European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

London, 23 February 2006
Doc. Ref. EMEA/180079/2005

POST-AUTHORISATION GUIDANCE

Human Medicinal Products

QUESTIONS AND ANSWERS ON THE APPLICATION OF THE SO-CALLED "SUNSET CLAUSE" TO CENTRALLY AUTHORISED MEDICINAL PRODUCTS

Please note that the final version of this document will also be integrated in the EMEA post-authorisation guidance.

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1. INTRODUCTION

This guidance document addresses questions that marketing authorisation holder (MAH) may have on this topic and gives practical aspects on how the EMEA will monitor any centrally authorised medicinal product never marketed within the EEA after the granting of the marketing authorisation (MA) and any complete cessation of marketing of a medicinal product where a three consecutive year period has elapsed, as leading to the invalidity of the marketing authorisation.

The monitoring of the so-called "sunset clause" provision will be based on the data related to marketing status of the medicinal product reported by the MAH.

Guidance on the marketing status reporting, the format and the timelines is given in the post-authorisation Q&A guidance document on '*the notification to the EMEA of actual marketing and cessation of placing on the market for centrally authorised medicinal products*' (Doc. Ref. EMEA/180078/2005).

In the future, the Agency intends to collect the marketing status information through an electronic reporting via a particular functionality within EudraVigilance Medicinal Product Dictionary (EVMPD) to facilitate the monitoring of a three-year period without marketing.

2. WHAT IS LEGAL BASIS?

The so-called 'sunset clause' is defined in accordance with Regulation (EC) No 726/2004, Article 14(4-6).

In the context of the sunset clause provision, the marketing authorisation of a centralised medicinal product will cease to be valid if:

- the medicinal product is not placed on the market within three years of the authorisation being granted or,
- where a medicinal product previously placed on the market is no longer actually present on the market for three consecutive years.

The European Commission may grant exemptions on public health grounds and in exceptional circumstances if duly justified.

This provision is also referred to in article 24(4-6) of the Directive 2001/83/EC, as amended.

3. DOES IT APPLY TO EXISTING PRODUCTS?

This new provision applies prospectively to all centrally authorised medicinal products from the date of entry into force of the Regulation i.e. 20 November 2005.

Therefore, for medicinal products which have been granted a marketing authorisation before 20 November 2005 and for which no more presentations are marketed in the Community at this date, the three-year period which may lead to the MA ceasing to be valid will start counting as of 20 November 2005.

4. WHAT ARE THE PRINCIPLES FOR THE MONITORING OF THE SUNSET CLAUSE PROVISION?

The marketing authorisation will remain valid if at least one presentation of the marketing authorisation is placed on the market in the Community (in at least one Member State) including Iceland, Norway and Liechtenstein.

The marketing authorisation of a centrally authorised medicinal product includes the initial marketing authorisation and all variations (e.g. additional presentations,…) and extensions (e.g. new strengths, new pharmaceutical forms,…) authorised for this specific medicinal product. This notion has been applied since the beginning of the centralised procedure and is reflected in the way the EU numbers are allocated to a specific centrally authorised medicinal product and all its presentations.

As referred to in the articles 14(4) and 14(5) of the Regulation, a three-year period without marketing may lead to the application of the sunset clause. This will start counting from two different points as detailed hereafter.

4.1 Marketing authorisation not followed by actual marketing

In accordance with the article 14(4) of Regulation (EC) No 726/2004, any marketing authorisation which is not followed by the actual marketing in the Community within 3 years after the granting of the authorisation shall cease to be valid.

However, the start of the three years period should be the date when the medicinal product can be placed on the market by the marketing authorisation holder i.e. as of the end of the 10-(or 11-) year period of market exclusivity of the reference medicinal product and at the end of other protection rules which must be respected.

4.2 Medicinal product previously marketed no longer actually present on the market

In accordance with the article 14(5) of Regulation (EC) No 726/2004, for any medicinal product previously placed on the market but no longer actually present on the market for three consecutive years, the marketing authorisation shall cease to be valid.

The term ‘no longer actually present on the market’ shall be understood in the same way as ‘ceased to be placed on the market’. Therefore, the sunset clause period shall start running from the last date of release into the distribution chain of the medicinal product.

5. WHAT ABOUT EXEMPTIONS?

According to the articles 14(6) of Regulation (EC) No 726/2004, the Commission may grant exemptions from the application of the sunset clause on public health grounds and in exceptional circumstances.

Exemptions can apply at any time of the marketing authorisation life cycle (i.e. at the time of the MA, during the MA life, or approaching the expiry of the sunset clause period) depending on the type of exemptions.

The MAH can already be aware at the stage of the marketing application that an exemption might be applicable, for instance:

- Medicinal products to be used in emergency situations, in response to public health threats duly recognised either by the WHO or by the Community (Decision No 2119/98/EC).

- Antimicrobial medicinal products such as antibiotics, antivirals and immunologicals (for active and passive immunisation) aimed at the prevention and/or treatment of disease caused by bio-terror agents in response to an emergency public health need.

It will be up to the MAH to justify why an exemption should apply based on public health grounds and in exceptional circumstances. Each justification should be notified to the Commission and will be considered on a case-by-case basis. A copy of such request should also be addressed to the EMEA.

6. WHAT ARE THE PROCEDURAL ASPECTS FOR MONITORING THE SUNSET CLAUSE?

Below is detailed the concept of the start and stop of the sunset clause period according to the main key-points of the marketing cycle of a medicinal product. This mechanism of the counting of the period without marketing of the product may need to be revised in the future according to the experience gained on the events that may affect the determination of the start and stop of the sunset timer.

The EMEA will monitor the application of the sunset clause provision via an electronic tool (so-called "sunset timer") which will run and be updated based on the marketing status data reported by the MAH for a specific medicinal product.

6.1 When is the sunset timer on?

Different situations lead to the start of the counting of the sunset clause period.

6.1.1 Granting of the Marketing Authorisation

At the time of the granting of the marketing authorisation, the medicinal product may not be immediately placed on the Community market. As a consequence, the sunset timer will start running from the granting of the marketing authorisation by the Commission or when the MAH can legally place the medicinal product on the market considering the market exclusivity and other protection rules which have to be respected.

The information about market exclusivity of the reference product is available to the EMEA but the information regarding other protection rules are not known by the Agency. MAHs are therefore advised to inform the EMEA of the expiry date of the other protection period to be respected as appropriate. This should be notified within 60 days from the date of granting of the marketing authorisation, otherwise the three-year period will start counting for a generic product after expiry of the 10 or 11 years of market exclusivity period of the reference medicinal product.

6.1.2 A temporary or permanent cessation of placing on the market the medicinal product

In accordance with the legal requirements, the MAH is responsible to inform the Agency of product cessation in placing on the market. When there is no longer any presentation of the medicinal product actually placed on the Community market, the sunset timer will start running from the last date of release into the distribution chain of the medicinal product.

6.2 When is the sunset timer off?

Different situations lead to the stop of the counting of the sunset clause period.

6.2.1 Initial placing on the Community market

The sunset timer will stop running at the time of the first placing on the market of one presentation in one Member State.

6.2.2 At the re-placing on the market after a temporary cessation of the whole medicinal product

As soon as a medicinal product is again placed on the Community market after a temporary cessation, the sunset timer will stop running at this date.

6.2.3 Exemption

As soon as an exemption is granted by the Commission for a medicinal product, the sunset timer will be stopped.

7. WHAT ABOUT THE EXPIRY OF THE SUNSET CLAUSE PERIOD?

The MAH should be aware of the overall timing with regard to the sunset clause period for their product and for taking any appropriate actions, should they wish to retain the marketing authorisation. However, at the time of the expiry of the sunset clause period, the EMEA intends to inform the European Commission and the MAH that the sunset clause provision should take effect according to either article 14(4) or article 14(5) of the Regulation (EC) No 726/2004.