Neutral Citation Number: [2022] EWHC 2847 (Pat)

IN THE HIGH COURT OF JUSTICE
BUSINESS AND PROPERTY COURTS OF ENGLAND AND WALES (ChD)
INTELLECTUAL PROPERTY LIST
PATENTS COURT

Royal Courts of Justice, Rolls Building
Fetter Lane, London, EC4A 1NL

Date: 10 November 2022

Before :

HIS HONOUR JUDGE HACON

- -

Between :

(1) TEVA PHARMACEUTICAL INDUSTRIES LIMITED **(2) TEVA UK LIMITED**	**Claimants**
- and -	
(1) NOVARTIS AG **(2) NOVARTIS PHARMACEUTICALS UK LIMITED**	**Defendants**

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- -

Tom Moody-Stuart KC and **Katherine Moggridge** (instructed by **Pinsent Masons LLP**) for the **Claimants**
Andrew Waugh KC and **Henry Ward** (instructed by **Bristows LLP**) for the **Defendants**

Hearing dates: 22-25 February, 28 February, 1 March, 3-4 March 2022

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Approved Judgment

I direct that pursuant to CPR PD 39A para 6.1 no official shorthand note shall be taken of this Judgment and that copies of this version as handed down may be treated as authentic.

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HIS HONOUR JUDGE HACON

Judge Hacon :

Introduction

1. The claimants (collectively "Teva") bring this action for revocation of two patents ("the Patents") owned by the first defendant, European Patent (UK) No. 2,964,202 ("EP 202") and European Patent (UK) No. 3,124,018 ("EP 018"). Teva also seek a declaration of non-infringement in relation to their product Teva DFX, used for iron chelation.

2. The second defendant is the exclusive licensee of the patents. I will refer to the defendants collectively as "Novartis". They counterclaim, alleging infringement of both patents. They say Teva DFX is an equivalent of the product protected by each of the patents.

Background to the invention

3. Since the 1960s iron chelation treatments, removing excess iron from a patient's blood, have been available using a compound called deferoxamine. Removing iron is typically required where the patient has been given a blood transfusion or is suffering from certain blood conditions. Up to the late 1980s the treatments required subcutaneous infusions lasting 8-12 hours at least 5 days a week. Aside from the major inconvenience in its administration and associated issues with patient compliance, deferoxamine had side effects which could be severe and even fatal.

4. In 1987 a product called deferiprone came into use with dosing needed 3 times a day. This was still far from ideal and there remained side effects.

5. A third drug, deferasirox was first marketed in the EU in 2006. It came as a dispersible tablet with the brand name Exjade and marked a significant advance since it could be taken just once a day, with correspondingly improved patient compliance. Less helpfully, each dose required between 3 and 7 tablets which had to be dispersed in water or other liquid, creating an unpalatable sludgy drink to be consumed on an empty stomach. Some patients suffered from side effects, principally in the form of nausea, vomiting, diarrhoea or abdominal pain.

6. The Patents claim a further improvement, being a swallowable film-coated tablet formulation of deferasirox.

Applications to amend the patents

7. The application for EP 018 was divided out of that for EP 202 and so they share the same priority date, 8 March 2013. Their specifications are almost identical; no material difference was identified during the trial.

8. Both Patents have been upheld in the Opposition Division of the EPO with amended claims. Appeals are pending. Before this court there are unconditional applications to amend the claims to bring them into line with the claims allowed by the Opposition Division. The proposed amendments to the claims of EP 018 bring them close to those

of EP 202. Novartis has also made a conditional application to further amend the claims of both Patents.

9. Such is the overlap between the specifications and proposed unconditional amendments of the two Patents that for the most part I can treat the two as one and will do so unless I state otherwise.

The skilled team

10. The parties were agreed that the skilled team consisted of three notional individuals: a clinician, a formulator and a pharmacokineticist. The formulator is the primary addressee since the Patents are teaching new formulations. He or she would be assisted by the clinician's advice on the medical view of iron chelation therapy, clinical requirements and any difficulties with existing therapies. The pharmacokineticist would provide input in the form of pharmacokinetic data relating to the active pharmaceutical ingredient ("API"), e.g. its bioavailability and half-life.

Common general knowledge

The law

11. Both sides referred to Arnold J's summary of the law on common general knowledge in *KCI Licensing Inc v Smith & Nephew plc* [2010] EWHC 1487 (Pat) at [105]-[112], approved on appeal: [2010] EWCA Civ 1260 at [6].

12. It was agreed that the following formed part of the common general knowledge in March 2013.

Clinical CGK

13. Principally three disorders – thalassaemia, sickle cell anaemia and some blood cancers – require repeated blood transfusions. The introduction of new blood on a large scale will cause a build-up of iron in the patient. The body has no mechanism for excreting iron and its accumulation, if left unchecked, can be fatal. Hence the need to remove excess iron by means of iron chelation therapy.

14. Thalassaemia is a genetic disorder which inhibits the production of haemoglobin. The severity of the condition varies. A distinction is made between transfusion dependent thalassaemia ("TDT") and non-transfusion dependent thalassaemia ("NTDT"). Patients requiring 8 transfusions or fewer per year are typically said to have NTDT, those requiring more than 8, and it may be many more than 8, have TDT. Thalassaemia is most common among people of Mediterranean, African (including North African), Southeast Asian and Chinese descent.

15. Sickle cell anaemia is also a genetic disorder. Red blood cells are produced in a deformed, sickle shape and become rigid in low oxygen environments. They pass less easily through narrow capillaries than do healthy, more malleable red blood cells, giving rise to occlusion of capillaries and ischaemia – the insufficient supply of blood to an organ or tissue. Sickled cells have a typical life span of only 16-20 days, compared with 120 days for healthy cells. This means that the rate of destruction of sickled cells can outpace replenishment, leading to anaemia. The condition is more common in those

of African, Middle Eastern, Indian, Caribbean, South and Central American and Mediterranean descent.

16. Myelodysplastic syndromes ("MDS") are blood cancers which affect the production of blood cells in the bone marrow. Patients with MDS have an increased risk of developing acute myeloid leukaemia. MDS may be due to genetic mutation and in such instances is most common among patients over 70 years old. Alternatively it may be caused by chemotherapy or radiotherapy inducing damage to bone marrow.

Formulation CGK

17. The approaches available to a formulator at the priority date were all standard but there were alternatives to be selected. There were at least two textbooks which formed part of the CGK and which would be consulted by a formulator. It was more straightforward to reformulate an existing approved medical product than to formulate for the first time.

18. The preferred and most common route of administration of a drug is the oral route, either using a swallowable tablet or by taking the drug dissolved or dispersed in a liquid. Swallowable tablets are the most popular among patients. Both swallowable and dispersible tablets are made from powdered, crystalline or granular API, almost always compressed, together with one or more excipients, i.e. binders, disintegrants, lubricants, diluents, glidants or surfactants. All relevant excipients were within the CGK. The Handbook of Pharmaceutical Excipients was also part of the CGK, providing information as to the properties, typical use, incompatibilities and the safety and regulatory status of all excipients used.

19. If the proportion of API in the tablet is to be high, the formulator must select excipients which maintain the processing attributes of the tablet despite their being present in relatively reduced quantity. To be avoided are excipients which negatively affect the pharmacokinetics of the formulation or which themselves cause adverse side effects.

20. Two commonly used fillers are microcrystalline cellulose ("MCC") and lactose. MCC has no significant toxic potential. Patients with lactose intolerance may react adversely to lactose in a formulation.

21. The two most commonly used surfactants are sodium lauryl sulphate ("SLS"), sometimes called sodium dodecyl sulphate ("SDS"), and Poloxamer 188 aka Pluronic F-68.

22. Some tablets are coated with a film. The coats fall into three categories. The first are simple water-soluble coats which serve to provide a characteristic colour or other appearance to protect the product from attrition during handling and transportation, to make counterfeiting difficult, to mask the taste of the drug, or all or any of the foregoing.

23. In the second category are enteric film coats. Such coats are functional in that they prevent dissolution in the stomach where pH is low and allow dissolution in the intestinal tract where pH is higher. This avoids acid degradation of the drug in the stomach and/or protects the stomach from the irritant effect of the drug and/or allows the drug to be preferentially absorbed downstream of the stomach.

24. The third category consists of sustained release coats. The coat is formulated to slow the rate of release of the drug and to sustain a consistent release over, typically, 6 to 12 hours.

25. 800mg total weight is generally considered the ceiling for a tablet that remains easy to swallow, although using a caplet shape may increase the ceiling to 1000mg. Self-evidently the API load is lower than the total weight.

26. Dispersible tablets are similarly formed by the compression of API and excipients. Although generally less acceptable to patients, they may have advantages over swallowable tablets such as providing faster absorption or allowing the administration of a larger dose per tablet. Some patients may find it difficult to swallow tablets and prefer a dispersible form. Dispersible tablets may have a simple film coat, but not an enteric or sustained-release coat because the latter two would interfere with dispersion.

27. There are three steps by which an API in a tablet becomes available in the blood stream. They are disintegration of the tablet, deaggregation of the tablet's contents and then dissolution of the API.

28. One of the necessary skills of a formulator is to give the formulation the required dissolution profile. The API must be released and then dissolve in the gastro-intestinal fluids so that it may be absorbed into the blood stream and thereby distributed around the body. APIs vary in their intrinsic solubility and may require a surfactant or other means to enhance solubility. There are standard *in vitro* test methods and dissolution equations which can be used to assist in attaining a suitable profile.

Pharmacokinetics CGK

29. Pharmacokinetics is the study of the effect of a drug over time, i.e. the kinetics of absorption, distribution, metabolism and excretion.

30. Generally, a dissolved drug will pass into the blood stream via the wall of the small intestine. It has a large surface area and typically the drug will take 3-5 hours to pass along and through the lumen. Food, particularly fat, slows the emptying of the stomach, which is why recommendations are given to take some drugs on an empty stomach, allowing faster passage to the small intestine. It also means that the pharmacokinetics of an orally administered drug will be affected by stomach contents when the drug is taken.

31. Pharmacokineticists use the term "bioavailability" to mean the rate at, and the extent to which, an API becomes available at the site of action in the body. There are alternative ways of measuring the bioavailability of a drug. Two principal means employ a graph of the amount of API in the systemic blood plasma over time. The first is AUC (area under the curve) which represents the total amount of unaltered API which enters the blood stream. The second is C_{max} which is the measure of peak plasma concentration.

32. AUC and C_{max} are used to assess the bioequivalence of two products containing the same drug, i.e. the extent to which the products can be considered to be therapeutically equivalent.

Dispersible deferasirox

33. Dispersible deferasirox was licensed in the EU in 2006. Published at the same time was an officially approved Summary of Product Characteristics ("SmPC") describing the properties and conditions of use. This included quite a long list of undesirable effects, special warnings and precautions for use. These were quoted in a Statement of Agreed Common General Knowledge provided by the parties and can therefore be taken to have been part of the CGK at the priority date.

Whether there was a preference for swallowable tablets

34. The Statement of Agreed Common General Knowledge included this:

> "Swallowable tablets (i.e. tablets meant for swallowing, i.e. not dispersed or chewed prior to ingestion; also known as 'conventional tablets') are the most common oral dosage form, due to advantages afforded both to the manufacturer (e.g. simplicity and economy of preparation, stability, and convenience in packaging, shipping and dispensing) and to the patient (e.g. accuracy of dosage, compactness, portability, and ease of administration)."

35. Novartis made much of the fact that there was nothing in the prior art to suggest that swallowable deferasirox had been proposed before the priority date. A central part of Novartis' argument on obviousness was a rhetorical challenge to Teva: why was there then no swallowable deferasirox before the priority date? I will consider that below but it does not displace, in fact it is fully consistent with, the CGK of the skilled team that having swallowable deferasirox in place of the dispersible product was an attractive goal if it could be achieved.

Geographical differences in common general knowledge

36. It was agreed that only the common general knowledge of a skilled team located in the UK is relevant in law. That point of law remains to be authoritatively decided, but the helpful agreement means that I need consider only CGK in this country. It makes little difference. The iron chelation community is international. Individuals travel, communicate with each other whether they travel or not and are aware of information generated outside their geographical base.

37. There was one minor distinction. It was common general knowledge that the proportion of patients with thalassaemia in the UK and elsewhere in Europe is higher than in the United States; the reverse is true of patients with sickle cell disease. Thalassaemia requires treatment either from birth or generally before the child is two years old, whereas sickle cell patients only require treatment when complications from the disease arise, in about 10% of cases, which may be at any age and may last throughout the patient's life. The UK-based skilled team's experience of patients' compliance with treatment and the consequences of non-compliance may therefore differ from that of their US equivalent.

Communication within the skilled team

38. The notional skilled team will be taken to interact to the same extent as would a real team addressing the same project, see *Alcon Eye Care UK Ltd v AMO Development, LLC* [2022] EWHC 955 (Pat) in which Mellor J discusses at [233]-[245] what would have taken place in the context of the technology with which that judgment was

concerned (ophthalmic systems for carrying out cataract surgery) and the correct approach to the instruction of experts replicating a real team in relation to the communication that there should be between the experts.

39. Evidence from both sides indicated that in real life the team would jointly produce a target product profile ("TPP") at the start of the project. The TPP would contain the known characteristics of the API and of the current formulation of the API. It would also contain clinically desirable attributes of a prospective new formulation provided by the clinician in the team.

40. It seems that there was little or no interaction between Novartis' three experts during the preparation of their evidence. That should have happened. Teva argued that this coloured the evidence of Novartis' formulator and I think that is possible.

41. By contrast, Teva sought to mimic real life by passing information from their expert clinician to their expert formulator. That was appropriate in principle because the most relevant communication within the team would consist of information going from the clinician to the formulator. But instead of having their expert clinician draw up her own list of relevant points, Teva's solicitors drafted and provided to the expert formulator a document intended to summarise the relevant information provided to them by the expert clinician. It was exhibited by Teva's expert formulator as "HH-2". HH-2 was the subject of considerable criticism by Novartis in its closing arguments, to which I will return.

The witnesses

42. Each side provided expert evidence from a clinician, a formulator and a pharmacokineticist.

Dr Farrukh Shah

43. Teva's clinician was Dr Farrukh Shah. Dr Shah is a Consultant Haematologist at the Whittington Hospital and since July 2021 has been Medical Director at NHS Blood and Transplant. Since 2004 her day-to-day clinical work has included the treatment of patients with thalassaemia or sickle cell anaemia. She has conducted clinical trials in relation to deferasirox in both dispersible and coated forms.

44. Dr Shah was the subject of a sustained attack by Novartis in closing. This largely came down to Novartis alleging that she had overstated the adverse gastrointestinal effect of dispersible deferasirox in her written evidence and had also overstated concern about lactose intolerance.

45. In cross-examination a leaflet for patients published in November 2015 by Dr Shah's hospital, the Whittington, was put to her. She was named towards the end as one of the haematology consultants at the hospital. It included this:

> "**Effects on the gut**
>
> These occur in about 11 per cent of patients, are typically mild and do not persist. They include stomach pain, nausea, and vomiting, diarrhoea or constipation. These symptoms rarely require dose adjustment or stopping treatment and tend

> to settle down over a few weeks. If these persist or you suffer from severe vomiting or diarrhoea every time you take Exjade, the doctor prescribing the treatment should be informed.
>
> Mostly these symptoms can be managed effectively by adjusting the time of day the medication is taken or taking it with food. Stomach ulcers have rarely occurred."

46. It is possible that leaflets provided to patients err on the side of reassurance to ensure patient compliance with the prescribed drug regime. Professor Nirmish Shah, Novartis' clinician, could not have emphasised more strongly the importance of patient compliance, particularly in the case of iron chelation treatments. In his first report he acknowledged that there were barriers to compliance in taking dispersible deferasirox, listing (i) steps needed to disperse the tablet in water or a beverage, (ii) the need to consume a relatively large amount of liquid, (iii) the unpleasant taste and texture of the liquid and (iv) the need for a patient to take the dispersible tablet on an empty stomach and not to consume food for 30 minutes afterwards. In cross-examination he acknowledged that GI side effects, which could be severe, were also a barrier to compliance.

47. The evidence overall was that dispersible deferasirox could cause severe side effects but not always and the effects could be temporary. On the other hand, such was the high importance of ensuring patient compliance, the skilled clinician would have thought it important to minimise these effects. In my view the attack on Dr Shah's credibility when she emphasised this was not merited.

48. Dr Shah's written evidence gave the impression that there were discussions in the field and with Novartis at the priority date about how to overcome compliance issues by way of a new formulation. In cross-examination it emerged that any such discussions happened after the priority date. This was unfortunate and had some limited significance, which I discuss below.

49. Novartis also alleged that Dr Shah's evidence was to be treated with caution because she was aware of a film-coated and swallowable preparation of deferasirox before she gave evidence. It is important where a witness has such knowledge for them to reflect on how it may influence them, see *Fisher and Paykel Healthcare Ltd v Flexicare Medical Ltd* [2020] EWHC 3282 (Pat), at [21]. But I was given no reason to suppose that Dr Shah did not understand her task as set out in her report or that she failed to focus on the knowledge of the skilled team at the priority date, such knowledge excluding the invention. It is not unusual for witnesses to give evidence about a claimed invention some time after the invention has become publicly known. There is a risk of this affecting their evidence but if the witness is diligent the risk will be low.

Dr Hiep Huatan

50. Teva's expert formulator was Dr Hiep Huatan. Dr Huatan is pharmaceutical consultant who provides product development services to pharmaceutical companies. Between 1995 and 2006 he worked for Pfizer Global Research and Development in Sandwich in the development of pharmaceutical formulations. As a consultant he has provided advice more widely on similar projects.

51. Dr Huatan was an honest witness taking quite scrupulous care to give accurate answers to the questions put to him. I think that he was genuinely puzzled as to why his evidence and that of Novartis' expert formulator, Dr Rigby-Singleton, differed. He was inclined to put it down to her lack of on-hand experience of formulating or reformulating drugs.

52. In cross-examination Dr Huatan spoke of the "routine" work of a formulator. It was put to him that by this he meant the work of a formulator that forms part of his or her job description and he agreed. In closing Novartis dismissed Dr Huatan's evidence regarding "routine" procedures as being therefore of no assistance in deciding whether a procedure was obvious. In giving his answer, Dr Huatan may well have thought it self-evident that routine tasks of the notional skilled formulator were part of their job description. However, I can see that a routine procedure and a procedure obvious to the notional skilled formulator may not in all circumstances be the same thing. Dr Huatan's evidence had to be considered in the round to assess what he meant. It was also necessary to bear in mind that Dr Huatan, like all the experts, was more skilled than the notional skilled person in his field. That said, I think that Dr Huatan was aware of this and tried to give evidence on matters as they would have been perceived by the skilled formulator.

Professor Jennifer Dressman

53. Teva's expert pharmacokineticist was Professor Jennifer Dressman. Professor Dressman has studied and taught pharmacokinetics in universities in Australia, the United States and Germany. She is the author of books on the subject and has worked on projects with several major pharmaceutical companies, with the Federal Drugs Administration and with the World Health Organisation, all of which have used her expertise in pharmacokinetics.

54. Novartis described Professor Dressman's evidence in cross-examination as being nit-picking in the extreme. I am sure that Professor Dressman was doing her best to assist the court but I think that occasionally she felt that she was obliged to resist on principle some points put to her that were not fully consistent with her reports. However, not much of her evidence was central to the issues in dispute.

Professor Nirmish Shah

55. Novartis' expert clinician was Professor Nirmish Shah, whom I have already mentioned. Professor Shah is Associate Professor of Medicine at the Duke University School of Medicine, North Carolina. He divides his time between treating patients with iron overload and conducting research into new treatments for such patients.

56. Teva criticised some omissions from Professor Shah's written evidence, particularly his failure to mention lactose intolerance in his first report. Teva rightly made no criticism of his evidence given in cross-examination. Professor Shah gave very clear answers to the questions put to him and made no attempt to argue Novartis' case.

Dr Shellie Rigby-Singleton

57. Novartis' expert formulator was Dr Shellie Rigby-Singleton. Dr Rigby-Singleton is director of Skyview Pharma Ltd which provides consultancy services regarding the development of pharmaceutical products. Since her post-doctoral research into drug-

membrane interactions she has worked in companies which advised pharmaceutical corporations on formulation and product development.

58. Teva suggested that Dr Rigby-Singleton's written evidence had been prepared with an eye to presenting Novartis' case in a favourable light. I think that there was something in this. She presented calculations about Teva's product on the assumption that it was not homogeneous although, as she accepted in cross-examination, the product was likely to be homogeneous. She said that she was somewhat regretful that she had not pointed this out in her report. There were other instances in which Dr Rigby-Singleton left me with the impression that she felt it important not to let down the side which had instructed her. I will refer to these in the context of my discussion of the prior art.

Professor James Houston

59. Novartis' expert pharmacokineticist was Professor James Houston. Professor Houston is Emeritus Professor at the University of Manchester, having been until 2019 Professor of Drug Metabolism & Pharmacokinetics and Director of the Centre for Applied Pharmacokinetic Research at that university. Much of Professor Houston's work has been carried out in collaboration with pharmaceutical companies.

60. Professor Houston was a very good witness, giving clear, unargumentative answers. It emerged that he knew little about formulation, which was not his field. Teva argued that this reflected the absence of any communication between Novartis' experts in the preparation of their evidence. Professor Houston accepted that in the real world, a team working on the reformulation of a drug would discuss the project.

The Patents

61. It is enough for me to refer to the specification of EP 202.

62. The background section sets out the prior art and its disadvantages, which I have discussed above. The summary of the invention includes this:

> "[0008] Typically, a drug product that shows faster dissolution will have a much higher exposure level when tested in humans. Surprisingly, in the current case, ExjadeTM (deferasirox) tablets formulated to have slower release showed much higher bioavailability and no food effects when compared with commercial dispersible tablets, which have a faster dissolution rate but which exhibit significantly lower exposure levels. The characteristics of the new swallowable (ingestible, orally administrable) tablets and sachets, such as its disintegration time and dissolution are uniquely needed to reach the intended exposure levels.
>
> [0009] An aspect of the present invention provides a coated tablet according to claim 1, comprising (a) deferasirox or a pharmaceutically acceptable salt thereof, and (b) at least one pharmaceutically acceptable excipient suitable for the preparation of tablets, wherein deferasirox or a pharmaceutically acceptable salt thereof is present in an amount of from 45% to 60% by weight based on the total weight of the tablet. The tablets are optionally enteric coated."

63. Novartis described the disclosure of paragraph [0008] as being of fundamental importance to the invention. The expectation before the invention was that dispersible tablets had higher bioavailability in the patient when compared to a film-coated swallowable tablet in the patient because, when taken, they were already disintegrated and to some degree disaggregated. Surprisingly, according to the Patent, the coated tablets of the invention had higher bioavailability than the prior art dispersible form.

64. The specification goes on to discuss the advantages of the invention, the manufacturing process and provides examples, including clinical studies. Paragraph [0050] describes these as indicating what it calls the "suprabioavailability" of the patented tablets revealed by graphs of the concentration of deferasirox in the patient against time and the figures for C_{max} (maximum concentration) and AUC (area under the curve) revealed by the graphs:

> "[0050] Six clinical studies have been initiated with corresponding pharmacology studies in healthy adult volunteers. Four studies have been completed and two studies are ongoing. In the initial clinical pharmacology study for variant selection (study 1), the tablet variant selected for development displayed suprabioavailability: both AUC and Cmax for the invented deferasirox formulation were approximately 40% higher compared to the current dispersible tablet (DT) at a single dose of 1500 mg. Therefore, the subsequent clinical pharmacology studies used strength-adjusted formulations (400 mg granules and 360 mg FCT to match the 500 mg DT), in line with EMA/618604/2008 Rev. 7, which states that 'If suprabioavailability is found, development of a lower dosage strength should be considered'."

65. These are the first two claims of EP 202 as unconditionally proposed to be amended:

> "*Claim 1*
>
> A swallowable film coated tablet ~~for oral administration~~ comprising deferasirox or a pharmaceutically acceptable salt thereof present in an amount from 45% to 60% by weight based on the total weight of the tablet, wherein the tablet is without sodium lauryl sulfate and lactose and comprises
>
> i. microcrystalline cellulose;
>
> ii. crospovidone;
>
> iii. povidone;
>
> iv. poloxamer 188;
>
> v. colloidal silicon dioxide;
>
> vi. magnesium stearate.
>
> *Claim 2*
>
> The swallowable film coated tablet ~~for oral administration~~ according to claim 1 wherein:

i. microcrystalline cellulose is present in a total amount of 10% to 40 % by weight based on total weight of the tablet;

ii. crospovidone is present in a total amount of 1% to 10 % by weight based on total weight of the tablet;

iii. povidone is present in a total amount of 1% to 5 % by weight based on total weight of the tablet;

iv. poloxamer 188 is present in a total amount of up to 2% by weight based on total weight of the tablet;

v. colloidal silicon dioxide is present in a total amount of 0.1% to 1% by weight based on total weight of the tablet;

vi. magnesium stearate is present in a total amount of 0.1% to 2% by weight based on total weight of the tablet;

vii. the coating comprises a functional or non-functional polymer."

66. These are the unconditional amendments sought for first two claims of EP 018:

"*Claim 1*

A swallowable film coated tablet ~~for oral administration~~ which contains deferasirox or a pharmaceutically acceptable salt thereof present in an amount of from 45% to 60% by weight based on the total weight of the tablet, and wherein the tablet contains 90 mg, 180 mg or 360 mg of deferasirox, ~~or a pharmaceutically acceptable salt thereof~~

wherein the tablet further comprises,

i. at least one filler in a total amount of 10% to 40 % by weight based on total weight of the tablet, wherein the filler is microcrystalline cellulose;

ii. at least one disintegrant in a total amount of 1% to 10% by weight based on the total weight of the tablet, wherein the disintegrant is cross-linked polyvinylpyrrolidone (crospovidone);

iii. at least one binder in a total amount of 1% to 5% by weight based on the total weight of the tablet, wherein the binder is polyvinylpyrrolidone (PVP);

iv. ~~optionally,~~ at least one surfactant in a total amount of ~~0.0%~~ up to 2% by weight based on the total weight of the tablet, wherein the surfactant is poloxamer;

v. at least one glidant in a total amount of 0.1% to 1% by weight based on the total weight of the tablet, wherein the glidant is colloidal silicon dioxide;

vi. at least one lubricant in a total amount of less than 0.1% to 2% by weight based on the total weight of the tablet, wherein the lubricant is magnesium stearate; and

vii. a coating~~.~~

and wherein the tablet does not contain sodium lauryl sulfate and does not contain lactose.

Claim 2

The swallowable film coated tablet ~~for oral administration~~ according to claim 1, wherein the tablet contains 90 mg of deferasirox ~~or a pharmaceutically acceptable salt thereof~~."

67. Hereafter, where I speak of the claims of the Patents, unless I state otherwise this should be taken mean the claims as unconditionally proposed to be amended.

Inventive concept – the parties' respective cases

68. Novartis formulated the inventive concept of both Patents in this way:

> "The provision of a swallowable film-coated tablet containing a high load of deferasirox with the excipients claimed (without sodium lauryl sulfate and lactose) having higher bioavailability compared with the Exjade dispersible tablets authorised and available to the public at the priority date and/or which has the benefits over the Exjade dispersible tablets authorised and available to the public at the priority date as described in the Patents and set out in the paragraphs listed in the Particulars of Infringement".

69. In closing, Novartis formally maintained this statement of the inventive concept but went on to argue, in what appeared to be an afterthought, that the inventive concept had another aspect: the provision of a tablet having a reduced food effect, i.e. can be taken with a light meal as opposed to an empty stomach. In argument Novartis put higher bioavailability and reduced food effect front and centre of their characterisation of the inventive concept. Otherwise, conspicuous by its absence was the range of deferasirox (45-60% of the total weight in the claim). By implication Novartis submitted that it is irrelevant to the inventive concept.

70. Teva argued that the range of deferasirox is the key feature of the inventive concept. Aside from the formulation being film-coated, there was nothing more to it. The inventive concept is:

> "A film-coated formulation with an amount of 45-60% deferasirox".

Inventive concept generally

71. The invention is prima facie that specified in the claim: see s.125(1) of the 1977 Act and *Conor Medsystems Inc v Angiotech Pharmaceuticals Inc* [2008] UKHL 49, at [17]. There is no reason to suppose otherwise in the present case. The inventive concept is the core of the of the invention claimed, see *Actavis UK Ltd v Eli Lilly & Co.* [2017]

UKSC 48, at [65]. Therefore the inventive concept of a claim cannot encompass matter which forms no part of the invention as a whole.

72. As I have noted, the core of Novartis' case on the inventive concept was that the Patents disclosed unexpected advantages of the swallowable tablets claimed: higher bioavailability and (as added in closing) reduced food effect. The existence of these advantages of the tablets of the claims was the new technical insight which Novartis say they contributed to the art.

73. Novartis further submitted, as they had to, that both higher bioavailability and reduced food effect form part of the invention as claimed, despite not being features of the claims. They advanced three arguments of law to support this contention.

74. The first was that invention may lie in discovering that a product has a particular property. This will give rise to a valid claim even if there is nothing inventive in making the product.

75. Novartis referred to *Conor Medsystems* (cited above) in support. The inventors in that case had discovered that stents coated with a known product called taxol markedly reduced restenosis. Restenosis is the re-constriction of an arterial channel provoked by the installation of a stent for the purpose and with the initial effect of expanding the channel. The judgment of the House of Lords focussed on claim 12 which claimed a stent coated with taxol "for treating or preventing recurrent stenosis". I was referred to this part of the opinion of Lord Hoffmann:

> "[17] … The invention means prima facie that specified in the claim: see s.125(1) of the 1977 Act. In the present case, the invention specified in claim 12 was a stent coated with taxol. There was no dispute that this was a new product. The question should therefore simply have been whether it involved an inventive step. As in the case of many product claims, there was nothing inventive in discovering how to make the product. The alleged inventiveness lay in the claim that the product would have a particular property, namely, to prevent or treat restenosis. (Compare *Pharmacia Corp v Merck & Co Inc* [2002] R.P.C. 41). So the question of obviousness was whether it was obvious to use a taxol-coated stent for this purpose. And this, as I have said, was the question to which the experts addressed themselves."

76. However, the purpose of a taxol-coated stent – to treat restenosis – was set out in the claim in issue the proceedings, claim 12. This purpose was thus at the core of the invention *as claimed* and was the inventive concept. Moreover, the inventive concept could not be stretched to constitute a concept outside that which was claimed:

> "[19] In my opinion, however, the invention is the product specified in the claim and the patentee is entitled to have the question of obviousness determined by reference to his claim and not to some vague paraphrase based upon the extent of his disclosure in the description."

77. It seems to me that if the key patent claim in *Conor Medsystems* had just been to a taxol-coated stent, the relevant question for inventive step would have been whether it was obvious to make such a stent at the priority date, no more.

78. Likewise, the relevant question for inventive step in the present case is whether it was obvious at the priority date to make a swallowable tablet as claimed, nothing more than that.

79. Novartis also relied on *Pharmacia Corp v Merck & Co Inc* [2001] EWCA Civ 1610, cited in *Conor Medsystems*, specifically this paragraph of the judgment of Aldous LJ:

> "[20] I agree with the judge. Nobody reading the specification could believe that the 'invention' was the compounds claimed in claim 1. The specification makes clear that the patentees had found a class of compounds that could be made which at least had anti-inflammatory action. It was that contribution that merited a 20 year monopoly. In my view the only question capable of argument is whether the compounds in the class were chosen merely for their anti-inflammatory action or because in addition they had reduced side-effects due to them being Cox II selective."

80. This paragraph must be read in context. Aldous LJ was dealing with an allegation that the claims were not supported by a technical contribution – in other words, they were claims to arbitrarily selected compounds and lacked inventive step for that reason alone. This allegation was rejected:

> "[61] The patent in this case claims a class of compounds. There is no technical contribution in a list of compounds which a skilled person would know how to make at the priority date. The 20-year monopoly was granted because of the disclosure in the specification that the class of compounds claimed had the quality disclosed in the specification. The invention or technical contribution justifying the monopoly claimed can only be that quality. I have already decided that the judge was right when he held that the specification would be read by the skilled person as disclosing that the claimed class of compounds had anti-inflammatory and/or analgesic effect with fewer and less drastic side-effects, the reduction in side-effects being due to Cox II selectivity. It is that disclosure which is the technical contribution and invention."

81. When Aldous LJ turned to consider obviousness over the cited prior art, all that was relevant was whether an inventive step was required to go from the prior art to the compounds claimed. Specifically, the prior art disclosed a particular 2,3 isomer; the question was whether it was obvious to make the 3,4 isomer, an isomer which would fall within claim 1. On the facts, it was. The anti-inflammatory and/or analgesic effect of the compounds claimed, also having fewer and less drastic side-effects, were irrelevant to this part of the analysis.

82. If product is obvious over a piece of prior art, the validity of a claim to that product cannot be salvaged by pointing to an unexpected "bonus effect" experienced when the product is used. In *Actavis Group PTC EHF v ICOS Corporation* [2019] UKSC 15, Lord Hodge (with whom Lady Hale, Lord Kerr, Lord Sumption and Lord Briggs agreed) reviewed principles of the law on inventive step relevant to that case. This was his final principle:

> "[73] Ninthly, it is necessary to consider whether a feature of a claimed invention is an added benefit in a context in which the claimed innovation is obvious for another purpose. In *Hallen & Co v Brabantia (UK) Ltd* [1991]

> R.P.C. 195 the Court of Appeal was concerned with an alleged selection patent for a self-pulling corkscrew which had a helix coated with polytetrafluoroethylene (PTFE) which was a known friction-reducing material. At the priority date PTFE had been used for several years to coat the helix of a twin-lever type corkscrew to aid its penetration into the cork. The PTFE-coated helix had this effect also on the self-pulling corkscrew, a fact which was obvious at the priority date. The PTFE coat when applied to a self-pulling corkscrew also had a non-obvious benefit of making a striking improvement in the extraction of the cork. The trial judge, Aldous J., held that the patent was invalid on the ground of obviousness because it was obvious to select the features of the claim for the first purpose notwithstanding that it was not obvious for the other purpose: [1989] R.P.C. 307, at pp.326-327. The Court of Appeal agreed with the judge, holding (pp. 215-216) that it was self-evident that a PTFE coating would improve the penetration by any corkscrew and that the 'golden bonus' or added benefit of the dramatic improvement in extraction of the cork would not found a valid patent as the claimed innovation was obvious for another purpose."

83. Novartis' second argument was that taking into account the technical effects of the claimed tablets as disclosed in the specification of the Patents aligns with the problem-solution approach of the EPO.

84. Ultimately, the justification said to have been expressed by Caliph Omar for burning the library of Alexandria (see *Kirin-Amgen Inc v Hoechst Marion Roussel Ltd* [2004] UKHL 46 at [46]) applies here by analogy: either the problem-solution approach is consistent with the *Pozzoli* approach (*Pozzoli SpA v BDMO SA* [2007] EWCA Civ 588, at [23]), in which case nothing is gained from considering problem-solution, or it is not, in which case I am bound by the relevant part of the *Pozzoli* judgment:

> "(1) (a) Identify the notional "person skilled in the art";
>
> (b) Identify the relevant common general knowledge of that person;
>
> (2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;
>
> (3) Identify what, if any, differences exist between the matter cited as forming part of the 'state of the art' and the inventive concept of the claim or the claim as construed;
>
> (4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?"

85. The third *Pozzoli* step requires the court to compare the inventive concept, or the invention *as claimed*, with the prior art. The fourth step requires consideration as to whether the differences between those two constitute an inventive step. Matter not within the claims is irrelevant.

86. Caliph Omar notwithstanding, I should say something about a possible difference between *Pozzoli* and problem-solution. The latter approach is set out in the EPO Guidelines for Examination, March 2022, G-VII, section 5:

> "In order to assess inventive step in an objective and predictable manner, the so-called 'problem-solution approach' is applied.
>
> In the problem-solution approach, there are three main stages:
>
> (i) determining the 'closest prior art',
>
> (ii) establishing the 'objective technical problem' to be solved, and
>
> (iii) considering whether or not the claimed invention, starting from the closest prior art and the objective technical problem, would have been obvious to the skilled person."

87. Section 5.2 of the Guidelines begins with this paragraph:

> "In the second stage, one establishes in an objective way the technical problem to be solved. To do this one studies the application (or the patent), the closest prior art and the difference (also called 'the distinguishing feature(s)' of the claimed invention) in terms of features (either structural or functional) between the claimed invention and the closest prior art, identifies the technical effect resulting from the distinguishing features, and then formulates the technical problem."

88. Thus, the difference identified in the second stage is that between the *claimed invention* and the closest prior art. If one takes the claimed invention to be just that: the invention as set out in the relevant claim, the technical problem to be solved cannot be assessed by reference to matter that is not within the claim, in particular a feature which, since it is absent from the claim, does not limit the scope of the claim. Alternatively, if the claimed invention can in this context include a technical effect referred to in the general description though not in the claim, the technical problem can be framed by reference to that technical effect.

89. Putting this alternative understanding of problem-solution another way, if a new product claimed in a patent was obvious at the priority date – say, the potassium salt in place of the sodium salt, and if when the modification was made it yielded a non-obvious and advantageous technical effect, the problem-solution approach will afford an inventive step to a claim to the product *as such*.

90. I take the view that on those hypothetical facts the *Pozzoli* analysis would not give rise to an inventive step. The differences of step 3 of *Pozzoli* are between the state of the art and either the inventive concept or the invention claimed as a whole, not the invention as discussed in the general description.

91. Of course, on the facts I have posited, the *Pozzoli* approach would not present any barrier to a finding of inventive step in relation to a claim limited directly or indirectly by reference to the advantageous technical effect.

92. I return to the judgment of Lord Hodge in *Actavis Group v ICOS*:

> "[93] In relation to the second submission, that the Court of Appeal's approach was in conflict with the EPO's problem and solution approach, it is important to recall Jacob L.J.'s words in *Actavis v Novartis* (above) ([26]) that no-one has ever suggested that the problem-and-solution approach is the only way to go about considering obviousness. Like the *Windsurfing*/*Pozzoli* approach, it provides a structured approach which may assist in avoiding the dangers of hindsight and may be more helpful in some cases than in others. No formula should distract the court from the statutory question: *Generics (UK) Ltd v Daiichi Pharmaceutical Co Ltd* [2009] EWCA Civ 646; [2009] R.P.C. 23, at [17] per Jacob L.J.
>
> [94] Further, there is considerable room for judgment and disagreement on the formulation of the objective technical problem to be solved."

93. Novartis' third argument was that it is not possible to ask and answer the questions set out by the Supreme Court in *Actavis UK Ltd v Eli Lilly & Co* [2017] UKSC 48, at [66], in relation to infringement of a claim without reference to the technical effects of the invention claimed, even if those effects form no part of the claims. It is trite law, the argument continued, that the inventive concept ought to be the same for validity and infringement.

94. I agree that the inventive concept of a claim should be the same for all purposes, although I am not sure that this has attained the status of trite law. Leaving that to one side, I fail to see the difficulty. I deal with this below in relation to the parties' arguments on infringement.

95. Novartis went on to say that their perceived difficulty in applying the *Actavis* questions was illustrated by my discussion of them in *Regen Lab SA v Estar Medical Ltd* [2019] EWHC 63 (Pat) (emphasis in bold added by Novartis' counsel):

> "[222] **Thus, the distinction between the invention as a whole and the inventive concept matters.** The invention is that which is claimed, see s.125(1) of the Patents Act 1977. **I take the inventive concept or core of the invention to be the new technical insight conveyed by the invention – the clever bit – as would be perceived by the skilled person.** This will be assessed by reference to the specification and the evidence."

96. Novartis argued that it is clear from the evidence that the clever bit of what is disclosed by the Patents is the higher bioavailability and reduced food effect of the tablets. Possibly so. But as I said in *Regen Lab*, the inventive concept is the new technical insight conveyed by *the invention* and the invention is that which is claimed.

97. This can also be viewed as a matter of construction. Although the description of the invention and the drawings are to be used to interpret the claims (see art.69 European Patent Convention), features disclosed only in the description are not to imported into a claim to impose a limitation that would not otherwise be there. In *Hewlett Packard GmbH v Waters Corporation* [2002] EWCA Civ 612, Aldous LJ said (at [34]):

> "No doubt the words of the claim have to be construed in the context of the whole specification having regard to what was the common general knowledge

> at the priority date: but it would not be right to imply a limitation into the words chosen by the patentee to define his monopoly."

98. Where the patentee has chosen the words of his claim such as to exclude mention of a feature referred to in the description, that feature forms no part of the claimed invention as a whole or, therefore, the inventive concept.

99. I return to the distinction between an allegation that a claim lacks inventive step for what might be called the standard reason, i.e. it is obvious over the prior art, and an allegation that it lacks inventive step because the alleged invention made no contribution to the art, see the discussion of *Pharmacia v Merck* above. Among the Grounds of Invalidity pleaded against the Patents, Teva allege that the claims of the Patents represent an arbitrary selection over the prior art which is not justified by any technical effect. This was advanced as a ground for finding that the claims lack inventive step because there was no contribution to the art and/or that they are insufficient. It led to cross-examination and argument concerning whether the technical advantages of improved bioavailability and reduced food effect stated in the Patents were plausible.

100. A patentee may identify a product, state in the patent specification that it has an identified technical advantage and claim the product. If the stated technical advantage is plausible so that the patentee has made a contribution to the art, the claim will not be found invalid as an arbitrary selection, whether for lack of inventive step, see for example *Generics (UK) Ltd v Yeda Research & Development Co Ltd* [2013] EWCA Civ 925 or for insufficiency, see for example *Idenix Pharmaceuticals Inc v Gilead Sciences Inc* [2016] EWCA Civ 1089. However, such a finding has no bearing on the separate issue as to whether the product is obvious over the prior art.

101. Where a product is claimed as such, the inventive concept is the existence of that product. The product was either obvious over the prior art to the skilled person at the priority date or it was not. Obviousness may often turn on whether the skilled person would have considered the possibility that certain products possess the relevant advantage and whether he or she would thereby, without invention, have identified the product. The relevant advantage of the product is thus commonly central to the investigation of obviousness. But it is not the same thing as the inventive concept of the invention as claimed.

102. This is more evident if the product is shown to have formed part of the prior art at the priority date. In that case the patentee may be entitled to a valid claim where the claim is limited directly or indirectly by reference to the newly identified advantage, but not a claim to the product as such. The position is no different if at the priority date the product was an obvious modification of a prior art product.

103. Were that not so, a claim to a product shown to have a surprising technical advantage, a product which is an obvious modification to a prior art product and fully within the contemplation of the skilled person, would not lack inventive step. This would be solely because the technical advantage is imported into the inventive concept. It seems to me that this would wrongly promote form over substance.

The inventive concept in the present case

104. I begin with claim 1 of EP 202. The issue is what the skilled team would perceive the inventive concept of the claim to be, having read the claim in the context of the whole specification and taking into account their CGK. Of the team, the skilled formulator would be the most significant member in this regard.

105. For the reasons given above, I take the view that higher bioavailability and reduced food effect cannot be imported into either the claims or the inventive concept. It makes no difference, if it is the case, that the skilled team reading the Patents would regard higher bioavailability and reduced food effect as the most significant technical insight conveyed by the description. They would read the claims and understand that this insight is not part of the inventive concept of the invention as the patentee has chosen to claim it. To give an extreme parallel: if the description had plausibly disclosed a product, identified by its chemical formula, as being an instant and permanent cure for iron overload, that would have potentially been a more profound technical insight. But if it were nowhere mentioned in the claims it would not form any part of the inventive concept as claimed.

106. The features of claim 1 can be divided into four: (a) a swallowable film-coated tablet, (b) the 45-60% range of deferasirox content, (c) the absence of SLS and lactose and (d) the six excipients.

107. As the parties agreed, the inventive concept is at root a swallowable film-coated tablet having certain features. A key issue is whether the 45-60% range of deferasirox content is one of them. Dr Huatan said this in his first report:

> "12.23 On the basis of the Skilled Formulator's knowledge that small changes can impact the quality, performance and processability of a formulation and the clear indications in the Patents that the 45% – 60% range is significant (and that a target of 56% is preferred and exemplified), the Skilled Formulator would consider strict compliance with the 45% – 60% in the claims of the Patents is intention of the patentee."

108. Dr Huatan maintained this view in cross-examination:

> "I cannot articulate my view clear enough that when you are doing a formulation and you provide that description, 45-60, there is often a much more tighter range of which is optimal and then as you work away, there will be a point that it will not work any more and as I have described, that has been the edge of failure, so therefore I see that range of 45-60 being a definitive range beyond which you will not work."

109. Dr Huatan's view on this was put to Dr Rigby-Singleton in cross-examination, who accepted it.

110. Dr Peter Rue was an expert formulator who gave evidence for Teva in the European Patent Office. This part of his evidence was endorsed by Novartis in the present trial and so can be taken as common ground:

> "*Drug loading*

> 5.4 Paragraph [0007] [of EP 202] states that drug loading in the tablet is 45% to 60%. This is repeated elsewhere in EP202, including in the claims. This is based on the acceptable size of the tablet and dose required. A formulator would work out how much of the drug was needed and the necessary amounts of essential excipients in order to make the tablet. Then the amount of filler required would be calculated. There is nothing special about the range that they have chosen. It is merely that this amount of active ingredient works with the chosen excipients. If a higher dose were required there is nothing to prevent them increasing the drug loading."

111. I think that Dr Rue's evidence can be reconciled with that of Dr Huatan. The skilled formulator would understand that the deferasirox content can be varied and could extend above the 60% top limit set in the claim. But this would be seen to require juggling with excipients in a manner not disclosed in the Patent. The skilled team is thus being told by the Patent that the range of deferasirox specified in the claim works using the excipients specified. The skilled team would not infer that the patentee was suggesting that the range by itself was individually inventive, but would take the inventive concept to lie principally in a swallowable film-coated tablet with 45-60% deferasirox as API in combination with the stated excipients.

112. This leaves the third feature: no SLS or lactose. The invention is that which is claimed and the words relating to this feature are strong: "wherein the tablet is without sodium lauryl sulfate and lactose". In my view this would therefore form an element of the inventive concept as the skilled team would understand it to be.

113. This is a case of the inventive concept consisting of a product having a particular combination of features. In this instance the combination consists of all the features of claim 1 of EP 202.

114. In stating the inventive concept I could just repeat the claim, but alternatively would characterise the inventive concept in this way:

> "A swallowable film-coated tablet containing deferasirox in an amount between 45% and 60% of total tablet weight, containing (i) microcrystalline cellulose, (ii) crospovidone, (iii) povidone, (iv) poloxamer 188, (v) colloidal silicon dioxide and (vi) magnesium stearate and containing no SLS or lactose"

115. The experts attached no inventive significance to the amounts of the excipients, either in claim 2 of EP 202 or in claim 1 of EP 018.

116. Novartis laid emphasis on the 90, 180 and 360mg content of deferasirox set out in the claims of EP 018 in a particular context. It was argued that these were clinically useful doses providing swallowable tablets of useful size because of the unexpected high bioavailability. This wrongly imports increased bioavailability into the invention and the inventive step. It was not suggested by Novartis that there was invention in any of the three doses as such and they formed no part of the inventive concept advanced by Novartis.

117. In fact the parties each advanced only one inventive concept for both Patents implying, in my view correctly, that there was just one inventive concept and that it is the same for both Patents. It is as stated above.

Construction

Total weight of the tablet

118. Claim 1 specifies that deferasirox or a pharmaceutically acceptable salt thereof must be present as 45-60% by weight, based on the total weight of the tablet. It was common ground that "total weight of the tablet" is not a term of art. The issue between the parties was whether that includes the coating. This turned out to have no real significance but since the argument was pursued I will decide the point of construction.

119. Teva say that in all but one instance of calculating the percentage of deferasirox in the tablets of the examples in the specification, the calculation is done by reference to the tablet without a coating. The exception is a formulation called variant A in paragraph [0047]. However when variant A is referred to in Table 3, total weight is without a coating. Dr Huatan said that in practice the skilled formulator would use the total weight of uncoated tablet to calculate the required coating. In argument, Teva elaborated on this, arguing that since a tablet is made first without a coating, it would be simpler to make it using percentages of the total at that stage, rather than adding the coat and then calculating percentages.

120. It seems to me that as a matter of ordinary English, the words "*total* weight of the tablet" quite strongly imply the whole thing, which would include the coat. The fact that it was convenient to present some or all of the examples with percentage figures for components in the uncoated tablet would not of itself modify that apparently clear meaning in the mind of the skilled person. Moreover, paragraph [0034] discusses the application of a coating to a "tablet core". This shows that the specification has language for an uncoated tablet which could have been used in the claims but was not. In my view, "the total weight of the tablet" would be taken to mean what at first it appears to mean: the weight of the whole thing, including the coating.

Validity

121. Argument was directed to claims 1 and 2 of the Patents. Teva allege that those claims lack inventive step over three cited items of prior art, taken with the common general knowledge. Teva also allege that the claims represent an arbitrary selection of integers differing from the prior art which confer no technical effect and that accordingly the claims lack inventive step and/or sufficiency for that reason.

122. These are the cited prior art documents:

(1) International Patent Application No. WO 2007/045445 ("Battung").

(2) International Patent Application No. WO 2009/067557 ("Zadok").

(3) Relative bioavailability of deferasirox tablets administered without dispersion and dispersed in various drinks, Séchaud R. et al., International Journal of Clinical Pharmacology and Therapeutics, 2008 Vol. 46, no. 2/2008, 102-108 ("Séchaud").

The law on inventive step

123. Novartis warned against hindsight, see *Wheatley v Drillsafe Ltd* [2001] RPC 7, particularly when the invention required a series of steps and the selection of a particular alternative at each step, see *Technograph Circuits Ltd v Mills & Rockley (Electronics) Ltd* [1972] RPC 346 and the well-known passage of Lord Diplocks's speech at 362:

> "The cross-examination of the respondents" expert followed with customary skill the familiar 'step by step' course. I do not find it persuasive. Once an invention has been made it is generally possible to postulate a combination of steps by which the inventor might have arrived at the invention that he claims in his specification if he started from something that was already known. But it is only because the invention has been made and has proved successful that it is possible to postulate from what starting point and by what particular combination of steps the inventor could have arrived at his invention. It may be that taken in isolation none of the steps which it is now possible to postulate, if taken in isolation, appears to call for any inventive ingenuity. It is improbable that this reconstruction a posteriori represents the mental process by which the inventor in fact arrived at his invention, but, even if it were, inventive ingenuity lay in perceiving that the final result which it was the object of the inventor to achieve was attainable from the particular starting point and in his selection of the particular combination of steps which would lead to that result."

124. Novartis also pointed to the dangers of attacks on the validity of a patent based on CGK alone, well signalled in the authorities, see *Ratiopharm GmbH v NAPP Pharmaceutical Holdings Ltd* [2008] EWHC 3070 (Pat) at [154]-[159] and *Accord Healthcare Ltd v Medac Gesellschaft für Klinische Spezialpräparate Mbh* [2016] EWHC 24 (Pat) at [120]-[124]. But Teva's case is not based on CGK alone. Teva may or may not be of the view that it could have pleaded a case solely based on CGK; that is by the way. Its formal case is that the Patents lack inventive step over the cited prior art in the light of the skilled team's CGK, bringing in train any inconvenient details there may be in the cited publications.

125. I return to the list of factors that may be taken into account when considering inventive step set out by Lord Hodge in *Actavis v ICOS*:

> "[65] First, it is relevant to consider whether at the priority date something was 'obvious to try', in other words whether it was obvious to undertake a specific piece of research which had a reasonable or fair prospect of success: *Conor v Angiotech* (above) at [42] per Lord Hoffmann; *MedImmune Ltd v Novartis Pharmaceuticals* UK Ltd [2012] EWCA Civ 1234; [2013] R.P.C. 27 , at [90] and [91] per Kitchin L.J. In many cases the consideration that there is a likelihood of success which is sufficient to warrant an actual trial is an important pointer to obviousness. But as Kitchin L.J. said in *Novartis AG v Generics (UK) Ltd* [2012] EWCA Civ 1623 , at [55], there is no requirement that it is manifest that a test ought to work; that would impose a straightjacket which would preclude a finding of obviousness in a case where the results of an entirely routine test are unpredictable. As Birss J. observed in this case (at [276]), some experiments which are undertaken without any particular expectation as to result are obvious. The relevance of the 'obvious to try' consideration and its weight when balanced against other relevant considerations depend on the particular facts of the case."

126. Teva also relied on Lord Hodge's fifth factor:

> "[69] Fifthly, the existence of alternative or multiple paths of research will often be an indicator that the invention contained in the claim or claims was not obvious. If the notional skilled person is faced with only one avenue of research, a 'one way street', it is more likely that the result of his or her research is obvious than if he or she were faced with a multiplicity of different avenues. But it is necessary to bear in mind the possibility that more than one avenue of research may be obvious. In *Brugger v Medic-Aid Ltd (No. 2)* [1996] R.P.C. 635 , at p.661, Laddie J. stated:
>
> > '[I]f a particular route is an obvious one to take or try, it is not rendered any less obvious from a technical point of view merely because there are a number, and perhaps a large number, of other obvious routes as well.'
>
> I agree. As a result, the need to make value judgments on how to proceed in the course of a research programme is not necessarily a pointer against obviousness."

127. There is potentially a fine distinction between the principle Lord Diplock had in mind in *Technograph* and Lord Hodge's fifth factor. A criterion by which the two may be reconciled is the degree to which hindsight is required to select a series of alternative steps in order to progress from the prior art to the claimed invention. This too was considered by Lord Hodge in *Actavis v ICOS*:

> "[72] Eighthly, the courts have repeatedly emphasised that one must not use hindsight, which includes knowledge of the invention, in addressing the statutory question of obviousness. That is expressly stated in the fourth of the Windsurfing / Pozzoli questions. Where the pattern of the research programme which the notional skilled person would undertake can clearly be foreseen, it may be legitimate to take a step by step analysis. In *Gedeon Richter Plc v Bayer Schering Pharma AG* [2011] EWHC 583 (Pat); [2011] Bus LR D153 , Floyd J. stated (at [114]):
>
> > 'I think that the guiding principle must be that one has to look at each putative step which the skilled person is required to take and decide whether it was obvious. Even then one has to step back and ask an overall question as to whether the step by step analysis, performed after the event, may not in fact prove to be unrealistic or driven by hindsight.'
>
> The obvious danger of a step by step analysis is that the combination of steps by which the inventor arrived at his invention is ascertained by hindsight knowledge of a successful invention. Lord Diplock warned against this in *Technograph Printed Circuits Ltd v Mills & Rockley (Electronics) Ltd* [1972] R.P.C. 346 , at p.362, a warning which judges have reiterated in later cases. I am not persuaded by Mr Speck's suggestion that Technograph is concerned only with a case in which a step by step approach was constructed by counsel on cross-examination in the absence of evidence of routine steps of research. The case contains a wider warning against the use of hindsight and has been interpreted as doing so. I agree with Birss J.'s analysis in *Hospira UK Ltd v Genentech Inc* [2014] EWHC 3857 (Pat) , at [240], where he stated:

> 'The particular point made in Technograph was that it was wrong to find an invention was obvious if it was only arrived at after a series of steps which involve the cumulative application of hindsight. In some circumstances success at each step in a chain is a necessary predicate for the next one and it is only the hindsight knowledge of the invention as the target which could motivate a skilled person to take each step without knowledge about the next one. In a situation like that, Technograph is important.'

But the Technograph warning has no bearing in a case in which the steps which the notional skilled person would take can readily be ascertained without the taint of hindsight."

128. A claim to a product which was within the contemplation of the skilled person as an obvious modification of a prior art product is a claim which lacks inventive step. It makes no difference that there was no incentive to make the modification, see *Asahi Medical Co Ltd v Macopharma (UK) Ltd* [2002] EWCA Civ 466:

> "[23] Mr Thorley also submitted that the judge had wrongly rejected his submissions … that an invention would not be obvious unless there was some motivation to implement the disclosure in the prior art and to take the steps required to arrive at the invention. In certain cases that can be right. Such cases are usually those where invention lies in the idea of taking a step. However, motivation may not be a requirement. The fact that nobody would dream of making a plate one inch bigger than the standard size does not mean that there would be invention in making one. In *Pharmacia Corporation v Merck & Co Inc* [2001] EWCA Civ 1610 , I cited this passage from the speech of Laddie J in *Hoechst v Celanese Corp v BP Chemicals Ltd* [1997] FSR 547 at 573:
>
> > 'Before a step from the prior art can be held to be obvious there must be some reason why the man skilled in the art would wish to take it. If he has a problem and the step would occur to him as a solution to it, then he has a reason. But there is no requirement that it be demonstrated that the step would have been expected to produce significant commercial advantages. The problem might be very small. The courts will assume that he may just want an alternative way of achieving essentially the same result as in the prior art. Thus mere workshop modifications, none of which would be expected to produce significant technical or commercial benefits are still obvious. To adopt an example sometimes given by Jacob J., if it is known to make a 5-inch plate, it is obvious to make a 5¼ -inch plate. Technicians and businessmen frequently want to make trivial variations in established or known products. Similarly if the prior art discloses two wooden parts held together by screws it would be obvious to glue them, even if so doing would not be expected to advance the industry. The notional addressee is likely to want to use materials readily at hand to make essentially the same thing as is disclosed in the prior art. That is sufficient motivation and the use of those materials is, accordingly, obvious. When the defendants argue that Hingorani or any of his readers is entitled to use any "natural extension" or "obvious variant" of his concept, they are correct if by that they mean the type of workshop modification or alternative discussed above. But it was not and

> could not be suggested by any witness that changing the medium from aqueous to organic and changing the resin was a mere workshop variant of what is set out in Hingorani.'

[24] I continued:

> '124. That statement of the law was, I expect, apt on the facts of that case, but should not be followed generally. A step from the prior art, albeit made without reason, can still be obvious. The judge categorises such a step as workshop modifications and, in so doing, introduces a test not in the statute, namely whether the step from the prior art was a workshop modification. The statutory test is obviousness and any modification which is obvious will not be patentable, whereas one which is not obvious will be. The true test, as made clear in *Windsurfing*, is to ask whether the invention was obvious. Whether or not there is a reason for taking the step from the prior art may well be an important consideration, but that does not mean that it is an essential requirement of a conclusion of obviousness.'

[25] The judge did not in paragraph 46 of his judgment fall into the error of principle that Mr Thorley submitted that he had. What he said in that paragraph has to be read in the light of the conclusion he had reached in paragraph 45. The judge concluded that the step from the prior art was a 'workshop variation' and therefore was an obvious step. Mr Thorley had submitted that it was not obvious because the skilled person would not in practice have thought of implementing it at all. If the step from the prior art lacked invention, then it mattered not whether anybody would have thought of implementing it. The public are entitled to make obvious modifications. Whether they would want to do so will depend upon a variety of factors which could include such things as cost and the attitudes of users."

129. One could add the qualification that the modification must have been seen as being possible at the priority date. A product may have been fully within the contemplation of the skilled person but he or she laboured under the belief that there was a technical barrier to making it. Showing there is no such technical barrier can be a contribution to the art which merits a patent. Jacob LJ explained this in *Pozzoli SpA v BDMO SA* [2007] EWCA Civ 588:

> "[25] …There is an intellectual oddity about anti-obviousness or anti-anticipation arguments based on 'technical prejudice.' It is this: a prejudice can only come into play once you have had the idea. You cannot reject an idea as technically unfeasible or impractical unless you have had it first. And if you have had it first, how can the idea be anything other than old or obvious? Yet when a patent demonstrates that an established prejudice is unfounded – that what was considered unfeasible does in fact work, it would be contrary to the point of the patent system to hold the disclosure unpatentable.
>
> [26] I put it this way in *Union Carbide Corp v BP Chemicals Ltd* [1998] R.P.C. 1, 13:

> 'Invention can lie in finding out that that which those in the art thought ought not be done, ought to be done. From the point of view of the purpose of patent law it would be odd if there were no patent incentive for those who investigate the prejudices of the prior art.'
>
> [27] Patentability is justified because the prior idea which was thought not to work must, as a piece of prior art, be taken as it would be understood by the person skilled in the art. He will read it with the prejudice of such a person. So that which forms part of the state of the art really consists of two things in combination, the idea and the prejudice that it would not work or be impractical. A patentee who contributes something new by showing that, contrary to the mistaken prejudice, the idea will work or is practical has shown something new. He has shown that an apparent 'lion in the path' is merely a paper tiger. Then his contribution is novel and non-obvious and he deserves his patent."

130. A claim lacks inventive step if any product falling within it was obvious at the priority date, see *Brugger v Medicaid Ltd* [1996] RPC 635, at 656. The EPO Board of Appeal provided the rationale in decision T 0939/92 (Triazoles) of 12 September 1995:

> "2.4.2. … it has for long been a generally accepted legal principle that the extent of the patent monopoly should correspond to and be justified by the technical contribution to the art (see T 409/91, OJ EPO 1994, 653, reasons Nos. 3.3. and 3.4, and T 435/91, OJ EPO 1995, 188, reasons Nos. 2.2.1 and 2.2.2). Now, whereas in both the above decisions this general legal principle was applied in relation to the extent of the patent protection that was justified by reference to the requirements of Articles 83 and 84 EPC, the same legal principle also governs the decision that is required to be made under Article 56 EPC, for everything falling within a valid claim has to be inventive. If this is not the case, the claim must be amended so as to exclude obvious subject-matter in order to justify the monopoly."

131. In the case of a claim based on the removal of a technical prejudice, that prejudice must therefore have been a barrier to the making of all products within the claim. To achieve this result a claim may contain a limitation to exclude products that were not subject to the technical prejudice. The absence of such a limitation may render the claim invalid for lack of an inventive step.

The role of HH-2

132. HH-2 was a short document and I will quote it in full:

> "SKILLED CLINICIAN'S INSTRUCTIONS TO SKILLED FORMULATOR
>
> As at the Priority Date, the Skilled Clinician would have made the following recommendations to the Skilled Formulator regarding the formulation of Dispersible Deferasirox as at the Priority Date:
>
> 1. Convert the dispersible to tablet formulation, so it is easier for patients to take.

2. If the medication has to remain dispersible then the removal of grittiness and soapy taste.

3. Removal of the need to take it on an empty stomach.

4. Removal or reduction of lactose so that patients with lactose intolerance can take the medication."

133. Teva's expert clinician, Dr Shah, gave this summary of her evidence in her first report (I omit here her misleading reference to discussions about a new formulation with Novartis before the priority date):

> "9.1 In summary, given the well-known issues with GI side effects and patient compliance, there was a motivation and need for a new formulation of Dispersible Deferasirox.
>
> …
>
> 9.3 The Skilled Clinician would have wanted to improve GI side effects and patient compliance (relating to the GI side effects, palatability, requirement to take it on an empty stomach and problems with dispersion). In order to do this, the Skilled Clinician would have recommended that the dispersible formulation be converted to a tablet formulation.
>
> 9.4 Although the Skilled Clinician would have largely left the composition of the formulation up to the Skilled Formulator, they would have wanted to have the lactose removed from a tablet formulation, given the well-known GI side effect issues that were caused by it in the thalassaemia and sickle cell patient populations. Further, given what was known about the unpalatable soapy taste, the Skilled Clinician would have instructed the Skilled Formulator to take steps to overcome this issue."

134. HH-2, prepared by Teva's solicitors, does not give an inaccurate picture of the wish list that, according to Dr Shah, would have been communicated by the skilled clinician to the skilled formulator during the preparation of the TPP.

135. Novartis had three points. The first was that HH-2 was headed "instructions", whereas the clinician would never literally instruct the formulator. That is true, but I am not persuaded that the heading had any effect on Dr Huatan's evidence.

136. The second point came from a search on BAIILI for "drug", "formulation" and "patents". Apparently only two results included any reference to a TPP. Therefore, it was argued, a TPP cannot have central importance to formulation cases. I find this not at all persuasive. The evidence from all the experts was that there would be a TPP which would emerge from discussions among the team hypothesised on the facts of this case. The most significant flow of information would pass from the clinician to the formulator, stating clinically desirable objectives. I have no idea whether a TPP was relevant to the facts and issues before the court in earlier reported cases.

137. The third point was that HH-2 was too short, was selective in the information conveyed and directed Dr Huatan towards the invention. Dr Huatan's evidence was therefore unreliable.

138. Dr Huatan's evidence about TPPs indicated that in real life a TPP is typically longer and more detailed than HH-2. He did not say that the skilled formulator could not carry out a reformulation of dispersible deferasirox if given HH-2. The question is whether Dr Huatan's evidence was unfairly influenced by HH-2 in a manner that he would not have been had he been given more fulsome and direct input from Dr Shah.

139. In their written closing submissions Novartis submitted that a number of matters should have been included in HH-2:

> "1) The skilled clinician understood that a dispersible was already the best Novartis could do;
>
> 2) The skilled clinician would have appreciated that a dispersible that better dispersed, so as to reduce the chalky gritty texture would improve compliance;
>
> 3) The skilled clinician would have appreciated that a dispersible that tasted better would improve compliance,
>
> 4) In relation to Dr Huatan's 6.9.2 [of his first report] there were the following side effects which are described as 'common' in the SmPC, all of would have been obstacles to compliance:
>
> 1) Headache;
>
> 2) Diarrhoea;
>
> 3) Constipation;
>
> 4) Vomiting;
>
> 5) Nausea;
>
> 6) Abdominal pain;
>
> 7) Abdominal distension;
>
> 8) Dyspepsia;
>
> 9) Transaminases increased;
>
> 10) Rash;
>
> 11) Pruritus;
>
> 12) Proteinuria.
>
> 5) In addition the SmPC identifies blood creatinine increase as 'very common. Yet HH-2 ignores all of 1, 3, 6, 7, 8, 9, 10, 11 and 12, and ignores blood creatinine increase.

6) There are also other, rarer, but much more serious side effects. Gastric ulceration is one example. Those side effects (and their cause, which was thought to be inadequate drug dispersion) play no part in any analysis in HH-2 (although they are illegitimately brought in to try and justify the removal of SLS as we have explained above).

7) HH-2's focus is on (2), diarrhoea. But as explained above, it is not even diarrhoea generally, but rather the 10% of diarrhoea that was severe, and the (unknown) percentage of that percentage which was suffered by lactose intolerant patients.

8) None of the side effects that are addressed in HH-2 relate to 'gastric irritation' (indeed there is no evidence at all in the case, with the possible exception of gastric ulceration), that any of the side effects result from 'gastric irritation'. So there is no motivation provided by HH-2 (or indeed anything else) to support Dr Huatan's claimed basis for removal of SLS, let alone the removal of it at GRAS levels.

9) There is no consideration whatsoever of the 'Pharmacokinetic profile of the drug substance with respect to features such as: oral absorption rate, which is a function of the solubility, rate of dissolution and permeability of the drug substance' (as per Dr Huatan's 6.9.3 above). Indeed, there were no discussions at all with the pharmacokineticist as Dr Huatan accepted at 3/30316-23.

10) As to 6.9.4 [of Dr Huatan's report], there is no real consideration of aesthetic attributes (e.g. colour, shape and size); the type of dosage form; the drug substance release profile (for example – immediate, delayed, sustained or modified release); the desired clinical attributes such as the therapeutic indication, route of delivery, dosage and dosage regimen; and the safety and efficacy performance attributes, including for example, improved tolerance to the medicinal product, reduction in one or more adverse effects, improved onset of drug substance action and / or an extended duration of action, save for the self-serving 'make the drug a swallowable tablet."

140. The first in the list implies that the skilled clinician would have known at the priority date that Novartis did not believe that it could improve on its dispersible product. That is an unhelpfully inaccurate characterisation of the evidence. I assume that it is based on Dr Shah having given written evidence that there were public discussions with Novartis before the priority date about how to overcome issues of compliance with the dispersible product by way of a new formulation and that in cross-examination it emerged that any such discussions happened after the priority date. Undoubtedly at the priority date Novartis believed that its dispersible product could be improved; the skilled team would not have known that, but neither was it shown to have expected the opposite.

141. I have earlier quoted the joint Statement of Agreed Common General Knowledge on pharmaceutical tablets in general and for convenience will repeat it here:

> "2. Swallowable tablets (i.e. tablets meant for swallowing, i.e. not dispersed or chewed prior to ingestion; also known as 'conventional tablets') are the most common oral dosage form, due to advantages afforded both to the manufacturer (e.g., simplicity and economy of preparation, stability, and convenience in packaging, shipping and dispensing) and to the patient (e.g. accuracy of dosage, compactness, portability, and ease of administration).
>
> 3. A coated tablet may be 'film coated' wherein a thin film is applied to the tablet surface to impart certain beneficial characteristics."

142. It seems to me probable that in discussions between the notional skilled team at the priority date about desirable improvements to dispersible deferasirox, the clinician would have said that a swallowable tablet was a desirable goal. The first point in HH-2 makes sense.

143. The second point in HH-2 impliedly acknowledges that the skilled clinician would not have known whether a swallowable tablet was possible. Maximising dispersibility and minimising grittiness are both improvements that the skilled clinician would plausibly suggest. The same goes for the third point.

144. As for the long list of side effects imparted by dispersible deferasirox, these were listed in the SmPC for Novartis' Exjade, quoted on the Statement of Agreed Common General Knowledge. There is a footnote which states "The parties are agreed that even if the SmPC for Exjade Dispersible Tablets was not common general knowledge, it contains the sort of information that the Skilled Clinician would acquire as a matter of routine." I am not entirely certain of the distinction being made there, but it implies that the information from the SmPC quoted in the Statement would have been known to the skilled clinician. Since the skilled clinician would have known of these side effects, it is to be expected that in the real world they would have been passed on to the skilled formulator. But I do not see what significant difference that makes. There was no suggestion that if the skilled formulator had been put on notice of the side effects, he or she would have made sure that lactose or SLS was part of the formulation, a matter of particular relevance. The same goes for matters such as release profile, dosage regimen and aesthetic attributes and indeed points (5) to (8) in Novartis' list. Novartis' argument was the other way around: that the existence of side effects would not of themselves have encouraged the team to formulate without lactose or SLS.

145. The lack of a pharmacokinetic profile was not shown to have influenced Dr Huatan's evidence in a material way. Nor the lack in HH-2 of the attributes referred to in (10).

146. In short, Dr Huatan was provided with less information than the notional skilled formulator would have been. But subject to one point, I am not persuaded that Dr Huatan's views on the way forward that the skilled formulator would have adopted were thereby skewed in a way that mattered.

147. For the reasons discussed above in the context of Dr Shah as a witness, I doubt that lactose would have figured much in the discussions between the notional skilled clinician and the formulator. It would have been there, but HH-2 probably overstates its significance.

148. Turning to the approach of the Novartis expert team, in contrast to Dr Huatan, Dr Rigby-Singleton gave her evidence as an expert formulator for Novartis without any input from her expert clinician colleague. I think that this is likely to have affected her evidence. Her views as to the priorities of the skilled team were necessarily entirely home grown and probably underestimated the likely clinical desire for improvement in patient compliance, amelioration of GI side effects, improving palatability by decreasing the soapy taste and grittiness and resolving problems of dispersion. Dr Rigby-Singleton probably also underestimated the likely clinical wish for a swallowable tablet to deal with most of these issues.

Battung

149. This patent application has the title "Dispersible tablets comprising deferasirox". The invention is summarised on page 2:

> "The present invention pertains to a dispersible tablet comprising an iron-chelating pharmacologically effective amount of [deferasirox] or a pharmaceutically acceptable salt thereof present in the amount of from 42% to 65% by weight based on the total weight of the tablet".

150. Just one formulation is exemplified, which has the same binder (microcrystalline cellulose), disintegrant (crospovidone), glidant (colloidal silicon dioxide) and lubricant (magnesium stearate) as required by claim 1 of EP 202. The differences in the Battung example are the filler (lactose) and the surfactant (SLS).

151. The specification discloses a range of possible excipients and goes further:

> "Reference is made to the extensive literature on the subject for these and other pharmaceutically acceptable excipients and procedures mentioned herein, see in particular Handbook of Pharmaceutical Excipients, Third Edition, edited by Arthur H. Kibbe, American Pharmaceutical Association, Washington, USA and Pharmaceutical Press, London; and Lexikon der Hilfsstoffe fiir Pharmazie, Kosmetik and angrenzende Gebiete edited by H.P. Fiedler, 4th Edition, Edito Cantor, Aulendorf and earlier editions which are incorporated herein by reference."

152. Alternatives are specifically mentioned. With regard to fillers and surfactants they are:

> "Fillers (1.1) according to the invention are lactose, especially lactose monohydrate, preferably lactose monohydrate (200mesh) and lactose spray dried, microcrystalline cellulose, especially PH 102, PH 101 or silicified microcrystalline cellulose, e.g. as known and commercially available under the Trademark ProsolvTM SMCC®90."
>
> …
>
> "Appropriate surfactants (1.4) according to the invention may be used: sodium laurylsulfate, quaternary ammonium salts, polysorbates, sorbitan esters and/or poloxamer. Preferably, the surfactant is sodium laurylsulfate."

153. Like the parties, I will address the *Pozzoli* approach by reference to inventive concept.

154. The differences between the Battung single example and the inventive concept are that in the inventive concept the deferasirox tablet is (i) swallowable, (ii) film-coated, (iii) contains poloxamer 188 instead of SLS as surfactant and (iv) contains microcrystalline cellulose ("MCC") instead of lactose as filler. The agreed CGK indicates that the first two can be taken together. This was confirmed by Dr Rigby-Singleton in cross-examination.

155. Much of the argument on inventive step advanced by Novartis assumed that increased bioavailability and/or reduced food effect formed part of the inventive concept. For the reasons given above, in my view they do not.

156. A further submission from Novartis was that if one considers all the fillers, disintegrants, binders, surfactants, glidants and lubricants proposed in Battung, there are 24,500 combinations and that there must be an inventive concept in selecting the particular six excipients of the inventive concept. This is a false mathematical argument. Four of the six excipients are disclosed in the single example in Battung. The differences are only in the surfactant and the filler.

157. Battung expressly discloses poloxamer as a suitable alternative filler. The inventive concept specifies poloxamer 188 but Dr Rigby-Singleton said that 188 would be one of the obvious choices among the poloxamers available. Battung expressly discloses MCC as an alternative filler.

158. There was an incentive to reformulate to create a product which minimised all or any of the known side effects of dispersible deferasirox. Low down the list, but present, was a mild incentive to have a product which omitted lactose to assist the relatively small number of patients who reacted badly to lactose. Dr Huatan said in his report that he believed that the skilled person would try MCC in place of lactose and was not challenged. In cross-examination Dr Rigby-Singleton agreed that MCC would be an obvious filler to select in place of lactose.

159. Dr Huatan said that in formulating a product like deferasirox, known to cause gastric irritation, using SLS would ring alarm bells because it, too, is a gastric irritant. Although SLS was a better surfactant than poloxamer, a formulator would be mindful about its use. Dr Huatan added that SLS and poloxamer work in essentially the same way. Dr Rigby-Singleton said that there would be no need to replace SLS if it was present in a concentration below that which causes irritation. But she added that a formulator would consider a range of surfactants and removing SLS would be a consideration. Poloxamer would be one of the alternatives the formulator would try, being a commonly used surfactant, in particular poloxamer 188.

160. Dr Rigby-Singleton said in cross-examination that there would have been no reasonable expectation that the combination of excipients of the inventive concept of the Patents would work. Despite being pressed and aside from saying that the formulator would have to test the new formulation, Dr Rigby-Singleton gave no reason for this lack of reasonable expectation. She did not say that there was some property of either poloxamer 188 or MCC which, either in itself or in combination with any other excipient, or with deferasirox, would be expected to cause problems. I had the impression that this was an instance of Dr Rigby-Singleton's cross-examination in which she felt duty bound not to let down Novartis. Dr Huatan thought that trying such a combination would be routine and I think he meant obvious. I prefer Dr Huatan's

evidence. I accept that the skilled person could not have been certain that the substitution of poloxamer 188 and MCC would not cause problems, but it would have been worth trying.

161. If the decision were taken by the skilled team at the priority date to reformulate deferasirox into a swallowable film-coated product, selecting MCC and poloxamer 188 would have been obvious to try with a reasonable expectation of success. This would not require the adoption of a *Technograph* step-by-step route to the inventive concept of the Patents, nor would it require hindsight having read Battung. It would require only the trial of a formulation that would have been within the contemplation of the skilled team as an obvious modification of the example in Batting.

162. I have found that the CGK of the skilled team would have included a preference for a swallowable film-coated product because of the significant advantages such products have over their dispersible counterparts and that subject to any technical prejudice directed to deferasirox in that regard at the priority date, this would apply to deferasirox.

163. The final question under this head is whether it would have been obvious to the skilled team to take the decision to reformulate into a swallowable tablet in the first place. The concept of deferasirox in swallowable film-coated tablet form must have been obvious because it was the preferred form for all orally administered drugs. Consequently, inventive step depends on whether the skilled team perceived that there was a technical barrier to achieving that goal.

164. Novartis' argued that there must have been a perceived barrier of that nature. If there had not been, one or both of Teva or Novartis would have made a swallowable deferasirox product "years before". How many years before was not made clear.

165. Speaking generally, the fact that those in the relevant industry could have made an invention claimed in a patent some significant time before the priority date, but failed to do so, can lead to an inference that the invention was not obvious. But it is not a cast iron inference in every instance because there may have been commercial or other non-technical reasons why those in the industry did not take the relevant step to make the invention.

166. In the present case Novartis has provided a plausible reason why swallowable deferasirox was not developed sooner than it was. Professor Shah said, unsurprisingly, that Novartis would have wished to market a medicine that was clinically, and therefore commercially, successful. It was part of Novartis' case that before their work on swallowable deferasirox, the expected bioavailability in "conventional tablets", i.e. swallowable film-coated tablets, was such that in order to provide patients with the required dose it would have been necessary to take too many of them. The necessary dose would have required patients to take so many tablets that there would have been problems with compliance. Alternatively, the patient would receive an insufficient dose of deferasirox from the number of tablets he or she was prepared to take. The product would not have been clinically or commercially successful. For a time Novartis felt it had to stick with the dispersible formulation.

167. If this is correct, there was no perceived technical barrier to making a product that would have fallen within the claims of the Patents. The expectation would have been that it would not be a commercially successful product but it would have been within the

claims. The false prejudice concerned the properties that such a product would have. Therefore this belief was only a barrier to developing a product for use in a regimen that would be acceptable to patients, a commercial product. It was not a barrier to performing the inventive concept of the claims.

168. In my view, at the priority date performing the inventive concept of the claims would not have required an inventive step. Claims 1 and 2 of both EP 202 and EP 018 lack inventive step over Battung.

Zadok

169. Zadok is a patent application disclosing a method of reducing or eliminating the tendency of an API contained in a pharmaceutical composition to agglomerate, thereby reducing bioavailability. The solution is to co-mill the API with at least two excipients. The milled (or micronized) mixture is added to the remaining excipients to form a dry blend which is compressed into a tablet. This one of the embodiments disclosed:

> "[0023] In a preferred embodiment, the above pharmaceutical composition is a high-dose pharmaceutical composition comprising about 20% to 80% by weight of a poorly water soluble active pharmaceutical ingredient (API), preferably deferasirox or a pharmaceutically acceptable sale thereof, wherein said API is co-milled in a dry process with at least two pharmaceutically acceptable excipient, to obtain a co-milled composition; Preferably, the pharmaceutical composition is in a unit dosage form. The unit dosage form is preferably in the form of a tablet. The tablet may be in the form of an oral dosage form, or in the form of a dispersible tablet."

170. The last sentence was given some attention having regard to what Dr Rigby-Singleton said about it in her first report. She said:

> "224. As mentioned above, the skilled formulator would consider that the disclosure [of Zadok] clearly relates to a dispersible tablet, as defined in paragraph [0029], as follows: 'As used herein, the term "a dispersible tablet" refers to a tablet which has to be dispersed in an aqueous phase, e.g. water, prior to ingestion'. This is different from EP 202, as the skilled formulator would understand that EP 202 relates to a 'swallowable film-coated tablet', which is a conventional tablet that is put in the mouth and swallowed with some water, and not dispersed prior to ingestion (see paragraph 210-211).
>
> 225. All of the examples detailed in Zadok are dispersible tablets. This is made clear in paragraph [0098], which states 'Dispersible tablets of deferasirox were prepared by […]'. It also states at the top of the table detailing formulation components 'Dispersible Tablets Formulations (125mg, unless otherwise noted).
>
> 226. For the reasons given above, the passing reference to a tablet would not change the skilled formulator's understanding that Zadok's teaching expressly relates to dispersible tablets. The skilled formulator would understand that the teaching of Zadok relates to the dispersible tablet formulations only. Indeed, there are 46 examples in Zadok, all of which relate to dispersible tablets. Not a single example relates to a swallowable film-coated tablet."

171. Dr Rigby-Singleton's insistence in her report that Zadok discloses only its claimed invention in the form of dispersible tablets, notwithstanding the words of paragraph [0023], was an example of her tendency to defend Novartis' case. In cross-examination she maintained what she had said. She was then shown claims 25 and 26 of Zadok:

> "25. The pharmaceutical composition of claim 23 or claim 24 in the form of a tablet.
>
> 26. The pharmaceutical composition of claim 25, wherein the tablet is a dispersible tablet."

172. Dr Rigby-Singleton observed only that claim 25 referred to a tablet, not a swallowable tablet.

173. Dr Rigby-Singleton did not suggest that any technical knowledge is necessary to understand paragraph [0023] or claims 25 and 26. The court can therefore make up its mind without any steering. I find Dr Rigby-Singleton's evidence on this surprising and unconvincing. For what it was worth, in cross-examination Dr Huatan expressed the view that in the last sentence of paragraph [0023] Zadok was discussing both a swallowable tablet or a dispersible tablet. Professor Shah, Novartis' clinical expert, was of the same view in cross-examination.

174. I agree with Dr Huatan and Professor Shah. It is hard to see what a "tablet … in the form of an oral dosage form", in contradistinction to "a dispersible tablet" could mean except a swallowable tablet. Similarly, following the usual principles of how patent claims are written, on the face of it the tablet of claim 25 must cover something more than a dispersible tablet and the only apparent candidate is a swallowable tablet. Novartis submitted that one must be wary of an alleged disclosure only contained in the claims, which may arise solely from an artefact in the drafting process aimed at obtaining maximum protection. I agree with the warning but not that it applies here. Paragraph [0023] discloses a swallowable tablet and claims 25 and 26 serve principally as confirmation of that.

175. Despite this dispute, the disclosure of a swallowable tablet was not central to Teva's case. Dr Huatan said that the skilled formulator would regard examples 25, 26, 37 and 39 as reasonable starting points for a reformulation project because of their favourable dissolution data and acceptable levels of excipients. They are all examples of a dispersible formulation. Dr Huatan referred to HH-2. The changes required to arrive at the inventive concept of the Patents were the same as those discussed in relation to Battung, with the additional qualification that the loading of deferasirox would be towards the upper section of the range disclosed in Zadok. As to the latter, Dr Huatan said that the skilled formulator would know that a swallowable tablet required a high dose of deferasirox and that he or she would recognise that this was confirmed by the recommendation of the daily dose in paragraph [0011] of Zadok:

> "[0011] Deferasirox is typically administered at an initial dose of about 20 mg/kg body weight, and the dose is adjusted up to a maximum of 30 mg/kg body weight. Thus for an average adult patient weighing about 70 kg, the recommended daily dose is between 1.4 and 2.1 g of deferasirox. The total tablet weight for this dose is about 1.7 g."

176. In his first report Dr Huatan said that it would have been obvious to the skilled formulator to reformulate any of the preferred examples in of Zadok to make the foregoing changes. He maintained his position in cross-examination.

177. Dr Rigby-Singleton accepted that if the skilled clinician raised concerns in relation to lactose, it would have been obvious to replace lactose as a filler and further agreed that MCC is the most common filler along with lactose. As I have said, replacing lactose would not have been high among the priorities communicated to the formulator but it would have been there. In cross-examination Dr Rigby-Singleton said that she would replace lactose with mannitol. It had poor flow characteristics but these could be overcome with flow aids. This was a new suggestion, not raised in her reports. I did not find it convincing evidence of what the notional skilled formulator would do.

178. Dr Rigby-Singleton accepted that it would have been obvious to replace SLS if the skilled clinician had raised concerns about gastric irritation. That would have been the case. Dr Huatan's evidence was that the skilled formulator would have gone to poloxamer as an alternative. Dr Rigby-Singleton accepted that it would have been an obvious choice and agreed that of the poloxamers available poloxamer 188 was the obvious choice.

179. On the foregoing evidence the question of inventive step over Zadok is much the same as that in relation to Battung. Novartis did not argue that having the content of deferasirox anywhere in the range of 45-60% was inventive over the disclosure of 20-80% in Zadok. Nor did Novartis press for any inventive significance in the ranges of excipients stated in claim 2 of EP 202 and claim 1 of EP 018.

180. I have found that a skilled team would have thought it obvious to reformulate dispersible deferasirox to make a swallowable tablet, though there may have been limited commercial pressure to try. Having read Zadok, a product within the claims of the Patents would have been within the contemplation of the skilled team as an obvious modification of examples set out in Zadok. The Patents lack inventive step over Zadok.

Séchaud

181. Séchaud is a paper by employees of Novartis in the *International Journal of Clinical Pharmacology and Therapeutics*, entitled "Relative bioavailability of deferasirox tablets administered without dispersion and dispersed in various drinks". It is a pharmacokinetic study which assessed the relative bioavailability of deferasirox in various drinks when compared with water, with and without dispersion:

> "The principal findings can be summarized as follows: (1) Deferasirox is chemically stable in all liquids tested but disintegration tests suggest that milk drinks and hot chocolate are less optimal for dispersing deferasirox due to the significant amount of time required for adequate dispersion; carbonated beverages induce important foaming; (2) the degree of dispersion does not affect the bioavailability of deferasirox; (3) deferasirox dispersed in orange juice is bioequivalent with deferasirox dispersed in water; (4) the bioavailability (AUC) is unaltered when deferasirox is dispersed in apple juice compared with tap water."

182. The authors conclude as follows:

> "Conclusions
>
> The data of this study show that orange and apple juice are viable alternatives to water for dispersing deferasirox tablets. Thus, in addition to water, patients are provided with a choice of juices for dispersion of deferasirox tablets. Additionally, the degree of dispersion does not affect deferasirox bioavailability. While these results provide reassurance that deferasirox therapy will not be compromised if a patient occasionally does not wait for complete dispersion of the tablet, it is strongly recommended that tablets be fully dispersed and that any remaining residue on the glass be re-suspended and ingested."

183. Séchaud has nothing to do with the formulation of deferasirox. Novartis argued that it provides no more pointers to a product within the claims of the Patents than does the CGK.

184. I have found that the skilled team would have considered the concept of making swallowable deferasirox tablets to be an obvious one. The clinical advantages would have been pressed by the skilled clinician. Within the contemplation of the skilled team would be making such a product using MCC as a filler, not lactose, and poloxamer 188 as a surfactant, not SLS.

185. Novartis' pointed to the final sentence of the conclusions in the paper which strongly emphasises the need for dispersible deferasirox to be ingested in a fully dispersed form. Dr Shah said that under no circumstances should patients take dispersible deferasirox without ensuring adequate dispersion. Novartis argued that therefore the skilled team reading Séchaud would have been warned off making a swallowable tablet that was entirely undispersed.

186. There are three problems with this argument. First, as Dr Shah's evidence implied, the dangers of taking the dispersible formulation when it is not fully dispersed were known. Séchaud added nothing there. Secondly, Séchaud is somewhat equivocal on this topic: complete dispersion is strongly recommended but if done occasionally it may not matter. Thirdly and not least, swallowable tablets have a dispersant. To make anything of this argument, it would have been necessary for Novartis to show that the dispersant in a swallowable tablet would not have been expected to disperse deferasirox adequately. I have no doubt that at least one of the experts would have raised this if it were a real concern. The absence of any such evidence suggests to me that the skilled team would have been satisfied that dispersion of the drug within a patient's GI tract from a swallowable tablet could be safely and easily achieved.

187. On the other hand, I think that Novartis' argument on the maths, discussed above in relation to Battung, has greater force. For a product within claim 1 of EP 202 to have been within the obvious contemplation of the skilled team, such a team would have to go further than contemplate a product with MCC as filler and poloxamer 188 as surfactant. All the excipients listed in claim 1 may be commonly used for their various purposes, but each is one of many alternatives. The skilled team reading Séchaud, unlike Battung and Zadok, is not given a starting formulation with most of the claim 1 excipients stated. Furthermore, Battung and Zadok both disclose high drug loading covering or overlapping the 45-60% range. Séchaud does not because it is not concerned with formulation.

188. I am not persuaded that Séchaud would teach the skilled team anything relevant that was not already part of their CGK. Nor am I persuaded that Séchaud would lead the skilled team to contemplate a product within claim 1 of EP 202 as an obvious alternative formulation. The same must follow for claim 2 and both claims of EP 018. The Patents do not lack inventive step over Séchaud.

Arbitrary integers

189. In closing Teva's counsel explained that its additional argument on obviousness, that each of the inventions clamed in the Patents represents an arbitrary selection over the prior art which is not justified by any technical effect, was advanced only if the court accepted Novartis' contention that the inventive concept included the benefits of unexpected bioequivalence and improved food effect claimed in the general specification. I have not, so I need not consider this argument.

Insufficiency

190. For the same reason I need not consider the argument on insufficiency.

Amendments

191. In letters dated 26 October 2021 Haydn Walker, the Hearing Officer acting for the Comptroller, set out his view regarding possible formal objections to the proposed amendments, that is to say those under s.14(5) of the 1977 Act (lack of clarity) and s.76(3) (added matter).

192. Teva endorsed the findings of the Hearing Officer, raised a further objection of double patenting and also maintained their position that none of the amendments would cure invalidity for lack of inventive step.

193. There was a further submission from Teva. They pointed out that Novartis (like Teva) had advanced only one inventive concept for all the claims of both Patents and all their proposed amended forms. If I were to find that the claims of the unconditional proposed amendments lacked validity, that must be the end of the matter: none of the claims in any proposed form could be valid because they all shared the same inventive concept.

194. I understand the logic of this argument and Novartis did not confront it, save to say that they were right about the inventive concept and therefore the claims in all their proposed forms are valid, subject only to formal objections. But I will consider whether the inventive concept of any formally allowable claim of the proposed conditional amendments is different and whether that affects my findings of lack of inventive step over Battung and Zadok.

195. Novartis said that the only reason for the proposed conditional amendments was to overcome a finding, if it were to be made, that the inventive concept of the unconditionally amended claims did not include a surprisingly increased bioavailability of deferasirox and a reduced food effect. It was not suggested that the conditional amendments would affect inventive step for any other reason.

<u>Amendments to EP 202</u>

196. The Hearing Officer raised no formal objection to the unconditional amendment to EP 202. I agree. But I have found it to be invalid for lack of inventive step.

197. This is claim 1 of the first conditional amendment of EP 202:

> "1. A swallowable film coated tablet for use in a method of treating iron overload ~~for oral administration~~ wherein the tablet comprises ~~comprising~~ deferasirox or a pharmaceutically acceptable salt thereof present in an amount from 45% to 60% by weight based on the total weight of the tablet, wherein the tablet is without sodium lauryl sulfate and lactose and comprises
>
> i. microcrystalline cellulose;
>
> ii. crospovidone;
>
> iii. povidone;
>
> iv. poloxamer 188;
>
> v. colloidal silicon dioxide;
>
> vi. magnesium stearate~~.~~
>
> wherein the method comprises swallowing said tablet."

198. I agree with the Hearing Officer that for the reasons he gives, this claim is clear, does not add matter and is supported by the description.

199. However, the amendment does not alter the inventive concept. The claim is broad enough to cover a swallowable tablet where the deferasirox has low bioavailability and high food effect. There is still no warrant to include increased bioavailability or reduced food effect as features of the inventive concept of this claim. The proposed claim lacks inventive step for the reasons given in relation to claim 1 of the unconditional amendment and this amendment is refused.

200. The second conditional amendment to claim 1 adds to the unconditional amendment the requirement that the film coating is non-functional. It was common ground that this means that the coat does not affect the release characteristics of the tablet. The third conditional amendment to claim 1 adds the same requirement to the first conditionally amended claim 1.

201. The Hearing Officer's view is that there is no support for this limitation in the description of the invention in the Patents outside example 5. The limitation therefore introduces an intermediate generalisation. I agree. The amendments are not allowable because the proposed claims would be in breach of s.76(3)(a) of the 1977 Act.

Amendments to EP 018

202. The Hearing Officer directs attention to the amendment to ingredient (iv) of the tablet of claim 1 as unconditionally proposed to be amended (see above). Aside from deleting "optionally" (about which no objection was raised by Teva or the Hearing Officer), the

range of poloxamer is changed from "0.0% to 2%" to "up to 2%". The Hearing Officer points out that "up to 2%" still includes 0% and therefore the amendment is unclear. I am not sure about that. I agree that the amendment is unclear in the sense that it is hard to see what difference it makes. But what matters under s.14(5)(b) of the 1977 Act is whether the claim, as proposed to be amended, would be clear. It seems to me that the skilled person would reasonably interpret "up to 2%" as meaning any value from 0% to 2% and would find that sufficiently clear.

203. In my view there is no formal objection to unconditionally amended claim 1 of EP 018 but the amendment is disallowed on the ground that the claims lack inventive step.

204. This is claim 1 of the first conditional amendment of EP 018:

> "1. A swallowable film coated tablet for use in a method of treating iron overload ~~for oral administration~~ wherein the tablet comprises deferasirox or a pharmaceutically acceptable salt thereof present in an amount of from 45% to 60% by weight based on the total weight of the tablet, and wherein the tablet contains 90 mg, 180 mg or 360 mg of deferasirox, ~~or a pharmaceutically acceptable salt thereof~~
>
> wherein the tablet further comprises,
>
> i. at least one filler in a total amount of 10% to 40 % by weight based on total weight of the tablet, wherein the filler is microcrystalline cellulose;
>
> ii. at least one disintegrant in a total amount of 1% to 10% by weight based on the total weight of the tablet, wherein the disintegrant is cross-linked polyvinylpyrrolidone (crospovidone);
>
> iii. at least one binder in a total amount of 1% to 5% by weight based on the total weight of the tablet, wherein the binder is polyvinylpyrrolidone (PVP);
>
> iv. ~~optionally,~~ at least one surfactant in a total amount of ~~0.0%~~ up to 2% by weight based on the total weight of the tablet, wherein the surfactant is poloxamer;
>
> v. at least one glidant in a total amount of 0.1% to 1% by weight based on the total weight of the tablet, wherein the glidant is colloidal silicon dioxide;
>
> vi. at least one lubricant in a total amount of less than 0.1% to 2% by weight based on the total weight of the tablet, wherein the lubricant is magnesium stearate; and
>
> vii. a coating~~.~~
>
> and wherein the tablet does not contain sodium lauryl sulfate and does not contain lactose, and wherein the method comprises swallowing said tablet."

205. Aside from the amendment to ingredient (iv), the Hearing Officer finds no formal objection to this claim. I agree. However, "for use in treating iron overload" does not introduce increased bioavailability or reduced food effect into the inventive concept. The claim lacks inventive step.

206. Claim 1 of the second conditional amendment adds the requirement that the coating is non-functional. As in relation to claim 1 of the second conditional amendment to EP 202, this amended claim adds matter and is disallowed pursuant to s.76(3) of the 1977 Act.

207. The Hearing Officer has no formal objection to conditional amendment 3 aside from "up to 2%" poloxamer. Aside from that point I agree, but the claims lack inventive step.

208. Conditional amendment 4 has the restriction to non-functional coating. For the reasons given above, this amendment is formally disallowed pursuant to s.76(3).

209. The Hearing Officer has no formal objections to conditional amendment 5 and I agree. But the claims lack inventive step.

210. Conditional amendments 6 and 7 include the requirement that the coating is non-functional and are therefore disallowed pursuant to s.76(3).

Double patenting

211. Teva's principal argument under this head is that proposed unconditionally amended claim 1 of EP 018 is coterminous with claim 2 of EP 202 as sought to be conditionally amended. From this, arguments about other claims and amendments flow.

212. On my finding about inventive step, the point does not arise.

Infringement

213. The product alleged to infringe, Teva DFX, is manufactured by a third party. There was a process description describing the means of manufacture, which is confidential in part and about which I need say little. The issue of infringement and Teva's application for a declaration of non-infringement turns solely on the percentage content of deferasirox in Teva DFX. Whether on Novartis' construction of "total weight" (which I have found to be correct) or Teva's construction, the deferasirox content of Teva DFX is, at its lowest, above the claimed range of 45-60%. The precise figures for Teva DFX are confidential, but on what is sometimes described in *Actavis* as a normal construction, Teva DFX is outside the claims. This is common ground.

214. Novartis argues that it nonetheless falls within the claim as an equivalent to the invention having asked and answered the *Actavis* questions. They are (*Actavis UK Ltd v Eli Lilly & Co* [2017] UKSC 48, at 66):

> "(i) Notwithstanding that it is not within the literal meaning of the relevant claim(s) of the patent, does the variant achieve substantially the same result in substantially the same way as the invention, i.e. the inventive concept revealed by the patent?

> (ii) Would it be obvious to the person skilled in the art, reading the patent at the priority date, but knowing that the variant achieves substantially the same result as the invention, that it does so in substantially the same way as the invention?
>
> (iii) Would such a reader of the patent have concluded that the patentee none the less intended that strict compliance with the literal meaning of the relevant claim(s) of the patent was an essential requirement of the invention?
>
> In order to establish infringement in a case where there is no literal infringement, a patentee would have to establish that the answer to the first two questions was 'yes' and that the answer to the third question was 'no'."

215. If Novartis' version of the inventive concept were correct Teva DFX would infringe as an equivalent. The 45-60% range of deferasirox does not figure in that inventive concept, which is all about the unexpected increased bioavailability and reduced food effect. The evidence indicated that Teva DFX benefits from those and I am not sure that it was in dispute.

216. Teva's inventive concept is almost entirely about the 45-60% range, so there would be no equivalence.

217. I have rejected both versions. For convenience I here repeat the inventive concept as I have found it to be:

> A swallowable film-coated tablet containing deferasirox in an amount between 45% and 60% of total weight and (subject to variation in conformity with the skilled person's common general knowledge) containing (i) microcrystalline cellulose, (ii) crospovidone, (iii) povidone, (iv) poloxamer 188, (v) colloidal silicon dioxide and (vi) magnesium stearate, and containing no SLS or lactose.

218. A view could be taken that a numerical range in a claim is never susceptible to stretching so as to allow for equivalents anywhere outside that range; a numerical range invariably implies strict compliance. I see two problems with such an approach. The first is that it invites the question whether a product or process 0.1% outside the range could never be an equivalent. Alternatively, what about 1% or 5%? If the concession is made that one cannot be absolutist and that depending on all the facts it may possibly be shown that there is an equivalent outside the claimed numerical range, and it seems to me that such a concession is unavoidable, then guidelines are needed to know when this will be the case. The only available guidelines are those in *Actavis*.

219. Secondly, in *Smith & Nephew plc v Convatec Technologies Inc* [2015] EWCA Civ 607, Kitchin LJ (with whom Briggs and Christopher Clarke LJJ agreed) stated (at [38]):

> "… the approach to be adopted to the interpretation of claims containing a numerical range is no different from that to be adopted in relation to any other claim."

220. This was endorsed by the Court of Appeal in *Jushi Group Co. Ltd v OCV Intellectual Capital LLC* [2018] EWCA Civ 1416, at [36]. *Smith & Nephew* pre-dates *Actavis*. *Jushi* was decided about a year after *Actavis*. I have assumed that the Court of Appeal

in *Jushi* was not drawing an unstated distinction, which it intended to be relevant in this context, between interpretation and scope. That would lead to the odd result that numerical claims need not always be strictly interpreted as a matter of normal construction but they must be under the doctrine of equivalents. On the further reasonable assumption that the principle quoted above from *Smith & Nephew* has not changed, the law on equivalents explained in *Actavis* applies to claims containing a numerical range just as much as it does to other claims.

221. Assuming that is correct, a numerical range may be more or less strictly applied in determining the scope of a claim, depending on all relevant facts.

222. By way of an example, referred to by both sides, *Regen Lab SA v Estar Medical Ltd* [2019] EWHC 63 (Pat) concerned a claim to a process for preparing a cell composition by centrifugation, comprising a series of steps. One of the steps involved buffered sodium citrate specified in the claim to be a 0.10 molar solution. The defendants supplied kits, the use of which led to the performance of a similar process save for two differences, one of which was that the buffered sodium citrate was a 0.136 molar solution. The inventive concept as found did not include the use of a buffer of any specific molarity. On the evidence the molarity of the sodium citrate in the variant was of no material significance and the answers to the *Actavis* questions were such that there was infringement by equivalence.

The arguments

223. The parties' arguments on infringement were ships passing in the night – unsurprisingly given the difference in their respective inventive concepts. One inventive concept points towards Teva DFX infringing the Patents, the other leads away from infringement.

The *Actavis* questions

224. The first question is whether Teva DFX achieves substantially the same result in substantially the same way as the inventive concept.

225. Teva DFX achieves exactly the same result in all aspects of the inventive concept except that its deferasirox content is above the 45-60% range. As discussed above, the evidence as a whole was that the range would be interpreted strictly when taken in context with all the specified excipients together. According to the CGK of the skilled formulator there could be leeway regarding the filler and the surfactant without changing the deferasirox content. But if the deferasirox content were to be changed, this would require change in the excipients as a whole. There was no evidence about the detail of this and it makes no difference to the inventive concept as presented in the Patents. The inventive concept is a swallowable film-coated tablet with fixed and specified features. The description of the Patents says that in combination they work. There may be other unexplained combinations which work, but those would be different inventive concepts. So far as this inventive concept is concerned, the skilled team would infer that the deferasirox range is to be strictly observed.

226. Despite the submission of Novartis, I see no difficulty in applying the first *Actavis* question to a product claim. In *Actavis* itself, claims 1 to 11 were use claims in Swiss

form, claims 12 to 14 were product claims. At [7] Lord Neuberger identified "the actual invention", which I take to be the inventive concept:

> "… a disclosure that pemetrexed could be administered safely if it was combined with a medicament with vitamin B12 …".

227. When Lord Neuberger turned to his newly formulated *Actavis* questions, he ruled (at [68]):

> "So far as the first question is concerned, there can be no doubt but that those products work in the same way as the invention: they all ultimately involve a medicament containing the pemetrexed anion and vitamin B12. Thus, they achieve substantially the same result in substantially the same way as the invention."

228. Where the inventive concept is a product, the variant achieves substantially the same result if it is substantially the same as that product. I was given little evidence to go on in assessing what qualifies as substantially the same product on the present facts. There was an assertion by Novartis in their written closing submissions that regulators allow for manufacturing tolerance and for Teva DFX to be released if the deferasirox is present in an amount that varies by 95-105% of the nominal value. I am not certain where that figure came from but it was put to Dr Huatan in cross-examination. He was insistent that while that is an accepted tolerance for the purpose of product regulation, when it came to formulation, the formulator would strictly adhere to the percentage value set, wherever it fell within the 45-60% range. As I understand him, there would otherwise be a tolerance in the formulating percentage on top of which there would be a further manufacturing tolerance. His point anyway was that the 45-60% range of the claim would be understood to be the range within which the formulator would fix a percentage figure for formulating the product and that would be strictly adhered to and therefore would be never higher than 60%.

229. The confidential range of deferasirox in Teva DFX in the evidence was taken from measurements of manufactured batches of Teva's product. That suggests to me that the confidential range already includes the manufacturing tolerance as it is in reality. But this was not explored.

230. I would add that no maths was done in Novartis' closing submissions in connection with the alleged 95-105% tolerance. My own check does not convince me that 95% of any relevant figure would result in something within the 45-60% range, even assuming that to be a relevant calculation. Further, for this argument to have force, Novartis would need to show that the 95-105% tolerance was within the CGK of the skilled team and would be seen by the team as a guide to whether one product was substantially the same as another. I was not shown any such evidence.

231. For the most part Novartis directed my attention to evidence of bioequivalence in their product and Teva DFX but this was on the basis of their preferred inventive concept and alleged similarities in bioavailability and food effect. It could not in any event be directly relevant since the relevant comparison is not between the parties' products but between Teva DFX and the inventive concept of the Patents.

232. I have found that in the present case the inventive concept of the Patents would be seen by the skilled team as requiring strict compliance with the 45-60% range of deferasirox. On that basis a variant will not be substantially the same as the inventive concept unless it strictly complies. I need not investigate with precision what compliance means numerically as matter of general principle. In my judgment Teva DFX does not comply.

233. This answer to the first *Actavis* question looks a great deal like an answer to the third. On the present facts they largely overlap. In the end, whether the result properly turns on the first or the third question, in my judgment the answer to the first question is no and/or the answer to the third is yes. Teva DFX falls outside the claims on both a normal construction and under the doctrine of equivalents.

Conclusion

234. The Patents lack inventive step over Battung and Zadok. Teva DFX does not fall within the scope of the claims of the Patents.