



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Procedural advice on publication of information on withdrawals of applications related to the marketing authorisation of human medicinal products

¹ Editorial revisions have been made to the table of withdrawal documents to ensure consistency.

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1. Introduction

This paper describes the publication of information on the withdrawals of marketing authorisation applications for human medicinal products. It updates the information in a reflection paper adopted by the European Medicines Agency (EMA) in September 2006, taking into account recent changes in EMA communication practices for certain types of applications as well as new guidance on the identification of personal data and commercially confidential information in marketing authorisation applications.^{2,3}

2. Legal basis and scope

The legal basis for the publication of information on the withdrawal of applications for marketing authorisation for human medicinal products is Article 11 of Regulation EC 726/2004, which states that:

“If an applicant withdraws an application for a Marketing Authorisation submitted to the Agency before an opinion has been given on the application, the applicant shall communicate its reasons for doing so to the Agency. The Agency shall make this information accessible and shall publish the assessment report, if available, after deletion of all information of commercially confidential nature”.

In September 2006, on the basis of Article 80 of Regulation (EC) No 726/2004,⁴ the EMA Management Board extended the publication requirement to withdrawn extension of indication applications and to withdrawals that take place after a CHMP opinion has been adopted but before the European Commission has issued a decision.

This paper also covers the publication of documents following the withdrawal of applications for other variations as well as extension applications. The principle is that the same level of transparency is applied to withdrawn applications as is applied to applications that receive a positive opinion. This means that a document (e.g. an assessment report) that would have been published for an application that received a positive opinion will also be published in the event of a withdrawal.

In addition to the application withdrawals mentioned above, this paper also covers communication on the outcomes of variation applications in cases where the initial scope of a variation included an extension of indication which has been removed from the final scope (see Section 5.). Although these cases are not strictly speaking withdrawals of application, similar levels of transparency are applied.

The deletion of commercially confidential information referred to in this paper is based on the two HMA/EMA guidance documents adopted in March 2012, the provisions of which are applicable to EMA publications on withdrawals of application.^{2,3}

3. Documents to be published on withdrawn applications

Applicant's withdrawal letter

When an applicant seeks to withdraw an application related to the marketing authorisation of a medicinal product, it shall communicate the reasons for doing so to the EMA.

A template for withdrawal letters to be used by applicants has been prepared by the EMA and, in line with Article 11 of Regulation EC 726/2004, includes a section on the reasons for the withdrawal. The

² http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/03/WC500124537.pdf

³ http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/03/WC500124536.pdf

⁴ Article 80 of Regulation (EC) No 726/2004: “To ensure an appropriate level of transparency, the Management Board, on the basis of a proposal by the Executive Director and in agreement with the Commission, shall adopt rules to ensure the availability to the public of regulatory, scientific or technical information concerning the authorisation or supervision of medicinal products which is not of a confidential nature.”

EMA recommends that applicants use the template and may request an applicant to resend a letter where insufficient information is provided. A template for withdrawal letters is included in Annex I of this document.

Withdrawal letters will be published on the EMA website for applications for new marketing authorisations, extensions of indication, and other variations or extension applications for which assessment reports would be expected to be published (see section on assessment reports below). The letter will have all personal contact information (addresses, emails, phone numbers and signatures) blanked out.

Question-and-answer (Q&A) document

A Q&A document will be published routinely following the withdrawal of new marketing authorisation applications and extensions of indication applications.

The Q&A document contains information in lay language on the scientific assessment of the product up to the time of the withdrawal. Where the CHMP has adopted an assessment report, the Q&A reflects the latest CHMP position on the application.

The Q&A in English will be published on the day after the next CHMP plenary meeting linked to the CHMP Meeting Highlights. The Q&A documents are first published in English, with translations in other official EU languages to follow.

A template for Q&As on withdrawn applications is included in Annex II of this document.

The EMA reserves the right to publish Q&As for other withdrawn applications should it be considered necessary or of public interest.

Withdrawal assessment reports

The EMA will publish the last adopted CHMP assessment report for all withdrawn applications relating to new marketing authorisations and extensions of indication. The last adopted CHMP assessment reports will also be published for other variations as well as extension applications in cases where an assessment report would have been published for a positive opinion.⁵

Prior to publication of any assessment report, the EMA will liaise with the applicant to delete all commercially confidential information. Guidance from the HMA/EMA documents adopted in March 2012 is applicable to withdrawals of application.^{6,7}

Assessment reports will be published within three months of the receipt of the withdrawal letter.

Procedural steps document

For all centrally authorised medicines, a document entitled 'Procedural steps taken and scientific information after authorisation' is published as part of the EPAR on the EMA website. It outlines the regulatory procedures that have taken place since the authorisation of the medicine. The procedural steps document should contain information on all applications withdrawn post-authorisation.

The inclusion of information on withdrawn applications in the procedural steps document is an important transparency tool providing information on the regulatory history of the product and the scientific evaluations that have taken place.

⁵ Information on the publication of assessment reports for positive opinions can be found in the EMA SOP on updating of the European Public Assessment Report for a human medicinal product (SOP/H/3012)

⁶ http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/03/WC500124537.pdf

⁷ http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/03/WC500124536.pdf

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Withdrawal EPARs

'Withdrawal European public assessment report (EPAR)' is a term used to describe the collection of all the relevant documents published on the EMA website following the withdrawal of an application: Q&A document (including translations), withdrawal letter and assessment report.

4. Post-opinion withdrawals

If an applicant withdraws an application after the CHMP has adopted a positive or negative opinion, but before the European Commission has issued a decision, the EMA will publish the relevant withdrawal documents described above, stating that the withdrawal occurred post-opinion. The timing of the publication of these documents is the same as for pre-opinion withdrawals (see table 6.)

5. Change of scope of variations involving an extension of indication

For several years, the EMA has been publishing specific communication on withdrawn extension of indication applications. In September 2011, this practice was extended to cases where the scope of the variation that initially included an extension of indication has been changed, resulting in a CHMP opinion that does not cover the extension of indication initially applied for. Although these cases are not strictly speaking withdrawals of application, the EMA considers that the same level of transparency that applies to withdrawn extensions of indication applications should apply to these variations.

In these cases the EMA will publish a Q&A document at the time of the CHMP opinion covering the outcome of the extension of indication evaluation. The CHMP assessment report will be published within four weeks of a European Commission decision along with an updated procedural steps document containing a description of the initial scope applied for and of the opinion finally granted.

6. Table of withdrawal documents to be published

Type of application	Documents	Timing
Withdrawn applications for a new marketing authorisation	Withdrawal letter	Published together with the Q&A
	Q&A	Day after next CHMP meeting linked to the CHMP Meeting Highlights
	Assessment report	Within three months of receipt of withdrawal letter
Withdrawn applications for extension of indication	Withdrawal letter	Published together with the Q&A
	Q&A	Day after next CHMP meeting linked to the CHMP Meeting Highlights
	Assessment report	Within three months of receipt of withdrawal letter
	Updated procedural steps document	At the time of the publication of the assessment report
Other withdrawn applications [†]	Assessment report [*]	Within three months of receipt of withdrawal letter
	Withdrawal letter [*]	At the time of the publication of the assessment report
	Updated procedural steps document	Within three months of receipt of withdrawal letter
Applications involving an extension of indication with subsequent change in scope (see section 5.)	Q&A	At the time of CHMP opinion
	Assessment report	Within four weeks of European Commission decision
	Updated procedural steps document	Within four weeks of European Commission decision when a decision is expected, or within two months of the CHMP opinion when no decision is expected.
<p>[*] To be published in cases where an assessment report would have been published for a positive opinion.</p> <p>[†] Q&As will be considered if there is public interest</p>		

7. Annexes

ANNEX I – Withdrawal letter template

(< FROM MAA ON HEADED PAPER >)

Date: <dd mmmm yyyy>

<CHMP Chairman>
European Medicines Agency
7 Westferry Circus
Canary Wharf
London
E14 4HB
United Kingdom

Subject: Withdrawal of <Product Name>, (INN), strength(s), pharmaceutical form(s) -
<EMA/H/product No.> OR <EMA/H/product No./X or II/nn>

Dear <CHMP Chairman>,

For the withdrawal of initial marketing authorisation application

I would like to inform you that, at this point of time, <Applicant's name> has taken the decision to withdraw the application for Marketing Authorisation of <Product Name>, (INN), strength(s), pharmaceutical form(s)>, which was intended to be used for <applied for Applicant's proposed indication>.

OR

For the withdrawal of Type II variation/ Annex I (Regulation 1234/2008) application linked to an extension of indication for a medicinal product already authorised

I would like to inform you that, at this point of time, <MAH name> has taken the decision to withdraw the application for <a new indication> <a change to the marketing authorisation> for <name of the product>, <to add <a <strength><pharmaceutical form>, > in the <treatment of /prophylaxis against/diagnosis of> <disease>.

This withdrawal is based on the following reasons <Please state the reasons for the withdrawal. The following is included as possible examples, amongst others>:

<identification of major manufacturing issues>
<identification of major pre-clinical issue>
<identification of major clinical issues>
<identification of major GxP issues>
<the CHMP considers that the data provided do not allow the committee to conclude on a positive benefit risk balance>
<Company's marketing strategy>
Other: <please elaborate>

<Please provide any further detailed comment as appropriate>
<Provide information on the consequences of the withdrawal on ongoing clinical trials and compassionate use programme>
<Provide additional information on any future plan for development of the product>

We reserve the right to make further submissions at a future date in this or other therapeutic indication(s).

I agree for this letter to be published on the EMA website.

Yours sincerely,

<Signature from the Applicant

ANNEX II – Questions & Answers document template

Questions and answers

Withdrawal of the marketing authorisation application for <X> (active substance/common name)

What is <X>?

What was <X> expected to be used for?

How is <X> expected to work?

What did the company present to support its application?

How far into the evaluation was the application when it was withdrawn?

What was the recommendation of the CHMP at that time?

What were the reasons given by the company for withdrawing the application?

What consequences does this withdrawal have for patients in clinical trials or compassionate use programmes?

<What is happening with <X> for the <treatment/prevention/diagnosis> of <other diseases>?>