OUTER HOUSE, COURT OF SESSION

[2017] CSOH 150

A371/17

NOTE BY LORD BANNATYNE

In the cause

(FIRST) ASTRAZENECA AB AND (SECOND) ASTRAZENECA UK LIMITED

Pursuers

against

TEVA UK LIMITED

Defender

Pursuers: Duncan QC, Pickard; Burness Paull LLP
Defender: Cormack (sol adv); Pinsent Masons LLP

16 November 2017

Introduction

[1] This matter came before me for a hearing prior to calling. At that stage the pursuers sought interim interdict to restrain the defender from launching Fulvestrant Teva onto the market in Scotland and thereby allegedly infringing three of the pursuers' patents: European Patent (UK) No 1, 250, 138 ("EP 138"); European Patent (UK) No 2, 266, 573 ("EP 573") and European Patent (UK) No 1, 272, 195 ("EP 195") (collectively "the patents").

[2] The first pursuer is the registered proprietor of the patents. The second pursuer sells and supplies Faslodex®, a breast cancer treatment which is protected by the patents, in the UK under exclusive licence from the first pursuer.

[3] The defender's position in short is that it considers the pursuers' claimed monopoly in terms of the patents to be an invalid one and separately with respect to EP 195, contends that the marketing of Fulvestrant Teva would not infringe EP 195. It wishes to enter the market with its own generic product Fulvestrant Teva. It would be a direct competitor to the pursuers' product.

The Patents

"(1) EP 138 entitled 'Fulvestrant Formulation', which was granted on 19 October 2005, has as its earliest priority date 10 January 2000 and which relates to the use of fulvestrant in the preparation of a formulation for administration by intra-muscular injection containing the compound fulvestrant in solution in a ricinoleate vehicle which additionally comprises at least one alcohol and a non-aqueous ester solvent which is miscible in the ricinoleate vehicle, for the treatment of a benign or malignant disease of the breast or reproductive tract. EP 138 has 31 claims in total. Claim 1 of EP 138 is to:

> 'Use of fulvestrant in the preparation of a pharmaceutical formulation for the treatment of a benign or malignant disease of the breast or reproductive tract by intra-muscular administration, wherein the formulation comprises fulvestrant in a ricinoleate vehicle, a pharmaceutically acceptable non-aqueous ester solvent, and a pharmaceutically acceptable alcohol, and wherein the formulation is adapted for attaining a therapeutically significant blood plasma fulvestrant concentration for at least 2 weeks.'

…

(2) EP 573 entitled 'fulvestrant formulation', which was granted on 17 June 2015, has as its earliest priority date 10 January 2000 and which relates to a novel sustained release pharmaceutical formulation adapted for administration by intra-muscular injection containing fulvestrant in solution in a ricinoleate vehicle which additionally comprises at least one alcohol and a non-aqueous ester solvent which is miscible in the ricinoleate vehicle, for use in the treatment of breast cancer. EP 573 has three claims in total. Claim 1 of EP 573 is to:

> 'A pharmaceutical formulation for use in the treatment of breast cancer by intra-muscular injection, wherein the pharmaceutical formulation comprises fulvestrant, a pharmaceutically-acceptable alcohol being a mixture of 10% weight of ethanol per volume of formulation and 10%

> weight of benzyl alcohol per volume of formulation, and the formulation contains 15% weight of benzyl benzoate per volume of formulation and a sufficient amount of a ricinoleate vehicle so as to prepare a formulation of at least 40mgml^{-1} of fulvestrant, wherein the ricinoleate vehicle is castor oil, and wherein the total volume of the formulation is 6ml or less.'

…

(3) EP 195 entitled 'use of fulvestrant in the treatment of resistant breast cancer', which was granted on 12 October 2005, has a priority date of 5 April 2000 and which relates to the use of fulvestrant in the treatment of breast cancer in patients who have previously been treated with tamoxifen and an aromatase inhibitor. EP 195 has six claims in total. Claim 1 of EP 195 is to:

> 'Use of fulvestrant in the preparation of a medicament for the treatment of a patient with breast cancer who previously has been treated with an aromatase inhibitor and tamoxifen and has failed with such treatment.'"

The Background

[4] On 12 March 2004 AstraZeneca received first EU approval to market Faslodex®.

[5] On 15 March 2016 marketing authorisation for Fulvestrant Teva was granted. The defender used abridged procedure citing Faslodex® as the reference medicinal product.

[6] On 9 August 2017 the defender presented a petition seeking revocation of EP 138 and EP 573.

[7] On 7 September 2017 the defender presented a petition seeking revocation of EP 195. In addition it lodged a summons which sought declarator that marketing and use of Fulvestrant Teva in the UK would not infringe EP 195.

[8] On 23 October 2017 the defender intimated to the pursuers that it intended to launch Fulvestrant Teva in Scotland before the rest of the UK and that Fulvestrant Teva would be made available for purchase by Health Boards and hospitals in Scotland on or after 1 November 2017.

[9] On 26 October 2017 the pursuers' agents wrote to the defender's agents seeking an undertaking that the defender would refrain from making Fulvestrant Teva available for purchase in Scotland pending final judicial determination of the various actions concerning the patents. On 27 October 2017 the defender refused to give the requested undertaking.

[10] On 31 October 2017 preliminary hearings took place before the Lord Ordinary in all four sets of proceedings. The defender offered an undertaking not to offer to dispose of or dispose of Fulvestrant Teva in the UK until the hearing on the motion for interim interdict was disposed of.

[11] EP 138 and EP 573 are due to expire on 8 January 2021 and EP 195 is due to expire on 2 April 2021.

Other Litigation with Respect to the Patents

[12] In 2006 the defender opposed EP 195. On 14 February 2013 the European Patent Office ("EPO") rejected EP 195 opposition on appeal and EP 195 was maintained unamended.

[13] On 8 July 2015 EPO found EP 138 valid in amended form after nine year opposition proceedings and B2 specification was published.

[14] On 16 March 2016 the defender opposed EP 573 and on 8 May 2017 the opposition division at EPO found EP 573 invalid. This decision is presently subject to appeal. With respect to litigations in Germany and Switzerland the position can be taken from the witness statement of Benjamin Hall who states as follows:

"**Germany**

The 138 Patent

30. Teva[1] has successfully revoked the German designation of the 138 Patent before the German Federal Patent Court. In its decision on 12 January 2017, the Court held that the 138 Patent is obvious over a combination of Howell and McLeskey (**Exhibit BAH6**). On 19 June 2017 AZ AB appealed the decision but there is currently no appeal hearing scheduled.

31. Prior to this decision, on 31 August 2016, an ex parte preliminary injunction was granted against Teva[2] by the Regional Court Düsseldorf in Germany and following an oral hearing before the Regional Court Düsseldorf on 29 November 2016, the preliminary injunction was upheld. However, following a request from Teva, the Higher Regional Court Düsseldorf suspended the enforcement of the preliminary injunction on 13 January 2017, on the basis that the German Federal Patent Court had held the 138 Patent to be invalid. Teva's appeal to the granting of the original preliminary injunction was heard on 2 November 2017. The Higher Regional Court Düsseldorf held that there was no basis for AZ AB's allegation that the decision of the Federal Patent Court that the 138 Patent was invalid, was evidently wrong. Consequently, AZ AB subsequently withdrew its request for a preliminary injunction.

The 573 Patent

32. On 21 September 2016 AZ AB sought injunctive relief against Teva[3] based on the 573 Patent. At an oral hearing on 7 February 2017, the Regional Court Mannheim in Germany dismissed AZ AB's application on the basis that the validity of the 573 Patent is not sufficiently certain to the degree necessary for the granting of a preliminary injunction ie there are serious doubts about the validity of the patent (**Exhibit BAH7**). Whilst AZ AB initially appealed the decision, the appeal was withdrawn after the Opposition Division held the 573 Patent to be invalid.

The 195 Patent

33. On 15 February 2017 AZ AB applied for a preliminary injunction against Teva[4] in Germany based on the 195 Patent. The application was dismissed by the

[1] The party to the proceedings was ratiopharm GmbH, a TPI group company.
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Regional Court Düsseldorf on 3 March 2017 due to a lack of temporal urgency.[5] (**Exhibit BAH8**). AZ AB's appeal of that decision, filed on 20 March 2017, was dismissed by the Higher Regional Court Düsseldorf on 10 May 2017, also on the basis of a lack of urgency for granting a preliminary injunction.

Switzerland

The 138 Patent

34. Teva[6] sought revocation of the 138 Patent in Switzerland. During these proceedings, AZ AB submitted four amended claim sets as auxiliary requests (referred to as Motions 1-4 in Switzerland). On 7 March, Judge Dr. sc, Nat, Dipl. Chem Hannes Spillmann rendered his Technical Opinion, which stated that the claims as granted and Motions 1-4 were invalid for lack of inventive step in light over Howell in combination with McLeskey and Motion 3 was also invalid for added matter (**Exhibit BAH9**). Following an oral hearing on 13 June 2017, the Swiss Federal Patent Court held by its decision dated 29 August 2017, that the 138 Patent as granted and Motions 1-4 were invalid for the same reasons as those expressed in the Technical Opinion (**Exhibit BAH10**).

35. At the oral hearing on 13 June 2017 AZ AB filed another auxiliary request with a new amended claim. While the Federal Patent Court found that such auxiliary request was inadmissible at that stage of the proceedings, it also stated in its decision that the new amended claim would be equally obvious over Howell in combination with McLeskey. On 13 October 2017 AZ AB appealed the judgment of the Swiss Federal Patent Court to the Swiss Federal Supreme Court.

The 573 Patent

36. Teva[7] also sought revocation of the 573 Patent in Switzerland. On 7 March, Judge Dr. sc, Nat. Dipl. Chem Hannes Spillmann rendered his Technical Opinion, which stated that the 573 Patent was invalid for lack of inventive step in light of Howell in combination with McLeskey (**Exhibit BAH11**). By virtue of its decision, dated 29 August 2017, the Swiss Federal Patent Court also held that the 573 Patent was invalid for lack of inventive step over a combination of Howell and McLeskey (**Exhibit BAH12**). On 13 October 2017 AZ AB appealed the judgment of the Swiss Federal Patent Court to the Swiss Federal Supreme Court."

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[5] A preliminary injunction may only be issued in Germany if it is necessary in order to avert considerable disadvantages and the urgency required for a ruling to be issued in summary proceedings is thus present.

[6] The party to the proceedings was Actavis Switzerland AG, a TPI group company.

[7] The party to the proceedings was Actavis Switzerland AG, a TPI group company.

[15] There was an addition in Holland the case of *Sandoz BV* v *Astrazeneca AB* C/09/513437/KGZA16-779 ("the Dutch case").

[16] In the Dutch case EP 138 was the subject of an invalidity attack based on the same prior art (McLeskey and Howell) that is relied upon by the defender in its EP 138 petition in this court. In those proceedings the first pursuer sought provisional relief against Sandoz BV to prevent infringement of the Dutch designation of EP 138 by launch of Fulvestrant Sandoz 50mg/ML. At first instance, Sandoz BV counterclaimed that EP 138 would be annulled in the proceedings on the merits due to *inter alia* lack of inventive step in light of Howell and McLeskey read together and McLeskey and common general knowledge. The provisional relief judge dismissed Sandoz BV's counterclaim and granted the first pursuer the injunctive relief sought. In a decision dated 31 October 2017 the Hague Court of Appeal upheld the first instance decision of the provisional relief judge and concluded at paragraph 4.31 that:

> "The conclusion, in the provisional opinion of the Court of Appeal, is that there are no serious realistic prospects that EP 138 will be annulled in proceedings on the merits…"

***Prima Facie* Case**

Approach of Court to the Issue of Prima Facie Case

[17] I did not understand the following exposition regarding the approach of the court set out in the defender's written submissions to be contentious:

> "A pursuer seeking interim interdict is required to show a *prima facie* or good arguable case, ie to show that he has "reasonable prospects" of establishing a right to interdict at proof. Where material is put forward by the defender in opposition to the motion, whether by defences or productions or statements made at the bar, that material will obviously have to be taken into account in assessing whether the pursuer has shown such a case. The court must look behind a pursuer's averments and give critical consideration to whether a *prima facie* case has been shown by the pursuer, on all the information laid before the court (*Schuh Limited* v *SHHH…Limited*

> [2011] CSOH 123 per Lord Glennie at paragraphs [13] and [16]; consistent with for example Lord Hamilton in *Waste Systems International Inc* v *Eurocare Environmental Services Ltd* 1999 SLT 198 at 201B)."

Submissions

EP 195

[18] Mr Duncan began his submissions by making two general points which he submitted apply as regards the issue of *prima facie* case with respect to the patents: first, the court should adopt the usual position in cases of this type and hold the ring while the underlying merits are determined and, secondly, that in the arguments being put forward on behalf of the defender the court was being asked to descend into a level of detail and make decisions which it could not make at this stage.

[19] Turning to the detail of his argument, the position advanced by the defender in its declarator of non-infringement as to why there was no infringement came to this: the defender accepts that Fulvestrant Teva will be used as a third therapy for certain sub-groups of patients, but it takes two points as to why this is insufficient for infringement:

(a) it argues that for one of these sub-groups (those who have previously received surgical treatment – the "first group"), Fulvestrant Teva will be used as a switch therapy after a fixed period of administration of tamoxifen and an aromatase inhibitor, and that this does not necessarily mean that those first and second therapies will have "failed" in the sense required by EP 195;

(b) it argues that for the other of these sub-groups (those who have not previously received surgical treatment – the "second group"), although the first and second therapies will have "failed" in the sense required by EP 195, nevertheless that group is a "very narrow subset of patients".

[20] As regards the case made by the defender Mr Duncan first made this point: even if it might be an answer to a patent infringement claim, such an argument cannot be successful at the interim interdict stage. Such issues raise points of claim construction as well as factual issues (eg what size are the patient sub-groups identified by the defender; is this a *de minimis* group etc), which this court cannot engage with at this stage. The above therefore is not a reason for finding there is no *prima facie* case.

[21] Beyond that, however, he had a specific response to the argument being advanced by the defender. He directed the courts attention to the Scottish Medicines Consortium advice about Faslodex®, which advice was issued on 8 February 2016 (6/9 of process) and in particular to the following section of the advice at page 5:

> "Clinical experts consulted by SMC considered that the place in therapy of fulvestrant would be as a treatment option after failure of anti-oestrogen and aromatase inhibitor therapy to avoid or postpone chemotherapy."

He submitted on the basis of the foregoing that there was a *prima facie* case that is obvious to a reasonable person in all the circumstances that Fulvestrant Teva will be used in accordance with the indication of EP 195. Resolution of the issues raised by the defender in its summons for declarator of non-infringement accordingly requires proof and are not capable for determination at this stage.

[22] With respect to the separate issue of the validity of EP 195 he referred to the EPO decision on validity. He also drew to my attention that in its decision EPO considered the first piece of prior art relied on by the defender, namely: Thurlimann and held it did not render the patent invalid. Secondly the other piece of prior art relied on by the defender was not even put before EPO showing its lack of significance or perhaps that no one was even aware of it. It could not be said against that background that there was no *prima facie*

case that the patent was valid. In any event the validity attack was not one which could properly be engaged with by the court at this stage.

[23] Mr Cormack's submissions with respect to the EP 195 patent were primarily directed to the issue of non-infringement. It was his position that so far as that issue was concerned no basis is averred in the present summons seeking interdict for the inference that it is known or obvious that Fulvestrant Teva will be used for treatment of a patient with breast cancer who previously has been treated with an aromatase inhibitor and tamoxifen and has failed with such previous treatment. An averred and evidence basis for this inference would be needed for the pursuers to have a *prima facie* case on this issue.

[24] The pursuers know the defender's position in relation to non-infringement as set out in its substantive action and make no attempt to address what the defender says.

[25] The defender identifies two groups of patients. In the first group the requirement and the claim that the use of fulvestrant correlate with failure of the previous treatment is not met. In the second group use of any third line treatment at all would be exceptional. These averments not having been addressed by the pursuer, further reinforces the absence of a *prima facie* case.

[26] As regards the document relied on by Mr Duncan, he described this as highly ambiguous. He directed the court's attention to two further passages in that document:

[27] Firstly at page 1 this is said:

> "Indication under review: for the treatment of post-menopausal women with oestrogen receptor positive, locally advanced or metastatic breast cancer for disease relapse on or after adjuvant anti-oestrogen therapy, or disease progression on therapy with an anti-oestrogen."

Secondly, at page 2 under the heading "Indication":

> "For the treatment of post-menopausal women with oestrogen receptor positive (ER+) locally advanced or metastatic breast cancer for disease relapse on or after

> adjuvant anti-oestrogen therapy, or disease progression on therapy with an anti-oestrogen."

The significance of these two passages was the use of the words "on or". The use of such words did not fit with claim 1 of EP 195. Thus the defender's position remained unmet.

[28] Mr Cormack's fall back position was this: if a *prima facie* case had been shown then it was a very weak one, for the reasons he had above advanced, and this should weigh in consideration of the issue of balance of convenience.

[29] Infringement was the principal argument with respect to EP 195. Mr Cormack accepted that EPO having upheld the validity of EP 195 then the court may be reluctant to hold that the pursuers have shown no *prima facie* case in respect of the validity of EP 195.

[30] However, his position on validity was this:

[31] In relation to the prior art Thurlimann:

1. EP 195 relates to the use of fulvestrant in the preparation of a treatment for a patient with breast cancer who has previously been treated with an aromatase inhibitor and tamoxifen and has failed with such treatment. Fulvestrant in this sense is a "third line" active agent.
2. Thurlimann discloses the use of fulvestrant as a second line active agent. It also discloses the use of other agents as third and fourth line agents and that active agents can be used interchangeably at the various stages in a sequential treatment strategy. No indication is given that this is not capable of applying to fulvestrant.
3. The difference between Thurlimann and EP 195, that fulvestrant is expressly identified as a third line agent in the latter, is *prima facie* not an inventive step.

[32] In relation to the prior art Iveson:

1. Fulvestrant is described in EP 195 itself as a pure anti-oestrogen [0010]-[0011]

2. Iveson describes the use of second and third line endocrine treatments as already being well known.
3. Iveson discloses the possibility of the use of pure anti-oestrogens as third and even fourth line endocrine treatments. It also cites Wakeling (1991) which identifies fulvestrant as a pure anti-oestrogen and describes its characteristics.

The position is of a *prima facie* cogent validity attack met so far with bare denial.

Discussion

[33] As regards validity there is at present the decision of EPO which has held the patent to be valid.

[34] That decision is in my judgment a piece of evidence upon which the pursuers can rely in advancing their position that there is a *prima facie* case. This was broadly recognised by Mr Cormack. I without difficulty hold that the pursuers have a *prima facie* case with respect to the issue of validity.

[35] On infringement it may be that the defender will be successful at proof, however, the dispute between the parties on this issue cannot be resolved at the stage of a hearing on interim interdict.

[36] I am persuaded that Mr Duncan is correct, for the reasons he advanced, that the issues raised by the defender cannot be resolved at this point and thus do not provide a reason for finding there is no *prima facie* case.

[37] Beyond that, I do not accept the defender's argument that the pursuers have failed to address the position advanced by the defender on non-infringement. It is correct that in the substantive action the pursuers' answers are not detailed. However, that is perhaps not surprising given the early procedural stage which that action has reached. However,

whatever the position in the pursuers' answers to that action, the pursuers do set forth a basis in the present proceedings as to why the defender's contentions are not well-founded. This is by reference to the Scottish Medicines Consortium advice. The passage relied on is relevant to the issue of non-infringement in that it appears to be the unanimous view of the clinical experts consulted that: "the place in therapy of fulvestrant would be as a treatment option after failure of anti-oestrogen and aromatase inhibitor therapy" (emphasis added).

[38] It is, on the face of it, at this stage, a piece of evidence supporting the pursuers' position on non-infringement.

[39] Mr Cormack points to two other passages in this document and argues that this shows a fundamental ambiguity within the document. He suggests therefore that the document does not support a *prima facie* case on the part of the pursuer.

[40] I would make two points regarding the submission made by Mr Cormack: first, on a critical consideration of the evidence there remains the passage founded on by Mr Duncan, which appears to go to the heart of the dispute between the parties, and cannot at this stage be swept aside, by consideration of the two other passages relied on by Mr Cormack. Secondly, the argument put forward by Mr Cormack with respect to this document tends to support the necessity for hearing evidence and shows that this dispute is not capable of resolution without such evidence and therefore the arguments put forward by the defender do not provide a reason for finding there is no *prima facie* case.

[41] I am satisfied for the foregoing reasons that the pursuers have shown a *prima facie* case with respect to validity and non-infringement of the patent.

Validity of EP 573 and EP 138

Submissions

[42] Mr Duncan began by summarising the defender's position on validity: the validity attack is based on a lack of inventive step.

[43] Given the nature of the argument he went on to say this: determination of questions of invalidity on the ground of lack of inventive step requires a multifactorial analysis of all the relevant evidence, including the expert evidence as to the identity, attributes and common general knowledge of the skilled person, the teaching that the skilled person would take from the prior art documents and the steps that the skilled person would consider it obvious to do in light of that teaching. It is not a point on which this court can take a view at this stage, and is not therefore a reason for finding that there is no *prima facie* case.

[44] He noted that it was foreshadowed in the defender's Note of Argument and other documents lodged by the defender that a principal part of its submissions today on the issue of *prima facie* case would be to refer to decisions in other jurisdictions with respect to the validity of these patents.

[45] It was his position that these decisions were not as persuasive as the defender sought to portray them. In particular EPO had upheld the validity of EP 138.

[46] In addition it had recently been upheld in the Dutch case both at first instance and appeal.

[47] He accepted that EP 573 had been held not to be valid by EPO. However, that decision was a matter of appeal.

[48] He recognised that in Germany and Switzerland there had been decisions with respect to both patents in which their validity had not been supported.

[49] However, he further advised the court that challenges based on the prior art relied upon by the defender had not prospered in the US with respect to related patents.

[50] When the whole picture was looked at, it was not as powerful as suggested by the defender.

[51] He particularly relied on the decision in the Dutch case in which the court had before it the prior art relied on by the defender in its present proceedings for invalidity and was in addition aware of the decision before EPO and the decisions in Germany.

[52] He submitted that on the basis of the above decisions it could not be said that the pursuers did not have a *prima facie* case. It was his position that the decisions tended to support the pursuers had a *prima facie* case.

[53] Beyond that he submitted that the pursuers did have a line of argument that it intended to advance in the substantive proceedings. That line would be the same or similar to the very detailed argument that was advanced in the Dutch case. Thus it could not be said on behalf of the defender that the pursuers were not putting forward any answer to the case on validity.

[54] Mr Duncan in addition made two short points with respect to the prior art in McLeskey and Howell which was relied upon by the defender: First, the argument against him with respect to McLeskey was this: a skilled person would go to McLeskey and then go to Howell and without an inventive step join the dots between these two pieces of work. He drew the courts attention to this at pages 697/8 of McLeskey:

> "Although the mechanisms of tamoxifen resistance described above should be amenable to alternative hormonal therapy, early results for small numbers of tamoxifen-resistant patients have shown that only about 30-40% of such patients have a positive response to subsequent ICI 182,780 or aromatase inhibitor therapy (13-20)."

[55] He drew the court's attention to the fact that Howell was No 19 where reference was made to "(13-20)". It was only referred to in the context of a not very positive research finding. It is one of no less than 91 papers referred to in McLeskey.

[56] It was his position that before one could make such a leap as the defender was contending should be made, there were a very large number of questions which the defender had to answer. These points were raised in Answer 25 in the substantive proceedings, which says as follows:

> "Denied. The Petitioner is called upon to identify: (i) what components of the formulation claimed in the Patents it avers are typical components of parenteral formulations; (ii) what components of the formulation claimed in the Patents it avers are typical components of intramuscular formulations; (iii) what properties of each of said components it avers constitute the common general knowledge of the person skilled in the art; (iv) what, if any, further knowledge of each of said components it avers constitutes the common general knowledge of the person skilled in the art; (v) what information set out in Pharmaceutical Dosage Forms; Parenteral Medications Volume 1, Edited by Avis, Liebermann and Lachman 1992 it avers constitutes the common general knowledge of the person skilled in the art; (vi) what other standard texts it avers the person skilled in the art would have consulted and what information set out in any such text it avers constitutes the common general knowledge of the person skilled in the art; (vii) what other knowledge it avers would have constituted the common general knowledge of the person skilled in the art at the earliest priority date of the Patents, namely 10th January 2000."

[57] Secondly, turning to Howell he submitted it did not disclose the excipients, used for stability.

[58] The onus was on the defender to show against the above background that it was obvious to combine these chemical resources in the way set out in Claim in the EP. That required expert evidence.

[59] Mr Cormack submitted that the defender's attack on validity is a straightforward one based on two pieces of prior art.

[60] In development of the above submission he stated as follows:

[61] In relation to the prior art Howell:

1. Howell discloses a castor oil based pharmaceutical formulation for use in the treatment of breast cancer by intramuscular injection, with the formulation comprising the active ingredient fulvestrant. Howell was a report of a study of the use of such a formulation in the treatment of breast cancer.
2. The only difference between Howell and EP 138/EP 573 is that Howell does not disclose that the castor oil based formulation used comprises at least one alcohol and an ester as required in the two patents. Standing that the patents themselves identify formulations which use alcohols and esters, it calls for explanation by the pursuers as to why use of same would not be obvious. This is not done and the pursuers have not shown a reasonable prospect of defeating the defender's case on this point.

[62] In relation to the prior art McLeskey:

1. McLeskey teaches the use of fulvestrant for the treatment of breast cancer in animals.
2. McLeskey further discloses a preformulated injection composition of fulvestrant at a concentration of 50mg/ml comprising a vehicle consisting of 10% ethanol, 15% benzyl benzoate, 10% benzyl alcohol, brought together with a castor oil-a formulation identical to that in EP 138 and EP 573.

[63] Even without Howell it would have been obvious to the skilled person to seek to use the formulation in humans. In any event, Howell is one of the literature citations in McLeskey. This is at least *prima facie* evidence that it would have been obvious to the skilled person to read them together (*Scinopharm Taiwan Limited* v *Eli Lilly & Company* [2009] EWHC 631 (Pat) at paragraphs [83]-[84]).

[64] The position is of a *prima facie* cogent validity attack met so far with bare denial.

[65] It was his position that no material had been provided which in any way counters the above and could base a decision at this stage that there were reasonable prospects of success in countering the defender's arguments on validity. The pursuers had not developed any case on validity. No attempt had been made to knock out the various decisions on validity made in other jurisdictions.

[66] For the foregoing reasons there was no *prima facie* case.

Discussion

[67] The starting point is that the onus of proving invalidity based on lack of an inventive step is on the defender.

[68] The defender in particular in advancing its argument that there is no *prima facie* case relies on a series of decisions on validity regarding these two patents in other jurisdictions.

[69] For a number of reasons, I do not believe that at this stage these cases are of the significance that the defender suggests and in particular I do not believe they show that there are no reasonable prospects of the pursuers countering the defender's argument on validity.

[70] First, all of the decisions do not point in the same direction. Parties who have challenged the patents have not always been successful.

[71] In the Dutch case, the challenge to validity, on similar grounds, as those before me, to EP 138 failed at first instance and thereafter failed on appeal.

[72] Moreover, EP 138 was held to be valid by EPO on 8 July 2015.

[73] Lastly, I am advised that challenges to related patents in the US on similar grounds have not prospered.

[74] I accept that against the foregoing the defenders are able to point to a measure of success in Switzerland and Germany in challenging the validity of the patents and that EPO has held that EP 573 is invalid as at 8 May 2017.

[75] Accordingly, the picture painted by the decisions in other jurisdictions is not a straightforward one. This is not a situation where every decision has gone against the pursuers.

[76] There has been divided success. This tends to suggest that this is a matter which is not sufficiently clear to allow me to hold at this stage that there is no *prima facie* case.

[77] It is also I believe worth bearing in mind when considering the significance of decisions in other jurisdictions the observation of Lord Hoffmann in *Conor Medsystems Inc* v *Angiotech Pharmaceuticals Inc* [2008] RPC 28 at paragraph 3:

> "There is still no European Patent Court. A European patent takes effect as a bundle of national patents over which the national courts have jurisdiction. It is therefore inevitable that they will occasionally give inconsistent decisions about the same patent. Sometimes this is because the evidence is different. In most continental jurisdictions, including the European Patent Office ('EPO'), cross-examination is limited or unknown. Sometimes one is dealing with questions of degree over which judges may legitimately differ. Obviousness is often in this category."

[78] The defender argued that the pursuers had not put any material before the court to entitle it to hold there was a *prima facie* case. I firstly believe that there is some force in Mr Duncan's point that at this stage there are a number of essential averments for the defender to make in the substantive action before it can expect a detailed reply from the pursuers.

[79] At Answer 25 in the substantive proceedings (which I have quoted in full earlier) the pursuers make a series of calls. These calls appear to me to seek relevant information from the defender and only when these are answered will the pursuers be able to develop its argument in detail with respect to the issue of validity.

[80] In any event Mr Duncan argues that he has set forth in his oral submissions the likely detailed line of the substantive argument which would be advanced on behalf of the pursuers with respect to validity. He relies on the arguments which were advanced in the Dutch case.

[81] It is perhaps instructive to look at the issues before the Dutch court on inventive step. This is dealt with at paragraphs 4.18 to 4.31 in its opinion where the following is said:

> "4.18 Sandoz also suggested Howell as the closest prior art. AstraZeneca argued, against this, that the document is not a reproduceable disclosure and cannot therefore be used as a starting point. Be that as it may, the Court of Appeal may leave this as a moot point, finding for the time being that the invention in terms of the patent would not be obvious to the average skilled person if he were starting from Howell. The only argument made by Sandoz to support its attack on the inventive step is that the average skilled person, starting from Howell, would come across McLeskey and that this combination would lead the average skilled person to the invention without inventive thought.
>
> 4.19 Astrazeneca denied that the average skilled person, starting from Howell, would come across McLeskey and that even if he were to do so, he would not pause to consider it. This may also remain a moot point, as the Court of Appeal finds for the time being that the average skilled person, starting from Howell and with knowledge of McLeskey, would not arrive at the invention in terms of the patent without inventive thought. This is explained below.
>
> 4.20 Proceeding from the differential measures between Howell and the invention in terms of EP 138, namely the composition of the fulvestrant formulation, one may proceed on the basis of the following objective technical problem: 'providing a fulvestrant formulation that is suited to the treatment of a benign or malignant illness of the breast or the reproductive tract'. Sandoz and AstraZeneca also proceed from this starting point. As AstraZeneca correctly argued, it follows from taking Howell as the starting point that it is intrinsic to being 'suited' to the treatment of (briefly) breast cancer that the positive research results disclosed in Howell are retained and thus that the fulvestrant formulation is tolerable and promotes a therapeutically significant plasma concentration for at least two weeks after administration by intramuscular injection.
>
> 4.21 Hypothetically assuming that the average skilled person comes across and takes note of McLeskey, he would find a number of fulvestrant formulations in it. The average skilled person would not simply start testing these formulations. He would only do so if, proceeding from Howell, on the basis of the disclosure in McLeskey, he had reasonable prospects of success in

solving the problem with one of the formulations disclosed in McLeskey or, as Sandoz puts in, if the average skilled person has a reasonable expectation that this is the fulvestrant formulation used in Howell and that it can thus solve the problem. This latter approach then presumes, as AstraZeneca correctly pointed out, that the average skilled person would perceive that the formulation disclosed in Howell was not a complete disclosure and did not include excipients. Also proceeding on this basis, the Court of Appeal considers that the average skilled person would not have this reasonable expectation of success and would refrain from undertaking research into the suitability of one or more of the formulations disclosed in McLeskey for the treatment of breast cancer.

4.22 According to established case law from the Technical Boards of Appeal of the European Patent Office, which should be followed by the Dutch Judiciary, a 'reasonable expectation of success' means 'the ability of the skilled person to reasonably predict, on the basis of existing knowledge before starting a research project, a successful conclusion to said project within reasonable limits'. Applied to the present case, the average skilled person would have a reasonable expectation of success if he could reasonably predict that research – into release and attained plasma profile over at least two weeks, as well as tolerability, after intramuscular administration – with the fulverstrant formulation disclosed in McLeskey would prove that this formulation was suited for the effective treatment of breast cancer. One must also take into account the nature and extent of the required research. As the research to be undertaken becomes more substantial, complex and/or time-consuming, he will place greater demands on his expectation about the results before embarking on such research than he would if he could simply and quickly have access to the research results.

4.23 The Court of Appeal rejects the submission by Sandoz that there is already a reasonable expectation of success – and the average skilled person would start testing a formulation – if he could already establish by means of 'standard tests' (of whatever nature and extent) whether a specific formulation had a specific result, or if he adopted a neutral 'try and see' attitude, without expectations. After all, this would amount to bypassing the –strict- condition that an invention may only be deemed to be obvious if the average skilled person *would* have arrived at the invention on the priority date, so that it is not enough that he *could* have arrived at the invention.

4.24 The position adopted by Sandoz, that the average skilled person would have suspected or seen the possibility, based on McLeskey, that the castor oil fulvestrant formulation was (or could have been) the same as that used in the Howell research, and that he would therefore simply start testing this, cannot therefore be accepted as correct. It follows from the correct application of the test to be applied in the problem solution approach – that an invention may only be regarded as obvious if the average skilled person <u>would</u> have arrived at the invention – that a pointer may be found in the prior art that would

prompt the average skilled person to look in a specific direction for the solution. The absence of 'preconceived opinions' or 'serious obstacles' (as argued by Sandoz) does not signify the actual existence of a (suspected) *possible* solution that can be investigated as a pointer or that – without a pointer – this would be sufficient to assume a reasonable expectation of success.

4.25 The origins of the castor oil fulvestrant formulation, provided by Zeneca, the legal predecessor of AstraZeneca, do not amount to a pointer. If all of this non-technical information may be considered in the context of the problem solution approach – which after all investigates whether a notional individual would reach a specific technical solution by making technical connections – then the average skilled person would still not assume with sufficient certainty, on this basis, that this formulation was the same as that used in the Howell research, which would generate the possibility of a reasonable expectation of success. Based upon his general professional knowledge, the average skilled person would know that before undertaking clinical tests as in the Howell research, this would be preceded by different tests, specifically including animal tests, in order to investigate for instance the stability and tolerability (side-effects) of a specific formulation. The McLeskey research did not investigate the castor oil fulvestrant formulation for therapeutic effect, but only used it to ensure that the production of oestrogen in the research mice was completely blocked in the research into the effect of FGF on the oestrogen-independent growth of breast cancer cells. The average skilled person would therefore perceive that only the (sufficiently high) concentration of fulvestrant was relevant to for this and that the formulation (and its effect on tolerability) added little to this. This is also apparent from the other fulvestrant formulations used in McLeskey, in which the fulvestrant was dissolved in 100% ethanol, a formulation that is unsuited to clinical use in humans. The average skilled person would therefore take into account that the formulation provided by Zeneca was one that it had itself used in pre-clinical animal trials (and that for precisely this reason could be made available free of charge without objection).

4.26 This is not altered by the fact that the formulation supplied by Zeneca is described as 'pre-formulated' in McLeskey. Based on the various statements made by the range of experts, the Court of Appeal is not for the time being convinced that this term would be understood by the average skilled person, in the context of the research reported on in the McLeskey publication, where the researchers themselves prepared a number of formulations, in any other way than that the castor oil fulvestrant formulation was supplied pre-prepared and therefore ready for use. There is not sufficient evidence for the assertion by Sandoz that the average skilled person would infer from the simply expression 'pre-formulated' that the formulation was intended for clinical research (more specifically Howell's research). This is all the more cogent as the combination of excipients was unusual and the formulation contained a high percentage of alcohol, as is also acknowledged by the party

expert for Sandoz, Prof, Vromans ('Vromans'), (5th opinion, paragraph 23). The Court of Appeal regards it as unbelievable that the average skilled person would imagine, precisely because of this unusual formulation, that it has been developed and was intended for clinical research, as stated by Vromans, In the provisional view of the Court of Appeal, and taking into account the findings already made at 4.25 above, the average skilled person would at the very least perceive that this formulation – just like the other formulations used in McLeskey that were typically intended for use in animal trials – had been prepared previously by Zeneca for use in the formulation phase (not necessarily leading to satisfactory results).

4.27 As previously held, the castor oil fulvestrant formulation in McLeskey is used exclusively as an oestrogen blocker in research into the influence of FGFs on hormone-independent breast cancer. That publication accordingly provides the average skilled person with no information at all on therapeutic effectiveness for the treatment of hormone-dependent breast cancer, for which the active ingredient fulvestrant is used in Howell. Nor does the uterus test provide him with this information. As already held above at 4.9, this can be used to demonstrate anti-oestrogen activity, but the uterus test has no predictive value for suitability in relation to breast cancer treatment, the more so as McLeskey does not mention the relevant data relating to the extent of anti-oestrogen activity (including in relation to the dose that is or can be administered to humans).

4.28 Nor does McLeskey contain any information concerning the pharmacokinetic characteristics (absorption, ie, the release of the active ingredient into the bloodstream, the blood plasma concentration and the elimination, ie, the breakdown of the active ingredient before it reaches the oestrogen receptors). In McLeskey, the formulation was administered subcutaneously to mice on a weekly basis. McLeskey does not disclose the resulting plasma profile. This means that one cannot see at this stage why the average skilled person would assume, with a reasonable expectation of success, that the weekly subcutaneous administration of castor oil formulation from McLeskey to mice would have the same pharmacokinetic characteristics as the fulvestrant formulation with intramuscular administration to humans once every four weeks, as disclosed in the Howell research, the more so because the relevant factors include not just the concentration of the active ingredient, which Sandoz appears to assume, but (especially) also the method of administration (which has an effect on bio-availability) and the combination of the excipients used. This is also reported in a publication by (among others) Vromans (Kalicharan and Vromans et al. *Spatial distribution of oil depots monitored in human muscle using MRI,* in *International Journal of Pharmaceutics* 505 (2016) 52-60), which states: '*Although many i.m [intramuscular – Court] oil depots for sustained drug delivery have been marketed, the rate and extent of drug release is often difficult to predict.'* and which mentions various factors that determine the pharmacokinetic characteristics of a drug. The Court of Appeal is therefore not at this stage sufficiently convinced by Vromans' statement (1st opinion

para 64 *et seq*.) that the average skilled person would consider that the formulation from McLeskey was the same – and would therefore have the same effects – as that used in the Howell study, due to the coincident concentration of fulvestrant.

4.29 Likewise, McLeskey teaches the average skilled person nothing about the tolerability of the castor oil fulvestrant formulation. The mere fact that the excipients used in this are each inherently normal for use in human drugs, as stated by Vromans (1st opinion, para 68) says nothing about the effect of the specific combination of these in the concentrations used. To the extent that the average skilled person could infer anything from McLeskey in relation to the tolerability of the castor oil fulvestrant formulation, this would be more of a cause for concern than reassurance. The percentage of alcohol (20% in a combination of equal parts benzyl alcohol and ethanol) in the formulation would create a sense of reticence in the average skilled person. In addition to the more practical problems with this volume of alcohol in the solution mentioned in the patent, there is no dispute that the average skilled person, based on his general professional knowledge, would know that a further problem with this would be that alcohols quickly disappear from a solution in oil after administration in humans, giving rise to a risk of irritation at the injection site (see *Schaupp,* paras 11-12, 31-32 and Vromans, 5th opinion, para 29). Given the poor solubility of fulvestrant in the oil remaining after diffusion of the alcohols, the average skilled person would expect that the fulvestrant would precipitate at the injection site, increasing the risk of irritation and, in serious cases, necrosis around the injection site. Because fulvestrant inhibits the growth of the tumour but cannot cure the cancer, fulvestrant injections will be administered over a longer period at the same site, namely the gluteus muscle. Contrary to the suggestion made by Sandoz, irritation/necrosis at the injection site is therefore a serious problem that a formulation expert would certainly wish to avoid. The fact that tolerability is an important aspect of a drug with intramuscular administration is also evidence from the fact that Howell explicitly reports that there was no irritation at the injection site (*'The long acting formulation of [fulvestrant] used in this study appeared well-tolerated locally at the site of injection despite the relatively large volume (5 ml) administered')*.

4.30 This leads to the conclusion that McLeskey contains no pointers that would prompt the average skilled person to start investigating the castor oil fulvestrant formulation it discloses, with a reasonable expectation that this formulation would be suited to the treatment of breast cancer, in the sense that the formulation was tolerable and would result in a sufficiently high blood plasma level for at least two weeks after intramuscular administration. The serious possibility that this formulation was an animal formulation, that it appeared to be insufficiently tolerable due to the percentage of alcohol combined with the poor solubility of fulvestrant, and also the absence of any indication of therapeutic effectiveness would restrain him from embarking

upon a long-term, costly research process that would include in vivo clinical trials on animals and humans.

4.31 The conclusion, in the provisional opinion of the Court of Appeal, is that there are no serious, realistic prospects that EP 138 will be annulled in proceedings on the merits, and that the challenged decisions should be upheld. Having regard to the injunctions against infringement already imposed in terms of EP 138, Sandoz has no interest in the injunction against enforcement by AstraZeneca, based on EP 1 669 073 and/or NL 1017075, which it is seeking in the counterclaim proceedings. This means that none of the grounds for appeal proposed by Sandoz will succeed."

[82] I have set out at some length the decision of the Dutch court in that I believe it clearly illustrates why it is impossible on the basis of the arguments I have heard to say that a case put forward, on the same basis as argued before the Dutch court, does not amount to a *prima facie* case.

[83] The pursuers' position when properly analysed is not merely a bare denial: with some justification, it says that it requires further information from the defender to fully develop its case; it says it believes it will run a line of defence broadly as set out in the Dutch case; it points to having had success in arguing the issue of validity in other jurisdictions based on arguing this line. I believe that when the foregoing is looked at, it is clear that a *prima facie* case has been put forward.

[84] Over and above the foregoing it does seem to me that this is once more a situation where the defender may prevail at proof, however, at this stage the dispute is not capable of resolution without expert evidence and full consideration following thereon. The issues raised by the defender do not provide a reason for finding there is no *prima facie* case.

[85] For the foregoing reasons I am clearly of the view that the pursuers have a *prima facie* case with respect to these two patents.

[86] Having held that the pursuers have a *prima facie* case with respect to the patents I turn to the second issue of balance of convenience.

[87] Mr Duncan contends that damages would not be an adequate remedy for the pursuers. In putting this forward he relied on the affidavit of Mr Drury-Dryden who is the oncology business unit director for the second pursuers.

[88] He submitted on the basis of the evidence contained in Mr Drury-Dryden's witness statement that the balance of convenience strongly favoured the pursuers.

[89] His position was that the pursuers would suffer irreparable and unquantifiable damage were the court not to grant interim interdict and they were ultimately successful.

[90] That such harm would result to a patentee in the case of the launch of a generic pharmaceutical product is well recognised (see: *Terrell on the Law of Patents* at 19-88 and 19-89).

[91] In elaboration of that submission he argued:

a. Unless restrained by *interim* interdict the Defender will launch the first generic competitor to Faslodex® on the market in Scotland: it has indicated its intention to do so on or after 1/11/17 and has further failed to give an undertaking that it will await final judicial determination of its Petitions and Summons for Non-Declarator;

b. As a consequence, the Second Pursuer will lose sales to the Defender as the Defender will almost certainly seek to undercut the Second Pursuer on price: this loss of sales could be extremely significant. As Mr Drury-Dryden explains in his witness statement, Faslodex® is made available on the NHS in Scotland via the Patient Assess Scheme ('PAS') and is supplied direct to pharmacies[8]. The Pursuers' assumption is that, if launched, Fulvestrant Teva would also be supplied direct to pharmacies and would be directly substitutable for

[8] §§15-17 Drury-Dryden

Faslodex®. Mr Drury-Dryden's assumption is that the '*vast majority*' of prescriptions for Faslodex® are written generically[9]. The consequence is that, once launched, Fulvestrant Teva would be expected to quickly capture a significant portion of the Faslodex® market. In addition, once a generic product was launched, NHS Scotland might open up a tender process in which case the Pursuers would have to directly compete with the Defender on price if it wanted to secure a contract: the consequence of that might be that the Defender would replace the Second Pursuer as the NHS supplier of fulvestrant in Scotland[10]. The Scottish market is a valuable one:

c. If Fulvestrant Teva is launched, the Pursuers will therefore lose their market rights to the valuable Scottish market as the holders of the various patent monopolies in respect of Falsodex® some 3 – 3 ½ years before that monopoly would otherwise have expired;

d. As Mr Drury-Dryden explains at §§27-32 of his statement, the broader impact of prolonged availability of generic product is impossible to quantify because of the large number of unpredictable factors which include: (i) the level of discount that the Defender will offer against the current Faslodex® price; (ii) whether multiple generic companies are waiting in the wings with granted UK marketing authorisations to the ready – Sandoz, Dr Reddy's and Actavis – and it is expected that if no *interim* interdict is awarded against the Defender, these generics will enter the market within a matter of weeks (§§33-35 Drury-Dryden);

[9] §§17-18 Drury-Dryden
[10] §19 Drury-Dryden

(iii) the effect on price if multiple generics do come onto the market; (iv) whether a new procurement process will be introduced by NHS Scotland;

e. If the Pursuers are ultimately successful at proof and obtain final interdict, they will find it very difficult, if not impossible, to re-establish the current Faslodex® price: §§46-48 Drury-Dryden;

f. The Pursuers are reasonably apprehensive that launch of a generic product will not only impact on their sales but also on their reputation – both with the NHS and with patients - §49 Drury-Dryden;

g. Faslodex® has recently been approved for further indications in the treatment of breast cancer and more are anticipated shortly: the market for Faslodex® is therefore likely to increase during the remainder of the monopoly period. This makes assessment of damages for patent infringement even more difficult in the future (see §36 Drury-Dryden).

[92] Beyond the above it was his position that the present case was one where if it subsequently transpired that the interdict ought not to have been granted, the defender would be adequately compensated in the event of an action for wrongous interdict. This was based on Mr Drury-Dryden's statement (at paragraphs 50-51).

[93] If the defender sought to argue that it would suffer unquantifiable damage were it to be subject to wrongous interdict, this would be based on a loss of first mover advantage argument. That is an argument commonly run by generics companies in these types of proceedings. However, such an argument was not convincing in light of the fact that there were multiple other generics waiting in the wings and accordingly any such advantage was likely to be short lived (see Drury-Dryden at paragraphs 33-35).

[94] Lastly, were the court to form the view that the defender may not be adequately compensated in damages if it turned out that *interim* interdict ought not to have been awarded, this is a case where the status quo favours the grant of *interim* interdict. At present the second pursuer is in the market with its own patented product and no other generic products are on the market. Maintaining the status quo pending final determination of this action is the best way to ensure that injustice is ultimately avoided.

[95] In contrast, the defender has shown no urgency to date in launching its product: it had its marketing authorisation in place since March 2016. In addition, the defender had been aware of the patents for some considerable time and yet has failed to clear the path prior to launch. This submission was made under reference to the chronology, which is set out earlier in this Note. The defender had opposed one of the patents as far back as 2006. In addition, it applied for its marketing authorisation on the basis of Falsodex® as the reference medical product back in 2014 and obtained its marketing authorisation for Fulvestrant Teva back in March 2016. Therefore it had plenty of time to clear the way in advance of its launch in Scotland. It had not taken this course. There was never any prospect of the proceedings which it had raised with respect to the validity of the patents being determined before 1 November 2017. The defender is a sophisticated player in the pharmaceutical litigation field and was well aware of the need to clear the way in advance of launch.

[96] Mr Cormack contended that damages would not be an adequate remedy for the defender.

[97] Mr Cormack commenced his argument by making two submissions:

(a) The defender had offered to keep full records of sale if *interim* interdict was refused until the final resolution of the substantive issues. This ensured that

any point regarding difficulty in quantifying the loss of the pursuers was answered.

(b) It is a very weak point to argue that loss is possible on the basis of other generic suppliers coming into the market.

[98] He submitted there was no specific information which was put forward on behalf of the pursuers that there would be entry at an early point. In addition Miss Jarvis (whose witness statement he relied on) expressly stated that the defender had no intelligence of an imminent launch by other generic producers.

[99] The pursuers offer no explanation of why they assert the likelihood of a price spiral which will be irreversible. This is because, in reality, significant, irreversible downward price pressure on the patent owner, which tends to support interim injunctions in generic litigation, will be absent in this instance. This is a very important point of distinction between the position in this case and "classic" generic litigation. This again should count heavily against the pursuers' case being regarded as a proper basis for the grant of interim interdict.

[100] There is a familiar competition in pharmaceutical patent cases at the interim relief stage: irreversible downward price spiral v loss of first mover advantage. The former is a key feature where interim relief may be granted to the patent owner.

[101] The pursuers effectively say that the defender should wait to clear the way. However, if the defender's case on the merits is correct, then it is entitled to enter the market now. There is no infringement of an invalid patent and it is not necessary to wait for revocation. As to the significance of clearing the way: see Terrell at 19-92/19-93; *Smithkline Beecham Plc* v *Apotex Europe Ltd* [2003] FSR 31. It is a factor but it does not necessarily

swamp other facts which point in a different direction (*Cephalon Inc* v *Orchid Europe Ltd* [2010] EWHC 2945 at [71]-[72]). The significance of clearing the way arises from concern about irreparable damage being done to the patentee in terms of irreversible price depression (see CIPA 61.12; this is warranted by the decision in *Smithkline* v *Apotex* – see especially [32]; [38]-[39]). Such is not a factor in the circumstances of this case which are not typical of generic pharmaceutical related litigation. This is explained in detail in the witness statement of Ms Jarvis which clearly distinguishes the present situation from the kind of case envisaged by the pursuers' unsupported averments.

[102] These are not principles of law, but rather matters which may be among those to be assessed on the evidence in the particular circumstances in assessing where the balance of convenience lies (*Cephalon* at [51]). The pursuers here put forward no evidence but treat these matters in effect as principles of law which is the wrong approach.

[103] Irreversible price reduction was not established on the evidence in *Cephalon* ([61] and [62]), where an interim injunction was refused. The balance of convenience in the present case is even more in the defender's favour than was the case in *Cephalon* (see [70]).

[104] Although the pursuers do not address it, the public interest is relevant: *Waste Systems International Inc* v *Eurocare Environmental Services Ltd* 1999 SLR 198 at 202B. It is significantly in the public interest that interim relief be refused to the pursuers in this case.

[105] He then turned to the statement of Ms Jarvis and took the following points from her statement:

[106] As Ms Jarvis explains with reference to the circumstances of the market, fulvestrant is administered via injection, predominantly in a hospital setting (Ms Jarvis [1.10]). It is not dispensed in the community pharmacies over the counter.

[107] Since its launch in 2004, the pursuers' Faslodex has been the only fulvestrant product available in the UK. It has a brand list price of …… per pack (Ms Jarvis at [3.6]).

[108] The next NHS tenders in respect of a group of oncology products, including fulvestrant, are scheduled for January 2019 in Scotland and May 2019 in England (Ms Jarvis at [6.2]).

[109] Although the pursuers do not say, it appears that they do not supply under a tender made and accepted by NHS Scotland or England, because to date fulvestrant has only been available from them and there was no need for them to tender [Ms Jarvis at [5.21], [6.3] and [6.4]).

[110] Because of the tender position, if Fulvestrant Teva is launched, the defender's sales team will need to pursue sales direct with individual hospitals on a sale by sale basis (Ms Jarvis at [7.1] and [7.4]). This will take time and effort and is not like a case where pharmacists switch to a generic *en masse* because they see a reduced price and more profit for them ([7.6]). The defender is willing and able to do this but it is a significant disincentive to other generic suppliers entering the market.

[111] Faslodex will not move categories in the UK Drug Tariff and will remain listed in Category Z at the pursuers' list price (Ms Jarvis at [5.14] and [7.5]). The usual concerns about movements between the categories in the Drug Tariff and the impact of that on pricing simply do not apply.

[112] An acceleration of the current tender schedule is liable only to occur if there are 2-3 generic suppliers established in the market. This is unlikely while the present litigations are pending.

[113] In the result, if interim interdict is refused, it seems that for the relevant period there will be two suppliers in the market, the pursuers and the defender. To the extent that the

pursuers lose sales to the defender, every sale will be recorded in the defender's sales records. The pursuers will readily be able to say what profit they have lost on each sale should they succeed in these litigations at the end of the day. To the extent that the pursuers also suffer loss because they reduce their price, on an *ad hoc* basis, to compete with the defender, they will also be readily able to quantify that loss. Because there will have been no structural change to the pricing, if the pursuers succeed at the end of the day they will be able to remove any *ad hoc* reductions in their price. There will be no downward price spiral. Damages which the defender is able to pay, will be a very good remedy for the pursuers.

[114] Finally, turning to what would happen were the defender to be subject to *interim* interdict and to succeed at the end of the day he said this:

[115] There will be very significant difficulties of quantification because it will likely not be possible to establish the dual supply arrangement with just the pursuers and the defender in the market. At the point at which the defender succeeds in the litigations at the end of the day, it is likely that other generic suppliers will enter the market so that (i) the defender will have to offer a substantially greater discount than would be the case in a dual market (Ms Jarvis at [8.2] and [8.3]); (ii) tenders may arise either because they are scheduled or because an interim tender is called; (iii) aside from the price implications of a tender situation, the defender may lose the tender and either be locked out of the market for the tender contract durations of between 3-5 years or, at best, have to undercut the pricing of the winning tenderer in order to make *ad hoc* sales, although this is unlikely to work [Ms Jarvis at [8.4]).

Discussion

[116] Both parties accepted that the other has the ability to pay any likely award of damages.

[117] So far as the strength of the pursuers' *prima facie* case is concerned, I do not believe that, as urged upon me by Mr Cormack (if I rejected his primary submission that a *prima facie* case had not been established) it can be characterised as a weak case. I do not for the same reasons as I have set out above in holding that there is a *prima facie* case believe that it is a weak case.

[118] Accordingly, I do not believe any issue of the weakness of the *prima facie* case is a factor which weighs at all in consideration of the balance of convenience.

[119] Given the above, I therefore believe the primary question in considering the balance of convenience is this: would damages be an adequate award for the pursuers if *interim* interdict was refused and they were successful at proof and would damages be an adequate award for the defender, if *interim* interdict was granted, and it was ultimately successful at proof. Or put another way: who is likely to suffer the most irreparable harm?

[120] As a starting point I accept Mr Cormack's submission that the defender's undertaking to keep records of sales is an important consideration as it means that the direct loss to the pursuers by the defender's drug being made available is easily quantified. I accept that this would allow one part of the pursuers' claim, namely: what sales it had lost to be fairly easily calculated.

[121] However, one of the principal bases upon which Mr Duncan advanced his position that irreparable and unquantifiable damage would be done to the pursuers related to concerns on their part about the impact of entry into the market of other generic

manufacturers and the irreversible downward price spiral that would result. Mr Cormack submitted that this part of the pursuers' case was weak. I do not accept that submission.

[122] It appears to me that when Mr Drury-Dryden's whole witness statement is had regard to that what is put forward is a strong case with respect to this particular aspect.

[123] Mr Drury-Dryden points out that three other companies have marketing authorisation for Fulvestrant (see paragraph 33). He then in his witness statement turns to look at two other generic launches in order to support his view on the impact on price of such entry(see: paragraphs 37 – 40). In the first generic launch three generic manufacturers launched generics within a few days of patent protection ending. In the other example to which he referred following a non-infringement decision two generic companies launched in under two months. With respect to how likely is the entry at an early point of other generic manufacturers there was also the evidence of *Sandoz* seeking to enter the Dutch market (see: the Dutch case).

[124] The above appeared to me to be reasonably strong evidence of likely early entry into the market of other generic manufacturers.

[125] On the other side Ms Jarvis' position, came to no more than this, that there was no market intelligence that these other manufacturers would enter in early course. Although it appeared to be accepted that if the defender were successful at proof there would be almost immediate entry by such generic competitors.

[126] The two previous launch examples used also showed the collapse of the price.

[127] The next issue was this: would such downward spiral be irreversible?

Mr Drury-Dryden at paragraph 44 said:

> "The ultimate outcome of premature generic entry would be: fulvestrant would be available at a significant discount for a significant period of time, and following the removal of generic manufacturers by a final injunction, any attempt by AZUK to

> charge a higher price would lead to a significant increase in NHS spend on fulvestrant as compared to the spend when generic products were available. Although such an increase would simply be a reassertion of the exclusivity to which AZUK would be entitled, as explained further below it might not be feasible to implement such an increase and the attempt to do so would cause harm to AZUK's relationship with NHS Scotland which is not capable of being compensated by monetary damages."

[128] He went on to say at paragraph 46:

> "As explained at paragraphs 24 to 45 above, although there are a number of ways in which the financial harm of a premature generic launch could materialise, it is clear that the reimbursement price of fulvestrant would be reduced for a significant period. The change in market is particularly difficult to assess given the extension of indications occurring in parallel. Any attempt by AZUK to increase prices back to pre-generic launch levels would be met with strong resistance from NHS Scotland. This resistance might be sufficiently strong to make it impossible for AZUK to increase its prices; if AZUK were to raise its prices, this is likely to and would have significant adverse consequences for AZUK's relationships with the NHS Scotland as a whole."

[129] Paragraphs 44 and 46 appear to me to reflect commercial sense. The pursuers could reinstate their price but that would not be in its wider commercial interests and would simply not reflect the commercial realities in the real world.

[130] It appeared to me that looking to the evidence of Mr Drury-Dryden that a rapid, severe and probably irreversible price spiral would result on the court not granting an *interim* interdict.

[131] The defender made great play in the affidavit from Ms Jarvis that the present case was not a classic generic pharmaceutical litigation case where there was an argument that there would be an irreversible downward price spiral resulting from the entry into the market of a generic product. It had to do this, in that if the present case fell into the classic category, there was a clear line of authority that interim relief should be granted. The core of this argument was that Falsodex would not move categories in the UK Drug Tariff. Thus there would be no structural price change which would be irreversible. It was not, as I

understood it, a matter of dispute that it was correct that if the defender's generic drug is introduced the patented drug would not move categories. However, Mr Duncan submitted that this was a distinction without a difference. I believe that that submission is correct. The important question is what will happen in the real commercial world?

[132] It appears to me that the answer to the above question is that the price would be highly unlikely to be restored to pre generic entry levels if the pursuers were ultimately successful. The pursuers could of course seek to restore the price, however, as pointed out by Mr Drury-Dryden in the commercial world that is simply not going to happen. Thus I believe this is a classic generic pharmaceutical case.

[133] In addition account has to be had to other matters: NHS Scotland deciding to have an earlier tendering process and the effect that this would have on the pursuers, the danger of damage to the pursuers' relationship with NHS Scotland and the extension of indications.

[134] For the above reasons I consider that damages would not be an adequate remedy for the pursuers if *interim* interdict was not granted and at Proof an interdict was granted.

[135] Turning to the question of the defender's position. The defender says that any loss which would be incurred by it would not be quantifiable should the court grant an interim interdict and ultimately the defender was successful at Proof.

[136] It in essence says that the loss is not quantifiable in that the defender would lose its first mover advantage and for the reasons set forth in Ms Jarvis' witness statement the loss of such status cannot be quantified. It is this loss of first mover advantage which in essence founds its case.

[137] In that I have accepted that the likelihood is that other generic manufacturers will enter the market at an early stage, should the court not grant interim interdict, I believe that

the fundamental basis for the defender's argument relative to the issue of unquantifiable loss falls at the first hurdle. There would I think be no significant first mover advantage.

[138] In early course the defender would, on the basis of my previous finding, be likely to lose its first mover advantage and thus losses would not likely be material from the loss of first mover advantage and I do not believe the difficulties in quantifying them would be as great as submitted by the defender.

[139] For the foregoing reasons I believe that the balance of convenience favours the pursuers.

[140] Had I thought that the situation was that each party's losses were in reality unquantifiable, then even in those circumstances, I would have held that the balance of convenience favoured the pursuers.

[141] In *Teva Pharmaceutical Industries Ltd* v *Actavis UK Ltd* 2015 EWHC 2604 (Pat) Mr Justice Arnold faced such a situation, that on both of the contesting hypotheses, put before him one side was going to suffer harm which would be difficult to quantify, and therefore there was the risk of irreparable harm.

[142] In seeking to deal with this issue, he said this:

> "In those circumstances the court's task is to adopt the course which appears least likely to cause the risk of ultimate injustice.
>
> 43. In determining which course is least likely to cause ultimate injustice, it is a council of prudence to preserve the status quo. In that connection, it seems to me that an important factor to take into account is Actavis failure to undertake what is familiarly known as 'clearing the path.'"

[143] I would adopt those observations. It seems to me in such circumstances that the appropriate course is to look at what is least likely to cause the risk of ultimate injustice. It also appears to me that in looking at this, a critical factor is the issue of "clearing the path".

[144] In the present case I believe that looking to the chronology, which I have set out earlier in this Note, the defender had it so wished could have cleared the path, prior to its proposed date of launch. It did not take steps to do so. The raising of the three substantive actions at the date at which they were raised offered no opportunity of a decision in these matters being reached prior to the date of launch. The defender had had its marketing authorisation for some considerable time. It was aware of the existence of the patents. It is clearly a major and sophisticated player in the pharmaceuticals world who would be in no doubt that the pursuers would seek to defend their patents. In these circumstances its failure to clear the path appears to me to be a crucial fact in deciding where the balance of convenience lies. Therefore had I been faced with the situation in this case as Mr Justice Arnold was in *Teva Pharmaceutical Industries Ltd* v *Actavis UK Ltd* I would have held that the balance of convenience favoured the pursuers.

Conclusion

[145] For the foregoing reasons I find that a *prima facie* case has been shown with respect to each of the patents and that the balance of convenience favours the pursuers with respect to the patents.

Decision

[146] I accordingly grant interim interdict in terms of the second conclusion as amended.

[147] I reserve the position regarding the expenses.