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Case No: CO/1366/2016

IN THE HIGH COURT OF JUSTICE
QUEEN'S BENCH DIVISION
ADMINISTRATIVE COURT

Royal Courts of Justice
Strand, London, WC2A 2LL

Date: 29/07/2016

Before :

Mrs Justice Whipple

- -

Between :

The Queen (on the application of Napp Pharmaceuticals Ltd)	**Claimant**
- and -	
Secretary of State for Health acting as The Licensing Authority	**Defendant**
-and-	**Interested Party**
Sandoz Ltd	

- -

Richard Gordon QC and Marie Demetriou QC (instructed by **Bristows LLP**) for the **Claimant**
George Peretz QC (instructed by **The Government Legal Department**) for the **Defendant**
Tom de la Mare QC and Ravi Mehta (instructed by **Olswang LLP**) for the **Interested Party**

Hearing dates: 6 July 2016

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Approved Judgment

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

Mrs Justice Whipple:

INTRODUCTION

1. This application for judicial review is brought by Napp Pharmaceuticals Ltd ("Napp"). The Defendant is the Licensing Authority established under the Human Medicines Regulations 2012. The powers of that authority are exercised by the Secretary of State for Health through the Medicines and Healthcare Products Regulatory Agency ("MHRA"). Sandoz Ltd is the interested party ("Sandoz"). Napp seeks judicial review of the MHRA's decision to grant marketing authorisations ("MAs") to Sandoz in relation to its product, Reletrans. Reletrans is a generic version of Napp's authorised product, BuTrans. At the heart of Napp's case is the scope and meaning of Article 10(3) of Directive 2001/83/EC on the Community code relating to medicinal products for human use (the "Medicinal Code"). Napp argues that Article 10(3), properly construed, provides protection for the clinical data provided by Napp in support of its application for an MA for BuTrans; alternatively, if the Court is in doubt, a reference to the Court of Justice of the European Union ("CJEU") is required under Article 267 TFEU in order to resolve the uncertainty.

2. Permission to bring this judicial review was granted by Cheema-Grubb J following an oral hearing on 25 May 2016. Permission had initially been refused on the papers by Irwin J (on 12 April 2016).

3. Napp was represented by Richard Gordon QC and Marie Demetriou QC, the MHRA by George Peretz QC, and Sandoz by Tom de la Mare QC and Ravi Mehta. I am grateful to all Counsel for their assistance in this case.

THE MEDICINAL CODE

4. Directive 2001/83/EC was implemented on 6 November 2001. It codified a series of existing directives, the earliest of which was Directive 65/65/EEC of 26 January 1965. The 2001 Directive was amended by Directive 2004/27/EC of 31 March 2004 (the "2004 amending directive"). Member States were required to implement the amendments by 30 October 2005. Article 10(3), on which this case turns, was introduced in its current form by the 2004 amending directive, but it reflected a provision which has formed part of the EU law code for many years, having been contained within the last sub-paragraph of Article 4.8(a) of Directive 65/65/EEC, before becoming part of Article 10(1)(a)(iii) of Directive 2001/83/EC (at those times commonly referred to as the "proviso").

5. The Medicinal Code in its current form is prefaced by a number of recitals. Of particular relevance are the following:

> "…
>
> (2) The essential aim of any rules governing the production, distribution and use of medicinal products must be to safeguard public health.
>
> (3) However, this objective must be attained by means which will not hinder the development of the pharmaceutical industry or trade in medicinal products within the Community.

> …
>
> (9) Experience has shown that it is advisable to stipulate more precisely the cases in which the results of toxicological and pharmacological tests or clinical trials do not have to be provided with a view to obtaining authorization for a medicinal product which is essentially similar to an authorized product, while ensuring that innovative firms are not placed at a disadvantage.
>
> (10) However, there are reasons of public policy for not conducting repetitive tests on humans or animals without over-riding cause."

The 2004 amending directive included the following relevant recital:

> "(14) Since generic medicines account for a major part of the market in medicinal products, their access to the Community market should be facilitated in the light of the experience acquired. Furthermore, the period for protection of data relating to pre-clinical tests and clinical trials should be harmonised."

6. The Medicinal Code is intended to apply to medicinal products for human use intended to be placed on the market in the Member States and either prepared industrially or manufactured by a method involving an industrial process (Article 2).

7. Article 6(1) provides that no medicinal product can be sold without first being authorised by the competent authorities of the Member State by grant of an MA. It is in the following terms:

> "1. No Medicinal product may be placed on the market of a Member State unless a marketing authorisation has been issued by the competent authorities of that Member State in accordance with this Directive or an authorisation has been granted in accordance with Regulation (EC) No 726/2004, read in conjunction with Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use (OJ L 378, 27.12.2006, p.1) and regulation (EC) No 1394/2007.
>
> When a medicinal product has been granted an initial marketing authorisation in accordance with the first subparagraph, any additional strengths, pharmaceutical forms, administration routes, presentations, as well as any variations and extensions shall also be granted an authorisation in accordance with the first subparagraph or be included in the initial marketing authorisations. All these marketing authorisations shall be considered as belonging to the same global marketing authorisation, in particular for the purpose of the application of Article 10(1)."

8. The second paragraph of Article 6(1) was inserted by the 2004 amending directive. It enables additional strengths, pharmaceutical forms, administration routes, presentations, variations and extensions (known as "line extensions") to be authorised under a global marketing authorisation or "GMA". It was common ground that a GMA is available where the line extensions have all been developed by the same company or by connected companies.

9. The procedure for obtaining an MA is outlined in Article 8, which requires an application to be made to the competent authority of the Member State concerned. The MHRA is the competent authority for the United Kingdom. The application is to

be accompanied by certain "particulars and documents" which are listed at Article 8(3). Those particulars include:

> "(i) results of:
>
> - pharmaceutical (physico-chemical, biological or microbiological) tests,
>
> - pre-clinical (toxicological and pharmacological) tests,
>
> - clinical trials."

10. Articles 10(1) and (2) provide for generic medicinal products to be authorised, subject to specific protections afforded to the innovator of the original (or "reference") medicinal product. Article 10(1), first paragraph, provides as follows:

> "By way of derogation from Article 8(3)(i), and without prejudice to the law relating to the protection of industrial and commercial property, the applicant shall not be required to provide the results of pre-clinical tests and of clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product which is or has been authorised under Article 6 for not less than eight years in a Member State or in the Community."

This is referred to as the "abridged" procedure. The "reference medical product" (or "RMP") is defined at Article 10(2)(a) as follows:

> "'reference medicinal product' shall mean a medicinal product authorised under Article 6, in accordance with the provisions of Article 8."

"Generic medicinal product" is defined at Article 10(2)(b) as follows:

> "'generic medicinal product' shall mean a medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies…"

As can be seen, "bioavailability studies", or "bioequivalence data" are required to demonstrate that the particular medicinal product is indeed a "generic" of the RMP.

11. Bioavailability and bioequivalence data are not defined further in the Medicinal Code, but some assistance as to their meaning is provided at Annex 1 to the Code. Under "Introduction and General Principles", paragraphs (1) and (2) of Annex 1 explain that the particulars and documents accompanying an application under Articles 8 and 10(1) shall be presented in accordance with the requirements set out in the Annex and in guidance published by the Commission. The particulars and documents must be presented as five modules, the fifth of which is "clinical study reports". Part 1 of the Annex, headed "Standardised Marketing Authorisation Dossier Requirements", describes the format and presentation of module 5, in the following terms:

> "- Clinical study reports
> - *Reports of Bio-pharmaceutical Studies*
> - Bio-availability Study Reports

- Comparative Bio-availability and Bio-equivalence Study Reports
- In vitro – In vivo Correlation Study Report
- reports of Bio-analytical and Analytical Methods"

Paragraph 5.2.1 explains these studies further as follows:

> "Bio-availability study reports, comparative bio-availability, bio-equivalence study reports, reports on in vitro and in vivo correlation study, and bio-analytical and analytical methods shall be provided."

12. The protections afforded to innovators of RMPs are set out in Article 10(1), in part in the first paragraph (see above) and further in the second and fourth paragraphs as follows:

> "A generic medicinal product authorised pursuant to this provision shall not be placed on the market until ten years have elapsed from the initial authorisation of the reference product.
>
> …
>
> The ten-year period referred to in the second subparagraph [above] shall be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorisation holder obtains an authorisation for one or more new therapeutic indications which, during the scientific evaluation prior to their authorisation, are held to bring a significant clinical benefit in comparison with existing therapies."

In summary, therefore, no application for authorisation of a generic version of an authorised drug can be made until 8 years have elapsed from the date the authorised drug (the RMP) was first authorised. No generic can be placed on the market until 10 years after that date. That 10-year period of protection can be extended to 11 years if, during the first 8 years, the innovator obtains an authorisation for one or more "new therapeutic indications" which bring "significant clinical benefit" in comparison with existing therapies. This is the "8+2+1" formula introduced by the 2004 amending directive. Previously, Member States had a choice of six or ten years' protection, without any possibility of extension.

13. Article 10(3) provides a procedure for authorisation of drugs that are variants of drugs which are already authorised, but are not generics. It provides as follows:

> "In cases where the medicinal product does not fall within the definition of a generic medicinal product as provided in paragraph 2(b), or where the bioequivalence cannot be demonstrated through bioavailability studies or in case of changes in the active substance(s), therapeutic indications, strength, pharmaceutical form or route of administration, vis-à-vis the reference medicinal product, the results of the appropriate pre-clinical tests or clinical trials shall be provided."

This is the "hybrid-abridged" procedure. The authorisation can only be granted if "appropriate pre-clinical tests or clinical trials" are provided. This plainly gives some latitude to the competent authorities of the Member State to decide what, in any given

case, is "appropriate". I shall return to the meaning of "appropriate" shortly. Data provided under Article 10(3) is referred to as "bridging data".

14. Finally, Article 10(5) provides further regulatory protection of clinical data for a period of one year (not cumulative), where an application is made for a "new indication" of a "well established" drug in circumstances where "significant" pre-clinical or clinical studies were carried out in relation to the new indication:

> "In addition to the provisions laid down in paragraph 1 where an application is made for a new indication for a well-established substance, a non-cumulative period of one year of data exclusivity shall be granted, provided that significant pre-clinical or clinical studies were carried out in relation to the new indication."

This additional protection was introduced by the 2004 amending directive. It was new to the Code.

15. The Medicinal Code is implemented into domestic law by the Human Medicines Regulations 2012. I was invited by all parties to consider their arguments by reference to the Medicinal Code, which is mirrored by the Regulations. I am content to do so.

FACTS

16. Buprenorphine is an opioid analgesic. It was first registered on 16 March 1992 by Schering-Plough under the brand name Temgesic, which was a sub-lingual tablet.

17. On 16 July 2003, Napp was granted an MA in Denmark for its own product, registered under the brand name Norspan (the name used in Denmark; the name used in some other countries, including the United Kingdom, is BuTrans). This was a seven day transdermal patch containing buprenorphine. The UK authority recognised that authorisation and granted a UK MA on 10 June 2005. The application to the Danish authorities had been made under Article 10(3) because BuTrans was delivered by a different route of administration (namely a trans-dermal patch as opposed to a sub-lingual tablet), and so it was not a "generic" version of Temgesic. Napp relied on Temgesic as the RMP for the purposes of Article 10(3). It supplied bridging data demonstrating the clinical effectiveness of BuTrans and its bioequivalence with Temgesic, this being the "appropriate" clinical data to support its application. Napp and its associated companies had conducted or commissioned 26 clinical trials and studies over a period of 9 years in order to obtain the appropriate bridging data. This was a considerable investment on its part. Since obtaining its MA, Napp has marketed BuTrans in doses of 5, 10, 15 and 20 µg /hour.

18. On 20 December 2013, Sandoz applied to the German authorities under the decentralised procedure (for which the Medicinal Code provides), seeking an MA for its product, Reletrans. Reletrans is a transdermal patch containing buprenorphine. It is a generic version of BuTrans. Sandoz applied under Article 10(3), and referred in its application to Temgesic as the RMP. In its cover letter Sandoz referred to the bridging data supplied by Napp to support its earlier Article 10(3) application in relation to BuTrans. The only new material supplied by Sandoz in support of its application was bioequivalence data which demonstrated that Reletrans was the bioequivalent of BuTrans.

19. On 12 January 2016, the decentralised procedure was concluded in Germany with a positive opinion in favour of Sandoz's application. The MHRA issued the UK MA to Sandoz on 10 February 2016.

20. In issuing that MA, the MHRA applied Chapter 4 of Title III of the Medicinal Code, as it is required to do by virtue of regulation 58(6) and (7) of the Human Medicine Regulations 2012.

CURRENT LITIGATION

21. By this judicial review, Napp challenges the MHRA's decision to issue an MA for Reletrans in the UK. Napp is pursuing parallel proceedings in the courts of other EU Member States, raising similar issues as are raised in this case. In short, Napp seeks to have Sandoz' MA for Reletrans set aside as unlawful, and to that end it seeks a reference to the CJEU to address what it suggests is a gap in the scheme of regulatory protection established by the Medicinal Code.

22. To complete the story, I should record that shortly before the hearing of this judicial review on 6 July 2016, Arnold J dismissed Napp's application to the Chancery Division to prevent threatened infringement by Sandoz of its patent relating to BuTrans (see [2016] EWHC 1517 (Pat), judgment dated 28 June 2016). Arnold J granted Napp permission to appeal to the Court of Appeal, and granted interim relief by way of injunction pending the appeal, which was to last until 16 August 2016 or further Order of the Court (see [2016] EWHC 1581 (Pat), judgment dated 28 June 2016). I am told that the patent appeal is listed for hearing by the Court of Appeal on 2 August 2016.

CLAIMANT'S CASE IN SUMMARY

23. Napp complains that the MHRA was wrong to have allowed Sandoz to rely on the bridging data provided by Napp in support of its Article 10(3) application for an MA for BuTrans. Napp contends that this was (as set out at [9] of the Claimant's Grounds):

    a. Not permitted under the Medicinal Code, which does not permit a generic applicant such as Sandoz to rely on the bridging data provided to support an authorisation under Article 10(3);

    b. In breach of the EU principles of legal certainty, legitimate expectation and /or fundamental rights; and

    c. In breach of the right to property contained in the Charter of Fundamental Rights of the EU.

24. More specifically, Napp argues that Article 10(3) requires an applicant to provide bridging data to establish the safety of its product by reference to the RMP (here, Temgesic, or product A). Article 10(3) does not permit such an applicant to rely on someone else's bridging data provided at an earlier date to support an earlier application under Article 10(3) for a different product (here, Napp's bridging data for BuTrans, or product B), and then simply to provide bioequivalence data to show that the index product (here, Reletrans or product C) is the bioequivalent of product B.

Napp argues that Article 10(3) precludes product C relying on the product B bridging data, for two main reasons: first, because it would be contrary to the principle set out in the Medicinal Code that authorisation cannot extend to a "generic of a generic"; and secondly, because to allow Reletrans' authorisation under Article 10(3) in this way, would mean that Napp's bridging data is entirely unprotected, which cannot have been what the Medicinal Code (or its authors) envisaged, because it would act as a disincentive to innovation. Napp argues that there is an apparent "lacuna" in the Medicinal Code which consists of silence in relation to the regulatory and data protection due to producers of drugs like BuTrans, and this must be the subject of a reference to the CJEU.

SCHEME OF THE CODE

25. Before turning to Napp's arguments, it is necessary to examine the scheme of regulatory protection set out by the Medicinal Code. The Medicinal Code is a comprehensive code. That Code reconciles a number of competing public and private interests many of which are revealed by the recitals. Those interests include the following: (i) safeguarding public health; (ii) not hindering the development of or trade in pharmaceutical products; (iii) encouraging and permitting the development of generic products while (iv) ensuring that innovators are not put at a disadvantage; (v) not conducting repetitive tests on humans and animals unless necessary.

26. The Code contains protections for innovators of new drugs: in essence, a period of 10 years, in some instances extendable to 11 years, before generic alternatives can be marketed; where the innovator develops line extensions of new drugs, those too can fall within the protections afforded by means of a GMA, but always subject to the existing 10-year period of protection – which can be extended to 11 years (by the 8+2+1 formula). By this means, the directive plainly balances the commercial interests of the innovator, in enjoying a period of exclusive marketing of the authorised drug, against the long term interests of the public in securing access to cheaper generic copies.

27. The directive does not specify any particular protection for bridging data supplied under Article 10(3).

28. Article 10(5) does, however, provide a period of data exclusivity for products which meet the criteria set out, namely, they are (i) new indications, of (ii) a well-established substance; in circumstances where (iii) significant pre-clinical or clinical studies were carried out in relation to the new indication. Products authorised under Article 10(3) are capable of falling within Article 10(5): Article 10(3) extends (amongst other things) to products which have different therapeutic indications, when judged by reference to the RMP.

29. There is no other protection contained within the Medicinal Code. Napp says this is an oversight (it calls it a "lacuna"). The counterargument, advanced by the MHRA and supported by Sandoz is that there is no lacuna; this is a deliberate policy choice. I shall return to that important issue after considering the relevant case law.

CASE LAW

30. Three cases decided by the European Court of Justice (as it was) have particular relevance to this case. They are:

a. Case C-368/96 *R v Licensing Authority established by the Medicines Act 1968 (acting by the Medicines Control Agency) ex p Generics (UK) Ltd and other cases* [1999] 2 CMLR 181 ("*Generics"*). This case involved three different cases on similar facts, raising similar issues. It is sufficient to outline the facts of the first case only in summary: on 29 January 1981 Bristol-Myers Squibb ("BMS") obtained an MA for a drug called Captopril, used to treat severe hypotension. BMS then obtained further MAs for new therapeutic indications for that drug. On 20 January 1993 Generics UK Ltd, a company carrying on business as a manufacturer of generic medicinal products, applied for MAs for generic versions of Captopril, under the abridged procedure. The regulator granted MAs for those indications which had been authorised for at least 10 years, but not for indications authorised for less than 10 years. On Generics' challenge, the High Court referred questions to the European Court of Justice. That Court advised that MAs should be given for all the therapeutic indications covered by the original application, whether those indications had been authorised for 10 years or not ([40] – [44], in answer to question 2).

b. Case C-106/01 *R (on the application of Novartis Pharmaceuticals UK Ltd) v The Licencing Authority established by the Medicines Act 1968 (acting by the Medicines Control Agency) and Others* [2004] CMLR 26 ("*Novartis"*). The facts in summary are these: in 1983, Novartis obtained an MA for Sandimmum, an immuno-suppressant. Novartis subsequently developed a related product called Neoral, which was authorised in May 1994 for all the same indications as Sandimmum. Neoral was not the bioequivalent of Sandimmum, and so the application for it was made under the hybrid-abridged procedure. In January 1999, the Medicines Control Agency, the statutory predecessor of the MHRA, granted MAs to SangStat for its product, SangCya, which was the bioequivalent of Neoral. SangStat's application was under the hybrid-abridged procedure. SangStat relied on Sandimmum as the RMP and included bioequivalence data demonstrating bioequivalence between SangCya and Neoral. The MCA relied on Novartis' bridging data for Neoral in granting the authorisation to SangCya. Novartis applied for judicial review of the MCA's authorisation of SangCya; the application was dismissed, but on appeal the Court of Appeal referred questions to the ECJ. The ECJ concluded that Novartis' bridging data for Neoral could not be accorded a further period of protection beyond that protection already afforded in relation to the original product, Sandimmum (see [58]), and that the competent authorities were entitled to refer to that bridging data provided in support of the application for Neoral, even if Novartis did not consent to that, see [67].

c. Case C-36/03, *R (Approved Prescription Services Ltd) v Licensing Authority, acting by the Medicines and Healthcare products Regulatory Agency* [2004] ECR I-11606 judgment, 9 December 2004 (*"APS"*). The facts in summary are these: Eli Lilly obtained an MA for Prozac capsules in November 1988. Eli Lilly then developed Prozac liquid which was authorised in October 1992 under the hybrid-abridged procedure. In 1999, APS applied for an MA under

> the hybrid-abridged procedure for its own product, Fluoxetine liquid, a generic version of Prozac liquid. APS relied on the similarity between that product and Prozac liquid. The MHRA rejected the application on the basis that Prozac liquid had not been authorised for 10 years or more, and invited a revised application using Prozac capsules as the RMP, requiring APS to supply the appropriate bridging data. APS challenged that decision. The High Court referred questions to the ECJ. By the time the matter came before the ECJ, *Novartis* had been decided. The Court concluded that an application for an MA for Product C (Fluoxetine liquid) could proceed under the hybrid-abridged procedure on the basis of similarity with Product B (Prozac liquid), where Product B was a new pharmaceutical form of Product A (Prozac capsules) and Product A had been authorised in the EU for the relevant period (at that stage, of six or ten years).

31. Those three cases were analysed by Moses J, as he then was, in *R (Merck Sharp and Dohme Ltd*) *v The Licensing Authority (Acting by the Medicines and Healthcare Products Regulatory Agency)* [2005] EWHC 710 (Admin) ("*MSD"*). From them, and from the Directive, he distilled the following principles (at [57]) (which I shall call the "Moses Principles"):

> "1. The primary objective of the Directive is to safeguard public health (see the Second Recital of the Directive and e.g. *Novartis* judgment at paragraph 30).
>
> 2. Article 10, as interpreted by the Court, provides a complete code as to the circumstances in which an applicant may cross-refer to data relied upon in support of a previous authorisation …
>
> 3. The identity of the applicant for authorisation is not a feature of the provisions of Article 10. It is irrelevant whether the applicant is an innovator which holds marketing authorisation for the original product or its development or a generic company which seeks authorisation (see the wording of the Directive at Articles 8 and 10).
>
> 4. Cross-reference to data relied upon in support of the authorisation of a product authorised for at least six or ten years or its development is permissible where product C is essentially similar to product A (*Generics*) or to product B (*Novartis* **and** *ApS*).
>
> 5. Product B is a development or line extension of product A if the differences between product B and product A are expressly identified in the proviso or "generally entail" or "generally imply" the difference in question between product A and product B (see *Novartis* at paragraph 66 of the judgment and *ApS* at paragraph 26).
>
> 6. The objective of ensuring that innovative firms are not placed at a disadvantage, identified in Recitals 3 and 9 of the Directive, is achieved by providing protection for a period of not less than six to ten years, a protection which is additional to that which is afforded by the domestic and Community laws of intellectual property and the additional supplementary protection afforded by Council Regulation 1768/92/EEC (*Generics* judgment paragraphs 73–76).

> 7. The expense and difficulty in producing and testing a product which is a development of the original authorised product is no ground for permitting a further period of data protection for the developed product (see *Generics* at paragraphs 46 to 48)."

32. He then turned to the facts of that case, which involved Fosamax 5mg, which had first been authorised to the Claimant ("MSD") in July 1993. MSD had then developed Fosamax Once Weekly 70mg, which was authorised in November 2000. A separate authorisation for Fosamax 70mg was required because the posology (or dosage) of Fosamax 70mg differed from Fosamax 5mg (and indeed from Fosamax 10mg which had also been developed by MSD in the meanwhile). Three generic drugs companies sought authorisations under the hybrid-abridged procedure to produce a generic version of Fosamax 70mg, relying on MSD's data supplied for both Fosamax 5mg and Fosamax 70mg. MHRA accepted the application(s) on that basis. MSD challenged the MHRA by way of judicial review. Moses J rejected MSD's submissions, and concluded that the generic drugs companies (and indeed the MHRA) were entitled to cross-refer to MSD's data supporting its application for Fosamax 70mg. Any other conclusion was inconsistent with the objectives of the Directive (see [77]). There was no "fatal gap" in regulatory protection afforded by the Directive; *Novartis* and *APS* were correctly decided; there was no need for a reference (see [80] – [87]).

ADVISORY SOURCES

33. The European Commission publishes a "Notice to Applicants" for those seeking authorisation of medicinal products. Volume 2A addresses Procedures for marketing authorisation. I was shown various versions of this Notice, dating back to 2001. In June 2013, the Commission introduced new text under the heading relating to Article 10 applications, sub-heading "Reference Medicinal Products" as follows (emphasis added):

> "…However, in those cases where a medicinal product authorised under Article 10(1) has been developed through an application submitted in accordance with Article 10(3) of Directive 2001/83/EC leading to a new indication, strength, pharmaceutical form, a marketing authorisation application of a subsequent generic of this medicinal product can include the new indication, strength, pharmaceutical form, etc. **To this effect, it will also be possible to refer to the data submitted to support the development."**

By this passage, the Commission appears to accept that bridging data submitted in support of an application under Article 10(3) can be referred to in an application for authorisation of a subsequent generic version of that drug. Certainly, there is no suggestion that any exclusivity applies to the bridging data already submitted, or that the subsequent generic application must be supported by its "own" bridging data.

34. I accept that the Notice to Applicants is not binding on me as a matter of law. But it carries some weight with me, as the ECJ has confirmed it should do: in *APS*, the Advocate-General (Jacobs) accepted that the Notice to Applicants lacked legal force ([70]), but said that it should be accorded some weight because it is a *"document which represents the harmonised views of the Commission and the competent authorities of the Member States as to how the Community legislation might workably be put into effect"* [71]. The Court agreed, at [27].

35. I was also shown minutes of meeting of the Co-ordination Group for Mutual Recognition and Decentralised Procedures, a group containing representatives of the competent authorities of the Member States ("CMDh"). At a meeting on 27 November 2013, the working party discussed potential applications under Article 10(3) , and suggested in terms that those applications should be based on Temgesic as the RMP, referring to Norspan in the cover letter, providing bioequivalence studies against Norspan. (As I have noted above, Norspan is the brand name for BuTrans elsewhere in the EU.) The CMDh was content for the applications to be made on a mixed basis, using data already supplied to support the authorisation for Product B.

36. These minutes are not legally binding either, but they carry some weight in demonstrating the collective view of the competent authorities that the combination of existing bridging data for Product B, along with bioequivalence studies for Product C against Product B, would be considered "appropriate" within Article 10(3).

ANALYSIS

Language of the Directive

37. So far as the Directive is concerned: Article 10(3) refers to "*appropriate"* pre-clinical tests or clinical trials. The provision is not specific about *who* must commission or produce those tests or trials. As a matter of ordinary language, if the intention had been to require a specific person or entity to produce such data, words to that effect could and should have been included. The obvious inference to draw, as a matter of ordinary language, is that the provision does not place any restriction on who compiles the bridging data, and that person may or may not be the person now making the application.

Scheme and Purpose of the Directive

38. Where bridging data has already been provided to support the application for Product B, there is no obvious reason why it should be repeated to support an application for Product C, if Product C is the same as or materially identical to Product B. The issue of paramount importance under the Medicinal Code is to show that Product C is safe and effective; and that can be done by showing that it is the same as or equivalent in effect to Product B, knowing that Product B has already been demonstrated as safe and effective by reference to Product A. That is why, in a case like the present, "appropriate" clinical data must include data demonstrating that Product C is the bioequivalent of Product B (as was done here, on the facts); that is consistent with Annex 1 which lists bioequivalence study reports as part of Module 5, relating to clinical data in the context of applications under Articles 8 and 10(1). That outcome is also consistent with the underlying policy of avoiding repeat tests on humans and animals so far as possible (recital (10)).

39. I can see no reason to read the provision as being subject to the restriction for which Napp argues. To read the word "appropriate" as being limited to data derived from pre-clinical tests or clinical trials undertaken by or on behalf of the party making the application, would be to go far beyond any exercise of construction, even strict construction, of a derogating provision in EU law. Instead, it would impose a significant limitation on the provision itself by reading in a separate and free-standing condition. The result would be at odds with the stated purposes of the Medicinal

Code, because it would lead to unnecessary repeat testing which is contrary to the public interest; it would also act as a disincentive to the development of generic alternatives which are in the public interest (see recital (14) of the 2004 amending directive).

40. That conclusion tallies with the scheme of regulatory protection contained within the Medicinal Code. Bridging data provided in support of an Article 10(3) application is not specifically protected, and will only benefit from protection if it comes within the limited scope of Article 10(5). It is common ground here that Article 10(5) would never have applied to BuTrans, which was not a "new indication" for the use of buprenorphine. Thus, quite simply, there is no protection for Napp's bridging data under the Code. I see no reason to conclude that this is a "lacuna". It is in my judgment a deliberate policy choice, to reflect and reconcile the wider objectives of the Code.

41. There is nothing offensive about that conclusion on the facts of this case. Schering-Plough produced a dossier of clinical data to support its original application for Temgesic. Schering-Plough was the innovator and its product and data was protected under Article 10(1), as it was contained in earlier directives, for the relevant period. Only once that protection had expired was Napp free to benefit commercially from Schering-Plough's dossier. It did so, and obtained authorisation for BuTrans relying in part on Schering-Plough's data. Only now, many years later, has a generic competitor presented an application for a product to rival BuTrans. But Napp was not the innovator. I see no strong reason, when balanced against the other purposes of the Code, why Napp should benefit from a fresh period of protection. Indeed, this argument was raised and dismissed in *Novartis*, where the Court said at [58] that *"documentation covering the new therapeutic indications of a medicinal product already authorised cannot be accorded a further period of protection…".*

The Case Law

42. The strong message which is delivered by all four of the cases outlined above, so far as is relevant to decide the instant case, is that data provided by one company in support of its application(s) for MAs for its own products can be relied on by third parties to support their applications, subject only to the express protections contained in the Code. Both *Novartis* and *APS* involved third party applications under Article 10(3). In each case the Court advised that the Code allowed the third party to rely on data already provided in support of an earlier application by a different applicant under Article 10(3). The Court did not suggest that the Directive afforded any protection to that data: quite the contrary, the Court concluded that *no* protection was due.

43. Napp argues that these four cases are materially different, because in each, the same company (or connected companies) developed Products A and B. That, so Napp argues, is not the case here. But these are distinctions on the facts which in my judgment are irrelevant. There is nothing in the Medicinal Code or the case law to suggest that the identity of the applicant has any relevance at all, indeed, quite the contrary: see Moses Principle 3, and this from *MSD* at [73]:

> "Article 10 makes no reference to the identity of the applicant. The right of a generic company to cross-refer to data is the same right exercisable by the

> competent authority to which the High Court and the European Court of Justice referred in *Novartis…*"

44. There is no reason why the outcome should be any different depending on the whether the innovator of Product A is, or is not, a company connected with the developer of Product B. After all, the development work in preparing the bridging data for a Product B application under the hybrid-abridged procedure (article 10(3)) will be the same, regardless of who undertakes that work.

45. Napp's arguments to the contrary lead to absurdity. Mr Gordon accepts that if BuTrans had been developed by Schering-Plough, that company would have had no protection for its bridging data under the Medicinal Code (Mr Gordon had to concede that much, given the European authorities). Yet he argues that Napp should have such further protection, simply because it is unconnected with Schering-Plough. But why? That would just create wholly unjustified discrimination between rival drug companies, based on the happenstance of whether the same or a different company had done the development work on Product B.

46. I conclude that the corporate identity and connections of the developer of Product B are not important to the analysis. Mr Gordon's grounds for distinguishing the European authorities are unfounded.

47. I agree with the Moses Principles. Moses Principle 4 would appear to be determinative of this case against Napp. Further, Moses Principles 3 and 6 appear to answer Napp's arguments as they are advanced here. Further, I note that Mr Gordon acted for the Claimant in *MSD*, and in that case too he advanced a submission that there was a "fatal gap" in the regulatory protection provided to his client by the Medicinal Code [82]. That argument was rejected by Moses J at [83], who refused to make a reference [87]; there was no appeal.

48. I conclude that the principles established in the case law are applicable to the case in hand and provide an insurmountable obstacle to Napp's claim.

Advisory Sources

49. If further support was needed for the conclusion that Napp's bridging data is not protected, it exists within the Commission's Notice to Applicants, and the CMDh's analysis of this case. Those sources are firmly supportive of the analysis of the Code, as it has been interpreted by case law, which I have arrived at above.

Remaining Arguments

50. I can find no support for Napp's arguments in the Code, the case law, or in any other material I have been shown. For completeness, I turn to deal with some of Napp's other arguments.

51. First, Napp argues that there can be no "generic of a generic", relying on Article 10(1) and 10(2). The definition of "generic medicinal product" makes it clear that the generic must be proved to be the bioequivalent of the RMP. This would exclude an application based on the bioequivalent of a generic formulation of an RMP, and so (as

all parties agree) there can be no "generic of a generic". But this clear prohibition is not replicated in Article 10(3), where the Code leaves the competent authorities of the Member States scope to determine what evidence is "appropriate". The provisions are different. It is clear that Article 10(3) does permit a third party to rely on data already held by the competent authorities relating to an earlier application under Article 10(3). It follows that Article 10(3) does permit "second generation" application (where Product C's application relies on a combination of data relating to Products A and B, together with its own bioequivalence data to demonstrate bioequivalence with Product B).

52. On this point, I record a submission by Mr Peretz, to the effect that the competent authorities would be precluded by the words of Article 10(3) from permitting a "third generation" application, for a notional Product D, where the application relied on data provided for Products A, B and C in combination with bioequivalence data establishing the equivalence of Product D to Product C. His submission is that the term "appropriate" is the safeguard (and effective prohibition) against an authorisation being permitted on that basis; the MHRA would not regard such an application to be based on "appropriate" data and would refuse it.

53. In answer, Mr Gordon argues that this is a yet further reason to doubt the MHRA's analysis of Article 10(3) because he says that the Medicinal Code was intended to provide a unified objective code for the authorisation of medicinal products in the EU and should not be construed in such a way as to confer "subjective" powers on the competent authorities of the Member States. But the language of Article 10(3) is clear: it does confer a discretion on the competent authorities of the Member States to decide what data is "appropriate" to support an application under the hybrid-abridged procedure. That discretion is to be exercised by the competent authorities in a manner consistent with the scheme and purposes of that Code, as part of the harmonised system established by the Medicinal Code, and subject always to judicial oversight. But it is built into the Code, and built into the harmonised system. It is not a reason for doubting the construction of the Code I have arrived at above.

54. Secondly, in its written case Napp argued that it was entitled to protection of its bridging data for all time, based on its interpretation of Article 10(3). By the time the matter came before me, Mr Gordon had forsaken that argument. He argued instead for a reference to the CJEU, on the basis that there was a lacuna in the Code, that clarity was needed. He suggested that the CJEU would be able to plug the gap, and relied on Case C-402/07 and C-432/07 *Sturgeon v Condor Flugdienst GmbH* as an example of the CJEU doing precisely that, in a different context. There are three answers. First, there is no gap, as I have already established. But secondly, and in any event, I agree with Mr Peretz that the proposition that Napp's bridging data should or might be entitled to open-ended protection under the Code is untenable. That would not reflect the scheme of the Code, which permits limited (express) protections for some products and data, in carefully defined circumstances, for a limited time. Nor would it fit with the wider purposes of the Code, outlined in the various recitals and above. Far from reconciling the competing public and private interests, that would promote the commercial interests of Napp above all other interests. Thirdly, and in any event, *Sturgeon* does not assist the Claimant. That case is far removed from this. The CJEU there identified a problem with Regulation 261/2004 (the "Denied Boarding Regulations"), which it resolved by interpreting the

Regulations as requiring passengers whose flights were delayed by three hours or more to be compensated in the same way as those whose flights were cancelled (see [61]). I can see no read- across from that case to this.

Conclusion

55. In summary, I reject Napp's first ground. Sandoz was permitted to rely on the bridging data provided to support BuTrans' application under Article 10(3); that data is not protected by the Medicinal Code. There is no lacuna, and no question which needs to be referred the CJEU. I am confident of this, and decline to make a reference.

56. Mr Gordon did not advance any arguments at the hearing in support of his second or third grounds. But they are surely moribund, once ground 1 is seen to be without merit.

57. I dismiss this application for judicial review.

THE *SYNTHON* POINT

58. Sandoz supports the MHRA's arguments on the interpretation of Article 10(3). I have dealt with those arguments above, and given my acceptance of them I have dismissed this application for judicial review. In its Acknowledgement of Service and skeleton argument, Sandoz raised a separate argument, to the effect that the MHRA was obliged to recognise the authorisation which had already been granted to Reletrans by the German authorities, and thus it had no discretion to refuse to authorise Reletrans under the decentralised procedure. In support of this argument, Sandoz relied on Case C-452/06 *R (on the application of Synthon BV) v Licensing Authority of the Department of Health* [2008] ECR I-07681, paragraph 25 of which provides as follows:

> "In accordance with the objective of abolishing all barriers to the free movement of medicinal products in the Community referred to in recitals 12 and 14 in the preamble to the directive, it is apparent from Article 28(4) that a marketing authorisation granted by a Member State must, in principle, be recognised by the competent authorities in other Member States within 90 days of receipt of the application and the assessment report from the reference Member State, and that that recognition is not dependant on the procedure followed by the reference Member State for granting that authorisation."

59. The MHRA disputes the principle which underpins this submission, namely that it lacked power to do anything other than recognise the German MA for Reletrans. The MHRA notes that the Court in *Synthon* confirmed at [29] that the competent authorities may call into question – and refuse to recognise – assessments conducted in other Member States where matter of risk to public health are concerned:

> "… a Member State to which an application for mutual recognition is made pursuant to Article 28 of Directive 2001/83 cannot call into question, on grounds other that those relating to the risk to public health, the assessments carried out by the reference Member State's authorities in the context of the procedure for evaluating the medicinal product."

The MHRA maintains that *if* it had perceived there to be a risk to public health, it would have been entitled to refuse to authorise Reletrans.

60. This debate has an air of the unreal about it. The MHRA did not consider there to be any risk to public health posed by Reletrans. It therefore did recognise the German assessment and authorised Reletrans under the decentralised procedure. Whether it was obliged to do so, or exercised a discretion to do so does not matter on the facts: it did so.

61. The *Synthon* point (as we referred to it at the hearing) is not going to assist in the determination of the case. It would be much better for that point to be decided, if it needs to be, in a case where it will actually make a difference, if such a case ever comes before the Court. It is a point of potential importance, going to the nature and scope of the MHRA's powers to refuse recognition of a drug, acting as a competent authority within the harmonised procedure. It is not helpful to determine that sort of issue in a vacuum, as I am invited to do in this case. I say no more about it.

DISPOSAL

62. The case against Napp is overwhelming. The Medicinal Code does not protect Napp's bridging data. The case law of the European Court and the domestic court provides a complete answer to Napp's arguments. The advisory bodies of the European Union have expressed themselves in accord with that case law and against the position advanced for Napp. There is no uncertainty such as to justify a reference.

63. This application for judicial review is dismissed.