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Case No: HC11 CO3027

IN THE HIGH COURT OF JUSTICE
CHANCERY DIVISION
PATENTS COURT

Royal Courts of Justice
Strand, London, WC2A 2LL

Date: 20/12/2012

Before :

MR JUSTICE ROTH

- -

Between :

(1) DR REDDY'S LABORATORIES (UK) LTD

(2) DR REDDY'S LABORATORIES LTD

Claimants

- and -

WARNER-LAMBERT COMPANY LLC

Defendant

- -
- -

Mark Brealey QC and Ms Julianne Kerr Stevenson (instructed by **Innovate Legal**) for the **Claimants**
Ms Kelyn Bacon and Mr Max Schaefer (instructed by **Arnold & Porter (UK) LLP**) for the **Defendant**

Hearing dates: 20, 21 and 22 November 2012

- -

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.

.....
Mr JUSTICE ROTH

Mr Justice Roth :

INTRODUCTION

1. This case concerns the interpretation of Regulation (EC) 1901/2006 ("the Paediatric Regulation") and its application in the process which led to the grant of a six month extension of the Supplementary Protection Certificate ("SPC") to the defendant for its medicinal product, atorvastatin. Atorvastatin is a very successful product used to treat elevated cholesterol-related complaints in both adults and children, marketed in the United Kingdom under the name "Lipitor".

2. The claimants (together "Dr Reddy's") are a substantial producer of generic medicines. The first claimant is a subsidiary of the second claimant but for the present purposes it is not necessary to distinguish between them. The defendant is a company within the Pfizer group and I shall refer to it, as it was throughout the trial, as "Pfizer". Pfizer is a leading and well-known manufacturer of pharmaceutical products.

3. Dr Reddy's apply to set aside the extension to the SPC granted to Pfizer under Article 36 of the Paediatric Regulation. Since this extension expired on 6 May 2012, the purpose of Dr Reddy's claim is now to establish a basis for the recovery of damages pursuant to a cross-undertaking given by Pfizer in a Consent Order of 17 November 2011. However, the issues for decision at this stage are whether the extension to the SPC for atorvastatin ("the paediatric extension") was validly granted and, if so, whether it should be revoked.

4. Dr Reddy's were represented at trial by Mark Brealey QC and Ms Julianne Kerr Stevenson, and Pfizer was represented by Ms Kelyn Bacon and Mr Max Schaefer. I am grateful for their written and oral arguments and the Court has also been substantially assisted by a full agreed statement of facts prepared in advance of the trial. Although a number of witness statements have been served, in the event neither side felt it necessary to cross-examine the other side's witnesses and, indeed, very little reference was made to the witness evidence in the course of the trial.

THE LEGISLATIVE REGIME

5. To assess this challenge to the paediatric extension, it is necessary to appreciate the scheme of the legislation. The following is intended as a general, and necessarily oversimplified, summary.

Marketing Authorisation

6. In the United Kingdom, as in most countries, authorisation is required to place a medicine on the market. Within the EU, the process of generating such marketing authorisation has been harmonised and in part centralised by what is referred to as the "Medicinal Products Code", which is now set out in Directive 2001/83/EC. For the most part, a marketing authorisation is issued nationally by the "competent authority" of the individual Member State, pursuant to an application made to that authority. However, Articles 32-34 of Directive 2001/83 provide for what is sometimes referred to as a "centralised referral" procedure. Under that procedure, the applicant may request an opinion from the Committee for Medicinal Products for Human Use

("CHMP"), which is the scientific advisory body to the European Medicines Agency ("EMA"). If the CHMP issues an opinion and report in favour of granting a marketing authorisation, that report is sent to the Commission, which then issues a decision in respect of the application. That decision, however, does not itself constitute the grant of a marketing authorisation but is addressed to the Member States which are then bound to act in accordance with the terms of the decision and issue their own, national, marketing authorisation.

7. In addition, it should be noted that Regulation (EC) 726/2004 introduced a centralised procedure for the grant of marketing authorisation for a limited range of products. For those products, a single, EU marketing authorisation may be granted. However, atorvastatin is not one of those products.

Supplementary Protection Certificate (SPC)

8. The provision of SPCs by way of extended patent protection for medicines was introduced in the EU in 1992. It is now governed by Regulation (EC) 469/2009 ("the SPC Regulation"). The rationale for the SPC, as stated in recital (4) of the SPC Regulation is that:

> "…the period that elapses between the filing of an application for a patent for a new medicinal product and authorisation to place the medicinal product on the market makes the period of effective protection under the patent insufficient to cover the investment to put into the research."

Since medicines, in particular those requiring lengthy and expensive research, will not be developed unless they have sufficient patent protection, there was also a concern that lack of extended protection would lead to the relocation of pharmaceutical research away to countries that offered better protection. As a result, some Member States introduced their own system of national SPCs and the EU regime was therefore also designed to introduce uniform protection across all Member States.

9. An SPC takes effect at the end of the basic patent period and extends the life of the patent for a period equal to that which elapsed between the date of lodging the application for the patent and the date of the first marketing authorisation, but subject in any event to a maximum period of five years: see Article 13 of the SPC Regulation.

Paediatric extension

10. Provision for a six-month extension to the SPC was introduced by the Paediatric Regulation which took effect on 26 January 2007. The background to this legislation was explained by Jacob LJ in *EI Du Pont de Nemours & Co v UK Intellectual Property Office* [2009] EWCA Civ 966, [2010] RPC 6, at [6]:

> "The Paediatric Regulation was to encourage specific research – and dissemination of knowledge about its results - into already known medicines as to their applicability for children. Prior to the Regulation there was no specific incentive for such research. If you discovered a new medicine you could patent it. You could then get an SPC if there was delay in getting an

> MA. And that was that. There was no particular requirement or incentive for going on to investigate whether the medicine was suitable (or unsuitable) for children or had particular application for children. The Paediatric Regulation provides an incentive – an extra six months of protection - for having conducted such research."

11. The context was further explained by the EU General Court in Case T-52/09 *Nycomed Danmark ApS v European Medicines Agency* (judgment of 14 December 2011). The court noted that at the date on which the Paediatric Regulation was adopted more than 50% of the medicines administered to children in Europe had not been authorised for such use and had not been subject to appropriate trials: para 39.

12. The objective of the Regulation is helpfully set out in the recitals, as follows:

> "(1) Before a medicinal product for human use is placed on the market in one or more Member States, it generally has to have undergone extensive studies, including pre-clinical tests and clinical trials, to ensure that it is safe, of high quality and effective for use in the target population.
>
> (2) Such studies may not have been undertaken for use in the paediatric population and many of the medicinal products currently used to treat the paediatric population have not been studied or authorised for such use. Market forces alone have proven insufficient to stimulate adequate research into, and the development and authorisation of, medicinal products for the paediatric population.
>
> (3) Problems resulting from the absence of suitably adapted medicinal products for the paediatric population include inadequate dosage information which leads to increased risks of adverse reactions including death, ineffective treatment through under-dosage, non-availability to the paediatric population of therapeutic advances, suitable formulations and routes of administration, as well as use of magistral or officinal formulations to treat the paediatric population which may be of poor quality.
>
> (4) This Regulation aims to facilitate the development and accessibility of medicinal products for use in the paediatric population, to ensure that medicinal products used to treat the paediatric population are subject to ethical research of high quality and are appropriately authorised for use in the paediatric population, and to improve the information available on the use of medicinal products in the various paediatric populations. These objectives should be achieved without subjecting the paediatric population to unnecessary clinical trials and without delaying the authorisation of medicinal products for other age populations.

…

> (6) The establishment of a system of both obligations and rewards and incentives has proved necessary to achieve these objectives. …"

13. Under the Paediatric Regulation, a Paediatric Committee ("PDCO") was established within the EMA. As noted in recital (8), it was to be a committee "with expertise and competence in the development and assessment of all aspects of medicinal products to treat paediatric populations."

14. As the General Court noted in *Nycomed*, the Paediatric Regulation provides a mechanism to compel pharmaceutical companies to envisage as a matter of course the possibility of the use in children of medicines which they develop. The "central element" of that mechanism is the paediatric investigation plan ("PIP") prescribed by the Paediatric Regulation. This is defined in Article 2(2):

> "'paediatric investigation plan' means a research and development programme aimed at ensuring that the necessary data are generated determining the conditions in which a medicinal product may be authorised to treat the paediatric population"

15. Subject only to a waiver or deferral granted by the EMA on the advice of the PDCO, any application for a new marketing authorisation for a medicine must include the results of studies conducted in compliance with an agreed PIP: Article 7. Further, for medicines which are already authorised and protected either by an SPC or by a patent which qualifies for the grant of an SPC, any application for authorisations of new indications, including paediatric indications and new pharmaceutical forms, must similarly include the results of such studies: Article 8. Provided that certain conditions are satisfied, the applicant is then entitled to a six-month extension of the SPC.

The scheme of the Paediatric Regulation

16. The procedure prescribed by the Paediatric Regulation involves a series of stages. The position of a patentee who wants either a new marketing authorisation for a medicine not previously authorised (ie under Article 7) or an authorisation of new indications or pharmaceutical forms of a product already authorised (ie under Article 8) can be summarised as follows:

    (i) The applicant draws up a draft PIP and submits it to the EMA (through the PDCO) for agreement: Article 15. Article 15(2) provides:

    > "The paediatric investigation plan shall specify the timing and the measures proposed to assess the quality, safety and efficacy of the medicinal product in all subsets of the paediatric population that may be concerned. In addition, it shall describe any measures to adapt the formulation of the medicinal product so as to make its use more acceptable,

> easier, safer or more effective for different subsets of the paediatric population."

(ii) The proposed PIP is assessed by the PDCO, which may request modifications to the plan. The PDCO then adopts an opinion, pursuant to Article 17(1):

> "…as to whether or not the proposed studies will ensure the generation of the necessary data determining the conditions in which the medicinal product may be used to treat the paediatric population or subsets thereof, and as to whether or not the expected therapeutic benefits justify the studies proposed. When adopting its opinion, the Committee shall consider whether or not the measures proposed to adapt the formulation of the medicinal product for use in different subsets of the paediatric population are appropriate."

(iii) The PDCO opinion is sent to the EMA which, subject to a procedure that entitles the applicant to have the opinion re-examined, adopts a decision annexing the PDCO opinion: Articles 18 and 25.

(iv) In its application for a marketing authorisation (whether a new authorisation or an authorisation of new indications) the applicant includes the decision of the EMA agreeing to the PIP and "results of all studies performed and details of all information collected in compliance with" the agreed PIP: Articles 7 and 8.

(v) The PDCO may be asked for its opinion as to "whether studies conducted by the applicant are in compliance with" the agreed PIP. That request may be made by the applicant prior to submitting its application for a marketing authorisation (ie stage (iv) above) or by the competent authority which has received the application: Article 23(2). The competent authority has to "take account" of the PDCO's opinion but is not bound by it: Article 23(3).

(vi) The competent authority which has received the application must verify that the PIP has been complied with: Article 23(1). This process is referred to as the "compliance check". However, although stage (v) above is optional, the parties agree that in practice the national competent authorities carry out the compliance check on the basis of an opinion to that effect from the PDCO.

(vii) If the compliance check is satisfied and a marketing authorisation (or extension to an existing authorisation) is granted, the results of all studies conducted in compliance with the PIP will be included in the summary of product characteristics ("SmPC"): Article 28(1); and the competent authority includes within the authorisation a statement indicating compliance with the PIP: Article 28(3).

(viii) If the application includes the results of all studies conducted in compliance with the PIP, the applicant receives a six-month extension to the SPC, but there is no such extension if the competent authority concludes that the studies do not conform with the PIP: Articles 36(1) and 24.

(ix) "Where there is a particular cause for concern", the competent authority as a condition for granting the marketing authorisation shall require that a risk management system be set up or that specific post-marketing studies be performed and submitted for review: Article 34(2). This provision continues:

> "The risk management system shall comprise a set of pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to medicinal products, including the assessment of the effectiveness of those interventions"

17. It will be necessary to consider further some of these provisions of the Paediatric Regulation, but three further aspects deserve mention:

(a) Even where completion of the PIP does not lead to the authorisation of a paediatric indication, if the results of the studies made in compliance with the PIP are included in the SmPC and, if appropriate, the product information leaflet, that will entitle the applicant to the reward of a paediatric extension: Article 36(1), second para. This is explained in recital (28):

> "Because the reward is for conducting studies in the paediatric population and not for demonstrating that a product is safe and effective in the paediatric population, the reward should be granted even when a paediatric indication is not authorised. However, to improve the information available on the use of medicinal products in the paediatric population, relevant information on use in paediatric populations should be included in authorised product information."

(b) The requirement to comply with a PIP can be waived by the EMA (on the advice of the PDCO) if it concludes that the product is likely to be ineffective or unsafe in all or part of the paediatric population, or that the disease or condition which the product is intended occurs only among adults, or that the product does not represent a significant therapeutic benefit over existing treatments for children. The applicant may apply for such a waiver or the PDCO may of its own motion advise that a waiver should be granted. The latter may be an important safeguard since the patentee would receive the significant benefit of a paediatric extension for seeking to establish whether the product can be used on children when it may be ascertainable at the outset that this would be inappropriate or unnecessary. See Articles 11-13.

(c) Provision is made for deferral of the initiation or completion of some or all of the studies in the PIP. Such a deferral may be requested by the applicant when submitting the proposed PIP or by the PDCO of its own motion. The conditions for a deferral are addressed below in the discussion of Dr Reddy's grounds of appeal.

THE PAEDIATRIC EXTENSION FOR ATORVASTATIN

18. Atorvastatin was a patented product that had a marketing authorisation at the time when the Paediatric Regulation came into force. Pfizer wished to apply for a

paediatric indication in that authorisation for certain high cholesterol conditions. Accordingly, Pfizer's application would fall under Article 8, combined with a limited category of waiver sought under Article 13. On 19 October 2007, Pfizer submitted its proposed PIP to the PDCO.

19. The PDCO requested certain modifications to the proposed PIP in discussion with Pfizer, and then issued its opinion and report on 4 June 2008 agreeing to the PIP, as there set out, and to a limited class of waiver.

20. On 20 July 2008, the EMA adopted a decision in accordance with the PDCO's opinion. The decision therefore (a) agreed the PIP and (b) granted a limited waiver.

21. The waiver is not material to the issues in this case. However, the terms of the PIP are at the heart of this case and it is necessary to summarise them. They can be taken from the positive opinion of the PDCO annexed to the EMA decision.

22. Pfizer had proposed new pharmaceutical forms for oral atorvastatin, more appropriate for children aged 6 years and above than the film-coated tablet which had previously been authorised.

23. The PIP required three clinical studies as follows:

Study Number	Area	Subarea	Description
1	Clinical	Bioequivalence	Bioequivalence study of the final age-appropriate oral atorvastatin formulation to the existing atorvastatin formulation in healthy adult volunteers
2	Clinical	Pharmacokinetic, safety	Steady-state, eight week pharmacokinetic study of atorvastatin in children and adolescents (aged 6 years to less than 18 years) with heterozygous familial hypercholesterolaemia using sparse PK sampling methodology and including flow-mediated artery dilatation assessments
3	Clinical	Safety	A 3-year study of the safety and follow-up study of efficacy of atorvastatin treatment of children and adolescents (aged 6 years to less than 18 years) with heterozygous familial hypercholesterolaemia

24. The PIP specified that the first study was to be completed by 30 September 2009 and the second study by 30 December 2009. The issues arise because of the terms of the third study. Those are set out in the PDCO Opinion under the heading "Risk Management Proposed at the Time of Marketing Authorisation". The objective of the third study is stated to be:

> "To provide data on the long-term follow-up of safety and efficacy in children and adolescents treated with Atorvastatin."

The study population is specified as at least 250 children and adolescents, of whom at least 50% are defined in terms which I was told means that they must be children under 11.

25. The study duration is specified as "three years". However, Pfizer explained (and this was not challenged) that this did not mean that the study could not continue for more than three years but that each individual child forming part of the study population would have to be subject to study for a period of three years.

26. Finally, the PIP specified that the study must be initiated by 31 March 2009. By contrast with the specifications for the first and second studies, the PIP does not stipulate a date of completion. Indeed, in the summary table of the three studies included in the Opinion, the date of completion of the PIP is specified as 31 December 2009 and the third study is referenced as required "to be initiated by the date of completion".

27. On 13 November 2009, pursuant to a request from Pfizer, the PDCO issued an opinion that Pfizer had complied with the PIP. The opinion was issued pursuant to Article 23(2) and (3). The appended report stated as regards the third study that Pfizer had "completed initiation". The report noted that the study was currently active in some countries and that 70 subjects had enrolled to date. The report concluded:

> "The PDCO adopted a positive opinion that the studies conducted by the applicant are in compliance with the agreed PIP. The agreed PIP was fully completed."

28. On 5 November 2009, Pfizer applied, pursuant to the centralised referral procedure in Article 29, for assessment by the EMA of its application for a marketing authorisation and for a decision to be adopted by the Commission in respect of the variation and an extension to the national marketing authorisations for atorvastatin held by members of Pfizer's corporate group, to include paediatric use for certain indications and approval of a new pharmaceutical form.

29. On 18 March 2010, the CHMP issued its assessment report. The report recommended that Pfizer be granted the marketing authorisation sought. The recommendation concluded:

> "Furthermore, CHMP takes note that the agreed [PIP] is fully completed and that the PDCO issued an Opinion on Compliance. CHMP reviewed the paediatric data subject to this plan and the result of these studies reflected in the Summary of Product Characteristics and, as appropriate, the Package Leaflet."

30. On 1 July 2010, on the basis of that report the Commission adopted a decision that the Member States should amend their national marketing authorisations for the relevant products. The recitals to the Commission's decision included the following:

> "Whereas…

> (3) It has been verified that the application includes the results of all studies performed and details of all information collected in compliance with the agreed [PIP].
>
> (4) Therefore the application complies with the requirements laid down in point (a) of Article 7(1) of [the Paediatric Regulation]."

31. The Commission's decision was addressed to the Member States and was implemented in the UK by the Medicines and Healthcare products Regulatory Agency ("MHRA"), being the national competent authority. The MHRA issued on 3 November 2010 its authorisations for each of the new pharmaceutical forms (a separate authorisation in respect of each tablet dosage) and on 16 November 2010 in relation to the variation of the summary of product characteristics regarding the existing authorisations to reflect the indications for paediatric use as set out in the annex to the Commission's decision. The MHRA authorisations include the statement referred to in Article 28(3) that the application complies with all the measures in the agreed completed PIP and also state that the SMPC reflects the results of those studies.

32. On 21 February 2011, Pfizer filed an application for an extension to the SPC for Atorvastatin in the UK. This was granted by the UK Intellectual Property Office ("the UK IPO") on 23 June 2011.

THE GROUNDS OF CHALLENGE

33. Dr Reddy's has advanced three grounds of challenge to the grant of the paediatric extension. Although expressed more extensively in the Re-re-amended Particulars of Claim, by the time of trial, they had been refined as follows:

    (1) The EMA acted *ultra vires* it powers under the Paediatric Regulation by approving a PIP that allowed Pfizer to defer completion of the third study. The circumstances in which studies in a PIP may be started but not finished are expressly defined by the Regulation and must be covered by a deferral under Article 20. No such deferral was applied for by Pfizer or granted in this case. Accordingly, the PIP was not lawfully approved under the Paediatric Regulation and Pfizer was therefore not entitled to the extension.

    (2) Pursuant to Article 45(3), a paediatric extension should be granted only when significant studies contained in the PIP have been completed. Here, none of the relevant bodies made an assessment as to whether either of the two studies which had been completed was significant; and, on the facts, they were clearly not significant.

    (3) Even if, contrary to ground (1), it was legitimate for the EMA to approve a PIP that required the initiation but not the completion of the third study, pursuant to Article 36 Pfizer was not entitled to a paediatric extension unless it included, within its application for a marketing authorisation, the results of the completed third study.

The jurisdiction to revoke a paediatric extension

34. Before considering those grounds, it is appropriate to address an important issue concerning the jurisdiction whereby the Court may revoke a paediatric extension. This arises under Article 16 of the SPC Regulation. Article 16(1) provides as follows:

> "The extension of the duration may be revoked if it was granted contrary to the provisions of Article 36 of the [Paediatric] Regulation …"

35. Pfizer submitted that this gives a discretion to the national body (in the UK, the Court) to revoke the paediatric extension on the basis set out, but not an obligation to do so. Dr Reddy's, by contrast, submitted that the extension must be revoked if it was contrary to the Paediatric Regulation.

36. In my judgment, the argument of Pfizer is correct. That the provision is to be interpreted in that way reflects not only its plain meaning, which I understand is the same in other language versions of the Regulation, but the contrast between Article 16 and the immediately preceding provision which concerns the invalidity of an SPC. Article 15(1) of the SPC Regulation provides that "the certificate *shall be invalid* if" (emphasis added) and sets out various grounds, including that it was granted contrary to the conditions for obtaining an SPC set out in Article 3. It seems to me clear from the contrasting wording of Article 15(1) and Article 16(1) that the use of the word "may" in the latter is deliberate.

37. Moreover, I consider that this construction makes good sense in policy terms. For example, one of the conditions for grant of a paediatric extension set out in Article 36(3) is that (save for a centralised EU authorisation under Regulation 726/2004) the product must be authorised in all Member States. If at the time the SPC was granted the product was not authorised in one of the 27 Member States but such authorisation was granted a few weeks later and before the period of paediatric extension would commence, the Court might well conclude that it would be inappropriate to revoke the extension. Indeed in *Du Pont de Nemours,* the Court of Appeal held that the fact that not all Member States had given marketing authorisations for the product at the time of the application for a paediatric extension did not preclude the application being rectified (under Article 10 of the SPC Regulation) once the missing authorisations had been obtained. Accordingly, if by error a paediatric extension was granted notwithstanding the absence of one of the necessary marketing authorisations, it would be anomalous if a third party's application to revoke the extension had to be granted although in the meantime the missing marketing authorisation had been obtained.

38. The circumstances in which an application to revoke a paediatric extension might be made and Article 36 might formally not be complied with are manifold, especially if Dr Reddy's is correct and a grant in conformity with Article 36 incorporates proper compliance with all the previous stages leading up to the application for a marketing authorisation. Although in many cases revocation might be appropriate, I consider it to be unduly formalistic if revocation had to be ordered in all such cases. Of course, if the language of the legislation mandated such a result, that would be the position. However, as I have explained, in my judgment, it stipulates the opposite.

39. I should add that I do not derive any assistance on this question of construction from section 72 of the Patents Act 1977 or Article 138 of the European Patent Convention that were prayed in aid by Mr Brealey. In the first place, they are part of a wholly different legislative regime. Secondly, quite different considerations of policy apply when a patent is substantively invalid from the situation where the grant of a right depends upon a series of steps taken by official or administrative bodies.

Ground 1

40. Article 36(1) provides:

> "Where an application under Article 7 or 8 includes the results of all studies conducted in compliance with an agreed paediatric investigation plan, the holder of the patent or supplementary protection certificate shall be entitled to a six-month extension of the [SPC]."

The foundation of Dr Reddy's argument is that in referring there to "an agreed paediatric investigation plan", Article 36(1) must mean a lawful PIP. In other words, if the EMA and PDCO do not have the power to approve the PIP in question, then compliance with it cannot properly entitle the applicant to the substantial reward of the extension. As Mr Brealey put it: "this case is about what is a lawful PIP".

41. But was the PIP that was agreed to by the EMA on the advice of the PDCO "unlawful"? Dr Reddy's contends that it was, on the basis that in effect the PIP provided for the deferral of completion of the third study although no deferral had been sought by Pfizer or, indeed, was granted under the specific provisions dealing with deferral in the Paediatric Regulation. Further, this meant that Pfizer could not include the results of all the studies in the PIP when applying for its marketing authorisation.

42. However, I consider that this mischaracterises the role of a deferral in the scheme of the Regulation, which is arranged in seven Titles. Deferrals are dealt with under Title II in section 2 of Chapter 3, the part of the Regulation that deals with the PIP. Articles 20-21 state, in so far as material:

> "20(1). At the same time as the paediatric investigation plan is submitted under Article 16(1), a request may be made for deferral of the initiation or completion of some or all of the measures set out in that plan. Such deferral shall be justified on scientific and technical grounds or on grounds related to public health. In any event, a deferral shall be granted when it is appropriate to conduct studies in adults prior to initiating studies in the paediatric population or when studies in the paediatric population will take longer to conduct than studies in adults.
>
> …
>
> 21(1) At the same time as the Paediatric Committee adopts a positive opinion under Article 17(1), it shall, of its own motion

> or following a request submitted by the applicant under Article 20, adopt an opinion, if the conditions specified in Article 20 are met, in favour of deferring the initiation or completion of some or all of the measures in the paediatric investigation plan."

43. The role of the deferral is further explained in recital (14):

> "In certain cases, the Agency should defer the initiation or completion of some or all of the measures contained in a paediatric investigation plan, with a view to ensuring that research is conducted only when safe and ethical and that the requirement for study data in the paediatric population does not block or delay the authorisation of medicinal products for other populations."

44. That was not the position in the present case at all. Atorvastatin had already been authorised for use in adults. Pfizer wished to market it for children in a new, more child-friendly formulation and wished a paediatric indication to be included accordingly in the SmPC. Pfizer was not seeking any further or amended marketing authorisation for its application to adults. Thus, there was no question of a paediatric study delaying authorisation for adults nor was it the case that the third study had to be delayed on safety grounds. Of course, since the PIP was to be completed by 31 December 2009 and the third study was a three year study (which as explained was likely in practice to take more than three years), it was obvious that the results of that study would not be available by the completion date. But that alone does not bring it within the statutory criteria for a "deferral".

45. As the General Court noted in *Nycomed*, by reference to recital (8) of the Regulation, the PDCO is the only body with "expertise and competence in the development and assessment of all aspects of medicinal products to treat paediatric populations": judgment, para 64. Requirements for a PIP are set out in Article 15(2):

> "The paediatric investigation plan shall specify the timing and the measures proposed to assess the quality, safety and efficacy of the medicinal product in all subsets of the paediatric population that may be concerned. In addition, it shall describe any measures to adapt the formulation of the medicinal product so as to make its use more acceptable, easier, safer or more effective for different subsets of the paediatric population. "

It is with regard to those requirements that the PDCO adopts an opinion in accordance with Article 17(1):

> "as to whether or not the proposed studies will ensure the generation of the necessary data determining the conditions in which the medicinal product may be used to treat the paediatric population or subsets thereof, and as to whether or not the expected therapeutic benefits justify the studies proposed."

46. The PDCO, as the expert committee, is obviously aware of the role of the PIP in relation to an application for a marketing authorisation and that the SMPC to be produced must reflect the results of studies conducted in compliance with an agreed PIP: Article 28(3). Evidently, the PDCO in the present case considered that sufficient data would be generated by the first two studies to provide the necessary information but that the third study should be commenced before the completion date of the PIP as part of a risk management system.

47. It is correct that such a risk management system appears to meet the criteria of Article 34(2) of the Regulation. On that basis, as Dr Reddy's accepted, it could have been required by the competent authority on the grant of the marketing authorisation as a study to be carried out thereafter. Pfizer had not proposed the third study as part of the PIP which it submitted to the PDCO. Indeed, when the PDCO suggested it, Pfizer's response was that it should be carried out outside the scope of the PIP. But the PDCO did not agree and included it in the PIP on the basis that I set out above. In my judgment, that does not render the PIP "unlawful" or "invalid". It had the beneficial effect that this study was started rather earlier than might otherwise have been the case, and enabled the PDCO to have control over the scope of the study.

48. At most, it might be contended that requiring the third study to be included as part of the PIP and not, as Pfizer had suggested, outside the PIP went beyond the strict power of the PDCO and the EMA under the Regulation. Dr Reddy's submitted that this was the position, pointing to the observation of the Court in *Nycomed* that the powers of the EMA are "circumscribed": para 98 of the judgment. However, suppose that the PDCO in its report stated that three studies would ensure the generation of the "necessary data determining the conditions in which the medicinal products may be used to treat the paediatric population" but that a fourth study, although not necessary for this purpose, should also be required because it might generate information that would be of scientific interest. If the EMA then issued a decision adopting this opinion, it could be contended that inclusion of the fourth study in that PIP was outside its power. On that basis, the EMA's decision might be open to legal challenge by the applicant. But if the applicant chooses not to challenge it but instead agrees to the PIP and follows its requirements, that does not render the PIP "unlawful" of "invalid". More particularly, if the applicant complies with the PIP and conducts those four studies, the fact that the fourth study arguably should not have been included does not deprive the applicant of its right to the "reward" of a paediatric extension under Article 36.

49. Accordingly, it is not necessary for me to decide whether the PDCO and the EMA in fact had power to include the third study here in the PIP. The fact is that Pfizer did not choose to contest the decision but agreed to the PIP. Since it is common ground that Pfizer then complied with what the PIP stipulated, I do not see that it is open to Dr Reddy's subsequently to challenge the grant of a paediatric extension on this basis.

50. If I were wrong on that point, and the third study should formally have been left outside the PIP so as to make it comply with Articles 15(2) and 17(1), I would regard this as a very technical breach. I emphasise that it is not the case that if the third study had to be left outside the PIP then the PDCO might have required an alternative to be included and completed; or that the second study, for example, would then have been more extensive. It is clear from the history of this matter that the PDCO considered that completion of the first two studies, as specified, by 31 December 2009

would generate the necessary data and enable the SmPC to be prepared for atorvastatin to be authorised for the paediatric population. The third study could then have been imposed as a post-authorisation requirement by the competent authority, and there is nothing in the Regulation to preclude the PDCO from making a recommendation as to what post-authorisation studies should be carried out. Faced with what I have described, on this basis, as a technical breach, I would regard this as an appropriate case for exercise of the Court's discretion under Article 16 of the SPC Regulation not to revoke the paediatric extension.

51. In the light of my decision, it is unnecessary to consider Pfizer's alternative argument that in any event the Court cannot revoke a paediatric extension on the basis of a defect in the PIP or an alleged failure by the applicant to comply with the PIP, where the competent authority has included with the marketing authorisation a statement pursuant to Article 28(3) indicating compliance. That submission was based on the wording of Article 16 of the SPC Regulation which states that the extension may be revoked if it was granted "contrary to the provisions of Article 36" of the Paediatric Regulation; and, secondly, on the provision in Article 36(2) of the Paediatric Regulation:

> "The inclusion in a marketing authorisation of the statement referred to in Article 28(3) shall be used for the purposes of applying paragraph 1 of this Article."

52. In *Du Pont de Nemours*, the Court of Appeal held that the only way an applicant can establish that a PIP has been complied with for the purpose of seeking a paediatric extension is by the inclusion in the marketing authorisation of an Article 28(3) statement. Hence the words, "shall be used" in Article 36(2) are mandatory. Accordingly, an applicant is precluded from seeking to persuade the UK IPO that it had complied with a PIP when it could not furnish such a statement from the competent authority.

53. However, although *Du Pont de Nemours* therefore established that the statement in the marketing authorisation is the exclusive basis for the determination of compliance, this does not mean that a third party is precluded by such a statement from seeking to revoke a paediatric extension under Article 16 of the SPC Regulation. If Pfizer's submission were correct, it would largely reduce the right of challenge under Article 16 to cover only the situation where the product had not been authorised in all Member States as required by Article 36(3) or, of course, where no Article 28(3) statement had been made. Ms Bacon did not shrink from this conclusion. She submitted that if the statement under Article 28(3) should not have been made by the competent authority, the only remedy of the third party was to bring separate proceedings to challenge the decision of the authority to make that statement. In the present case, that would have meant starting judicial review proceedings seeking to quash the decisions of the MHRA of November 2010. It may be that Dr Reddy's could have started such proceedings but I do not see a good reason to limit the scope of the express statutory right of challenge under Article 16 in that way. It should be noted that a third party, such as a generics producer, would have no particular objection to the marketing authorisation; what it objects to is the extended patent life bestowed by the paediatric extension. Where there is an express statutory power in the legislative regime to challenge that paediatric extension, my present view is that Pfizer was being over-formalistic in seeking to read the language of Article 16(1) in

the narrow way urged upon the Court. However, in the light of my conclusion on the basic argument of Dr Reddy's under ground 1, it is unnecessary to reach a final view on this point.

Ground 3

54. Since it is closely related to Ground 1, it is logical next to address Dr Reddy's Ground 3.

55. Article 36(1) requires the application to include the results of all studies "conducted in compliance with an agreed [PIP]…" Dr Reddy's argued that since the application here did not include the results of the third study, this condition was not satisfied.

56. I regard this submission as misconceived. Since the PIP did not require completion of the third study by the completion date of the PIP but only its initiation, Pfizer did what was required of them by the PIP. The terms of the PIP were therefore complied with. Accordingly, if Ground 1 does not succeed, I see no basis for the challenge to succeed on Ground 3.

Ground 2

57. Dr Reddy's second ground turns on the proper interpretation of Article 45(3). It is necessary to set out most of Article 45:

> "1. By 26 January 2008, any paediatric studies already completed, by the date of entry into force, in respect of products authorised in the Community shall be submitted by the marketing authorisation holder for assessment to the competent authority.
>
> The competent authority may update the summary of product characteristics and package leaflet, and may vary the marketing authorisation accordingly. …
>
> 2. All existing paediatric studies, as referred to in paragraph 1, and all paediatric studies initiated prior to the entry into force of this Regulation shall be eligible to be included in a paediatric investigation plan, and shall be taken into consideration by the Paediatric Committee when assessing applications for paediatric investigation plans, waivers and deferrals and by competent authorities when assessing applications submitted pursuant to Article 7, 8 or 30.
>
> 3. Without prejudice to the previous paragraph, the rewards and incentives of Articles 36, 37 and 38 shall only be granted provided that significant studies contained in an agreed Paediatric Investigation Plan are completed after the entry into force of this Regulation.
>
> 4. In consultation with the Agency, the Commission shall draw up guidelines to establish assessment criteria for the

> significance of studies for the purposes of applying paragraph 3."

58. The Paediatric Regulation entered into force on 26 January 2007. Pfizer contends that the requirement in Article 45(3) that significant studies contained in the PIP must be completed after that date is a transitional provision which has no application in the present case. Dr Reddy's submits that it applies in all cases, and that it was not satisfied here. In that regard, it is also necessary to refer to Article 28(3), of which the final sentence states:

> "For the purpose of the application of Article 45(3), this statement shall also indicate whether significant studies contained in the agreed [PIP] have been completed after the entry into force of this Regulation."

That provision concerns the statement to be made by the competent authority within the marketing authorisation.

59. Article 45 appears in the Title of the Paediatric Regulation headed "Communication and Co-ordination". Article 45(1) is clearly a transitional provision concerning paediatric studies already completed before 26 January 2007. Article 45(2) is also a transitional provision: it permits both studies *completed* prior to the Paediatric Regulation coming into force (ie studies covered by Article 45(1)) and studies *initiated* prior to the Paediatric Regulation coming into force to be included in a PIP. It also requires all these studies to be taken into account when any application concerning a PIP and a marketing authorisation is assessed.

60. Article 45(3) is expressly stated to be without prejudice to Article 45(2). Hence it clearly has the effect that if studies completed before the Paediatric Regulation entered into force are included in the PIP, the reward of a paediatric extension will be granted only if the PIP also requires studies to be completed after the entry into force of the Regulation and if those studies are "significant". The valuable reward of the paediatric extension is therefore not given only for studies completed prior to 26 January 2007, or for those studies and some non-significant studies completed thereafter.

61. Literally read, the language of Article 45(3) could be of general application. However, if that were the legislative intention, its expression does not accord with the structure of the Regulation viewed as a whole. It would be expected then to appear in Article 36, or at least in a provision in the Title of the Regulation headed "Rewards and Incentives"; or, possibly, in Title II concerning "Marketing Authorisation Requirements".

62. There is nothing in the recitals which helps on this question of interpretation but, in my view, assistance can be derived from the Commission's Guidelines drawn up pursuant to Article 45(4): OJ 2008 C243/1. The templates for the compliance statement to be made by the competent authority under Article 28, as set out on page 12 of the Guidelines, indicate that the statement of significance for the purpose of Article 45(3) only has to be made where a PIP contains some studies completed before the entry into force of the Regulation. Somewhat confusingly, final section 3 of the Guidelines then proceeds on the basis that Article 45(3) applies only to studies

initiated before, albeit completed after, the entry into force of the Regulation, whereas the wording of Article 45(3) and, indeed, the Commission's suggested templates set out at the end of the immediately preceding section of the Guidelines indicate that it applies whenever a PIP contains studies completed before the entry into force of the Regulation. Despite this element of confusion, it is nonetheless clear that the Guidelines regard Article 45(3) as a transitional provision and not one which applies in every case.

63. I consider that further assistance is provided by the statutory history. Both sides referred me to the travaux préaratoires, each contending that it supported their preferred interpretation.

64. The Paediatric Regulation originated in a proposal presented by the Commission in September 2004. What is now Article 45 originated as Article 44 of the Commission's draft. Draft Article 44(3) read as follows:

> "No paediatric studies, as referred to in paragraph 1 [ie completed before the entry into force of the Regulation], which have at the date of entry into force of this Regulation already been submitted for assessment in the third country, shall be taken into consideration for the rewards and incentives provided for in Article 36, 37 and 38."

This was explained in the Commission's Explanatory Memorandum as follows:

> "Pharmaceutical companies have, in some cases, already conducted clinical trials in children. However, frequently, the results of these studies have not been submitted to Competent Authorities and have not resulted in updates to product information. To deal with this issue, it is proposed that any studies completed before this proposed legislation is adopted will not be eligible for the rewards and incentives proposed for the EU. …"

65. When this draft was considered in the working party of the Council, the French delegation proposed replacing this paragraph by a provision to the opposite effect:

> "If studies, as referred to in paragraph 1, are included in an approved paediatric investigation plan they can be taken into consideration for the rewards and incentives provided for in Articles 36, 37 and 38, including when they have already been submitted for assessment in a third country."

66. In discussion of this proposal the Commission responded that "the intention of this Article was to force use of data from studies already performed in other countries but not to give rewards for such studies since this would create an incentive to withhold data until this Regulation entered into force."

67. This discussion led to further refinement of the drafting by the working party of the Council, which in its report of 22 June 2005 proposed that draft Article 44(3) should read:

> "Any paediatric studies, as referred to in paragraph 1, which have at the date of entry into force of this Regulation already been submitted for assessment in a third country, shall not, on their own, be sufficient to qualify for the rewards and incentives provided for in Articles 36, 37 and 38."

68. In its report of 20 July 2005, the European Parliament proposed an amendment to Article 36 of the draft Regulation, the provision that (as in the final Regulation) dealt with the eligibility for a reward. Part of that amendment excluded the grant of a paediatric extension for products whose active substance already benefitted from a patent covering the same paediatric use or formulation. The Commission responded on 10 November 2005 with an amended draft Regulation, taking account of the various proposals of the Parliament. But the Commission did not accept this particular amendment, stating as follows:

> "This amendment would run counter to the objective, central to this Regulation, of stimulating research into medicines for children. New paediatric research into substances which may already have paediatric indications covered by a patent or supplementary protection certificate (for instance, to extend the use of the product to other paediatric subpopulations or to better adapt it to the specific needs of children) would be discouraged. Moreover, it would discourage paediatric research by third parties (different holders of patents or supplementary protection certificates). This would also be difficult to reconcile with the purpose of the [SPC Regulation] which aims at giving sufficient protection to all research, including new applications of an existing product.
>
> However, and in line with the purpose of this amendment, it is appropriate to clarify in the Regulation that the rewards associated with a completed agreed Paediatric Investigation Plan should only be triggered by research completed after entry into force of the Regulation. In this way, it will be ensured that any extension of the supplementary protection certificate or of market exclusivity under Articles 36 and 37 of this Regulation is based on new paediatric research."

This led to the introduction of Article 44(3) in the draft with wording that became Article 45(3) of the final Regulation.

69. Similarly, the Council in its Common Position adopted on 10 March 2006 (OJ 1996 C132E/1) commented as regards the Parliament's proposed amendment:

> "The Council cannot agree to the first part of the amendment, which relates to patents. A basic patent (protecting the molecule) covers all medicinal uses of the substance, hence it covers also any paediatric medicinal use. A specific paediatric patent only exists in the case of a so-called 'usage patent'. The Commission proposal prolongs the basic patent; in such circumstances it would be difficult to operate the 'non-

> cumulative' test set out in the first part of the amendment and it would go against the objective of stimulating innovation and research. However, consistent with the spirit of the amendment, the Council considers that there is a need to clarify that the rewards and incentives which resulted from completion of an agreed paediatric investigation plan should only be available if at least some significant research was completed after the entry into force of the Regulation."

70. Accordingly, although the legislative history of Article 45(3) is somewhat tortuous, I consider that it supports the interpretation of that provision as a transitional provision designed to address the issue of pre-existing research.

71. Mr Brealey emphasised that the commercial benefit of a paediatric extension can be substantial, since it provides six months additional patent protection for all purposes and is not merely restricted to paediatric use of the product. He submitted that it was entirely logical as a matter of policy that such a significant benefit should not be granted in the absence of significant new research being completed. Although at first glance attractive, I am not persuaded by this submission. Patent protection is inevitably a blunt instrument, with the period of protection unrelated to the degree of effort or expense involved in the production of an invention provided that the criteria for a patent are satisfied. Such general sentiments cannot override the legislative intention as indicated by the structure and drafting history of the Paediatric Regulation.

72. In the present case, I note that the PDCO in its positive opinion on compliance with the PIP stated that it considered that the second study "could be considered significant". In granting the market authorisations to Pfizer, the MHRA in its accompanying statements included the sentence:

> "Significant studies contained in the agreed PIP have been completed after the entry into force of [the Paediatric Regulation]."

That appears to be the formal statement envisaged by Article 28(3). This suggests that the MHRA may have considered that Article 45(3) does apply in this case or, possibly, it included that statement out of an abundance of caution. However, whatever the explanation, the approach of the MHRA cannot affect the proper construction of the legislation.

73. In my judgment, the *ex ante* control of the studies to be included in a PIP is governed by the criteria in Article 17(1), buttressed by Article 6(2) which provides:

> "When carrying out its tasks, the Paediatric Committee shall consider whether or not any proposed studies can be expected to be of significant therapeutic benefit to and/or fulfil a therapeutic need of the paediatric population."

I accept that the criteria applicable under those provisions are different from the criteria for significance under Article 45(3) as set out in Part 4.2 of the Commission's Guidelines. Nonetheless, I am entirely satisfied for the reasons set out above that

Article 45(3) is not of general application and does not apply when all the studies included in a PIP were initiated after the Paediatric Regulation came into force. I should add that although this is a question of the proper interpretation of the Paediatric Regulation, I see no need to refer this question to the European Court of Justice for a preliminary ruling.

74. Accordingly, it is again unnecessary to consider Pfizer's alternative argument that even if Article 45(3) does apply, the statement by the competent authority that significant studies were here completed after the Regulation came into force is conclusive for the purposes of Article 36. This argument mirrors that advanced as regards compliance with a PIP for the purpose of Article 36(1) and, for the same reasons as I expressed in that context, I am doubtful that it is correct.

75. Dr Reddy's advanced an alternative argument under its Ground 2 to the effect that on the facts of the present case even on a narrow interpretation of Article 45(3) the provision was engaged because Pfizer had conducted and completed studies on the paediatric use of atorvastatin prior to 27 January 2007 and those studies are referred to in the report of the PDCO advising approval of the PIP. However, this submission, which was pursued somewhat faintly by Mr Brealey, is wholly unsustainable. Although the PDCO indeed referred to and took account of such studies when assessing the PIP, as it was obliged to do by Article 45(2), it is quite clear that the studies included in the PIP are restricted to the three specific studies set out above.

76. Finally, I should note that in the event that the court had decided that Article 45(3) applied in the present case, Pfizer wished to contend on the facts that the first two studies met the criteria of significance, whereas Dr Reddy's sought to argue that this point was not open to Pfizer if a proper assessment of significance had not been carried out by either the competent authority or the EMA. However, pursuant to directions given on 27 June 2012, the issue as to whether or not those studies individually or cumulatively were significant was held over pending the outcome of this trial; and in the light of this judgment it does not need to be resolved.