Intellectual Property Office

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11 June 2020

REGULATION (EC) 469/2009 CONCERNING THE SUPPLEMENTARY PROTECTION CERTIFICATE FOR MEDICINAL PRODUCTS

APPLICANT	Chugai Seiyaku Kabushiki Gaisha and Tadamitsu Kishimoto
ISSUE	Whether the extension to the duration of SPC/GB12/034 should be revoked under Article 16(1) and (2) of Regulation (EC) 469/2009
HEARING OFFICER	Dr L Cullen

DECISION

1. This decision relates to a request to revoke the extension to the duration for a supplementary protection certificate ("SPC"), SPC/GB12/034, in the name of Chugai Seiyaku Kabushiki Kaisha (Chugai Pharmaceutical Co., Ltd)[1] and Tadamitsu Kishimoto[2] ("the proprietors") which relates to the product "*Tocilizumab*".

2. *Tocilizumab* is the active substance in the medicinal product "*RoActemra*" which is used in the treatment of rheumatoid arthritis and, of interest in the present case, was subsequently approved to treat systemic idiopathic juvenile arthritis in children.

3. The SPC relies on basic patent EP(UK) 0783893 B1, entitled "*Inhibition of abnormal growth of synovial cells using IL-6 antagonist as active ingredient*", and on the centralised European marketing authorisation EU/1/08/492/001-006 for the medicinal product "*RoActemra*" in the name of Roche Registration GmbH with an address in Germany. The SPC was applied for on 2nd August 2012 and was granted by the Intellectual Property Office (IPO) on 1st December 2014. Following expiry of the basic patent and payment of the necessary fees, the SPC entered into force on 7th June 2015 for the maximum 5-year duration allowed under Article 13 of Council Regulation (EC) 469/2009 ("the SPC Regulation")[3]. As a consequence, the SPC expired on 6th

[1] Chugai Pharmaceutical Co., Ltd and Roche Registration GmbH are part of the Hoffman-La Roche pharmaceutical company.

[2] Tadamitsu Kishimoto is a professor at the Graduate School of Frontier Biosciences at Osaka University in Japan.

[3] Regulation (EC) No. 469/2009 of the European Parliament and of the Council of 6 May 2009 concerning the creation of a supplementary protection certificate for medicinal products is a

June 2020.

4. An application for an extension of the duration of this SPC (also referred to as a paediatric extension) under Article 7(3) of the SPC Regulation was filed on 11th May 2018, with the necessary fee and supporting materials confirming that the testing of the medicinal product for use in the paediatric population had been completed successfully and the marketing authorisation (MA) updated accordingly. This application was granted on 10 December 2018 and provides for an extension of the duration of the SPC until 6th December 2020.

5. D Young & Co Intellectual Property, the agent acting for the proprietors, wrote to the Intellectual Property Office (IPO) on 3rd June 2020 requesting that the extension to the duration of this SPC be revoked under Article 16 the SPC Regulation because it was granted contrary to the provisions of Regulation (EC) No 1901/2006 ("the Paediatric Regulation")[4], specifically Article 36(5) of that regulation.

6. The reason stated in the agent's letter for seeking revocation was that the proprietor had applied for, and successfully obtained, a one-year extension of the period of marketing protection for the medicinal product *RoActemra* "*on the grounds of a new paediatric indication, systemic juvenile idiopathic arthritis (sJIA), which brings a significant clinical benefit in comparison with existing therapies, in accordance with Article 14(11) of Regulation (EC) 726/2004*." Regulation (EC) 726/2004 (the EMA Regulation)[5] established the European Medicines Agency (EMA) and the procedures for granting a centralised marketing authorisation for a medicinal product valid within the whole territory of the European Union.

7. The letter from the agent made clear that the proprietor was not seeking revocation of the SPC itself. It also did not provide any information on why the paediatric extension was applied for initially.

8. I thank the applicant for bringing this matter to the attention of the IPO before the expiry of the SPC, albeit only 3 days before so, and before the start of the extension to the duration of the SPC.

The Relevant Law

9. The point at issue concerns the interplay of Article 16 of the SPC Regulation, Article

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codification of Council Regulation (EEC) 1768/92 of 18 June 1992 concerning the creation of a supplementary protection certificate for medicinal products which had been amended substantially several times. Regulation (EC) 469/2009 supersedes Regulation (EEC) 1768/92. Annex II to Regulation 469/2009 indicates the correlation between the recitals and Articles in Regulation 1768/92 and those in Regulation 469/2009.

[4] Regulation (EC) No. 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for Paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No. 726/2004.

[5] Regulation (EC) No. 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.

36 of the Paediatric Regulation and Article 14(11) of the EMA Regulation.

The SPC Regulation

10. Article 1(e) of the SPC regulation defines '*an application for an extension of the duration'* of an SPC as follows:

> *For the purposes of this Regulation, the following definitions shall apply:*
> *(a) …. ;*
> *(b) …. ;*
> *(c) …. ;*
> *(d) 'certificate' means the supplementary protection certificate;*
> *(e) 'application for an extension of the duration' means an application for an extension of the duration of the certificate pursuant to Article 13(3) of this Regulation and Article 36 of Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use*

11. Article 13 of the SPC regulation, entitled 'Duration of the certificate', reads as follows (my emphasis added in bold):

> *1. The certificate shall take effect at the end of the lawful term of the basic patent for a period equal to the period which elapsed between the date on which the application for a basic patent was lodged and the date of the first authorisation to place the product on the market in the Community, reduced by a period of five years.*
>
> *2. Notwithstanding paragraph 1, the duration of the certificate may not exceed five years from the date on which it takes effect.*
>
> *3.* ***The periods laid down in paragraphs 1 and 2 shall be extended by six months in the case where Article 36 of Regulation (EC) No 1901/2006 applies. In that case, the duration of the period laid down in paragraph 1 of this Article may be extended only once****.*
>
> *4. ……..*

12. Article 16 of the SPC Regulation, entitled 'Revocation of an extension of the duration', reads as follows (my emphasis added in bold):

> *1.* ***The extension of the duration may be revoked if it was granted contrary to the provisions of Article 36 of Regulation (EC) No 1901/2006.***

*2. **Any person may submit an application for revocation of the extension of the duration** to the body responsible under national law for the revocation of the corresponding basic patent.*

The 'extension of the duration' referred is the extension as defined in Article 1(e) of the SPC Regulation and Article 36 of the Paediatric Regulation.

The Paediatric Regulation

13. Article 36 of the Paediatric Regulation, which sets out the rewards and incentives available for carrying out testing of medicinal products in children, reads as follows (my emphasis added in bold):

*1. **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 period referred to in Articles 13(1) and 13(2) of Regulation No 1768/92.***

The first subparagraph shall also apply where completion of the agreed paediatric investigation plan fails to lead to the authorization of a paediatric indication, but the results of the studies conducted are reflected in the summary of product characteristics and, if appropriate, in the package leaflet of the medicinal product concerned.

2. 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.

3. Where the procedures laid down in Directive 2001/83/EC have been used, the six-month extension of the period referred to in paragraph 1 shall be granted only if the product is authorised in all Member States.

4. Paragraphs 1, 2 and 3 shall apply to products that are protected by a supplementary protection certificate under Regulation (EEC) No 1768/92, or under a patent which qualifies for the granting of the supplementary protection certificate. They shall not apply to medicinal products designated as orphan medicinal products pursuant to Regulation (EC) No 141/2000.

***5. In the case of an application under Article 8 which leads to the authorisation of a new paediatric indication, paragraphs 1, 2 and 3 shall not apply if the applicant applies for, and obtains, a one-year extension of the period of marketing protection for the medicinal product concerned, on the grounds that this new paediatric indication brings a significant clinical benefit in comparison with existing therapies, in accordance with Article 14(11) of Regulation (EC) No 726/2004** or the fourth subparagraph of Article 10(1) of Directive 2001/83/EC.*

The 'six-month extension' to the duration of the SPC as set down in Article 36(1) is also commonly referred to as the 'paediatric extension'.

The EMA Regulation

14. Article 14(11) of Regulation (EC) 726/2004 (the EMA Regulation)[6] reads as follows (my emphasis added in bold):

> *Without prejudice to the law on the protection of industrial and commercial property, medicinal products for human use which have been authorised in accordance with the provisions of this Regulation shall benefit from an eight-year period of data protection and* ***a ten-year period of marketing protection, in which connection the latter period shall be extended to a maximum of 11 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.***

The 'period of marketing protection' is the period of time during which a generic version of the medicinal product cannot be placed on the market even though the generic medicinal product has been granted a valid marketing authorisation[7].

15. The additional one-year extension to the period of marketing protection is only obtained if the holder of the MA provides evidence that the medicinal product provides a significant clinical benefit for a new therapeutic indication. An application from the marketing authorisation holder (MAH) to vary the authorisation in this way is assessed by the EMA, in this case by the Committee for medicinal products for Human Use (CHMP). If the CHMP adopts a positive opinion, the variation is granted by the European Commission. The conditions under which the medicinal product is used to achieve this new indication are described in the updated summary of product characteristics (SmPC) for the MA. The updated SmPC is published in the revised European public assessment report (EPAR)[8] after the variation to the MA has been

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[6] Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.

[7] For information on how the period of marketing protection works see the explanation of EU marketing authorisation legislation, procedures and guidelines provided by the European Commission at https://ec.europa.eu/health/human-use/legal-framework_en; in particular, *Part 6: Data Exclusivity and Marketing Protection* of Chapter 1: Marketing Authorisation of Volume 2A: Procedures for Marketing Authoristion at https://ec.europa.eu/health//sites/health/files/files/eudralex/vol-2/a/vol2a_chap1_201507.pdf.

[8] A European public assessment report (EPAR) is published for every human (or veterinary) medicine application that has been granted or refused a marketing authorisation by the European Commission and is publically available on the EMA website here. The EPAR is published following an assessment by EMA of an application submitted by a pharmaceutical company seeking authorisation of the medicinal product. An EPAR provides public information on a medicine, including whether it was assessed positively or negatively by EMA. The EPAR is referred to in Article 13(3) of the EMA Regulation, which requires EMA to publish a public assessment report for each centrally authorised medicine together with a public-friendly overview. The EPAR comprises a series of documents and

granted by the European Commission.

Analysis

16. Article 16(2) of the SPC Regulation makes clear that "*any person*" may seek the revocation of the extension upon application to the "*body responsible under national law for the revocation of the corresponding basic patent"*. In the UK, the relevant body is the Intellectual Property Office. I am satisfied that the term "*any person*" includes the holder of the SPC as in this case. I conclude that the request for revocation is allowable.

17. In support of their request, the agent provided a copy of the assessment report prepared by the Committee for medicinal products for Human Use (CHMP) of the European Medicines Agency (EMA), in response to the application from the holder of the marketing authorisation, Roche Registration GmbH, for a type II variation to include systemic juvenile idiopathic arthritis as a new therapeutic indication that brought a significant clinical benefit in comparison to existing therapies[9]. The applicant highlighted the following text in this report (on page 2):

> "*Furthermore, the MAH requested consideration of this application under Article 14(11) of Regulation (EC) No 726/2004 and submitted a justification that the application concerns a new therapeutic indication which is claimed to bring a significant clinical benefit in comparison with existing therapies."*

Having looked at this report, I note that the preceding paragraph on this page states that:

> "*The initially applied wording for extension of indication reads as follows:*
> *"RoActemra is indicated for the treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 2 years of age and older, who have responded inadequately to previous therapy with one or more NSAIDs and systemic corticosteroids. RoActemra can be given as monotherapy or in combination with MTX"."*

I note also that the section of this report entitled "3. Conclusion" (on page 72) states:

> "*On 19 May 2011 the CHMP considered this following variation to be acceptable and agreed on the amendments to be introduced in the*

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reports including: (i) a lay summary: (ii) details about the marketing authorisation holder; (iii) product information (such as the package leaflet and summary of product characteristics); and (iv) reports on the assessment carried out at EMA. The reports on the assessment include the scientific conclusions of the relevant EMA committee, providing the grounds for the committee opinion on whether, or not, to approve an application. EPARs are published on the EMA's website once the European Commission has issued a decision granting or refusing the marketing authorisation. For further detail see https://www.ema.europa.eu/en/ medicines/what-we-publish-when/european-public-assessment-reports-background-context.

[9] This is identified in the EPAR and assessment history as EMA Procedure Type II variation no EMEA/H/C/000955/II/0015.

Summary of Product Characteristics, Annex II Labelling and Package Leaflet.

Furthermore, the CHMP reviewed the data submitted by the MAH taking into account the provisions of Article 14(11) of Regulation (EC) No 726/2004 and considered the indication to be new and that it is held to bring a significant clinical benefit in the absence of existing therapies (see appendix).”

18. The assessment history for *RoActemra* published as part of the EPAR[10] indicates that the Commission Decision confirming the variation to the marketing authorisation was granted by a decision of the European Commission dated 1st August 2011, following the positive opinion of the CHMP issued on 19 May 2011. The European Commission is the competent body responsible for granting MAs, including any variations, on the recommendation of the EMA. The grant of the variation to the MA for *RoActemra* by the European Commission confirms that the condition set down under Article 14(11) of the EMA regulation has been meet.

19. Article 36(5) of the Paediatric Regulation as set out above, makes clear that should the holder of the MA successfully obtain a one-year extension of the period of marketing protection, the earlier provisions in this article (see parts (1), (2) and (3) of Article 36) concerning an extension of six-months to the duration of the SPC cannot be applied. In effect, this article makes clear that one has to choose which of the two rewards available for carrying out testing of medicinal products in children to have – either a regulatory one, i.e., an extension to the period of marketing protection or an intellectual property one, i.e., an extension to the duration of the SPC; but it is not possible to have both.

20. In this case, as the letter from the agent has stated and the documents from the EPAR discussed above confirm, the MAH had already obtained the additional year to the marketing protection when the application for the extension to the duration of the SPC was made. As a consequence, the extension to the duration of this SPC was granted contrary to the provisions of Article 36 of the Paediatric Regulation and as such, I am satisfied that it should be revoked in accordance with Article 16(1) of the SPC Regulation.

Conclusion

21. Taking all of the above into account, I consider that the request for revocation of the six-month extension to the duration of supplementary protection certificate SPC/GB12/034 made by the proprietor of this SPC is allowable.

22. The holder of the MA provided in support of SPC/GB12/034 had previously gained a one-year extension to the period of marketing protection for the medicinal product

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[10] See assessment history section of EPAR for RoActemra, document entitled “*RoActemra: EPAR - Procedural steps taken and scientific information after the authorisation*”, document no. EMA/247046/2020 (here)

RoActemra which comprises the active product *tocilizumab*, the subject of this SPC. As such, the paediatric extension granted for SPC/GB12/034 was granted contrary to the provision of Article 36(5) of the Paediatric Regulation. Therefore, the paediatric extension is revoked under Article 16(1) of the Regulation.

Appeal

23. Any appeal must be lodged within 28 days after the date of this decision.

Dr L CULLEN
Deputy Director, acting for the Comptroller