

ENGLAND AND WALES / JUDGMENT

Generics (UK) Limited & Ors v AstraZeneca AB

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Neutral Citation Number: [2025] EWCA Civ 903 IN THE COURT OF APPEAL (CIVIL DIVISION) ON APPEAL FROM THE HIGH COURT OF JUSTICE, BUSINESS AND PROPERTY COURTS OF ENGLAND AND WALES, INTELLECTUAL PROPERTY LIST (Ch), PATENTS COURT Dr Michael Tappin KC sitting as a Deputy High Court Judge

[2025] EWHC 1012 (Pat) Case No: CA-2025-001040 Royal Courts of Justice Strand, London, WC2A 2LL Date: 16 July 2025 Before : LORD JUSTICE PETER JACKSON LORD JUSTICE ARNOLD and LORD JUSTICE STUART-SMITH

- ----- Between :

(1) GENERICS (U. K.) LIMITED

(2) TEVA PHARMACEUTICAL INDUSTRIES Claimants/ Respondents LIMITED AND TEVA UK LIMITED

(3) GLENMARK PHARMACEUTICALS EUROPE LIMITED

- and - ASTRAZENECA AB

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- ----- Defendant/ Appellant Thomas Hinchliffe KC, Stuart Baran, Thomas Lunt and Dheemanth Vangimalla (instructed by Freshfields LLP) for the Appellant Tom Mitcheson KC and Adam Gamsa (instructed by Taylor Wessing LLP) for Viatris Tom Mitcheson KC and Tim Austen (instructed by Pinsent Masons LLP) for Teva Tom Mitcheson KC and Kathryn Pickard KC (instructed by Powell Gilbert LLP) for Glenmark Hearing dates : 25-26 June 2025

- ----- Approved Judgment This judgment was handed down remotely at 10.30am on 16 July 2025 by circulation to the parties or their representatives by e-mail and by release to the National Archives. Judgment Approved by the court for handing down. Generics v AstraZeneca Lord Justice Arnold:

Introduction

1. 2. 3. 4. 5. 6. This appeal requires this Court once again to consider the concept of plausibility when determining the validity of a patent. It has many similarities with *Sandoz Ltd v Bristol-Myers Squibb Holdings Ireland Unlimited Company* [2023] EWCA Civ 472,

[2023] RPC 12 (“*Sandoz v BMS*”), although there are differences. One of the main differences is that the appeal also requires the Court to consider the concept of arbitrary selection from the prior art. The Defendant (“AstraZeneca”) was the proprietor of European Patent (UK) No. 1 506 211 entitled “C-aryl glucoside SGLT2 inhibitors and method” (“the Patent”), which expired on 14 May 2023, and is the proprietor of UK Supplementary Protection Certificates Nos. SPC/GB13/021 and SPC/GB14/050 (“the SPCs”) based on the Patent, which expire on 13 and 14 May 2028. The claims of the Patent relate to a compound called dapagliflozin, marketed by AstraZeneca under the trade mark Forxiga pursuant to a marketing authorisation granted on 14 November 2012, which is used to treat diabetes. The Claimants contend that the Patent was invalid, and therefore the SPCs are invalid. There is no challenge to the claimed priority date of 20 May 2002. AstraZeneca acquired the Patent from Bristol-Myers Squibb (“BMS”) in 2014. Dapagliflozin is an inhibitor of the sodium-dependent glucose co-transporter protein SGLT2. SGLT2 is responsible for the re-uptake of glucose in the proximal tubule of the kidney back into the bloodstream. SGLT2 inhibitors are understood to reduce blood glucose levels by preventing glucose reabsorption into the blood, thereby facilitating excretion into the urine. The Claimants contend that the Patent was invalid for lack of inventive step and/or insufficiency. In summary they plead that: i) ii) the Patent did not make it plausible that dapagliflozin is an SGLT2 inhibitor, a selective SGLT2 inhibitor or useful for treatment of diabetes; and the Patent did not make a technical contribution over International Patent Application No. WO 01/27128 A1 (“WO 128”) filed by BMS and published on 19 April 2001, but rather merely made an arbitrary selection of dapagliflozin from the class of compounds disclosed in WO 128 without disclosing any advantage for dapagliflozin compared to that class. WO 128 discloses a class of compounds defined by an extremely broad Markush formula, Formula I, that are said to be SGLT2 inhibitors. It also describes a narrower (but very broad) class defined by Formula IA and a still narrower (but broad) class defined by Formula IB. It is common ground that dapagliflozin falls within the class defined by Formula IB and differs in only one respect from a member of that class described in Example 12 of WO 128. Originally the Claimants also contended that it was obvious (in the conventional sense) to arrive at dapagliflozin as an SGLT2 inhibitor from the disclosure of WO 128, but that allegation was not pursued in their closing submissions at trial. Judgment Approved by the court for handing down. *Generics v AstraZeneca* 7. 8. After a seven day trial Dr Michael Tappin KC sitting as a Deputy High Court Judge held that the Patent was invalid on both grounds pursued by the Claimants for the reasons given in an impressive judgment running to 282 paragraphs dated 28 April 2025 [2025] EWHC 1012 (Pat). AstraZeneca appeals with permission granted by the judge on eight grounds. I expedited the hearing of the appeal because the market for dapagliflozin is a large one and

the Claimants (and a number of other generic pharmaceutical companies) are currently restrained by interim injunctions and undertakings from launching generic dapagliflozin products. It is worth noting that Dr Tappin KC was particularly well-qualified to hear this case, since he not only has a degree in chemistry and a doctorate in biochemistry, but also had the experience gained from appearing as counsel in (among many other cases) *Sandoz v BMS*. The law concerning plausibility 9. Article 52(1) of the European Patent Convention (“EPC”) provides that European patents “shall be granted for any inventions” provided that (among other things) they “involve an inventive step”. Article 56 provides that an invention “shall be considered as involving an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art”. Article 83 requires that an application for a European patent “shall disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art”. Article 100 provides the grant of a European patent may be opposed on grounds that include lack of patentability under Article 56 and failure to comply with Article 83. Article 138(1) provides that a European patent may be revoked with effect for a Contracting State by the courts of that State on grounds that again include lack of patentability under Article 56 and failure to comply with Article 83. Sections 1(1)(a), 3, 14(3) and 72(1) of the Patents Act 1977 give effect in the United Kingdom to Articles 52(1), 56, 83 and 138(1) EPC. None of those provisions mentions the criterion of plausibility. It has been developed through the case law initially of the Boards of Appeal of the European Patent Office and latterly of the courts of the Contracting States including the UK. 10. I traced the development of the law in my judgment in *Sandoz v BMS* at [7]-[42]. It is pointless to repeat the exercise, and so I will take that exposition as read and only recapitulate the key points. Given the arguments on the present appeal, however, it is worth putting the law into context by first explaining a fundamental aspect of patent law. First to file 11. So far as I am aware, all patent laws in the world now operate on the “first to file” basis. (The USA used to be an exception, but that has ceased to be the case since the America Invents Act 2011). Without descending into detail, this essentially means that the first person to file an application to patent a particular invention is entitled to any resulting patent to the exclusion of any later applicant. Thus the date on which the application is filed, or the priority date if earlier, is critical. (The priority date is the date of an application by the same applicant in respect of the same invention filed up to one year earlier. The priority system enables an applicant to file an initial application in one country followed by multiple subsequent applications in other countries.) It is by reference to that date that issues of patentability are assessed. Thus Judgment Approved by the court for handing down. *Generics v AstraZeneca* 12. 13. 14. it is by reference to the state of the art at that date that it is determined whether the claimed invention meets the core requirements of novelty, inventive step and industrial application. And it is by reference to the common general knowledge of the person skilled in the art at that date that the patent is interpreted, and that inventive step and sufficiency of disclosure are assessed. It is a cardinal principle of patent law that hindsight should, so far as is humanly possible, be excluded from these assessments. As has often been pointed out, it would be unfair to inventors if inventive step were to be assessed with

hindsight, since many inventions appear obvious after the event. It can readily be seen that it would undermine this system if applicants for patents were permitted to add information (what patent lawyers call “subject-matter”) to the information that is contained in their applications after the application date or, where applicable, the priority date. For this reason, patent laws typically contain substantive rules which are designed to prevent this. In the case of the EPC, the key two rules are Article 87(1), which provides that priority can only be claimed in respect of “the same invention”, and Article 123(2), which provides that “[a] European patent application or a European patent may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed”. These provisions are implemented in the UK by sections 5(2) and 76 of the 1977 Act. The jurisprudence both of the Boards of Appeal and of national courts establishes that these rules are strict ones. It would also undermine this system if applicants were permitted to rely upon information (other than common general knowledge) that is not present in the application (or priority document) when filed as establishing the patentability of the invention. That would also be objectionable for another reason, namely that it would be contrary to the “patent bargain” discussed by Lord Sumption in *Generics (UK) Ltd v Warner-Lambert Co LLC* [2018] UKSC 56, [2019] Bus LR 360 (“Warner-Lambert”) at [17]. In short, this is the principle that the reward of a 20 year monopoly is bestowed on the proprietor of a patent in return for the disclosure of the invention to the public in the patent application. It does not follow from the principles discussed in the preceding paragraphs that, in the event of dispute, evidence dating from after the relevant date cannot be relied upon as establishing the position as at that date. In this jurisdiction the court receives evidence from suitably qualified expert witnesses whose primary function is to educate the court as to the common general knowledge of the skilled person or team at the relevant date, and hence to inform the court of any technical considerations which are material to the issues it has to consider. Such evidence is necessarily given after the event, and frequently long after the relevant date, but the experts are instructed to try to avoid hindsight. Furthermore, evidence as to subsequent events can cast light on the position as at the relevant date. It is sufficient to give three examples of this. First, the reaction of the scientific community when an invention is first made public may help to show that it was not obvious. Secondly, in rare cases, evidence that the invention has achieved commercial success by fulfilling a “long-felt want” may also help to show the same thing. Thirdly, evidence of subsequent attempts to perform the invention (or evidence that can be treated as a proxy for such evidence) may be relied upon to show that the disclosure in the application was insufficient. Judgment Approved by the court for handing down. *Generics v AstraZeneca* 15. There is, however, a fundamental distinction between relying upon later evidence to cast light on the position as at the relevant date on the one hand, and on the other hand permitting patent applicants and proprietors to rely upon information that could not have been available to the skilled reader of the patent application at the relevant date, either because it did not yet exist or because it was secret, as establishing the patentability of an invention. *Warner-Lambert* 16. It is common ground that the decision of the majority of the Supreme Court

in Warner-Lambert is authority binding on this Court as to the standard to be applied when assessing the sufficiency of disclosure of a medical use invention. (The claimed invention in Warner-Lambert was a second medical use, but AstraZeneca does not suggest, at least in this Court, that a distinction can be made between first and second medical use claims.) The majority adopted a standard which has subsequently come to be referred to as “ab initio plausibility”, meaning in essence that the application when read together with the common general knowledge must positively make it plausible that the invention will achieve the claimed technical effect. The minority preferred a standard which has subsequently come to be referred to as “ab initio implausibility”, meaning in essence that the application when read together with the common general knowledge should not give rise to doubt as to whether the invention will achieve the claimed technical effect. 17. For present purposes it is sufficient to cite two passages in the judgment of Lord Sumption for the majority. The first passage sets out the principle (emphases and line breaks added in [37]): “36. The principle is that the specification must disclose some reason for supposing that the implied assertion of efficacy in the claim is true. Plausibility is not a distinct condition of validity with a life of its own, but a standard against which that must be demonstrated. Its adoption is a mitigation of the principle in favour of patentability. It reflects the practical difficulty of demonstrating therapeutic efficacy to any higher standard at the stage when the patent application must in practice be made. The test is relatively undemanding. But it cannot be deprived of all meaning or reduced ... to little more than a test of good faith. 37. Plausibility is not a term of art, and its content is inevitably influenced by the legal context. In the present context, the following points should be made. First, the proposition that a product is efficacious for the treatment of a given condition must be plausible. Second, it is not made plausible by a bare assertion to that effect, and the disclosure of a mere possibility that it will work is no better than a bare assertion. Judgment Approved by the court for handing down. Generics v AstraZeneca But, third, the claimed therapeutic effect may well be rendered plausible by a specification showing that something was worth trying for a reason, ie not just because there was an abstract possibility that it would work but because reasonable scientific grounds were disclosed for expecting that it might well work. The disclosure of those grounds marks the difference between a speculation and a contribution to the art. This is in substance what the Technical Board of Appeal has held in the context of article 56, when addressing the sufficiency of disclosure made in support of claims extending beyond the teaching of the patent. In my opinion, there is no reason to apply a lower standard of plausibility when the sufficiency of disclosure arises in the context of EPC articles 83 and 84 and their analogues in section 14 of the Patents Act. In both contexts, the test has the same purpose. Fourth, although the disclosure need not definitively prove the assertion that the product works for the designated purpose, there must be something that would cause the skilled person to think that there was a reasonable prospect that the assertion would prove to be true. Fifth, that reasonable prospect must be based on what the TBA in Salk (para 9) called ‘a direct effect on a metabolic mechanism specifically involved in the disease, this mechanism being either known from the prior art or

demonstrated in the patent per se.’ Sixth, in Salk, this point was made in the context of experimental data. But the effect on the disease process need not necessarily be demonstrated by experimental data. It can be demonstrated by a priori reasoning. For example, and it is no more than an example, the specification may point to some property of the product which would lead the skilled person to expect that it might well produce the claimed therapeutic effect; or to some unifying principle that relates the product or the proposed use to something else which would suggest as much to the skilled person. Seventh, sufficiency is a characteristic of the disclosure, and these matters must appear from the patent. The disclosure may be supplemented or explained by the common general knowledge of the skilled person. But it is not enough that the patentee can prove that the product can reasonably be expected to work in the designated use, if the skilled person would not derive this from the teaching of the patent.” 18. In the second passage Lord Sumption rejected Warner-Lambert’s argument that the courts below were wrong to reject experimental data generated after the relevant date as establishing the plausibility of the claimed technical effect for the reasons he gave at [40]: Judgment Approved by the court for handing down. *Generics v AstraZeneca* “This submission also is contrary to the legal basis of this particular head of insufficiency. We know that pregabalin works for the treatment of ... neuropathic pain, because like any other medicament on the market, it underwent demanding clinical trials after the priority date, the results of which were made public. On that basis it received marketing authorisation for ... neuropathic pain. This is always the case for a commercially valuable medicament, and no other kind will be worth litigating about. The question is not whether it works but whether the contribution to the art consisting in the discovery that it can be expected to work has been sufficiently disclosed in the patent. The inherent difficulty of demonstrating this before clinical trials is taken into account in the modest standard (ie plausibility) which is applied to test it. ... This does not mean that subsequent data is never admissible in a dispute about sufficiency, but the purpose for which it is admitted is strictly limited. Where the asserted therapeutic effect is plausible in the light of the disclosure in the patent, subsequent data may sometimes be admissible either to confirm that or else to refute a challenger’s contention that it does not actually work... But it cannot be a substitute for sufficient disclosure in the specification.” *Sandoz v BMS* 19. The principal legal issue in *Sandoz v BMS* was whether the same standard as that adopted in *Warner-Lambert* was applicable to the assessment of both sufficiency and inventive step in the case of a claim to a single chemical compound i.e. a pure product claim. This Court held that it was for the reasons I gave at [92]: “... It is true that, as Lord Sumption noted at [23], the concept of plausibility originated as a response to over-broad claims, in particular claims to whole classes of compounds, as in *Agrevo*. *Idenix* is an example of its application in that context by the courts of this country. It is also true that, as Lord Sumption noted at [19]-[20], that the concept was also found to be of utility in addressing one of the problems with second medical use claims. Nevertheless the concept was applied by the Board of Appeal to a claim to single compound in *BMS/Dasatinib*, which was one of the cases relied upon by Lord Sumption (and one of the cases reviewed by the Enlarged Board in *G 2/21*). As the

Claimants point out, the present case is strikingly similar to BMS/Dasatinib. Moreover, BMS/Dasatinib does not stand on its own, because the claim in Johns Hopkins, which was another of the cases relied upon by Lord Sumption and reviewed by the Enlarged Board, was effectively a claim to a specific molecule. The concept has also been applied by this Court in Generics v Yeda to a claim to what was in substance a single product, albeit a product comprising a mixture of polypeptides. Furthermore, the underlying principles are Judgment Approved by the court for handing down. Generics v AstraZeneca applicable as much to claims to single chemical compounds as to claims to classes of compounds and second medical use claims. The fundamental principle is that the scope of the patent monopoly must be justified by the patentee's technical contribution to the art. This remains so whether the scope of the claim is broad or narrow. Thus when considering inventive step it is necessary to consider what technical problem the claimed invention solves. If it is not plausible that the invention solves any technical problem then the patentee has made no technical contribution and the invention does not involve an inventive step. Equally, when considering insufficiency it is necessary to consider whether the specification sufficiently discloses the claimed invention. If it is not plausible that the invention solves any technical problem then the patentee has made no technical contribution and the specification does not disclose any invention. It follows that, in order for a claim to a single chemical compound to be patentable, the application must make it plausible, when read in the light of the skilled person's common general knowledge, that the compound has the utility asserted for it. Moreover, it makes no difference whether the claim incorporates the use of the compound as a technical feature or whether the claim is simply to the compound per se and the assertion of utility is only to be found in the specification. This is because, as explained above, there is no invention in merely identifying a new chemical compound; invention can only lie in identifying its utility." 20. 21. G 2/21 22. It should be noted that in that case it was common ground between the parties, as I explained at [4], that it made no difference whether the issue was viewed as one of inventive step or one of sufficiency. As explained in more detail below, this is not common ground in the present case. BMS applied to the Supreme Court for permission to appeal on two grounds. Ground 1 was that Warner-Lambert was not of general application, but was confined to the special case of second medical use claims. Ground 2 was that the Court of Appeal had erred in its approach to the standard required by Warner-Lambert. By order dated 31 October 2023 the Supreme Court (Lord Reed, Lady Rose and Lord Stephens) refused permission to appeal "because the application does not raise an arguable point of law". Paragraph 3.32 of Supreme Court Practice Direction 3 states that "[t]he reasons for refusing permission to appeal should not be regarded as having any value as a precedent". Nevertheless, this Court cannot ignore the fact that the Supreme Court considered that the grounds were not sufficiently arguable to justify the grant of permission to appeal. As explained in more detail below, some of AstraZeneca's grounds of appeal concern the decision of the Enlarged Board of Appeal in case G 2/21 [2023] OJ EPO A85. This decision was rendered about four weeks before the hearing in Sandoz v BMS. I discussed it in my judgment in that case at [43]-[53]. Having regard to the

arguments in this case, it is necessary to consider it afresh. Judgment Approved by the court for handing down. *Generics v AstraZeneca* 23. 24. 25. 26. 27. In G 2/21 the Enlarged Board of Appeal considered three questions about the circumstances in which it was permissible to rely on so-called “post-published evidence” (evidence which post-dates the application or priority date) as demonstrating or supporting a technical effect when assessing whether the claimed invention complies with the requirement for an inventive step. In answering the questions referred, the Enlarged Board began by noting at [23] that, according to the settled jurisprudence of the Boards of Appeal, “the assessment of inventive step is to be made at the effective date of the patent on the basis of the information in the patent together with the common general knowledge then available to the skilled person”. To use a term employed by the Boards of Appeal in other contexts, this is the “gold standard”. The Enlarged Board then noted at [24]-[26] that the EPO routinely employs the so-called “problem and solution approach” to the assessment of inventive step. It is not necessary for present purposes to describe this approach, but it is important to note that it forms an important part of the background to the questions referred to the Enlarged Board and that it is not employed by the courts of the UK (other than, on occasion, as a cross-check), nor is it widely employed by the courts of other EPC Contracting States. The first question asked whether post-published evidence must be disregarded “on the ground that proof of the effect rests exclusively on the post-published evidence” (emphasis in the original). The Enlarged Board considered this question at [27]-[56]. Its answer was that “evidence submitted by a patent applicant or proprietor to prove a technical effect relied upon for acknowledgement of inventive step may not be disregarded solely on the ground that such evidence, on which the effect rests, had not been made public before the filing date of the patent and was filed after that date”. This is not really an answer to the question referred, which was not about whether evidence can be excluded solely on the ground that it post-dates the relevant date, but whether a technical effect can be relied upon which rests exclusively on post-dated evidence. Perhaps for that reason, although the referring Board of Appeal only asked its second and third questions on the premise that the answer to the first question was yes, the Enlarged Board considered them anyway. In its decision to refer (T 116/18 Sumitomo/Insecticide compositions, unreported, 11 October 2021) the referring Board had identified what it regarded as two divergent lines of Board of Appeal case law. The first line, represented by decisions such as T 1329/04 Johns Hopkins/Factor-9

[2006] EPOR 8 and T 488/16 Bristol-Myers Squibb/Dasatinib [2019] EPOR 24, it labelled “ab initio plausibility”. The second line, represented by decisions such as T 578/06 Ipsen/Pancreatic cells (unreported, 29 June 2011), it labelled “ab initio implausibility”. The distinction it saw between these two lines was that, in the first, post-published evidence could be taken into account if, based on the information in the application and the skilled person’s common general knowledge, the skilled person would have considered the technical effect plausible. In the second line, post-published evidence could be taken into account if, based on the information in the application and the skilled person’s common general

knowledge, the skilled person would not have considered the technical effect implausible. Judgment Approved by the court for handing down. *Generics v AstraZeneca* 28. 29. The Enlarged Board began its consideration of these questions by observing at [58] that that it considered “the conceptional notion inherent in the term ‘plausibility’, which is often used as a generic catchword, as not being a distinct condition of patentability and patent validity, but a criterion for the reliance on a purported technical effect”. This observation chimes with what Lord Sumption said in *Warner- Lambert* at [23] and [36]. From [60] onwards, the Enlarged Board embarked on an analysis of the “jurisprudence regarding the reliance on a technical effect for inventive step”. It began with some “general considerations”, referring among other cases to *Ipsen*. At [66]-[68] it considered cases in the “ab initio plausibility” or “type I” line of case law identified by the referring Board, including *Johns Hopkins* and *BMS/Dasatinib*. In

- [69] it considered cases in the “ab initio implausibility” or “type II” line. It expressed its “intermediate conclusion” as follows: “70. The Enlarged Board takes note of the classification done by the referring board in respect of the case law of the boards of appeal concerning the relevance of post-published evidence to prove an asserted technical effect for acknowledgement of inventive step ...
71. However, when analysing the case law in more detail and irrespective of the conceptual terminologies for what questions 2 and 3 refer to as two distinct plausibility approaches, the Enlarged Board understands from the case law of the boards of appeal as common ground that the core issue rests with the question of what the skilled person, with the common general knowledge in mind, understands at the filing date from the application as originally filed as the technical teaching of the claimed invention.
72. Applying this understanding to the aforementioned decisions, not in reviewing them but in an attempt to test the Enlarged Board’s understanding, the Enlarged Board is satisfied that the outcome in each particular case would not have been different from the actual finding of the respective board of appeal. Irrespective of the use of the terminological notion of plausibility, the cited decisions appear to show that the particular board of appeal focussed on the question whether or not the technical effect relied upon by the patent applicant or proprietor was derivable for the person skilled in the art from the technical teaching of the application documents.” 30. In other words, the Enlarged Board regarded the two lines of case law as being reconcilable. In each case, the core question being addressed was what the technical teaching of the application was to the skilled person with the common general knowledge in mind at the filing date, and whether the technical effect relied upon by the patent applicant or proprietor was derivable from that technical teaching. 31. Although the reference was only concerned with inventive step, at [73]-[77] the Enlarged Board considered the case law of the Boards of Appeal regarding Judgment Approved by the court for handing down. *Generics v AstraZeneca* sufficiency, in particular in the context of second medical use claims. It noted at [74] that the issues of sufficiency of disclosure (Article 83) and inventive step (Article 56) were “to be treated separately”. It also noted that in second medical use

cases a technical effect, usually a therapeutic effect, was a feature of the claim and that such cases involved the use of a known therapeutic agent for a new therapeutic application. It was therefore “necessary that the patent ... renders it credible that the known therapeutic agent ... is suitable for the claimed therapeutic application”. 32. The Enlarged Board expressed its “intermediate conclusion” with regard to these cases at [77] as follows: “The reasoned findings of the boards of appeal in the decisions referred to above make clear that the scope of reliance on post published evidence is much narrower under sufficiency of disclosure (Article 83 EPC) compared to the situation under inventive step (Article 56 EPC). In order to meet the requirement that the disclosure of the invention be sufficiently clear and complete for it to be carried out by the person skilled in the art, the proof of a claimed therapeutic effect has to be provided in the application as filed, in particular if, in the absence of experimental data in the application as filed, it would not be credible to the skilled person that the therapeutic effect is achieved. A lack in this respect cannot be remedied by post-published evidence.” 33. At [78]-[85] the Enlarged Board turned to consider decisions of courts of EPC Contracting States “with regard to the reliance on technical effect for inventive step”. In particular, at [84]-[85] it considered judgments of the UK courts, including Warner-Lambert and the High Court judgment in Sandoz v BMS. It expressed its “intermediate conclusion” as follows: “86. Like the EPC, none of the legal systems of the EPC Contracting States provide for an explicit patentability requirement for what the referring decision discusses and addresses with what is referred to in questions 2 and 3 under the term ‘plausibility’. 87. Notwithstanding the fact that the aforementioned decisions were taken on the decisive facts of the case in hand and the particular submissions made by the parties to those proceedings, the Enlarged Board recognises a certain degree of common ground that the courts of the EPC Contracting States, when confronted with the examination of an asserted technical effect in the assessment of inventive step and with the question whether a patent proprietor may rely on post-published evidence to confirm that technical effect, ponder on the technical teaching of the claimed subject-matter that the person skilled in the art, with the common general knowledge in mind, understands from the patent application.” Judgment Approved by the court for handing down. Generics v AstraZeneca 34. In other words, the Enlarged Board interpreted the decisions of the national courts as approaching matters in a similar manner to the Board of Appeal decisions which it had summarised in [71]-[72]. 35. At [88]-[95] the EBA set out its “concluding considerations”, including the following: “92. The term ‘plausibility’ that is found in the case law of the boards of appeal and relied upon by the referring board in questions 2 and 3 of the referral and the reasons for it, does not amount to a distinctive legal concept or a specific patent law requirement under the EPC, in particular under Article 56 and 83 EPC. It rather describes a generic catchword seized in the jurisprudence of the boards of appeal, by some national courts and by users of the European patent system. 93. The relevant standard for the reliance on a purported technical effect when assessing whether or not the claimed subject-matter involves an inventive step concerns the question of what the skilled person, with the common general knowledge in mind, would understand at the filing date from the application as originally filed as the technical teaching of the claimed invention. The

technical effect relied upon, even at a later stage, needs to be encompassed by that technical teaching and to embody the same invention, because such an effect does not change the nature of the claimed invention.

94. Hence, a patent applicant or proprietor may rely upon a technical effect for inventive step if the skilled person, having the common general knowledge in mind, and based on the application as originally filed, would consider said effect as being encompassed by the technical teaching and embodied by the same originally disclosed invention. 95. The Enlarged Board is aware of the abstractness of some of the aforementioned criteria. However, apart from the fact that the Enlarged Board, in its function assigned to it under Article 112(1) EPC, is not called to decide on a specific case, it is the pertinent circumstances of each case which provide the basis on which a board of appeal or other deciding body is required to judge, and the actual outcome may well to some extent be influenced by the technical field of the claimed invention. Irrespective of the actual circumstances of a particular case, the guiding principles set out above should allow the competent board of appeal or other deciding body to take a decision on whether or not post-published evidence may or may not be relied upon in support of an asserted technical effect when assessing whether or not the claimed subject-matter involves an inventive step.” 36. Accordingly, the Enlarged Board answered the second and third questions in its order as follows: Judgment Approved by the court for handing down. *Generics v AstraZeneca* “A patent applicant or proprietor may rely upon a technical effect for inventive step if the skilled person, having the common general knowledge in mind, and based on the application as originally filed, would derive the said effect as being encompassed by the technical teaching and embodied by the same originally disclosed invention.” 37. It is clear, and undisputed by either party in the present case, that, in expressing itself in the way that it did, the Enlarged Board was deliberately eschewing the language of plausibility. What is less clear is whether the test it laid down differs in substance from one of plausibility, and if so how. There is a substantial dispute as to how that test is to be understood and applied. It is common ground that the test appears to involve two limbs: the skilled person would derive the technical effect as being, first, encompassed by the technical teaching of the application, and secondly, embodied by the same originally disclosed invention. The dispute particularly focusses on the second limb. The law concerning arbitrary selections 38. 39. The judge set this out at [39]-[59]. Save in one respect, there is no dispute as to the accuracy of that account, and so I can summarise it briefly. Making an arbitrary selection from the prior art is not inventive. The question is therefore what distinguishes an arbitrary selection from an inventive selection. The answer to that question is that an inventive selection makes a technical contribution to the art, whereas an arbitrary selection does not. The leading authority on this distinction is *Dr Reddy’s Laboratories (UK) Ltd v Eli Lilly & Co Ltd* [2009] EWCA Civ 1362, [2010] RPC 9, in which this Court adopted the principles applied by the Boards of Appeal. The test established in that case was succinctly summarised by Floyd LJ in *Generics (UK) Ltd v Yeda Research & Development Co Ltd* [2013] EWCA Civ 925, [2013] Bus LR 1329 at [49(4)]: “... a selection from the prior art which is purely arbitrary and cannot be justified by some useful

technical property is likely to be held to be obvious because it does not make a real technical advance ...” This principle has found particular application where the application or patent claims a chemical compound selected from a genus of compounds disclosed in a prior document. It is not necessary to show that the prior document contains some pointer to the later claimed compound. (If there were such a pointer, the complaint of arbitrary selection would be unnecessary because the later compound would be obvious in the conventional sense.) In order to rebut the charge of arbitrary selection in such a case, the applicant or patentee must show that the claimed compound achieves what in *Dr Reddy’s Jacob LJ* at [52] called “a real technical advance” and Lord Neuberger of *Abbotsbury MR* at [109] called “a particular technical result”. 40. The judge summarised the law at [59] as follows: “Overall, I do not perceive any material difference between the case law of the EPO and the UK case law (which is to be expected, given that the intention of the Court of Appeal in *Dr Judgment Approved* by the court for handing down. *Generics v AstraZeneca Reddy’s* was to adopt the EPO approach). The requirement is for the claimed invention to in fact constitute a technical advance and for the patent to disclose enough to make that technical advance plausible. If the patent claims a compound selected from a previously disclosed genus of compounds which are said to have a particular property, then that requirement is not satisfied if the compound does not in fact have some different or improved property compared to those previously individually disclosed (a new effect or an increase in an effect), or the patent does not make such improved property plausible.” The skilled team 41. The judge found that the Patent was addressed to a skilled team comprising (i) a medicinal chemist and (ii) a biochemist or pharmacologist with experience in glucose transporter proteins and diabetes. The expert witnesses 42. The Claimants called Professor Bernard Thorens (biology/pharmacology) and Dr Paul Edwards (medicinal chemistry). AstraZeneca called Professor Clifford Bailey (biology/pharmacology) and Professor Barry Potter (medicinal chemistry). The judge found that all four witnesses had done their best to assist the court and that the areas of dispute between them on matters which were for expert evidence were fairly limited. Common general knowledge 43. 44. The judge set out the common general knowledge of the skilled team at [71]-[144] and [206]-[218]. Given the scope of the issues on the appeal, I will take those passages as read. It is only necessary to explain four points. First, the process of drug discovery proceeds through a number of stages, including the identification of a target, the generation of “hits” (compounds that show potential activity against the target), selection of “lead” compounds (those that show most promise), optimisation of leads through structural modifications, pre-clinical development and clinical trials. Activity is normally measured initially by *in vitro*, and later by *in vivo*, assays. A key property of a candidate compound is its potency, often expressed as IC₅₀ (half the maximal inhibitory concentration) or EC₅₀ (half the maximal effective concentration). Lower values indicate a more potent compound. It was common, at the stage of hit identification, to use an *in vitro* assay with a cut-off of 10 µM (i.e. to detect compounds with an IC₅₀ of 10 µM or less). However, compounds with such a level of potency would not be regarded as acceptable as a drug. For that, medicinal chemists would generally be looking for IC₅₀s in the low nanomolar range or better. 45. Secondly, SGLT2 was a known target at

the priority date. It had been isolated, cloned and characterised in humans. It was found to be expressed in the kidney. Judgment Approved by the court for handing down. *Generics v AstraZeneca* 46. 47. Thirdly, phlorizin is a naturally-occurring compound which was discovered in the early 1800s and was later noted to produce glycosuria and reduce blood glucose levels. It was demonstrated in the 1960s that phlorizin inhibits renal glucose reabsorption, and the skilled biologist/pharmacologist would be aware of studies using phlorizin, including to lower blood glucose in animal models. The skilled biologist/pharmacologist would (at least) assume that phlorizin inhibits SGLT2. Phlorizin was not suitable for the treatment of diabetes because it produced undesirable side-effects. Fourthly, the investigation of SGLT2 inhibitors as potential treatments for diabetes had become an established field by the priority date. Among others, a group of scientists employed by the Japanese pharmaceutical company Tanabe Seiyaku were active in this field. The Patent 48. It is common ground that there is no material difference between the Patent and the application which preceded it, and therefore it is possible in this case to determine the issues by reference to the Patent. The judge set out the disclosure of the Patent at [145]-[184]. For the purposes of the appeal, the following summary using the headings and sub-headings in the specification will suffice. Field of the invention 49. The specification states at [0001]: “The present invention relates to C-aryl glucosides which are inhibitors of sodium dependent glucose transporters found in the intestine and kidney (SGLT2) and to a method for treating diabetes, especially type II diabetes, as well as hyperglycaemia, hyperinsulinemia, obesity, hypertriglyceridemia, Syndrome X, diabetic complications, atherosclerosis and related diseases, employing such C-aryl glucosides or in combination with one, two or more other type antidiabetic agent and/or one, two or more other type therapeutic agents such as hypolipidemic agents” Background of the invention 50. 51. The specification sets out the background to the invention at [0002]-[0009]. The judge found that much of this was common general knowledge. Work on phlorizin “or closely related analogs” is referred to in [0004] and [0007], including a 6 month study of “an SGLT2 inhibitor” in diabetic rats by Tanabe Seiyaku. At [0010] the specification acknowledges that two items of prior art “disclose C-aryl glucoside SGLT2 inhibitors for treating diabetes”. The first is WO 128, which it says in [0011] discloses compounds which “are reported to be inhibitors of the SGLT2 transporter and consequently represent a mode for treatment of diabetes and complications thereof”. Judgment Approved by the court for handing down. *Generics v AstraZeneca* Description of the invention 52. This section begins: “[0013] In accordance with the present invention, a C-aryl glucoside compound is provided which has the structure [labelled I] [i.e. dapagliflozin] including pharmaceutically acceptable salts thereof, all stereoisomers thereof, and all prodrug esters thereof.

[0014] The compound of formula I possesses activity as inhibitors of the sodium dependent glucose transporters found in the intestine and kidney of mammals and is useful in the treatment of diabetes and the micro and macrovascular complications of diabetes such as retinopathy, nephropathy, and wound healing.” 53. The specification goes on in [0019] to state: “The term ‘other type of therapeutic agents’ as employed herein refers to one or

more anti diabetic agents (other than SGLT2 inhibitors of formula I) ...” Detailed description of the invention 54. This section begins by describing how dapagliflozin can be made. It then sets out a list of definitions. It then gives a long description of how dapagliflozin, pharmaceutically acceptable salts, stereoisomers and prodrug esters may be used. The only parts of this that either side suggests are relevant are references in [0051], [0052], [0053], [0074] and [0102] to “the SGLT2 inhibitor of formula I”. 55. The specification then states at [0114]: “SGLT2 inhibitor activity of the compounds of the invention may be determined by use of an assay system as set out below.” 56. Assay for SGLT2 activity. Under this sub-heading the specification states at [0115]: “The mRNA sequence for human SGLT2 (GenBank #M95549) was cloned by reverse-transcription and amplification from Judgment Approved by the court for handing down. Generics v AstraZeneca human kidney mRNA, using standard molecular biology techniques. The cDNA sequence was stably transfected into CHO cells, and clones were assayed for SGLT2 activity essentially as described in Ryan et al. (1994). Evaluation of inhibition of SGLT2 activity in a clonally selected cell line was performed essentially as described in Ryan et al., with the following modifications. Cells were grown in 96-well plates for 2-4 days to 75,000 or 30,000 cells per well in F-12 nutrient mixture (Ham’s F-12), 10% fetal bovine serum, 300 ug/ml Geneticin and penicillin-streptomycin. At confluence, cells were washed twice with 10 mM Hepes/Tris, pH 7.4, 137 mM N-methyl-D-glucamine, 5.4 mM KCl, 2.8 mM CaCl₂, 1.2 mM MgSO₄. Cells then were incubated with 10 µM [14C]AMG, and 10 µM inhibitor (final DMSO =0.5%) in 10 mM Hepes/Tris, pH 7.4, 137 mM NaCl, 5.4 mM KCl, 2.8 mM CaCl₂, 1.2 mM MgSO₄ at 37°C for 1.5 hr. Uptake assays were quenched with ice cold 1X PBS containing 0.5 mM phlorizin, and cells were then lysed with 0.1% NaOH. After addition of MicroScint scintillation fluid, the cells were allowed to shake for 1 hour, and then [14C]AMG was quantitated on a TopCount scintillation counter. Controls were performed with and without NaCl. For determination of EC₅₀ values, 10 inhibitor concentrations were used over 2 log intervals in the appropriate response range, and triplicate plates were averaged across plates.” 57. 58. Claims 59. I have italicised the word “inhibitor” which appears twice in this paragraph and is central to some of the arguments. Although it is not a point relied on by the Claimants, it may be noted that the last sentence does not identify the “10 inhibitor concentrations”. The reference for the paper by Ryan et al. is given in [0116]. Example. From [117]-[128] the specification describes in detail the preparation and characterisation of dapagliflozin. It does not set out any results from the assay for SGLT2 activity described in [0115] for dapagliflozin. The only claims relied upon by AstraZeneca for its appeal are claims 2 and 15. Claim 15 is dependent on claim 14. AstraZeneca applied unconditionally to amend claim 14 as shown below: “2. 14. The compound as defined in Claim 1 having the structure [formula I i.e. dapagliflozin]. Use, in the manufacture of a medicament for treating or delaying the progression or onset of diabetes, diabetic retinopathy, diabetic nephropathy, delayed wound healing, insulin resistance, hyperglycaemia, elevated blood levels of obesity, fatty acids or glycerol, hypertriglyceridemia, Syndrome X, diabetic complications, hyperlipidemia, Judgment Approved by the court for handing down. Generics v AstraZeneca atherosclerosis or hypertension, or for increasing high density lipoprotein

levels, of a compound as defined in claim 1. 15. The use as defined in claim 14 where the SGLT2 inhibitor compound has the structure [formula I i.e. dapagliflozin].” 60. In making the application to amend claim 14, AstraZeneca made no admission that the specification did not support the claim to efficacy in respect of the deleted diseases, but nor did it advance any case that it did. WO 128 61. The judge set out the disclosure of WO 128 alongside that of the Patent at [145]- [184]. Comparison of the two documents shows that the text of the Patent was largely copied from that of WO 128, but omits a substantial amount of material contained in WO 128. The principal difference between the two documents is that, as explained in paragraph 5 above, WO 128 discloses and claims three classes of what are said to be SGLT2 inhibitors. The narrowest class is represented by Formula IB shown below. 62. In addition, WO 128 describes 15 “Working Examples” in which the preparation and characterisation of specific compounds are described in detail. It also gives a more summary description of the preparation and characterisation of a further 65 Examples. One of the Working Examples described in WO 128 is Example 12. This describes the preparation and characterisation of the compound shown below. 63. 64. This compound differs from dapagliflozin only in that the group at the R4 position is -OMe (-OCH₃ or methoxy) whereas it is -OEt (-OC₂H₅ or ethoxy) in dapagliflozin. So far as the assay is concerned, the content of the two documents is the same: a passage at page 52 line 9 to page 53 line 12 of WO 128 is identical to the specification Judgment Approved by the court for handing down. Generics v AstraZeneca of the Patent at [0114]-[0116]. Like the Patent, WO 128 contains no results from the assay. 65. The final point to note is that WO 128 states, while acknowledging prior art, at page 7 lines 14-19: “Other disclosures and publications which disclose SGLT2 inhibitors include the following: K. Tsujihara et al, Chem. Pharm Bull. 44, 1177-1180 (1996) M. Hongu et al, Chem. Pharm Bull. 46, 22-23 (1998) M. Hongu et al, Chem. Pharm Bull. 46, 1545-1555 (1998) A. Oku et al, Diabetes, 48, 1794-1800 (1999)”. These four papers all emanated from Tanabe Seiyaku. The judge’s judgment Plausibility 66. The judge approached the issue of plausibility by asking himself the three questions proposed by Birss LJ in Akebia Therapeutics Inc v FibroGen Inc [2021] EWCA Civ 1279, [2022] RPC 7 at [53] for addressing claims to classes of products: “First one must identify what it is which falls within the scope of the claimed class. Second one must determine what it means to say that the invention works. In other words what is it for? Once you know those two things, the third step can be taken: to answer the question whether it is possible to make a reasonable prediction the invention will work with substantially everything falling within the scope of the claim.” 67. 68. It was common ground that the answer to the first question is that claim 2 is limited to the single compound dapagliflozin, while claim 15 is limited to the use of that compound in the manufacture of a medicament for treating or delaying the progression or onset of diabetes (“treating diabetes” for short). It was also common ground that the answer to the second question in the case of claim 15 is that “working” means treating diabetes. That is the relevant technical effect. As for claim 2, AstraZeneca did not advance any case that the identification of dapagliflozin per se was a technical contribution (i.e. without identifying any useful properties of dapagliflozin). The judge concluded at [232] that: “... what it means

to ‘work’ for the purpose of the second Fibrogen step in respect of claim 15 is treating etc. diabetes, in the sense of having sufficient efficacy to treat diabetes, and in respect of claim 2 is either (a) the same as in the case of claim 15 or (b) reducing blood or plasma glucose in Judgment Approved by the court for handing down. Generics v AstraZeneca vivo with sufficient efficacy to allow it to be used as an experimental tool.” 69. 70. 71. 72. 73. On the appeal AstraZeneca confined its case to finding (a), which made it unnecessary for the Claimants to pursue a respondents’ notice challenging finding (b). The judge considered the third question at [233]-[262]. He began by noting that Prof Thorens and Prof Bailey were in agreement that the mechanism proposed in the Patent, i.e. that SGLT2 inhibition would lead to a reduction of blood/plasma glucose in vivo and hence an effect on the diabetes disease state was a plausible one, given the support provided by the phlorizin and Tanabe Seiyaku studies referred to in

[0004] and [0007]. The question was whether the Patent disclosed enough to make it plausible that dapagliflozin has activity as an SGLT2 inhibitor which is sufficient to have a useful effect on the diabetes disease state. The issue between the parties was whether the statements in the Patent referring to dapagliflozin as an SGLT2 inhibitor were a bare assertion, as the Claimants contended, or verbal statements of an experimental result, albeit without numerical data, as AstraZeneca contended. The crux of this dispute was the correct interpretation of [114] and [115]. So far as [114] was concerned, the judge interpreted this as a statement that the assay described in [115] could be performed to determine SGLT2 activity. As for [115], it was common ground that, given that this was expressed in the past tense, it was to be taken as a description of an assay that had been carried out. The judge noted, however, that what was used in the assay was “inhibitor”. There was nothing to tell the reader what the inhibitor was. The judge went on: “239. Further, I accept the Claimants’ submission, supported by their cross-examination of Prof. Bailey, that the skilled person reading the Patent would understand that the assay could have been performed by the patentee on other compounds, either in the validation of the assay, in which case phlorizin might have been used as the inhibitor, or in assessing the SGLT2 inhibitory activity of other compounds. The fact that paragraph

[0115] tells the reader that the assay has been performed on an inhibitor does not tell the reader that it has been performed on dapagliflozin. 240. The reader might guess that had been done, but that is not the same as a disclosure that it has been. While Prof. Bailey and Prof. Potter said that the reader would understand that the assay had been performed on dapagliflozin, that was based on their assumption that a pharmaceutical company would not apply for a patent (let alone be granted one) if it did not have data to support the assertion that dapagliflozin was an SGLT2 inhibitor. That is a bootstraps argument, and in my judgment the assumption is not a permissible one to make Further, both Dr Edwards and Prof. Potter said that the fact that 20g Judgment Approved by the court for handing down. Generics v AstraZeneca dapagliflozin had been made did not make any difference to the assessment of whether it had been assayed.

241. Overall, I reject AZ's characterisation of the Patent's description of dapagliflozin as an SGLT2 inhibitor as a verbal statement of an experimental result. On the contrary, it is an assertion unsupported by any experimental results.

242. As Warner-Lambert makes clear, a priori reasoning can provide an alternative basis for plausibility of an effect. However, the Patent contains no reasoning, based on structural similarities or otherwise, to support the suggestion that dapagliflozin is an SGLT2 inhibitor.”

74. The judge explained that AstraZeneca relied on structural similarities between dapagliflozin and phlorizin as giving the skilled team “additional reassurance” that dapagliflozin would be an SGLT2 inhibitor. Having identified five differences between the structures of dapagliflozin and phlorizin, the judge went on: “245. It was quite clear from the evidence of Dr Edwards and Prof. Potter that, given the CGK that small structural differences can make large differences to activity, the number and nature of the differences between dapagliflozin and phlorizin were such that no prediction could be made, based on the activity of phlorizin, about the activity of dapagliflozin as an SGLT2 inhibitor. The most that could be said was that the removal of the O-glucoside bond might reduce the risk of hydrolysis of dapagliflozin compared to phlorizin, and that the glucose moiety in dapagliflozin might interact with SGLT2. However, I accept Dr Edwards' evidence that the presence of the glucose moiety, together with the two phenyl rings, does not provide the skilled team with the ability to make a reasonable prediction that dapagliflozin would be an SGLT2 inhibitor. 246. Indeed, AZ accepted that the similarities (such as they are) with phlorizin would not on their own be sufficient to make plausible the assertion that dapagliflozin was an SGLT2 inhibitor. It relied on them only to ‘reinforce the confidence’ that the skilled team would be given by ‘the positive assay result’. However, in my judgment there is no ‘positive assay result’ disclosed in the Patent for the reasons explained above.” 75. Next, the judge explained that there was a debate between the parties as to whether the skilled team when presented with the Patent would obtain and study any of the documents referred to in it, and if so which. The judge directed himself that this was “a context- and fact-dependent question, and thus it depends firstly upon the wording of the specification and secondly on the evidence” (Akebia Therapeutics Inc v FibroGen Inc [2020] EWHC 866 (Pat), [2020] RPC 15 at [218]). 76. The judge went on: Judgment Approved by the court for handing down. Generics v AstraZeneca “248. Prof. Potter's view was that the skilled medicinal chemist reading the Patent would see the reference to WO 128 at paragraph [0011] and look it up. I accept that - in my judgment a skilled medicinal chemist presented with a statement that dapagliflozin is an SGLT2 inhibitor but no experimental data to support it, and a statement in paragraph [0011] that compounds of a Markush formula which covers dapagliflozin have been reported in WO 128 to be SGLT2 inhibitors, would want to obtain WO 128 to see whether it contained SAR information that could be used to assess the claim of SGLT2 inhibition for dapagliflozin. Of course, if the skilled medicinal chemist were to obtain WO 128, they would find that it too contains no experimental data, and therefore no SAR information which might make it plausible that dapagliflozin was an SGLT2 inhibitor, let alone indicate what its EC 50 might be. 249. Prof. Thorens and Prof. Potter said that the

skilled team presented with the statements in paragraphs [0004] and [0007] of the Patent about the Tanabe Seiyaku 6 month rat study (or their equivalents in WO 128) would want to find out more about that work. However, no attempt was made to recreate the kind of search that would have been done at the priority date to locate that work. The skilled team which had WO 128 would, however, see that it contained a number of references to prior work on compounds which are said to be SGLT2 inhibitors. Those references include the papers by Tsujihara et al., Hongu et al. and Oku et al. ...; in my judgment the skilled team would regard those as potential sources for the Tanabe Seiyaku work referred to in paragraphs [0004] and [0007]. Further, Prof. Potter said that the skilled medicinal chemist would want to look at materials cited in WO 128, including those papers, and would be interested in any SAR information they contained. Therefore, in my judgment the skilled team which had WO 128 (which for the reasons explained in the previous paragraph, the skilled team reading the Patent would have done) would also look at the four Tanabe Seiyaku papers which it cites. 250. Even a brief consideration of those papers would reveal that the SAR work conducted by Tanabe Seiyaku indicated strict structural requirements for activity of phlorizin analogues. The position can be summarised by setting out the abstract of the first Hongu et al. paper (which follows on from the Tsujihara et al. paper which had shown a benefit of removing the 4'-hydroxy group from the first phenyl ring, referred to as the B ring by Tanabe Seiyaku): 'A novel series of 4'-dehydroxyphlorizin derivatives was synthesised and the effects of these compounds on urinary glucose excretion were evaluated in rats. There Judgment Approved by the court for handing down. Generics v AstraZeneca was a strict structural requirement for activity. Introduction of a small substituent or a flat ring at the 3- and/or the 4-position on the A ring was permissible, but any change at the bridge part between the A and B rings or in the sugar moiety resulted in complete lack of activity. The 6'-OH group on the B ring was also necessary, and even small structural modifications of the 6'-OH group reduced the activity considerably. Among the compounds synthesised, the 5-benzofuryl derivative 25 [T-1095a] was the most potent and was selected as a new lead for further structure-activity relationship investigations.' 251. This emphasises the importance, in phlorizin analogues, of retaining the structure of the linker between the two phenyl rings, and the hydroxy group on the first phenyl ring that has the ability to hydrogen bond to the carbonyl in the linker. Both those features are absent in dapagliflozin, and so the skilled team considering the Tanabe Seiyaku papers would find nothing to suggest that dapagliflozin would be an SGLT2 inhibitor. Indeed, in my judgment the message that they convey, namely that structural features of phlorizin analogues (which are absent from dapagliflozin) are important for activity, would give the skilled team reason to doubt whether dapagliflozin would be an SGLT2 inhibitor.

252. As neither WO 128, nor the Tanabe Seiyaku papers which it cites, contain any information to support the suggestion that dapagliflozin is an SGLT2 inhibitor, it is not necessary to consider whether it would be permissible to rely on information in these cross-referenced documents to establish or support a case of plausibility applying the approach in Warner-Lambert." 77. Finally, the judge considered the question of potency: "253. AZ repeatedly

asserted that the teaching of the Patent was that ‘positive results’ had been obtained in the assay of dapagliflozin. However, even if one were to accept (which I do not) that the teaching of the Patent was that dapagliflozin had been assayed, that begs the question as to what the ‘positive results’ were. Even if the skilled person were to understand the Patent as disclosing that dapagliflozin had been assayed and determined to be an SGLT2 inhibitor, it does not disclose the EC50 that had been obtained (or even how it compared with that of phlorizin).

254. Nor, on the evidence, did the description of the assay mean that any positive result must have been a EC50 in a range which would confer utility. Dr Edwards said, and Prof. Bailey accepted, that the potency could have been in the millimolar Judgment Approved by the court for handing down. Generics v AstraZeneca range. AZ submitted that the assay could have been one with a 10 μ M EC50 cut-off, and that a compound which passed such an assay would have been a ‘hit’. I do not think there was anything in the evidence to suggest that the skilled team would have understood the assay to have such a cut-off, but in any event, on the evidence a ‘hit’ in itself is not a compound with practical utility
255. AZ submitted that the statements in the Patent that dapagliflozin was an SGLT2 inhibitor useful for the treatment of diabetes must be read as teaching that the EC 50 for dapagliflozin was such that it would be useful to treat diabetes. I agree with the Claimants’ characterisation of this as another bootstraps argument. On the contrary, the Patent makes bare assertions that dapagliflozin is an SGLT2 inhibitor and useful to treat diabetes.” 78. Having quoted two passages from the cross-examination of Prof Bailey in [256], the judge went on: “257. Overall, the evidence was that not every compound which produced a measurable EC50 in an in vitro SGLT2 inhibition assay would have been regarded as plausibly having a useful effect on ... the diabetes disease state. Indeed, while my conclusion does not depend on this, the skilled team which had the Tanabe Seiyaku papers cited in WO 128 would, as Prof. Potter accepted, note that Tsujihara et al. presents results showing that some compounds which had SGLT2 activity in vitro were indistinguishable from the control in vivo and so were categorised as inactive. 258. The skilled team which had the Tanabe Seiyaku papers cited in WO 128 would also note that Oku et al. provides the IC50s for phlorizin (160 nM against both SGLT1 and SGLT2) and for [a compound designated] T-1095a (20 nM against SGLT1 and 5 nM against SGLT2). It also presents the results of a study of T-1095a in diabetic rats, though it does not appear to be the study referred to in paragraphs [0004] and [0007] of the Patent (the source of that study was not clear from the materials in the case). There is nothing in the Tanabe Seiyaku papers to displace the skilled team’s CGK about potency requirements for an SGLT2 inhibitor which could be useful to treat diabetes. They provide the IC50 for phlorizin as a benchmark for someone seeking an experimental tool to lower blood/plasma glucose. However, as I have said, the Patent provides no information on the EC50/IC50 of dapagliflozin. 259. The absence of information about the EC50 of dapagliflozin is significant. The skilled team cannot reasonably predict any useful effect on ... the diabetes disease state from merely being told that dapagliflozin is an SGLT2 inhibitor. Judgment Approved by the court for handing down. Generics v AstraZeneca 260. For the reasons I have given above, in my judgment the Patent does not disclose enough to

make it plausible that dapagliflozin ... will treat etc. diabetes.” Arbitrary selection 79. The judge explained at [266]-[268] that AstraZeneca’s case at trial was that it was not necessary for dapagliflozin to have greater efficacy than (or be in any other way superior to) any of the other compounds encompassed by the disclosure of WO 128, including the compounds of the Examples. AstraZeneca did not advance any case that dapagliflozin was, so far as utility for the treatment of diabetes was concerned, any different in its properties to any of the other compounds of WO 128 (and in particular to the compound of Example 12). 80. In those circumstances the judge held as follows: “269. in my judgment that means that the Patent does not make a technical contribution over WO 128. There is nothing in the Patent nor in the evidence at trial to indicate that dapagliflozin is anything other than an arbitrary selection from the genus of compounds disclosed by WO 128. 270. 271. 272. The argument advanced by AZ was that the Patent made it plausible that dapagliflozin was an SGLT2 inhibitor which ... was useful to treat etc. diabetes, whereas that was not made plausible by WO 128. That, AZ submitted, taught the skilled person something new and so was a technical contribution. In my judgment there is some sleight of hand going on here. A technical contribution needs to be both present in fact and made plausible by the specification I do not see how making something plausible can in itself be a technical contribution. Indeed AZ did not plead a technical contribution consisting of making something plausible - it pleaded (correctly, in my judgment) actual properties of dapagliflozin as being technical contributions. Even if this argument were a permissible one, in my judgment it does not work in this case. The parties were agreed that, in order for the arbitrary selection case to add anything to the plausibility case, it is necessary to assume that the Patent does make it plausible that dapagliflozin is an SGLT2 inhibitor which ... is useful to treat etc. diabetes. That requires me to approach matters on the basis that the Patent would be understood as disclosing that dapagliflozin had been assayed and had generated an EC50 which meant that it would plausibly ... be useful to treat etc. diabetes. 273. If that is so, then in my judgment WO 128 must also be understood as disclosing that compounds which it discloses had been assayed and had generated EC50s which meant that Judgment Approved by the court for handing down. Generics v AstraZeneca they would plausibly ... be useful to treat etc. diabetes. Prof. Potter (whose view was that the skilled medicinal chemist reading the Patent would assume that dapagliflozin had been tested) said this: ‘While the Medicinal Chemist would not be able to identify which of the compounds encompassed by WO 128 were tested in the assay, they would not doubt that the assay had in fact been used in relation to some of them. While no biological data are provided, it would be a reasonable assumption that at least the Examples - for each of which characterisation data are provided, indicating that they were synthesised - would have been tested for activity using this assay.’ 274. Therefore, on this approach the skilled team would understand that the compound of Example 12 of WO 128 (amongst others) had been tested and produced an EC50 which meant that it would plausibly ... be useful to treat etc. diabetes.” 81. The judge went on to refer to Prof Potter’s evidence that the skilled medicinal chemist would regard the statement in WO 128 that the compounds of Formula IB are SGLT2 inhibitors and useful in the treatment etc. of diabetes as being a prediction based on assay results of the

compounds of the Examples, and continued: “277. There was no suggestion that any particular compounds covered by formula IB would be regarded as likely exceptions to the prediction - in particular there was no suggestion that the skilled medicinal chemist would regard a compound with R 1 = Cl and/or R4 = OEt as being a likely exception. On the contrary, Prof. Potter’s evidence was that the skilled medicinal chemist would have no expectation that a compound with an alternative alkoxy group would have better, the same or worse activity data than one with a methoxy group (as in Example 12). 278. Therefore, on the hypothesis on which I am considering matters, WO 128 contains what the skilled team would regard as a plausible prediction, based on assay data for the compounds of the Examples, that compounds of formula IB (including dapagliflozin with its close relationship to Example

- 12) will be SGLT2 inhibitors and that they will ... be useful to treat etc. diabetes.
279. All that the Patent does (on that hypothesis) is to verify that WO 128’s prediction of SGLT2 inhibitory activity and utility is correct in the case of dapagliflozin. It does not show that dapagliflozin has properties that are in any way different from those predicted by WO 128. On that hypothesis, while the Patent may make it more plausible that dapagliflozin ... be useful to treat etc. diabetes, it does not make that plausible for Judgment Approved by the court for handing down. *Generics v AstraZeneca* the first time. So I reject AZ’s argument which I have recorded in paragraph 270 above.” AstraZeneca’s grounds of appeal 82. AstraZeneca’s grounds of appeal fall into three groups. Grounds 1-3 concern the judge’s interpretation of the Patent. Grounds 4-6 concern the law as to plausibility. Grounds 7 and 8 concern arbitrary selection. Grounds 1-3: interpretation of the Patent 83. 84. Ground 1 is that the judge wrongly assessed the disclosure of the Patent at [238]-[241] when he found that it did not comprise a verbal statement of an experimental result. AstraZeneca relies on the principle, which is not in dispute, that the skilled person or team reads a patent with a “mind willing to understand, not a mind desirous of misunderstanding” (*Generics (UK) Ltd v Yeda Research and Development Co Ltd*
- [2012] EWHC 1848 (Pat) at [192]). Given that the Patent is all about dapagliflozin, that it contains repeated references to “the SGLT2 inhibitor of formula I” and that the purpose of the assay described in [0115] is to measure “SGLT2 activity of the compounds of the invention” as stated in [0114], AstraZeneca contends that the skilled team would understand that the “inhibitor” referred to in [0115] must be dapagliflozin. The Claimants point out that, as Lord Diplock emphasised in *Catnic Components Ltd v Hill & Smith Ltd* [1982] RPC 183 at 242, “a patent specification is a unilateral statement by the patentee, in words of his own choosing”. Even so, if the issue were one purely of language, AstraZeneca’s argument might have some merit. A patent, however, is a technical document addressed to technical readers. It is to be read through the eyes of the skilled person or team having the common general knowledge. Read in that way, I have no hesitation in agreeing with the judge.

85. What would immediately strike the skilled team about [0115] is that it does not identify the “inhibitor”. It is purely a description of a method. If one is looking for linguistic clues, it is noticeable that it does not even refer to “the inhibitor”, which might be taken to be a reference to a specific, even if unidentified, inhibitor. It simply uses the word “inhibitor” as a generic term for the substance being tested. If [0115] was intended to record a test that had been performed on dapagliflozin, then it would surely have said so. Nothing would have been easier, and there is no good reason why that statement should not have been made, if that were the case. 86. 87. Furthermore, the skilled team would note that [0115] does not itself contain even a verbal statement of a result. It does not say, for example, “the inhibitor was found to have SGLT2 activity”, let alone “significant [or suitable or some other such term] SGLT2 activity”. Again, nothing would have been easier, and there is no good reason why that statement should not have been made, if that were the case. AstraZeneca contended in paragraph 4 of its grounds of appeal and paragraph 16 of its skeleton argument that the judge ought not to have relied upon the expert evidence to which he referred at [239] to resolve what is properly a matter of documentary interpretation for the court. I did not understand counsel for AstraZeneca to pursue this contention in oral argument, but in any event I would reject it. The judge made a Judgment Approved by the court for handing down. *Generics v AstraZeneca* 88. 89. 90. 91. finding in [239], based on the expert evidence, as to a technical consideration which would bear upon the skilled team’s reading of the Patent, namely that the assay described in [0115] could have been performed on other compounds either in validating the assay or in assessing the SGLT2 inhibitory activity of other compounds (such as one or more of those described in WO 128). It follows that the Patent must be interpreted with that consideration in mind. The judge did not make the mistake of treating the expert evidence as determinative of the issue of interpretation. Instead, counsel for AstraZeneca focussed his argument on the proposition that the evidence did not establish that the skilled team would think that only other compounds had been tested and dapagliflozin had not. This argument makes the very mistake which AstraZeneca’s abandoned argument accused the judge of making, namely of treating the issue of interpretation as being one for expert evidence. In interpreting the Patent, what matters is that [0115] gives the skilled team no reason to think that dapagliflozin has been tested when there are alternative possibilities which are equally consistent with the language used. Ground 2 is that the judge wrongly assessed the disclosure of the Patent at [253]-[260] when he found that the Patent did not disclose enough to make it plausible that dapagliflozin will treat diabetes. AstraZeneca contends that the judge should have found that the assay result was that dapagliflozin had been shown to be an SGLT2 inhibitor at a useful level of activity. The sole basis for this contention is the repeated references in the specification to dapagliflozin as an SGLT2 inhibitor useful for the treatment of diabetes. This argument can only get off the ground if AstraZeneca succeeds on ground 1. Even on that assumption, however, I do not accept it. As the judge rightly said, it is a bootstraps argument. The repeated references in the specification to dapagliflozin being an SGLT2 inhibitor useful for the treatment of diabetes are pure assertion. Even if the skilled team understood [0115] to mean that dapagliflozin had been tested and found to demonstrate

some unspecified degree of SGLT2 inhibition, there is no information in the Patent as to: (i) what level of SGLT2 potency was obtained, even in purely verbal terms; or (ii) more specifically, the EC50 value that was determined; let alone (iii) whether the EC50 value was sufficient to confer utility. The judge made findings in [254] and [257], based on the expert evidence, that the potency could have been in the millimolar range, which would not have been enough for practical utility, and that not every compound which produced a measurable EC50 in an in vitro SGLT2 inhibition assay would have been regarded as plausibly having a useful effect on the diabetes disease state. AstraZeneca's only real answer to this was to attack the judge's findings as being unsupported by the evidence of Prof Bailey which the judge quoted in [256]. This is not a ground of appeal for which AstraZeneca has permission. In any event, it is a hopeless argument. The evidence of Prof Bailey provided ample support for the judge's finding and it did not stand alone, as the judge made clear. Counsel for AstraZeneca pointed out that the first passage quoted by the judge was in the context of WO 128, and only the second in the context of the Patent, but there is nothing in this point because the disclosures of the documents are the same with respect to the assay. Judgment Approved by the court for handing down. *Generics v AstraZeneca* 92. Ground 3 is that, had the judge correctly interpreted the patent, he should have concluded that the claimed inventions were plausible even applying the standard laid down in *Warner-Lambert*. This depends on AstraZeneca succeeding on both grounds 1 and 2, and therefore does not arise. Grounds 4-6: the law concerning plausibility 93. 94. 95. 96. AstraZeneca accepts that, if it fails on grounds 1-3, then claim 15 is insufficiently disclosed applying the *Warner-Lambert* standard. On that hypothesis, AstraZeneca nevertheless contends that claim 2 is valid. In outline, AstraZeneca argues that claim 2 satisfies the requirement of inventive step because the skilled team reading the Patent at the priority date would have no legitimate doubt that dapagliflozin would be useful for the treatment of diabetes, and that the invention of claim 2 is sufficiently disclosed because, as is common ground, the Patent discloses how to make dapagliflozin. Before considering grounds 4-6 in detail, I would point out that claim 2 is significantly broader than claim 15. It covers all uses of dapagliflozin (including for the treatment of the diseases deleted from claim 14, as well as wholly unrelated diseases, and non-pharmaceutical applications), while claim 15 is limited to the use of dapagliflozin for the treatment of diabetes. As a matter of basic principle, a broader claim to monopoly requires more justification than a narrower claim. Yet AstraZeneca contends that the patentability of claim 2 should be subject to less stringent criteria than claim 15. Moreover, this contention is advanced even though precisely the same disclosure in the Patent is relied upon as supporting both claims. Counsel for AstraZeneca was unable to provide any convincing justification for this. I would also point out that, as the judge recorded, AstraZeneca does not contend that the identification of dapagliflozin was a patentable invention. This is because the mere identification of a new chemical compound requires no invention: see e.g. *T 939/92 Agrevo/Triazoles* [1996] EPOR 171 at [2.5.3], *Pharmacia Corp v Merck & Co Inc* [2001] EWCA Civ 1610, [2002] RPC 41 at [20] (Aldous LJ) and *Idenix Pharmaceuticals Inc v Gilead Sciences Inc* [2016] EWCA Civ 1089 at [116] (Kitchin LJ). AstraZeneca's argument for patentability rests upon the proposition that dapagliflozin is

useful for the treatment of diabetes. Thus AstraZeneca simultaneously argues that (i) what makes the difference between claim 2 and claim 15 is that claim 2 does not include the therapeutic effect of dapagliflozin as a functional feature of the claim whereas claim 15 does, and (ii) the invention of claim 2 is patentable because of the therapeutic effect of dapagliflozin. Again, counsel for AstraZeneca did not provide any convincing justification for this. Ground 4 is that the Warner-Lambert test sets too high a standard for plausibility, and must be revisited in the light of G 2/21. Ground 5 is that, in the light of G 2/21, the Court should have treated claim 2, as a claim to a product per se, differently to claim 15, as a claim comprising a functional technical feature. The plausibility of the former should be assessed under inventive step, and the plausibility of the latter under sufficiency of disclosure, with different standards for plausibility applying in those cases: *ab initio* implausibility in the former case and *ab initio* plausibility in the latter case. Judgment Approved by the court for handing down. *Generics v AstraZeneca* 97. 98. 99. The short answer to ground 4 is that, as I have already noted, it is common ground that Warner-Lambert is binding on this Court with respect to the sufficiency of medical use claims. Counsel for AstraZeneca did not argue that G 2/21 provided any basis for this Court to apply a different test of plausibility in such cases, and he accepted that the Enlarged Board's (in English terms, *obiter*) conclusion at [77] was consistent with that of the majority in Warner-Lambert. Accordingly, counsel for AstraZeneca concentrated his argument on ground 5. As he accepted, *Sandoz v BMS* is *prima facie* binding authority to the opposite effect. Furthermore, he did not challenge the reasoning in *Sandoz v BMS* at [92] quoted in paragraph 19 above. He nevertheless submitted that this Court was free to depart from *Sandoz v BMS*, and should do so, on the basis of the exception to the rule that a previous decision of this Court is binding on this Court (and on lower courts) recognised in *Actavis UK Ltd v Merck & Co Inc* [2008] EWCA Civ 444, [2009] 1 WLR 1186 at [95]: "we are free to decide what this court is to do if it finds that its earlier interpretation of the [EPC] is clearly inconsistent with a settled interpretation given by the Boards of Appeal" (Jacob LJ giving the judgment of the Court of Appeal). As counsel for AstraZeneca emphasised, decisions of the highest authority in this jurisdiction have recognised the desirability, in the absence of any supranational court with jurisdiction to interpret the EPC, of the UK courts following the settled jurisprudence of the Boards of Appeal: see, for example, *Human Genome Sciences Inc v Eli Lilly and Co* [2011] UKSC 51, [2012] RPC 6 at [87] (Lord Neuberger). It is important that a harmonised approach to the interpretation of the EPC is adopted by the courts of the Contracting States even if that means the UK courts adopting an interpretation that is contrary to the interpretation they would have adopted if left to their own devices: see, for example, *John Wyeth & Brother Ltd's Application* [1985] RPC 545 at 565-567.

100. Counsel for AstraZeneca's principal submission was that G 2/21 is itself sufficient basis for this Court to depart from *Sandoz v BMS*. Although G 2/21 was considered in *Sandoz v BMS*, it had been common ground between the parties in that case that it made no difference whether the issue was viewed as one of inventive step or as one of sufficiency, whereas AstraZeneca contends that it makes a significant difference. As a result, G 2/21 had been

misinterpreted in *Sandoz v BMS*. His secondary submission was that subsequent decisions of the Boards of Appeal and of courts of other EPC Contracting States confirm that G 2/21 was misinterpreted in *Sandoz v BMS* and supported AstraZeneca's reading of it. 101. So far as G 2/21 is concerned, counsel for AstraZeneca emphasised that the Enlarged Board had expressly differentiated between inventive step and sufficiency at [73]-[77] (see paragraph 31 above). He argued that it followed that the Enlarged Board could not have intended to apply the same criteria to inventive step as to sufficiency, and in particular sufficiency of medical use claims. I acknowledge the force of this argument, but the question remains how the criteria articulated by the Board as being applicable to the assessment of inventive step are to be understood and applied.

102. Counsel for AstraZeneca submitted that the first limb of the test asks whether the relevant technical effect is part of what is taught by the document. If it is not, then it cannot be relied upon as a putative inventive step. The second limb is a question of Judgment Approved by the court for handing down. *Generics v AstraZeneca* technical substance in light of the skilled addressee's technical understanding: in essence, whether the skilled addressee would understand, in light of their common general knowledge, that the subject-matter of the claim has the technical effect relied upon. 103. I did not understand counsel for the Claimants to dispute counsel for AstraZeneca's reading of the first limb. As counsel for the Claimants expressed it, it is a disclosure test. Nor did counsel for the Claimants really take issue with counsel for AstraZeneca's formulation of the second limb as set out in the preceding paragraph (which I have taken verbatim from paragraph 43 of AstraZeneca's skeleton argument).
104. Where counsel parted company was with regard to counsel for AstraZeneca's further submission that the second limb has no requirement for a positive teaching in the specification rendering the effect plausible, and is therefore akin to the *ab initio* implausibility test. Counsel for the Claimants disputed this.
105. Apart from the Enlarged Board's differentiation between inventive step and sufficiency, counsel for AstraZeneca's principal argument in support of this submission was that the Enlarged Board had treated the *ab initio* plausibility lines of cases as being reconcilable with the *ab initio* implausibility line of cases. He submitted that this could only be the case if one "levelled down" to the *ab initio* implausibility standard. Counsel for the Claimants riposted that that would mean that the *ab initio* plausibility line of cases were wrongly decided, and yet the Enlarged Board had affirmed them. 106. The conclusion I draw from these arguments, revisiting G 2/21 after an interval of two years since *BMS v Sandoz*, is that, while the Enlarged Board clearly intended to get away from the debates over plausibility in the context of inventive step, the truth of the matter is that the distinction between *ab initio* plausibility and *ab initio* implausibility is inescapable. The *ab initio* plausibility standard requires the claimed technical effect to be rendered plausible by the technical content of the application read with the skilled person or team's common general knowledge. The *ab initio* implausibility standard permits a technical effect to be claimed that is not implausible in the

light of the technical content of the application read with the skilled person or team's common general knowledge. As is demonstrated by the arguments in Warner- Lambert, Sandoz v BMS and the present case, this difference can be decisive where the application claims a technical effect without providing either experimental data or theoretical reasoning to support that claim. 107. I would add that, as Lord Sumption pointed out in Warner- Lambert at [40], the difference between the two standards only really matters in cases where it has subsequently been demonstrated that the technical effect is indeed achieved. In cases like Sandoz v BMS and the present one, the technical effect has subsequently been proved not merely by the in vitro data that is missing from the specification, but also by in vivo experiments and then by clinical trials. In those circumstances it is tempting for courts and tribunals to be swayed by that hindsight knowledge. Tempting as it is, this is contrary to principle for the reasons explained in paragraphs 11-13 above. 108. I am therefore not persuaded that G 2/21 itself justifies this Court departing from Sandoz v BMS. I turn next to consider subsequent decisions of the Boards of Appeal Judgment Approved by the court for handing down. Generics v AstraZeneca and of the national courts. 109. So far as decisions of the Boards of Appeal are concerned, AstraZeneca primarily relies upon the decision of the referring Board of Appeal when it came to apply the Enlarged Board's answers to the questions: T 116/18 Sumitomo/Insecticide compositions, unreported, 28 July 2023. The Board of Appeal began at [11.1] by expressing the view that the Enlarged Board's focus in [93] on the application as filed and the filing date "is intended to prevent the filing of applications directed purely to speculative (armchair) inventions made only after the filing". It reiterated this point at [11.8]. I note that this chimes with the reasoning of Lord Sumption in Warner- Lambert at [22] and [37 (third)].

110. At [11.10] the Board held that, for the first limb of the Enlarged Board's test to be satisfied, "the purported technical effect together with the claimed subject-matter need only be conceptually comprised by the broadest technical teaching of the application as filed", which did not mean that "said effect need ... be literally disclosed in it by way of a positive verbal statement".
111. At [11.11] the Board held that the second limb was satisfied unless the following question was answered in the affirmative: "would the skilled person, having the common general knowledge on the filing date in mind, and based on the application as filed, have legitimate reason to doubt that the purported technical effect can be achieved with the claimed subject-matter?". The Board went on in [11.12] to reject the appellant's argument that the second limb was only satisfied if "the application as filed contains experimental proof that the purported proof that purported technical effect is actually achieved with the claimed subject-matter". I note that Warner- Lambert does not require experimental proof. On the contrary, plausibility may be demonstrated by experimental data falling short of proof or even by a priori reasoning unsupported by data: see Lord Sumption at [37 (fourth) and (sixth)]. The Board also held at [11.13] that it was not necessary for the application as filed to contain "a positive verbal statement about the purported technical effect".

112. At [12] the Board expressly disagreed with this Court's decision in *Sandoz v BMS*. It also partially disagreed with the Court of Appeal of the Hague in the case discussed below. 113. 114. In AstraZeneca's skeleton argument no reliance was placed upon any Board of Appeal decisions other than T 116/18. It was acknowledged in paragraph 88 that there were other Board of Appeal decisions that had sought to apply G 2/21 and that "they do not all take an identical approach to what G 2/21 means". In oral argument counsel for AstraZeneca asserted that T 116/18 had been followed in "60-70" decisions, but he did not take the Court to any of these, and only made passing reference to two or three of them. The Claimants relied upon T 314/20 Boehringer Ingelheim/Glucopyranosyl- substituted benzene derivative (unreported, a decision dated 19 November 2023, but the written reasons for which were only handed down on 20 December 2024) as demonstrating that the Boards of Appeal had not yet arrived at a settled interpretation of G 2/21. In this decision the Board agreed at [6.13.4] with T 116/18 that the purpose of the requirements laid down in G 2/21 was to prevent speculative applications for inventions which were only made after the filing date. At [6.13.5]-[6.13.11] the Board Judgment Approved by the court for handing down. *Generics v AstraZeneca* 115. 116. identified two issues with the reasoning in T 116/18. The first issue was that there was an inconsistency in the reasoning: the Board had stated that the Enlarged Board had not referred to any of the plausibility standards in its order, but instead adopted new requirements, and yet the Board had interpreted the second limb as imposing the ab initio implausibility standard. The second issue was that some of the Board's inferences were not supported by the text of G 2/21. As the Board explained in [6.14], however, it did not need to reach a conclusion as to the correct test to be applied for the purpose of the case at hand. In these circumstances it seems to me that it is not yet possible to say that the Boards of Appeal have adopted a settled view as to how the test in G 2/21 is to be interpreted and applied. Turning to decisions of courts of other EPC Contracting States, AstraZeneca focussed on (translations of) decisions from the Netherlands, Spain and Switzerland, while the Claimants focussed on a decision from Norway. Before discussion of these decisions, it should be noted that many of the decisions cited in oral argument or referred to in the parties' skeleton arguments concerned parallel decisions concerning the apixaban patent that was in issue in *Sandoz v BMS*. It is common ground that many other courts reached different conclusions to those reached by the UK courts. What matters for present purposes is the reasons for those differing conclusions. It is not uncommon for the courts of different EPC Contracting States to reach different conclusions on the same issue because of differences in the evidence and/or arguments. In the UK, an important aspect of the decisions is that Meade J made a finding, based on the expert evidence, that the skilled team would be aware of other potential reasons for apixaban having been prepared in greater quantities compared to other examples than the reason contended for by BMS, namely that apixaban was the most promising candidate of those exemplified in the application. This evidence does not appear to have featured in a number of the other decisions. There were also differences in the arguments. Finally, the reasoning of the courts differed from one another.

117. Of the Dutch decisions cited, it is sufficient to refer to those in the first case, which concerned an application for a preliminary injunction against a number of generic companies from marketing apixaban. The District Court of The Hague refused the injunction on the ground that the patent was probably invalid. The Court of Appeal disagreed and granted the injunction: [NL:GHDHA:2023:1593]. The Court considered G 2/21 at [6.5]-[6.13]. The generics argued that a stated technical effect may only be invoked if the skilled person “already understands from the patent application that the stated effect is actually achieved with the invention and the problem is actually solved, at least that this is made plausible”. The Court rejected this argument ([6.5]). The Court interpreted “would derive” in paragraph 2 of the Enlarged Board’s order as having the same meaning as the word “derivable” used in [72] ([6.6]-[6.7]). It noted that the Enlarged Board had differentiated between inventive step and sufficiency, and held that it would be incompatible with this to interpret G 2/21 as requiring that the alleged effect had been plausible when assessing inventive step ([6.8]-[6.9]). It agreed with BMS that the technical teaching of a patent “must be understood as ‘what is taught to the [skilled person] about how the technical problem can be solved with technical resources’” [6.10]. As can be seen from what the Court went on to say in [6.18] and [6.21.3] about the fact that the application disclosed a test with which the skilled person could easily determine that apixaban had a favourable Judgment Approved by the court for handing down. *Generics v AstraZeneca* Ki value, this amounts to an acceptance of the argument rejected by Lord Sumption in *Warner-Lambert* at [53] that it is enough for the application to encourage the skilled person to carry out simple tests identified in the application to confirm the efficacy of the claimed product if carrying out such tests would indeed show that the product is likely to be efficacious. That argument was not revived in *Sandoz v BMS*. 118. The Court then said at [6.12]: “Contrary to what [the generics] argue, this interpretation of G 2/21 by the Court of Appeal does not lead to a free pass for speculative patents. After all, the fact that protection is granted based in a purely speculative patent for an invention that is only made afterward is prevented because it is required that the technical effect is already included by the technical teaching of the application and embodies the same invention that is disclosed therein. Moreover, it is established that EP 415 does not concern a speculative patent. BMS undisputedly argued that the inventors had already determined the favourable affinity and selectivity of apixaban experimentally prior to the submission of the application.” 119. The first two sentences appear to accept that speculative patents are not permitted by G 2/21. Counsel for AstraZeneca did not defend the reasoning in the second two sentences, which acquit BMS of speculative patenting on the basis that it had positive experimental data in respect of apixaban which it did not include in the patent application. This was not something relied upon by BMS in the English litigation, but it is also a point mentioned in a number of the other decisions. I cannot agree with this for the reasons given in paragraph 13 above. If reliance by the applicant upon secret data is ruled out, as it should be, then I remain of the view that I expressed in *Sandoz v BMS* at [93] that it is not possible to determine whether a claimed invention is speculative other than by assessing whether the application read in the light of the common general knowledge makes it plausible. As Lord Sumption said in *Warner-Lambert* at [37(third)], “[t]he disclosure of

those grounds [sc. reasonable scientific grounds for expecting that it might well work] marks the difference between a speculation and a contribution to art”.

120. An appeal by the generic companies to the Dutch Supreme Court was rejected without reasons, from which it may be inferred that the Supreme Court agreed with the reasoning of the Advocate General in his opinion dated 20 December 2024 that the Court of Appeal had made no error justifying cassation. It is sufficient to note that the Advocate General expressed the view that G 2/21 “did not give an unambiguous answer” to the question of the extent to which the technical effect must have made plausible ([4.7]) and “does not solve all problems with plausibility inventiveness” ([4.11]) and that each case turned on its facts ([4.10] and [5.26]). Again, the Advocate General relied on what BMS had actually done before filing the patent, and not what was included in the patent, as an answer to the charge of speculative patenting ([5.8] and [5.14]).
121. Turning to Spain, AstraZeneca relied upon a decision of the Supreme Court concerning apixaban: Judgment 635/2015 dated 24 April 2025. It is common ground that that Court followed T 116/18 and applied an *ab initio* implausibility test. It does Judgment Approved by the court for handing down. *Generics v AstraZeneca* not appear that the Court was made aware of T 314/20. Furthermore, in concluding that the *ab initio* implausibility test was satisfied, the Court considered it significant that the ability of apixaban to inhibit Factor Xa, and its selectivity, “could be verified with tests described in the application”. The Court noted that the Court of Appeal of the Hague had reached the same conclusion concerning the application of the G 2/21 test to the apixaban patent.
122. As for Switzerland, AstraZeneca relied upon a decision of the Swiss Federal Patent Court concerning apixaban in *Mepha Pharma AG v Bristol-Myers Squibb Holdings Ireland Unlimited Co* dated 5 March 2024. As the Claimants pointed out, however, the Court held at [39] that: “If the criterion that the claimed technical effect is considered by the skilled person to be embodied in the invention as originally disclosed is understood as the Boards of Appeal did in decision T 116/18 and T 1989/19 [a decision not cited to this Court that the Swiss Court stated had followed T 116/18], namely that this criterion is fulfilled if the skilled person has no reason to doubt that the invention achieves the technical effect, speculative applications are not prevented. In the case of a technical effect claimed in the original application without any basis, there are no reasons for its occurrence, but often also no reasons against its occurrence – especially since, in practically significant cases, it has subsequently been found that the invention achieves the claimed effect.” This is a clear, and to my mind convincing, rejection of the *ab initio* implausibility standard.
123. The Court went on later in the same paragraph to interpret the second limb of the test in G 2/21 as follows (footnotes omitted): “The second criterion is fulfilled if the technical effect is obvious to a person skilled in the art, taking into account the general knowledge at the time of filing, based on the application as filed. Experimental data or an express statement on the technical effect are not necessary for this purpose. However, since the purpose of derivability is to prevent abusive speculative applications, the hurdle must not be set too high, otherwise inventions that are worthy of protection will not be protected.”
124. I

presume that by “obvious”, the Court meant “apparent”. In determining that this test was satisfied in the instant case, the Court held that it would not be unreasonable to expect the skilled person to determine the inhibition constants of all 110 examples disclosed in the application, and that when they did so they would find that apixaban had a K_i value of 0.08 nm and therefore conclude that apixaban was a potent and effective Factor Xa inhibitor ([42]). This reasoning is similar to that of the Dutch and Spanish courts, but it makes explicit the extent of the burden that this approach places on the public to carry out experiments that the patentee has not done (or if it has done them, not disclosed the results of) if the test is applied, as it should be, to the Judgment Approved by the court for handing down.

Generics v AstraZeneca 125. application. (If the invention is only plausible because of information in the granted patent which is not present in the application, then the patent is invalid for added matter: see *Sandoz v BMS* at [3] and [53].) Inspired by the passage from the Swiss Court’s decision that I have quoted in paragraph 123 above, counsel for AstraZeneca argued that speculative patent applications were unobjectionable, and that it was only abusive speculative patents that were objectionable. I am unable to accept this submission for two reasons. First, it does not seem to me to be supported by the decision. The Swiss Court accepted that “so-called ‘armchair’ inventions should not be rewarded with exclusive rights” ([39]). Its point was that it was important not to set the hurdle against speculative applications too high (a point which Lord Sumption recognised in *Warner-Lambert* at

[36] and [37(third)]). As we have seen, the Board of Appeal in T 116/18 and the Court of Appeal of The Hague agreed that speculative applications should not be permitted. Secondly, I am unable to see what distinguishes an abusive speculative application from a non-abusive speculative application. Certainly, counsel for AstraZeneca was unable to articulate any workable criterion for distinguishing the two. 126. The Norwegian Court of Appeal in a decision concerning apixaban dated 3 March 2024 expressly rejected BMS’s argument that G 2/21 had “lowered the requirement for plausibility”. On the contrary, it held that: “The decisive factor for whether a technical effect can be built upon in the assessment of inventive is whether at the time of application, based on the BMS application in combination with the general subject knowledge, it appeared credible – i.e. plausible – to the expert team that this effect would be achieved.” On the facts, the Court considered that this test was satisfied. The reasoning was largely based on structural considerations rejected by Meade J on the evidence before him. 127. The conclusion I draw from this brief review of the case law of courts in other EPC Contracting States is that we are some way from unanimity as to what test G 2/21 lays down and how to apply it. There appears to be an emerging consensus that speculative patents are not permitted, but little agreement as to what constitutes a speculative patent.

128. Accordingly, neither the jurisprudence of the Boards of Appeal nor the case law of courts of other Contracting States justifies a departure from *Sandoz v BMS* any more than G 2/21 itself does. 129. Even if AstraZeneca were to prevail on the law, and to establish that the correct standard to be applied to the assessment of inventive step was the ab initio implausibility, or no legitimate reason to doubt, standard, the Claimants contend that the Patent fails to satisfy

even that standard. In support of this contention the Claimants rely, first, on the judge's finding at [251] that the four Tanabe Seiyaku papers cited in WO 128 "would give the skilled team reason to doubt whether dapagliflozin would be an SGLT2 inhibitor", and secondly, the judge's finding in Judgment Approved by the court for handing down. Generics v AstraZeneca

- [259] that the absence of information about the EC50 of dapagliflozin means that the skilled team cannot reasonably predict any useful effect on diabetes. 130. In my judgment the answer to the second contention is straightforward: there is nothing in the judge's findings to suggest that the absence of information about the EC50 of dapagliflozin would in itself give the skilled team a reason to doubt the efficacy of dapagliflozin to treat diabetes if they would not otherwise doubt the efficacy of dapagliflozin.
131. AstraZeneca advances two answers to the first contention in the alternative. The first answer is that there is an apparent inconsistency between the judge's reasoning at [247]-[251] and what he said in [252] and [262]. At [248] the judge found that the skilled team reading the Patent would also read WO 128, and at [249] he found that they would also read the Tanabe Seiyaku papers. It is on this basis that he made his finding in [251]. Despite this, the judge went on to say in [252] that "it is not necessary to consider whether it would be permissible to rely on information in these cross-referenced documents to establish or support a case of plausibility applying ... Warner-Lambert". Moreover, in [262] he declined to decide whether the Patent satisfies a "legitimate reason to doubt" test on the ground that his findings of fact should be sufficient for a higher court to apply whatever test is appropriate. AstraZeneca contends that the better reading of the judgment is that the judge did not in fact make a finding about the effect of the Tanabe Seiyaku papers, since he did not decide whether they could be relied on. The Claimants dispute this. 132. In my view the better reading of the judgment is that the judge made findings at [248]-[251] that the skilled team would follow the cross-references and as to the conclusion they would draw from the Tanabe Seiyaku papers. In [252] he pointed out that this did not assist AstraZeneca. He left open the question of whether it was legally permissible for AstraZeneca to rely upon such information to establish or support plausibility. Although he did not spell out his reasons for leaving that open, it seems to me that it is probable that he considered that it was debatable applying Warner-Lambert whether it was permissible to go outside the four corners of the patent read together with the common general knowledge. By parity of reasoning, and having regard to [262], it seems to me that he also left open the question whether it was legally permissible for the Claimants to rely upon such information to establish or support *ab initio* implausibility.
133. Although the judge left those questions open, I consider that the logic of the judge's reasoning applies whatever the test is. I see no reason why the skilled person or team should be confined to the four corners of the patent if it contains cross-references to other documents which they would follow up for the purposes of deciding whether the claims made were plausible or implausible. For the reasons the judge gave at [248] the skilled team

reading the Patent would read WO 128 for that purpose, and for the reasons he gave in [249] they would also read the Tanabe Seiyaku papers. Having done so, they would reach the conclusion he set out in [251]. It follows that the skilled team would have legitimate reason to doubt that dapagliflozin is an SGLT2 inhibitor. That in turn means that they would have legitimate reason to doubt that it would be useful for the treatment of diabetes. 134. That takes me to AstraZeneca's second answer to this point. If necessary, AstraZeneca contends by ground 6 that the judge erred (i) in taking the Tanabe Judgment Approved by the court for handing down. *Generics v AstraZeneca Seiyaku* papers into account and (ii) in finding that they would give the skilled team reason to doubt whether dapagliflozin would be an SGLT2 inhibitor. The difficulty that AstraZeneca faces with this ground of appeal is that it is a challenge to findings of fact made by the judge after hearing expert evidence.

135. AstraZeneca nevertheless submits that these findings were not open to the judge on the evidence. AstraZeneca argues that finding (i) was not open to the judge because none of the experts gave evidence that the skilled team reading the Patent would cross-refer first to WO 128 and then to the Tanabe Seiyaku papers. AstraZeneca argues that finding (ii) was not open to the judge because the upshot of Prof Potter's evidence was that what was said about the compound called T-1095a "cannot inform you positively or negatively" about dapagliflozin. 136. I do not accept these arguments. In the case of finding (i), this was open to the judge on the evidence he referred to in [248] and [249]. In the case of finding (ii), it is fair to note that the judge did not expressly refer to the evidence of any of the experts in [251]. As counsel for the Claimants pointed out, however, Prof Potter was a cross-examined on this topic over 42 pages of transcript, and his evidence cannot be reduced to the soundbite relied upon by AstraZeneca. Furthermore, the judge had the advantage of being able to read the papers and see the experts cross-examined on them. This Court was not even provided with copies of the papers. This is island-hopping with a vengeance. Thus AstraZeneca has not demonstrated that the finding was not open to the judge. On the contrary, it appears to be supported by the abstract from the Hongu et al paper which the judge quoted at [250]. Grounds 7-8: arbitrary selection 137. It must be assumed for the purposes of considering grounds 7 and 8 that at least claim 2 of the Patent is free from objection on plausibility grounds.
138. Ground 7 is that the judge was wrong in his approach to the issue of arbitrary selection. Ground 8 is that the judge failed properly to assess the contribution of WO 128 when considering whether the Patent made a technical contribution. Although counsel for AstraZeneca argued these two grounds together, it is important to distinguish between them. 139. The starting point for ground 7 is the final sentence of [59]. For convenience I will set this out again: "If the patent claims a compound selected from a previously disclosed genus of compounds which are said to have a particular property, then that requirement is not satisfied if the compound does not in fact have some different or improved property compared to those previously individually disclosed (a new effect or an increase in an effect), or the patent does not make such improved property plausible."

140. AstraZeneca contends that this is wrong in law, and that the judge ought to have held that, where the prior art merely asserted that the genus had a given advantage or property without rendering it plausible, then a subsequent patent may make a technical contribution by making the same assertion in respect of a selected Judgment Approved by the court for handing down. Generics v AstraZeneca compound and rendering it plausible. The judge rejected this argument at [271], but AstraZeneca argues that he was in error. I disagree. As the case law discussed by the judge makes clear, a selection from the prior-disclosed genus is only inventive if the selection makes a technical contribution because the selected compound in fact has some useful property which means that the selection is a technical advance. Mere plausibility is not enough for this purpose.
141. AstraZeneca also argued in its grounds of appeal that the technical contribution of the Patent was not merely that it made a plausible claim that dapagliflozin would be useful for the treatment of diabetes, but rather it made a claim to that effect which turned out to be true. This argument was rightly not pursued in AstraZeneca's skeleton argument or oral submissions, because it is contrary to the way AstraZeneca put its case at trial as the judge explained at [266]-[268].
142. Given that I have rejected ground 7, success on ground 8 would not suffice for AstraZeneca to overturn the judge's conclusion on arbitrary selection. I shall nevertheless address it. AstraZeneca argues that the judge went wrong because he compared what the Patent contributed to what WO 128 said, whereas he should have compared what the Patent contributed with what WO 128 contributed. AstraZeneca does not dispute that the relevant wording in the Patent is the same as that in WO 128, but it nevertheless contends that the quality of the disclosures is quite different. WO 128 makes an assertion about a class of compounds which it is common ground would at its narrowest (those covered by Formula IB) include millions of compounds, whereas the Patent is confined to dapagliflozin. AstraZeneca relies upon the principle, which is not in dispute, that it is easier to show a claim of narrow scope is plausible than a claim of broad scope. 143. In my judgment the judge was correct to reject this argument for the reasons he gave at [272]-[279] (see paragraphs 80-81 above). I would only add two points. First, counsel for AstraZeneca sought to attack the judge's analysis of the expert evidence, but the judge's findings are amply supported by that evidence. Secondly, counsel for the Claimants made a striking submission in support of the judge's reasoning. Given the disclosure in WO 128, BMS could have filed 50 patent applications for compounds falling within Formula IB, including an application in respect of the compound of Example 12, and subsequently abandoned all 50 other than the one for dapagliflozin. On AstraZeneca's argument, none of those applications would have been objectionable on the ground of arbitrary selection. What this submission highlights is the complete absence from the Patent of any basis for distinguishing between dapagliflozin and other compounds falling within Formula IB of WO 128 such as the compound of Example 12.

Conclusion

144. For the reasons given above I would dismiss the appeal. In summary, the judge correctly interpreted the Patent. Applying *Sandoz v BMS*, as he was bound to do, he correctly concluded that the Patent did not make it plausible that dapagliflozin would be useful for the treatment of diabetes, and therefore both claims 2 and 15 were invalid for both lack of inventive step and insufficient disclosure. Even if the standard applicable when considering inventive step for claim 2 is whether the skilled team would have legitimate reason to doubt that dapagliflozin would be useful for the treatment of diabetes, on the judge's findings the skilled team would have legitimate Judgment Approved by the court for handing down. *Generics v AstraZeneca* 145. reason to doubt this. Turning to arbitrary selection, the judge was correct to hold that the Patent claims a compound arbitrarily selected from the genus disclosed in Formula IB of WO 128 because the Patent makes no technical contribution compared to WO 128: the disclosure with respect to the assay is identical, and AstraZeneca does not even argue for this purpose that dapagliflozin is in fact superior in any of its properties to any of the compounds disclosed in WO 128, and in particular the compound of Example 12. The judge made it clear that he reached his decision with regret given that dapagliflozin had proved to be successful, but as he rightly said at [281] "later findings about dapagliflozin do not enter the picture and my task has been to assess the validity of the Patent based on its disclosure". The judge went on to observe that it was not for him to speculate about why the Patent was drafted in the way that it was, and in particular why it contained no data about the performance of dapagliflozin. It may be no coincidence, however, that the application for the Patent was filed by BMS at around the same time as the apixaban application. As discussed above, in the apixaban litigation courts of other EPC Contracting States have accepted that, at the time of filing the application for that patent, BMS had data in respect of apixaban which it did not include in the application. There is no evidence before this Court as to whether the same was true of dapagliflozin and the application for the Patent. Even if that were the case, I have explained above why applicants for patents should not be permitted to rely upon data which they choose to keep secret when filing their applications. Lord Justice Stuart-Smith: 146. I agree. Lord Justice Peter Jackson: 147. I also agree.

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Prepared on 23 October 2026 · Esheria