30 April 2013
EMA/239916/2013
Committee for Medicinal Products for Human Use (CHMP)

Overview of comments received on the draft on the Procedural advice on the submission of variations for annual update of human influenza inactivated vaccines applications in the centralised procedure

Interested parties (organisations or individuals) that commented on the draft document as released for consultation.

1. Vaccines Europe

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
1.	Vaccines Europe welcomes the opportunity to comment on the Procedural advice on the submission of variations for annual update of human influenza inactivated vaccines applications in the centralised procedure (EMA/CHMP/BWP/99698/2007 Rev. 2). In addition, please note that the comments that will be provided to EMA in the context of the public consultation of the Quality Module of the Guideline on Influenza Vaccines will be in line with the observations made on this guideline.	
	Vaccines Europe would like to highlight that according to the proposed timelines for the annual update, the Marketing Authorisation Holder (MAH) is requested to submit additional clinical data (if applicable) on day 45. We consider that in order to be able to submit the additional data as early as possible, the MAH should be informed earlier than at Day 45.	The EMA acknowledges the need to know as soon as possible whether additional clinical data are required. As for this year, the EMA whenever possible will communicate information on the annual update prior to the submission of the annual update application (e.g. during 'annual strain selection' meeting with stakeholders or pre-submission meeting,…)
	Ideally, we would like to suggest that the eventual need for clinical data would be included in the annual EU recommendation on strains to be used for the manufacture of the seasonal influenza vaccine. In addition, in order to shorten the procedure and promote flexibility, MAHs should have the possibility to submit this requested additional data before Day 45. As	Deadlines as mentioned in the guideline should be seen as maximum deadlines. Applicants are reminded to discuss any particularities for their application during a pre-submission meeting.

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	a result, no clock off period would be needed.	

2. Specific comments on text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
Page 3 1. Introduction 3rd paragraph	1.	Comment: Add clarification on the need to produce and release pilot/full scale of batches of the specific annual influenza vaccine for clinical trials Proposed change (if any): As soon as the reagents for standardisation are made publicly available by the WHO collaboration centres, the manufacturers will qualify monovalent bulks and will produce and release pilot/full scale of batches of the specific annual influenza vaccine for clinical trials **if these are necessary/ requested by CHMP**.	Text is amended as follows: As soon as the reagents for standardisation are made publicly available by the WHO collaboration centres, the manufacturers, , will qualify monovalent bulks and will produce and release pilot/full scale of batches of the specific annual influenza vaccine for clinical trials, **where appropriate**.
Page 7 Module 1 Point 1.3.1.	1.	Comment: For the revised SmPC, Labelling and Package Leaflet, minor changes on the product information (e.g. change in the telephone number of the local representative in the leaflet) could be introduced during the annual update variation, if agreed by the PTL and the rapporteur. Furthermore, the note also states that "the year of the season should not be part of the name of the medicinal product but should be included in the section **1** of the SmPC and corresponding sections of labelling". This is not currently the case for all CP vaccines. For several vaccines, in the SmPC, the year is only mentioned in section **2**. For the concerned products this will mean an additional change in the product	Proposal is not agreed. Only changes related to the new strains used may be introduced in these texts. No change of the wording. Proposed deletion is agreed. This topic does not fall within the scope of this guideline and will be discussed in other appropriate guidance. Deletion of the following text: ~~**The year of the season should not be part**~~

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		information. It has to be noted here that this process differs from one vaccine to another and its need should be further discussed outside of this guideline. Moreover, it has to be taken into account that it is rather late now (April 2013) for timely approval and implementation, i.e. before the next annual update for the season 2013/2014. We therefore suggest removing this sentence. Proposal change: Amend the note on Point 1.3.1. as follows: ~~Only c~~**C**hanges related to the new strains used **and minor changes on the product information as agreed by the PLT/rapporteur** may be introduced in these texts. ~~The year of the season should not be part of the name of the medicinal product but should be included in section 1 of SmPC and corresponding sections of labelling. (At submission of the of variation application, the full set of annexes of the product information in all languages should be submitted to the Agency and MSs electronically in accordance with the CHMP members distribution list as published the Agency website).~~	~~**of the name of the medicinal product but should be included in section 1 of SmPC and corresponding sections of labelling. (At submission of the of variation application, the full set of annexes of the product information in all languages should be submitted to the Agency and MSs electronically in accordance with the CHMP members distribution list as published the Agency website).**~~
Page 8 Section 3.2 Module 3 1st paragraph	1.	Comment: A definition of what "relevant and adequate sections" are is not provided in the guideline. We are of the opinion that for the variation dossier the relevant information will be the information that has been updated. Therefore, when providing the Quality Documentation only the information that has been changed should be included.	Proposal is not agreed. 'relevant and adequate sections' should be understood as the information supporting the strains subject to the annual update No change to the wording.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		Proposed change: Amend the first paragraph of Section 3.2.1. – Module 3 as follows: "Please note that **for this Module** only **the updated / new information on the different sections of the CTD dossier** ~~relevant and adequate sections of the CTD variation application~~ should be submitted. ~~All sections not felt to be necessary should however be justified adequately in the Summary/Overview."~~	
Page 8 Module 3 Point 3.2.S.2.4.	1.	Comment: We would like to confirm that the Control of Critical Steps and Intermediates point should only be completed for products with intermediates. Proposed change: Add clarification that 3.2.S.2.4 only applies to products with intermediates.	Proposed change is not agreed. 3.2.S.2.4 applies to the control of critical steps and to the control of intermediates . Critical steps are also possible if there are no intermediates. No change to the wording.
Page 9 Module 2 Points 2.5 & 2.7	1.	Comment: It should be clarified (as it is the case for the Quality Overall Summary Page 7 – Section 3.2.1. – Module 2 – Point 2.3.) that it is an addendum that needs to be submitted. Proposed change: Amend 2.5 and 2.7 as follows: 2.5 Clinical Overview **(addendum to " previous" Clinical Overview)**	Proposal is agreed. Amended text: 2.5 Non-clinical Overview **(addendum to previous Clinical Overview, if appropriate)** 2.7 Clinical Summary **(addendum to previous Clinical Summary, if appropriate)**

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		2.7 Clinical Summary (**addendum to "previous" Clinical Summary)**	
Page 9 Module 5 Point 5.3.6. Last paragraph	1.	Comment: Due to the changes introduced by the Pharmacovigilance legislation, PSURs are assessed by the PRAC. In addition, PSURs must be submitted within 70 days after the Data Lock Point, which date likely is earlier than the submission of the clinical data in the annual update procedure. In other words, despite it only is an encouragement (whereas the 70 day submission deadline is a legal requirement), there seems to be little to no added value to include the PSUR in the annual update dossier or cross reference to the previous PSUR submissions. Proposed change: Delete the 4th bullet: "Finally, applicants are encouraged to include the following PSURs in the clinical data package (for eCTD submissions, a cross reference to the previous PSUR submissions is sufficient): * PSUR covering the period 1 September- 30 April of the previous season * PSUR covering the period 1 May - 31 August of the last but one season. "	Proposal is agreed. Deletion of the following text: ~~**"Finally, applicants are encouraged to include the following PSURs in the clinical data package (for eCTD submissions, a cross reference to the previous PSUR submissions is sufficient):**~~ ~~*** PSUR covering the period 1 September- 30 April of the previous season**~~ ~~*** PSUR covering the period 1 May - 31 August of the last but one season. "**~~