SUBMISSION OF COMMENTS ON PROPOSAL FOR REVISION OF THE VARIATIONS REGULATIONS

COMMENTS FROM JOHNSON & JOHNSON/ANNE PAPIN
GENERAL COMMENTS
In general, the draft proposal addresses many of the issues industry has had with the current Regulation and is moving in a positive direction. However, the practical implementation is difficult to foresee and may necessitate further revision. The role of the EMEA will be further strengthened and the extra burden that will be placed on EMEA staffing is of some concern.
The Regulation should specify that rejection of Type IA variations may only occur where any of the elements listed in paragraph 1 of Annex III is missing.
It should be stated that, once the Regulation is implemented, Competent Authorities should not request additional national documents (eg, notarisation /authentification of signed documents and certificates).
Draft guideline on classification of variations attached to the draft Regulation There are some general concerns that the information provided in the guideline should be comprehensive to minimize different interpretations of that information. 'Design space' should be defined clearly.

SPECIFIC COMMENTS ON TEXT

GUIDELINE SECTION TITLE		
Line no[1]. + paragraph no.	**Comment and Rationale**	**Proposed change (if applicable)**
Throughout draft	All occurrences of 'one month' should be amended to '30 days for consistency and clarity. It should be clarified that 'days' refer to 'calendar days'	
p5, Art. 5,	'The Agency shall deliver this recommendation within 60 days following receipt of the request '. This appears to be lengthy for the determination of the classification of a variation that excludes assessment of the actual variation. It is suggested that this time is reduced to a maximum of 30 days.	'The Agency shall deliver this recommendation within 30 days following receipt of the request '.
p7, Art. 9	Timelines should be added to:	2. …If the notification fulfils the requirement laid down in the first

[1] Where available

	2. … If the notification fulfils the requirement laid down in the first subparagraph, the relevant authority shall acknowledge receipt of a valid notification. 3. …Where the notification is accepted, the relevant authority shall close the procedure in accordance with Article 21(1).	subparagraph, the relevant authority shall acknowledge receipt of a valid notification within 14 days. 3. …Where the notification is accepted, the relevant authority shall close the procedure within 5 days in accordance with Article 21(1).
p8, Art. 10	Timelines should be added to: 2. …If the application fulfils the requirement laid down in the first subparagraph, the relevant authority shall acknowledge receipt of a valid application. 4. Within the period laid down in paragraph 3, the relevant authority may request the holder to provide supplementary information within a time limit set by that competent authority. 5. Within the period laid down in paragraph 3, the relevant authority shall, where it reaches a final opinion on the application, close the procedure in accordance with Article 21(1).	2. …If the application fulfils the requirement laid down in the first subparagraph, the relevant authority shall acknowledge receipt of a valid application within 14 days. 4. Within the period laid down in paragraph 3, the relevant authority may request the holder to provide supplementary information within 90 days. The holder may request to extend this period with appropriate justification. 5. Within the period laid down in paragraph 3, the relevant authority shall, where it reaches a final opinion on the application, close the procedure and inform the holder that the variation is approved in accordance with Article 21(1).
p10, Art. 12	2. Within one month following receipt of the elements referred to in paragraph 1, the competent authority of the reference Member State shall close the procedure in accordance with Article 21(2).	2. Within one month following receipt of the elements referred to in paragraph 1, the competent authority of the reference Member State shall inform the holder of the validity of the notification and close the procedure in accordance with Article 21(2).
p10, Art. 13	Timelines should be added to: 2. …If the notification fulfils the requirement laid down in the first subparagraph, the competent authority of the reference Member State shall acknowledge receipt of a valid notification. 3. …Where the notification is accepted by the competent authority of the reference Member State, that competent authority shall close the procedure in accordance with Article 21(2).	2. …If the notification fulfils the requirement laid down in the first subparagraph, the competent authority of the reference Member State shall acknowledge receipt of a valid notification within 14 days. 3. …Where the notification is accepted by the competent authority of the reference Member State, that competent authority shall close the procedure within 5 days in accordance with Article 21(2).
p11, Art. 14	Timelines should be added to: 2. …If the application fulfils the requirements laid down in the first subparagraph, the competent authority of the reference Member State shall acknowledge receipt of a valid application and inform the holder and the other relevant authorities of the date of the start of the	2. …If the application fulfils the requirements laid down in the first subparagraph, the competent authority of the reference Member State shall acknowledge receipt of a valid application within 14 days and inform the holder and the other relevant authorities of the date of the start of the procedure laid down in paragraphs 3 to 6.

	procedure laid down in paragraphs 3 to 6.	
p12, Art. 14	Timelines should be added to: 4. Within the period laid down in paragraph 3, the relevant authority may request the holder to provide supplementary information within a time limit set by that competent authority.	4. Within the period laid down in paragraph 3, the relevant authority may request the holder to provide supplementary information within 90 days. The holder may request to extend this period with appropriate justification.
p14, Art. 18	Timelines should be added to: 2. … If the notification fulfils the requirement laid down in the first subparagraph, the Agency shall acknowledge receipt of a valid notification. 3. … Where the opinion of the Agency on the notification is favourable, the Agency shall close the procedure in accordance with Article 21(3).	2. … If the notification fulfils the requirement laid down in the first subparagraph, the Agency shall acknowledge receipt of a valid notification within 14 days. 3. … Where the opinion of the Agency on the notification is favourable, the Agency shall close the procedure within 5 days in accordance with Article 21(3).
p14, Art. 19	Timelines should be added to: 2. …If the application fulfils the requirements laid down in the first subparagraph, the Agency shall acknowledge receipt of a valid application. 4. Within the period laid down in paragraph 3, the Agency may send the holder a request for supplementary information within a certain time limit set by that the Agency. The procedure shall be suspended until such time as the supplementary information has been provided. In this case the period laid down in paragraph 3 may be extended for a further period to be determined by the Agency.	2. …If the application fulfils the requirements laid down in the first subparagraph, the Agency shall acknowledge receipt of a valid application within 14 days. 4. Within the period laid down in paragraph 3, the Agency may send the holder a request for supplementary information within 90 days. The holder may request to extend this period with appropriate justification. The procedure shall be suspended until such time as the supplementary information has been provided. In this case the period laid down in paragraph 3 may be extended for a further period to be determined by the Agency.
p17 & 18, Art. 21	This article appears confusing and unclear and should be revised for clarity and to keep timelines as short as possible.	
p19, Art. 24	The proposed procedure may be positive. However, there appears to be no defined mechanism to make the EMEA opinion binding on the relevant Competent Authorities and therefore it is unclear how this procedure may work in practice. The worksharing procedure needs a mandate for acceptance of the EMEA opinion by the relevant Competent Authorities and a timeline for these authorities to implement the opinion after completion of the worksharing procedure. A time limit of not more than 30 days should be specified for implementation of the EMEA opinion by the relevant Competent Authorities.	

	It is suggested that the EMEA appoints a RMS for each worksharing procedure. It would be helpful to clarify who conducts the assessment work and how is this recognized by other relevant Competent Authorities. There is a need for transparency around this procedure.	
p24, Annex II	The legal possibility to group variations in one application for one MA or for several MAs (for example many changes to an SmPC or a number of IA/IB variations, or class labelling) is welcomed. However, it seems that in most cases the variations still have to be consequential. Consideration should be given to expanding the cases in which variations can be grouped.	
	Grouping of the same application for various strengths and pharmaceutical forms of the same product having the same active substance so be added to Annex II.	14. All variations in the group relate to products having the same active substance.
Draft Detailed Guideline Referred To In Article 6(1)(A): Conditions For Classification Of Variations		
p31, change 13.b	The conditions listed still include number 5, although 5 is striked through in the list of conditions.	13.b Conditions 2, 3, 4
p34, 37, 38, 42 & 45, changes 19, 26, 31, 37, 44.	It is considered that where the specifications are being tightened in response to a previous commitment, it would seem reasonable that these should be Type IA variations and that condition 1 should be deleted from these changes. For situations where the tightening of the specification limits cannot be implemented as agreed in a previous commitment, a new change should be introduced categorized as a Type IB variation.	**x. In response to a commitment, change in specification of an excipient/of the immediate packaging of the finished product/to in-process tests or limits applied during the manufacture of the product/of the specification of the finished product/in specification of a measuring device or administration device for veterinary medicinal products.** Condition: The tightening of the specification limits cannot be implemented as agreed in the commitment. Type IB
p42, change 38.a	The conditions listed still include number 5, although 5 is striked through in the list of conditions.	38.a Conditions 1, 2, 3, 4 (see below)
p42, change 38	It is suggested that 38 be expanded to include deletion of a test procedure as a Type IB variation with the condition that deletion of the test procedure does not have a substantial potential to have a negative impact on the quality, safety or efficacy of the medicinal	d. Deletion of a test procedure Conditions: 5 IB Conditions 5: Deletion of the test procedure does not have a substantial potential to have a negative impact on the quality, safety or efficacy of the

	product concerned.	medicinal product concerned.
p46, change 46	Change 46 should be applicable to biosimilars also.	**46. Change in the summary of product characteristics*, labelling and package leaflet/insert of a generic <u>or biosimilar</u> medicinal product* following a Commission Decision for a referral for an original medicinal product in accordance with Article 30 of Directive 2001/83/EC or Article 34 of Directive 2001/82/EC**