European Medicines Agency

London, 5 October 2006
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OVERVIEW OF COMMENTS RECEIVED ON REFLECTION PAPER ON PUBLICATION OF WITHDRAWALS

Table 1: Organisations that commented on the draft Guideline as released for consultation

	Name of Organisation or individual	Country
1	The European Federation of Pharmaceutical Industries and Associations (EFPIA)	EU
2	The Association of the European Self-Medication Industry (AESGP)	EU
3	The Pharmaceutical Research and Manufacturers of America (PhRMA)	USA
4	Dutch Genetic Alliance/European Genetic Alliance's Network (VSOP/EGAN)	The Netherlands/EU
5	International Plasma Fractionation Association (IPFA)	The Netherlands
6	Merck Sharp & Dohme (MSD)	EU

As the full text of all received comments are included in this overview, the comments will not be published separately.

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Table 2:Discussion of comments

GENERAL COMMENTS - OVERVIEW
Outcomes of general comment have been addressed in the section "Specific comments", as appropriate.
[EFPIA] EFPIA welcomes and supports initiatives to increase transparency opposite all stakeholders and does particularly respect the right for the patient to be able to access information about their medication. In particular EFPIA supports the availability of information on withdrawals to patients and to practitioners. However it is important to ensure that the provision is accurate and informative, and that the commercial prospects of a company and its ability to meet its obligations to shareholders are not damaged unwittingly. The applicant may have legal obligations in relation to announcements to investors which will also need to be considered. The applicant should therefore be involved in the drafting of any Press Releases, and in drafting Q&A documents, and sufficient time should be allowed to accommodate this. This also concerns any information which is provided on the consequences in terms of development of the product, compassionate use programmes/clinical trials and use of the product. The company planning the development is best placed to advise on future consequences etc. and can make a valuable contribution to ensuring that the information provided is accurate and informative. Throughout the main text of this reflection paper, references are made to the need for the company to share information about ongoing clinical trials and compassionate use programmes. Only at the very end within the penultimate question in the Q&A template is it mentioned that this information should be "in line with CHMP advice/recommendation" and that information should be given on "previous CHMP opinions on compassionate use programmes for the product" – if any. This aspect is important and should be incorporated in the reflection paper or applicable future guidance more prominently than it is at present. It is also important to recognise that the company will be in communication with patients in clinical trials and compassionate use programmes using the most appropriate route - via the clinical investigators. It is important that "mixed messages" are not given, so information in the Q&A should be general advice (for example for patients to consult their doctor as was included in the recent Orathecin withdrawal Q&A document). For more specific information a good approach would be for the EMEA draft the Q&As using the information supplied by the company in the withdrawal letter, since the template does request companies to provide information on development consequences, compassionate use, etc. EFPIA members are keen to work with the Agency to ensure that information to practitioners and patients is useful to them and accurately reflects all the knowledge available both from the company and the Agency. **[AESGP]** In order to improve clarity, we would like to suggest adding a chart summarising the different scenarios including timelines as well as to revise the structure of the document (for example, timelines are addressed in sections 3 and 4, the content of the documents is addressed in sections 4 and 6).

[PhRMA]
The legal basis for the Proposal is Article 11 of Regulation (EC) No 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 commercially confidential information"*.

The Proposal also relies on Article 80 of the Regulation, which entrusts the Agency's management board with ensuring an appropriate level of transparency by making regulatory, scientific or technical information concerning the authorisation or supervision of medicinal products, which is not confidential, available to the public.

PhRMA welcomes and supports initiatives designed to increase transparency vis-à-vis stakeholders. However, special care should be taken to properly implement the policy that is expressed in the two legal provisions and to strike an appropriate balance between the various interests at stake. The distinction between the transparency principles laid down in Article 11 and in Article 80 should be reflected in the EMEA guidance and practices and there is also a clear need to preserve confidentiality of commercial information, among others by providing appropriate procedural guarantees for the affected pharmaceutical companies.

In addition, more attention should be given to the needs of the core audience, *i.e*. the patients. Only the potential benefit to the patients should dictate the information to be given and the way to present it.

Finally, it is important to take into account the diversity of reasons that can lead to the withdrawal of an application. A withdrawal can be based on an expectation that the CHMP will conclude that the product is not efficacious, not safe or not of sufficient quality. More often, however, an application will be withdrawn because there are not enough data available at the moment and the extra data cannot be gathered during an even prolonged clock stop. The 1998 General Report of the Agency states, for instance, based on a first systematic review of withdrawals of applications:

> "Most of the withdrawals appear to be due to premature applications, with applicants unable to provide adequate additional information, data and responses even with a longer clock stop."

Thus, in most cases, a withdrawal of an application is totally non-conclusive. This should be taken into account when information on withdrawals is made public.

Therefore, the Proposal should be amended to render it more consistent with Regulation 726/2004, in particular Article 11 thereof, and to strike a fairer balance between transparency and company interests, including confidentiality.

[VSOP/EGAN]
In general we agree with the content of the paper.

[IPFA]

To make sure that confidentiality would be respected and that the item "Company's marketing strategy" will be allowed enough space to not reveal confidential issues

Starting date of implementation is unrealistic, since the end of consultation is March 23rd, 2006. There have been some withdrawals since application after November 2005. This regulation should not be retroactive. The new date for implementation should be immediate after adoption by the CPMP.

[MSD]

MSD supports EMEA's general policy to operate in a transparent manner and provide adequate information to the public. However, we believe that the active publication of withdrawal letters and Q&A documents prepared by the EMEA is not justified by the legal provisions in Article 11 of Regulation 726/2004 and is in general inappropriate. Article 11 only provides for making information of the withdrawals "accessible" and for the WPARs/EPARs to be published.

We believe that a general active publication policy for the applicant's withdrawal letter, together with an extensive Q&A document, is overemphasising the withdrawal action. Clearly, the amount of documentation published for withdrawal actions is unbalanced compared to the publication efforts made for approvals which are granted for new medicines, indications or line extensions. Q&A documents should only be developed if there is a clear need to inform the public of any consequences of the withdrawal from a public health perspective.

Hence, we oppose that the withdrawal letter from the company is generally published on the EMEA website. Instead, this letter should be made available by the EMEA only upon request and after redaction of personal information, which should remain confidential for personal data protection reasons. We further request that the Q&A document is only developed in cases where the withdrawal action has an impact on public health and where it is likely that the public will benefit from more background information. In such cases, we believe that the applicant is responsible to provide such information on potential consequences in terms of the development of the product, compassionate use programmes or the use of the product already on the market. Therefore, MSD proposes that the company develops such Q&A document and provides it to EMEA.

MSD fully agrees that the publication of the WPARs/EPAR updates follows the general EMEA publication policy for the EPARs.

SPECIFIC COMMENTS ON TEXT		
2. Legal basis and scope		
Line no.[1] + paragraph no.	**Comment and Rationale**	**Outcome**
Paragraph 1 Line 10	**[IPFA]** There will be no Assessment Report if the withdrawal occurs before the Assessment Report. Change text to: *The Agency shall make this information accessible and shall publish the assessment report, if yet available, after deletion of commercially confidential information"*	Not agreed. No possibility to amend wording of legislation.
	[PhRMA] The scope of the Proposal may be questioned in views of the wording of Article 11 of Regulation 726/2004. The Proposal goes beyond the principle expressed in Article 11: • The Proposal provides that the concept of withdrawal of an application covers not only the initial marketing authorisation applications but also the applications for a new indication and the applications for line extensions (Annex II to Regulation (EC) No 1085/2003 on variations). However, the scope of Article 11 is expressly limited to "*application for a marketing authorisation*." It does not include applications for new indications or applications for variations. Furthermore, publicising withdrawals of applications for line extensions may cause unnecessary concerns to many patients and, more broadly, to the medical community. • The Proposal imposes the publication of withdrawal documents for withdrawals occurring as from day one of the centralised procedure until the Commission decision. However, Article 11 expressly limits the transparency obligation to withdrawals that occur "*before an opinion has been given [by the CHMP] on the application*."	The publication of the withdrawal of an application includes the initial authorisation applications as well as applications for extensions of marketing authorisations as set out in Annex II to Regulation (EC) No 1085/2003. See EMEA Management Board transparency measures for publication of information on withdrawal of type II variations for new indication and withdrawal occurring between CHMP opinion and EC decision. See also outcome on PhRMA comments on Subsection "Q&A".

[1] Where applicable

	• The Proposal envisages the publication of several documents: an EMEA press release, the applicant's withdrawal letter, a Q&A prepared by the CHMP, and a withdrawal public assessment report (WPAR) or, in cases of applications for a line extension or a variation, an update of the EPAR. The Q&A would be a summary of the CHMP evaluation of the application at the time of withdrawal and CHMP views on the application. The WPAR/updated EPAR, which would be based on the assessment report, would highlight the major issues leading to the withdrawal. However, the only information to be publicised under Article 11 are "*this*" information, *i.e.* the reasons for the withdrawal given by the applicant, and the assessment report, and the latter only if available at the time of withdrawal. Article 11 does not expressly envisage the publication of any other document or information whether coming from the applicant or the EMEA.	

3. Documents to be made available to the public – timelines

Line no.[2] **+ paragraph no.**	**Comment and Rationale**	**Outcome**
Paragraph 1 Line 24	**[EFPIA]** As indicated in the general comments, the company needs to be involved in the drafting of the press release. Add after *"….in an EMEA Press Release"* - new text: ***"which will be supplied to the company for review and input at least a week before release"***	Not agreed. EMEA press release to be published at the time of the withdrawal. However, EMEA Press Release will only contain factual data (announcement of the withdrawal and reasons given from the applicant in the withdrawal letter)
	[MSD] As justified above under general comments, MSD recommends amending the bullets as follows: o A "Q&A" document will be developed by the applicant in cases	Not agreed. The Agency has the obligation to provide information to the general public about medicinal products evaluated by the Agency (Article 57.1(m) of Regulation (EC) No 726/2004). The Q&A document will translate the scientific information contained in the

[2] Where applicable

	where the withdrawal has an impact on public health and the public needs to be informed about potential consequences. This document will be provided to EMEA together with the withdrawal letter and is published on the EMEA website as soon as possible after the withdrawal press release. o The withdrawal letter from the applicant will be made available from the EMEA upon request and after redaction of personal confidential information.	assessment report, if available, into a document understandable by the general public (the Q&A). If an assessment report is not available at the time of the withdrawal, the Q&A document will not contain any detail of the evaluation of the product by the CHMP, and will provide only factual data on the product itself. Not agreed, according to Article 11, the Agency shall make accessible the applicant's reasons for withdrawing.
	[PhRMA] The Proposal imposes the publication of various documents and extensive information without specific policy reasons and on the basis of incorrect assumptions. The rationale behind Article 11 of Regulation 726/2004 is to inform the public about the withdrawal of a marketing authorisation application and the reasons for the applicant to do so. Article 11 is part of the general transparency trend started by the Community several years ago. Publicising the occurrence of, and reasons for, a withdrawal reaches the transparency objective set by Article 11 and no other, additional information is necessary to this end. This is even more relevant where the Proposal calls for the same information to be published several times. Indeed, the Q&A would include the CHMP views on the application at the time of withdrawal and so would the WPAR/updated EPAR although in a more detail manner. The Q&A as envisaged by the EMEA thus is unnecessary, in particular the sections "what was the recommendation of the CHMP at the time" and "what were the main concerns of the CHMP". This would be explained in detail, and thus more accurately, in the WPAR/updated EPAR. Furthermore, the Proposal does not provide policy reasons that require as much information on withdrawals to be made public. The product will by definition not be marketed until a new application successfully goes through the review procedure and the patients using the product under compassionate use programs or in a clinical trial can be adequately informed under the relevant regulatory rules. Finally, the breadth of the information to be provided under the Proposal is such that it seems more designed for competitors than for patients. The information required for transparency purposes under Article 11 is adequately	See also outcome on PhRMA comments on Subsections "Q&A" and "WPAR".

	provided by publishing a press release indicating the withdrawal and the reasons given by the applicant to do so. The other documents envisaged by the Proposal thus are not necessary for transparency purposes and, again, one may wonder about the policy reasons that could justify publishing the withdrawal letter, a Q&A and a WPAR/updated EPAR in addition to a press release and, as the case may be, the (non-confidential) assessment report. If nevertheless publication of the withdrawal letter is deemed necessary, it is important to allow the letter to be signed in the name of the applicant (typically a company) only and to have the name of the person authorised for communication mentioned in a cover e-mail or cover letter, which is not made public. There is no need to require the name of the person authorised for communication to be made public and avoiding publication of the individual's name is also in line with basic data privacy principles. This will require an amendment of the template in Annex 1 to the Proposal. On the other hand, sound policy reasons justify focusing the resources of the EMEA on areas that are the most relevant. The Proposal would force the Agency to allocate significant human and time resources in finalising the assessment report as well as preparing and publishing the Q&A and WPAR/updated EPAR, although this is not required under Article 11 and the transparency objective is already reached by the publication of a press release. Sound policy reasons also justify limiting useless information in the EPAR. In cases of line extensions or variations, the Proposal would lead to adding information about the withdrawal and reasons for the withdrawal to the EPAR, regardless of whether it is relevant for the current product. Furthermore, the publication of documents other than a press release and a non-confidential version of the assessment report (if a report already exists), is based on the assumption that "*CHMP views on an application cannot be considered as "commercially confidential information" and therefore should not raise any comments from the applicants*." This assumption is not correct. Certain actions of the CHMP or information used by the CHMP in connection with an application are considered of confidential nature by applicants. It therefore is not accurate that all CHMP actions, opinions or decisions may be disclosed to the public without further consideration.	Comment related to individual privacy for signature of the Applicant withdrawal letter agreed. Comment related to "commercially confidential information": details on these issues should be addressed in the EMEA document on principles to be applied for deletion of commercially confidential information.

4. Structure and content of the documents to be published		
Line no.[3] + paragraph no.	**Comment and Rationale**	**Outcome**
Subsection "Applicant's withdrawal letter"	**[AESGP]** The matters related to the template letter and letter itself seem to have been slightly confused in the two paragraphs of this section. We propose the following re-phrasing: "***The applicant will prepare a letter for announcing the withdrawal which will be published by the EMEA. This letter will include a section on the reasoning behind the withdrawal.*** ***To that effect and in order to ensure that the level of information provided is similar from one withdrawal to the other, the EMEA has prepared a template letter which applicants are recommended to use. The template letter is included in Annex 1 of this document***."	Comments have been taken into account to rephrase the subsection
Subsection "Q&A"	**[AESGP]** We appreciate the fact that the Q&As will be sent to the applicant for review before publication. However, we should like to remark that the Q&As document does not only present the CHMP's views but also concerns the medicine and its potential on-going use in clinical trials or compassionate use programs on which the applicant may wish to comment. In addition, we think it would be useful to include a timeline for review. In light of the above, we would suggest deleting the sentence reading "*The CHMP views on an application […] raise any comments from the applicant*" and slightly reword the following sentence as follows: ***"The applicant will be provided with the "Question and Answer" document for a 5-working day review before its publication."***	Comments have been taken into account. 5-day consultation period is not possible since procedure will only allow consultation for a maximum of 1 day during the CHMP week.

[3] Where applicable

	In case of ongoing use of the medicine in clinical trials or compassionate programs, we recommend that special considerations be given in the writing of the respective section in the Q&A in order not to frighten patients who may be involved in the trials / compassionate use programs. A sentence should be added both in the body of the reflection paper and on the Q&A template (annex 2) to that effect.	
Subsection "Q&A"	**[EFPIA]** We have serious concerns about the proposal to provide a "summary of the CHMP evaluation at the time of the withdrawal" in the Q&A document. This would be in the Sections headed "What was the recommendation of the CHMP at that time?" and "What were the main concerns of the CHMP?" It does not seem to be in the public interest to routinely publish such a summary on an application for a medicine which is not to be made available as part of a routine practice. This information is speculative in the sense that it deals with the CHMP's "provisional opinion" i.e. what it might have recommended or decided if the procedure had continued. However, this cannot be predicted and stated with certainty. It is highly sensitive and potentially disadvantages the applicant in relation to its competitors who may use this information to estimate the likelihood and timing of any re-submission of the application. Within the Q&A document this information is likely to be presented simplistically and out of context regarding the full background and content of the application dossier and all considerations and factors the CHMP have considered. The WPAR, if available, should be better in that at least it will have this in context. We propose that these sections of the Q&A are replaced by a link to the WPAR if available, rather than have an unsatisfactory summary included in the Q&A. (This approach would be in line with the text of the legislation which does not require the Q&A at all or such a summary in particular to be published – only the reasons for withdrawing the application given by the applicant and the WPAR 'if available').	Not agreed. The Q&A document aims to provide the information on the withdrawal to the patients and the general public in a language, which is easily understandable by them. The information contained in the document will not be different that the one contained in the assessment report. In order to ensure that the summary is satisfactory, the text will clearly state that the applicant will have the opportunity to comment the Q&A document before it is published The publication of Q&A document for withdrawal of application is consistent with EMEA current practice to publish Q&A documents once the procedure for evaluation of an application for marketing authorisation by the CHMP has finalised, irrespective if the opinion of the CHMP is positive, negative. The Q&A clearly states that the position of the CHMP is provisional.

Subsection "Q&A" **Page 4, line 5**	**[EFPIA]** As indicated in the general comments, EFPIA believes that the company planning the development is best placed to advise on future consequences, compassionate use programmes/clinical trials, etc. of a withdrawal and can make a valuable contribution to ensuring that the information provided is accurate and informative. In addition, in certain situations, CHMP views on an application may contain details that could potentially affect intellectual property rights. Delete from "*the CHMP views on an application….*" To the end of that paragraph i.e. *to "…. prior to its publication"* and replace with: ***"the CHMP views on an application cannot be considered as "commercially confidential" information. Nevertheless, to ensure the document is accurate and informative regarding development consequences, compassionate use programmes/clinical trials and any existing products the company will be involved in the preparation of Q&A, by providing a draft to the company for review and input at least two weeks before issue".***	Agreed. The applicant will advise on future consequences, compassionate use programmes/clinical trials, etc. of a withdrawal. This information is expected to be provided in the withdrawal letter (see template), and will be used for the preparation by the Q&A document by the EMEA. The text will be modified (see previous comment) to clearly state that the applicant will have the opportunity to comment the Q&A document before it is published. Two weeks consultation period is not possible since procedure will only allow consultation for a maximum of 1 day during the CHMP week.
Subsection "Q&A" **2nd para**	**[MSD]** A publication of Q&A documents should only be made in cases where the withdrawal action has an impact on public health, i.e. when the withdrawal affects patients directly in cases where they use the product either for licensed treatment, in compassionate use programs and/or in clinical trials. We strongly disagree with the statement that the CHMP views on an application can generally not be considered as "commercially confidential information". They are based on confidential data submitted by the applicant and hence, can include sensitive information. We propose that the Q&A is developed and provided by the applicant who is responsible for ensuring that the potential consequences of the withdrawal action are adequately addressed and managed. Rephrase paragraph: "If the withdrawal has an impact on public health, a Q&A document should be made available as soon as possible after the EMEA press release. This document is developed by the applicant and provided to the EMEA together with the withdrawal letter. If applicable, it will include potential consequences in terms of	Not agreed. It remains EMEA responsibility to provide adequate information to the public about medicinal products evaluated by the CHMP.

	development of the product, compassionate use programs, ongoing clinical trials and use of the product when it is already on the market."	
Subsection "WPAR"	**[PhRMA]** The Proposal organises a system by which the assessment report would be finalised by the CHMP although the application has already been withdrawn. However, Article 11 makes clear that the assessment report should be published "*if available*". Furthermore, Article 11 envisages the publication of the assessment report and not of a WPAR/updated EPAR. Although based on the assessment report, the WPAR/updated EPAR is different from the assessment report as it highlights the major issues leading to the withdrawal. Such document is not necessary because the applicant has the obligation to disclose the reasons for the withdrawal and the latter are only known by the applicant.	Comment accepted. The Withdrawal Public Assessment Report will be prepared on the basis of the latest assessment report adopted by the CHMP.
Subsection "Q&A"	**[PhRMA]** Article 11 calls for information to the public only about the withdrawal, the reasons given by the applicant for such withdrawal ("this information") and any already available assessment report. The templates withdrawal letter and Q&A included in the Proposal contain much more information than is required under Article 11, including commercially confidential information like future plans for development of the product. It is possible that Article 80 of the Regulation provides a basis for disclosing other information, but this should be limited to information for which there is a clear policy need for enhanced transparency and in respect of the basic principles expressed in the legislation. Article 80 only organises access to and availability of existing documents and in principle does not allow for the creation of new documents by the authorities, even for transparency purposes. In addition, any reliance on a possible implied legal basis should be combined with even stronger guarantees for the protection of the commercial interests of the companies involved.	Not agreed. (see previous comments) The Q&A document aims to provide the information on the withdrawal to the patients and the general public in a language, which is easily understandable by them. EMEA discussed this approach at the occasion of different meeting with Patients and Consumers Organisations. Company's future plan for the development of the product will reflect information given by the company in the withdrawal letter (see template) and as such will be used for the preparation by the Q&A document by the EMEA. The publication of Q&A document for withdrawal of application is consistent with EMEA current practice to publish Q&A documents once the procedure for evaluation of an application for marketing authorisation by the CHMP has finalised, irrespective if the opinion of the CHMP is positive, negative. The text has been modified to clearly state that the applicant will have the opportunity to comment the Q&A document before it is published.

Subsection "WPAR"	**[AESGP]** Remarks on the sub-section: We would like to draw attention on the fact that in most cases, the application will be re-submitted and therefore it is critical to provide the appropriate information without scaring patients. In case of re-submission, the new EPAR should address why/how the new submission addresses the issues or concerns which led to the withdrawal. We suggest to clearly indicate this in the text. In addition, the product could already be approved in other regions so the wording of the WPAR should avoid any possible negative impact on the other authorisations. We think this should be mentioned.	Agreed. The intention is not to scare patients, but to avoid it by providing the information in the most appropriate way. This is particularly important when a product is withdrawn, but is authorised for another indication. Adequate information must provide clear information to the public, i.e. on the level of safety of the authorised product.
Subsection "WPAR"	**[AESGP]** Third, fourth and fifth paragraphs: We fully support the making available of the appropriate information to patients; however this should not undermine companies' business or competition aspects. Therefore, we would like to propose the following wording (with reference to the text provided in the Notice to Applicants): "***Applicants will receive the adopted AR from the EMEA for a 10 working day review period. Applicants are then required to identify within this timeframe those issues which they consider to be commercially confidential. Such issues should be notified and justified by the applicant to the EMEA. Upon receipt of the applicant's response with those issues which the applicant considers to be commercially confidential, the EMEA will prepare a WPAR, taking into account the obligations of the Regulation, transparency and confidential considerations***." In addition, in case of important disagreements, the holding of a teleconference should be made possible between the EMEA (project manager in charge of redacting the WPAR) and the applicant to discuss those issues and reach agreement on wording.	The original text in the reflection paper is already clear enough, and it is not against the proposed wording.

Subsection "WPAR"	**[EFPIA]** Several paragraphs refer to "commercially confidential information', confidentiality aspects. In this regard it would be important to acknowledge that in a pre-opinion phase many data in the assessment can be regarded as "commercially confidential" especially if the company intends to resubmit the application at a later stage, even though the general principles are the same as those set forth in the '*EMEA document on principles of* "*commercially confidential information for the publication of an assessment report'*	The applicant will receive the AR and will have the opportunity to comment on commercially confidential information.
Subsection "WPAR" **(Lines 19-21/ para. 5 of subsection)**	**[EFPIA]** It is not clear if the EMEA will let the applicant know whether its proposed deletions of commercially confidential information have been accepted. It is suggested to add a sentence at the end of the paragraph currently reading "After deletion of commercially confidential information, the CHMP will have the opportunity to comment on the WPAR/EPAR update. However, the EMEA will ultimately decide whether or not to introduce the comments with regard to confidentiality aspects" to clarify that **"The applicant will be provided with the WPAR/EPAR final document prior to its publication".**	Agreed. Added to paragraph 6 of subsection.
Subsection "WPAR" **Lines 22-23/ para. 6 of sub-section**	**[EFPIA]** This paragraph states that "the major issues leading to the withdrawal should be clearly highlighted" in the final WPAR/EPAR" It is assumed that "the issues" referred to in this paragraph are the reasons based on which the applicant decided to withdraw its application and already given in the withdrawal letter. It would be helpful to make this clear.	The referred paragraph has been updated in line with above comments. The WPAR/EPAR update will provide the provisional views of the CHMP and will highlight the main concerns raised by the CHMP.
Subsection "WPAR" **Para 2 of subsection**	**[IPFA]** What in the case of withdrawal before LoQ? This is clear when the various steps are described under 5. Timetable ~~*The assessment report from the CHMP is available after day 120 List of Questions (LoQ) in case of initial Marketing Authorisation Applications*~~	Not agreed. It is important to stress when the assessment report is considered available.

	~~*and applications for extensions of marketing authorisations as set out in Annex II to Regulation (EC) No 1085/2003*~~	
Subsection "WPAR" **4th para, line 3**	**[MSD]** MSD believes that the company should provide a proper justification for requesting deletion of commercial confidential information. Please delete "substantiated and…"	Agreed.
Subsection "WPAR" **6th para, line 2**	**[MSD]** We agree that the WPAR/EPAR update includes the major issues leading to the withdrawal of the application are clearly highlighted. This is another argument, why we believe a Q&A document does not provide additional information.	The Q&A does not provide additional information, but translates the scientific information from the WPAR into lay language, so that the patients and the general public can easily understand this information.
	[PhRMA] The Proposal does not strike a fair balance between transparency and confidentiality of commercial information. A fair balance between transparency and confidentiality is essential to promote pharmaceutical research and fair competition in the pharmaceutical sector. Protection of confidential information is even more important at the application stage because almost all information and documents contained in the marketing authorisation dossier are confidential. Although the Proposal stresses several times the need to protect commercially confidential information, it organises the disclosure of information provided by the applicant without granting him the procedural rights that would guarantee that no commercially confidential information is indeed disclosed. The issue is even more acute as the Proposal does not set clear rules on what information is considered confidential. The Proposal states that the concept of "commercially confidential information" will be the same as this set in the "EMEA document on principles of commercially confidential information for the publication of an assessment report." This document, however, is not publicly available so that pharmaceutical companies do not know what information will really be protected. Once that document is released, a new version of the Proposal -- taking into account comments received so far -- should be published for further consultation. Under the Proposal the applicant would be consulted before the	Applicant will be given the opportunity to review Q&A and WPAR/EPAR update to delete commercially confidential information. EMEA document on principles for deletion of commercially confidential information has been released for consultation prior to finalisation. The final version should be read in conjunction with this reflection paper.

	publication of the Q&A and WPAR/ updated EPAR. However, the applicant would not be able to comment or propose amendments to the Q&A. Such possibility only exists for the WPAR/updated EPAR. In addition, no recourse is organised for the cases where the applicant and the EMEA disagree as to the confidential nature of information. Such recourse is most relevant where the information contained in the Q&A or WPAR/updated EPAR may be detrimental to the applicant and the effect an undue publication cannot be undone. Given the sensitive nature of the information, the applicant should be closely involved in the drafting of each document to be published. The applicant should be consulted in a meaningful way, with clear opportunities to submit comments and propose amendments to both the Q&A and the WPAR/updated EPAR. A mechanism should be set up for resolving different views between the applicant and the EMEA as to the content of each document, which should among others allow a reassessment at a higher administrative level. Strict deadlines should be fixed for the applicant and the EMEA and for each step of the process. Such guarantees will delay the publication of the Q&A and the WPAR/updated EPAR. However, Article 11 of Regulation 726/2004 does not impose a timeframe for providing the information on a withdrawal and the public is informed immediately about the withdrawal and reasons for it by the EMEA press release. Without procedural guarantees granted to the applicants for protecting their commercially confidential information, the Proposal strikes an unfair balance to the detriment of pharmaceutical companies.	

5. Timetable for the publication of documents depending of the stage of the procedure at the time of the withdrawal (initial applications and applications for new indications – variations type II-and Annex II applications linked to a new indication)		
Line no.[4] + paragraph no.	**Comment and Rationale**	**Outcome**
	[MSD] For completeness, please include a timetable that reflects the evaluation procedure and publication requirements for generic products seeking an initial marketing authorisation.	No need to provide specific clarification. Timetable for generics is included in general timetable.
6. Elements to be considered for the preparation of the "Question and Answer" document and the assessment report		
Line no.[5] + paragraph no.	**Comment and Rationale**	**Outcome**
First bullet first sentence **Page 5/11**	**[EFPIA]** As indicated in Section 4 and 5 an assessment report is not available prior to the adoption of the List of Questions. The first sentence may be confusing and it is suggested to modify it: "*Before information on a withdrawal can be published by the EMEA, the CHMP assessment report* ***if available (i.e. if the application was withdrawn after the adoption of the list of questions)****, will have to be finalised and adopted by the CHMP"*	Agreed.
Second bullet in Section 6 **Page 6/11, line 5**	**[EFPIA]** After '*As patients could be involved in clinical trials or compassionate use practical advice for patients on this aspect will be included in the documents to be published by the EMEA."* Add the following text: ", ***using the information provided by the company in the withdrawal letter and after consultation with the company***	Not agreed. Even if this information will be given using the information provided by the company, it could be possible to use information from the CHMP (i.e. from previous CHMP opinions on compassionate use for the same product). The fact that the company will have the possibility to see and comment on the documents is already in the document, and there is no need to repeat it here.

[4] Where applicable
[5] Where applicable

	[EFPIA] The wording for the reasons for withdrawal will be very sensitive. This is especially so when an application for a new indication is withdrawn and the product remains on the market for already authorised indications, or when resubmission or further development activities are planned. Consideration should be given to the wording so that it is "patient friendly" and does not give rise to unnecessary alarm. It should be noted that consideration will be given to the wording of these documents so that the key message is conveyed in a "balanced" way, that is easy for the lay public (including patients) to understand without becoming unnecessarily alarmed.	As clearly stated in the template Q&A document, neither text nor modification will be added when informing of the reasons for the withdrawal. The information will be limited to that stated in the applicant's withdrawal letter. EMEA fully agrees on the second statement and consideration will be given to the wording of these documents so that the key message is conveyed in a "balanced" way, that is easy for the public (including patients) to understand without becoming unnecessarily alarmed.
7. Starting date of the implementation.		
Line no.[6] + paragraph no.	**Comment and Rationale**	**Outcome**
	[IPFA] Starting date of implementation is unrealistic, since the end of consultation is March 23rd, 2006. There have been some withdrawals since application after November 2005. This regulation should not be retroactive. The new date for implementation should be immediate after adoption by the CPMP. *It is proposed to start the implementation of this new provision of the legislation ~~with the first withdrawal of an initial marketing authorisation application or application for new therapeutic indication occurring after 20 November 2005~~ immediately after adoption by the CPMP.*	According to legislation, information on withdrawals has been published for withdrawals of applications occurring after 20 November 2005

[6] Where applicable

GUIDELINE SECTION TITLE: ANNEX 1 – Withdrawal letter template		
Comment and Rationale		**Proposed change (if applicable)**
Last line	**[EFPIA]** The identity/signature of the person who signed the letter on behalf of the company should not appear on a publicly accessible website. It is appropriate that the template letter states that the letter must be signed and who should sign it. However EFPIA believes the identity of the signatory **does not need** to appear on the website and this should be made clear.	Agreed. The template letter has been modified to allow the letter to be signed in the name of the applicant (company) and not to require the name of the person authorised for communication to be made public. This is also in line with general comments received from Pharma.

GUIDELINE SECTION TITLE: ANNEX 2 – Question & Answer document template		
Comment and Rationale		**Proposed change (if applicable)**
Heading 5 **How is X expected to work?**	**[EFPIA]** We believe that details on principal mechanism of action of a withdrawn product is commercially sensitive information valuable to the competitors but of no value to the public especially once a marketing application has been withdrawn. It is suggested that this heading is deleted from the template.	Most of times this information is already of public domain at the time of the withdrawal. If confidentiality does not apply for commercial reasons, this information is of relevance for the general public in order to understand the product.
Heading 6	**[EFPIA]** We believe that information on endpoints may be commercially sensitive information valuable to competitors but of no value for the public, especially once a marketing authorisation has been withdrawn. We believe it is appropriate to delete the last sentence under this heading ~~*"Briefly describe the endpoint."*~~	Same previous comment applies
Page 11, line 4	**[EFPIA]** It does not seem appropriate to formulate a firm hypothesis on the possible outcome of the procedure *"The CHMP had no major concerns* ~~*and the application could have been approved*~~ ***at this point in the procedure*** *"*	The text has been modified in order to clearly express that CHMP's views are provisional.

	[VSOP/EGAN] However we were wondering whether the same should be applicable to type II large manufacturing changes. We can envisage such changes where a withdrawal of the application could have an impact e.g. on the product supply. I would therefore recommend to add both in the withdrawal letter template as well as in the Q&A document: <provide information on consequences for the product supply> Also in both documents we would prefer to see information on impact on safety and efficacy in registered indications as well. We can imagine that a withdrawal for a new indication based on new safety concerns could cause worries at the general public for the safety in a current indication. So immediately under the statement regarding clinical trials we would suggest to add: <provide information on the safety and efficacy of product X in the already registered indication>.	Publication on withdrawal of Type II variation application for manufacturing changes is not foreseen by the legislation. Agreed. The template of the Q&A has been updated to make clear that such information will be included.