Maritime and Commercial High Court dated 25 June 2015. Pharmacists in Denmark were required to label the dispensed product with the condition for which the medicine was to be taken. The court was able to find that the pharmacists were directly infringing in those circumstances, it appears by treating the application of the label as the final step in the "manufacturing" required by the claim. The claim against the manufacturer for indirect infringement appears to have failed on the grounds related to the wording of the injunction.

197. I think this Danish case illustrates how technical the law in this area is in danger of becoming. If a pharmacist merely forms the intention of dispensing pregabalin for pain he or she is not committing a "downstream act of manufacture" whereas if a label is applied to the product there can be direct infringement by the pharmacists and indirect infringement by the manufacturer. It is unfortunate that the patentee's right to a return for his contribution to the art should turn on such technical distinctions.

198. At paragraph 93 of *Warner-Lambert CoA* I referred to *Schering v Teva* Case HA ZA 10-437, a decision of the District Court of the Hague dated 10 November 2010, and at paragraph 95 to *Novartis v Sun* a decision of the Court of Appeal of the Hague dated 27 January 2015. *Schering* was a case where the relevant patient group had been carved out of the SmPC. I pointed out, in the passage which I cited in paragraph 93 of *Warner-Lambert CoA*, that the court did envisage that there could be infringement where it was established that doctors were in fact prescribing for the relevant group. *Novartis* was a case of indirect infringement. The known use was a mere 3% of the market, the remaining 97% being for the patented indication.

199. Since then, by a judgment of 25 November 2015, the Hague District Court has decided the main proceedings in the *Novartis* case. It dismissed the contributory infringement claim because there was no downstream act of manufacture, a conclusion for which it relied heavily on the judgments of Arnold J in this case. However it has adjourned for further consideration the question of whether there was direct infringement. Thus, at least so far as direct infringement is concerned, the position in the Netherlands at first instance remains open.

200. Finally Mr Speck referred us to a recent decision of the EPO in decision *T 1673/11* concerning an attempt in opposition proceedings to amend a claim from a Swiss-form claim to an EPC 2000 claim. The TBA took the view that a Swiss form claim was limited to the product "packaged and/or provided with instructions for use in the treatment of" the new indication (infantile Pompe's disease). This seems to be an

acceptance of the "only packaging will do" approach. Interestingly the TBA appears to have considered the direct product of the process in the case of a Swiss-form claim to be a product with the packaging as well. This would be to treat the requirement for packaging as if it were a step in the claimed process, rather than merely evidence of the requisite mental element. That again goes beyond the common approach of the parties in this case.

201. These cases continue to show a spectrum of different approaches. Some countries have gone for the "only packaging will do" approach. Some countries look more generally for some element of encouragement of the use of the drug for the new use by the manufacturer before being prepared to find infringement. Others look to see what steps have been put in place in the marketplace to prevent use for the prohibited indication. I do not think a universal principle has yet emerged.

202. Mr Speck submits, however, that the views I expressed in *Warner-Lambert CoA* go too far, and are out of line with the main stream of European authority. What is required is that the manufacturer "aims for or targets" the patented indication. The court should adopt that approach, he submits, because of the consequences of the approach in *Warner-Lambert CoA*. He argues, firstly, that if a manufacturer is liable if he reasonably foresees that some of his drug will be used for the treatment of pain, he will be using the process, and the whole of his output will infringe. Secondly, because all his output will then become the direct product of the process, it will be an infringement in the hands of the pharmacist whatever the mental state of the pharmacist. The patentee will therefore be able to stop pharmacists from supplying the drug at all, irrespective of the indication for which it is dispensed.

203. Mr Miller points out that, at least so far as the pharmacist is concerned, the same is true whatever form the mental element of the manufacturer is required to take. In any case, he submits, this is a consequence of which the court was aware in *Warner-Lambert CoA*.

204. Mr Speck responds that if one adopts the aiming or targeting approach, the manufacturer has control over whether he infringes. He can sell the product for the non-patented indications without incurring liability, provided that he does not aim for or target the patented one. He accepts that the consequence of crossing the line will be the same, but the element of control is essential if access to the lawful market is not to be rendered impractical.

205. I recognise, as I recognised in *Warner-Lambert CoA*, that the case where a manufacturer foresees use for the patented treatment, but takes all reasonable steps within his power to prevent it happening, represented a hard case. However, I do not think the answer is to adopt a test of purely subjective intention. Indeed I detected in Mr Speck's submissions on this occasion a recognition that a purely subjective test is not correct and that the mental element needs to be judged objectively.

206. I think the debate in this case has been distorted by reference to notions of subjective intention. I have no doubt that an objective approach is necessary. From an objective standpoint one would normally regard a person to intend what he knows or can reasonably foresee as the consequences of his actions. That is the test which I formulated in *Warner-Lambert CoA*.

207. If that is the basic test to be adopted, what is sufficient to negative the existence of intention? In my judgment the absence of the patented indication from the label cannot conceivably be sufficient to negative the intention. Mr Speck recognised that there could be objective factual circumstances where the absence of a label identifying the patented indication did not negative intention, for example a manufacturer who proposes to sell far more of the drug than the market for the non-patented indication could bear.

208. Viewed in this way I think the answer becomes clear. The intention will be negatived where the manufacturer has taken all reasonable steps within his power to prevent the consequences occurring. In such circumstances his true objective is a lawful one, and one would be entitled to say that the foreseen consequences were not intended, but were an unintended incident of his otherwise lawful activity. I think this approach is in line with that adopted in the decision of the Tribunal de Grande Instance, in that it recognises an obligation on the manufacturer to take steps if he is to enter the market where he stands to benefit from the patentee's contribution to the art.

The submissions of the Secretary of State

209. Mr Silverleaf QC, who appeared for the Secretary of State for Health as intervener, supported Mr Speck's submissions for Actavis but submitted in addition that assistance on the correct scope of claims in the Swiss form could be derived from elsewhere in the law, in particular the law about joint tortfeasors and the criminal law of accessory liability. He submitted that, as a general principle, the law does not impose liability as an accessory on the basis of a mental element which is less demanding than that of the person primarily responsible. He referred us, for example, to the recent decision of the Supreme Court in *Fish & Fish v Sea Shepherd UK and others* [2015] UKSC 10 at paragraphs 37 to 44.

210. I think that the policy considerations which are in play in the present case are different from those which apply in the case of joint torts and crime. There is in any event no general principle of the kind identified by Mr Silverleaf which permeates the whole of the law or even the law of tort. A principal may be liable for the act of his agent done within the scope of the agent's authority without sharing the agent's intention; an employer may be vicariously liable for the intentional acts of an employee which the employer does not intend.

211. In the area of patent infringement, as section 60(2) demonstrates, statute has intervened to make a person liable for supplying another with the means to infringe when he knows or ought to know of the intentional use by others. That is sufficient to show that there are different policy considerations in play here.

The judge's application of Warner-Lambert CoA

212. In *Warner-Lambert CoA* I said that a manufacturer who knew or could reasonably foresee that some of his drug would intentionally be used for treating pain would be making use of the patentee's inventive contribution in the same way as a manufacturer who actively desired that result. At paragraph 127 I said that the skilled person would understand that the patentee was using the word "for" in the claim to require that the manufacturer knows (and for this purpose constructive knowledge is enough) or can reasonably foresee the ultimate intentional use for pain.

213. The judge's analysis of the factual scenario surrounding Actavis' marketing of Leceant is undoubtedly comprehensive, but I think Mr Miller is correct in saying that in deciding whether there was intentional use for pain the judge considered the state of mind of the three participants in the process, namely the prescribing doctor, the pharmacist, and the patient.

214. So far as the doctor was concerned, the judge concluded that the necessary intention was not present. It has to be remembered that the necessary intention was that Actavis' product Lecaent should intentionally be used for pain. There was no doubt that doctors intended the drug pregabalin to be used for pain. However doctors would either prescribe Lyrica, Warner-Lambert's branded product, which could not give rise to infringement, or prescribe generically, in which case the doctor would not know whether the pharmacist would dispense Lyrica or Lecaent.

215. Turning to the pharmacist the judge held that he would not normally have the necessary intention either. He will simply intend to dispense the drug which is on the prescription. The pharmacist will have the information which the doctor lacks in the case of a generic prescription, namely the brand of drug (Lyrica/Lecaent) which is to be dispensed, but will lack information which the doctor has, namely the indication for which the drug was prescribed. Turning to the patient, the judge held that the patient's intention was not relevant. The patient intended to take whatever drug the doctor had prescribed for whatever condition the doctor had prescribed it for.

216. I think the judge fell into error in seeking to dissect the requirement for intentional treatment of pain in this way. Because claims in this form rely for their novelty on the purpose of the use of the drug, it is only essential that the manufacturer is able to foresee that there will be intentional use for the new medical indication. Intentional use is to be distinguished from use where the drug is prescribed for a different indication and, without it in any sense being the intention of the treatment, a pain condition is in fact treated.

217. The issue which the judge was called upon to decide was whether Actavis knew or could foresee that at least some of the prescriptions written generically for pregabalin to treat pain would in fact be fulfilled with Lecaent. Had Warner-Lambert succeeded in upholding valid claims on which they relied for infringement, it would then have been necessary to decide whether, at any of the various dates analysed by the judge, that test of knowledge or foresight was satisfied. If so the judge should have gone on to consider whether Actavis had taken all reasonable steps in their power to prevent Lecaent from being used to treat pain.

Indirect infringement

218. In *Warner-Lambert CoA* I considered that the case of indirect infringement did not meet the standard for striking out. I said this at paragraph 138:

> "138. … I consider it is arguable to say that when section 60(2) speaks of "putting the invention into effect", it may be legitimate to look not just at whether any one person is carrying out the invention in a sense which would give rise to liability of that person for an act of infringement. It may be that the invention is put into effect if pregabalin is manufactured by one

> person and supplied to another who intentionally uses it for the treatment of pain. In those circumstances, a person who supplies pregabalin with the requisite knowledge (i.e. that prescribed in section 60(2) itself) does provide means suitable and intended to put the invention into effect, albeit by the combination of manufacturer and user, rather than by any one person alone. It may be that this is the reasoning which underlies the decisions in the Dutch and German cases which I have referred to."

219. The judge, at paragraph 682 of the main judgment, quoted part of that reasoning, and said that he did not understand it. At paragraph 684 he said:

> "684. The fundamental difficulty with Pfizer's claim under section 60(2) remains, as it has always done, that claims 1 and 3 of the Patent are claims to processes of manufacture, but there is no act of manufacture by any party downstream from Actavis, nor even the prospect of such an act. This is so even if manufacturing (or "preparation", to use the word in the claims) for this purpose includes packaging with appropriate instructions. In particular, there is no act of manufacture by pharmacists, nor any prospect of such an act. It follows that, although there is no difficulty in concluding that Lecaent's active ingredient is "means, relating to an essential element of the invention, for putting the invention into effect", Lecaent is not suitable for putting, or intended to put, the invention into effect: either the invention has already been put into effect by the time that Lecaent leaves Actavis' hands or it is not put into effect at all. Accordingly, I conclude that Actavis have not infringed claims 1 and 3 of the Patent pursuant to section 60(2)."

220. Mr Miller advanced two reasons why the claim under section 60(2) could succeed as an alternative claim. The first depended on giving "invention" a wider meaning in section 60(2), so as to escape the shackles of section 125 which states that the invention is that which is specified in the claim, except where the context otherwise requires. I do not think that argument can prevail in the light of the decision of this court in *Menashe Business Mercantile Ltd v William Hill Organisation Ltd* [2002] EWCA Civ 1702, [2003] 1 WLR 1462 at [24] (Aldous LJ).

221. Mr Miller's second reason built on paragraph 138 of *Warner-Lambert CoA*. He submitted that the process of the invention would be put into effect by the subsequent ascription of purpose by the pharmacist to generic pregabalin supplied by a manufacturer. Although one way in which this might be done was by an express statement on a label applied by a pharmacist, this was not the only way.

222. Mr Speck supported the judge's reasoning. He was prepared to accept, at least for the purposes of argument, that the application by a pharmacist of a label ascribing the patented indication could be an act of manufacture. However, in the absence of any such step, the manufacture was complete at the stage that the product left the manufacturer. Indirect infringement was impossible in these circumstances.

223. On this issue I prefer Mr Miller's submissions. I think there is a danger in translating section 60(2) into a requirement for a "downstream act of manufacture". What is required is that means are provided which are for putting the invention into effect.

224. The invention in the present case is the use of pregabalin in the preparation of a pharmaceutical composition for treating pain. As the example of labelling by a pharmacist shows, that process is not completed when the pregabalin has been formulated into a pharmaceutical composition by a manufacturer. The process of preparing the composition can continue through any packaging step performed by the manufacturer and includes the labelling step performed by the pharmacist. I agree with the Danish court's conclusion to that effect in *Warner-Lambert Company LLC and another v Krka d.d. and another*, a case which I do not think was cited to the judge.

225. I have already concluded when considering direct infringement that the significance of a packaging step is only that it demonstrates the necessary intention. I am therefore unable to understand why other acts of the pharmacist in preparing the composition for delivery to the patient cannot also be regarded as relevant acts of preparation, if done with the necessary intention. I cannot agree with the judge that there is no relevant act of preparation by pharmacists, nor any prospect of such an act.

Conclusion

226. Arnold J's conclusions on the sufficiency of the claims as they stood before him were correct. The judge was also entitled to come to the conclusion that the late application to amend the claims amounted to an abuse of process. It followed that the action fell to be dismissed.

227. If my Lords agree, it would follow that the appeals of both parties should be dismissed.

Post-script

228. Since this judgment was largely prepared in draft, we have had our attention drawn by Warner-Lambert to three further decisions in corresponding actions in France, Sweden and Spain on the issues of sufficiency and infringement. Both sides have made submissions on these three cases.

229. The decision in France is that of the Tribunale de Grande Instance (Judges Ancel, Barutel and Senel) dated 8 July 2016 in *Generics (UK) Limited v Warner-Lambert Company LLC*. The court rejected Mylan's case of insufficiency, relying in particular on a passage of cross-examination of Dr Scadding in these proceedings, and other material which was before Arnold J. Having read the decision, I am not persuaded that its reasoning undermines the conclusions which I have reached. The court appears to have relied on hyperalgesia and allodynia as a sufficient unifying characteristic. For reasons which I have explained, the judge was entitled to reject the reliance placed on that characteristic.

230. The decision in Sweden is that of the Stockholm District Court (Judges Derebörg and Högström, sitting with Patent Court Judge Siösteen and a technical adviser) dated 12 August 2016 in *Actavis Group PTC ehf v Warner –Lambert Company LLC*. That

court was presented with different evidence from that before Arnold J. In addition it considered that the mention of the existence of the Bennett and Kim assays in the patent, tests which are for peripheral neuropathic pain, and without any experimental results, could render the invention plausible across the breadth of the claim. That is a view with which I have already expressed my disagreement. Whilst paying tribute to the quality of the decision, I am not persuaded by this judgment that my view was wrong.

231. The decision in Spain is that of the Barcelona Court of Appeal (Judges Martin, Espa and Vega) dated 5 July 2016 in *Warner-Lambert and another v Laboratorios Cinfa SA and others*. The court allowed an appeal by Warner-Lambert in interim injunction proceedings, holding that there was indirect infringement because there was a real likelihood that generic pregabalin would be used for pain. The court appears to have proceeded on the basis that (downstream) direct infringement is not a pre-requisite of a finding of indirect infringement: see paragraph 83 of the translation. Whilst the decision might be thought broadly to support Warner-Lambert's position, it is fair to say that it does not expressly endorse the argument which I have accepted. I have not placed any reliance on it.

Lord Justice Kitchin

232. I agree.

Lord Justice Patten

233. I also agree.