



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

18 September 2018
EMA/CHMP/BWP/637549/2018
Committee for Medicinal Products for Human Use (CHMP)

Overview of comments received on 'Questions and Answers on Bovine Spongiform Encephalopathies (BSE) and vaccines' (EMA/CHMP/BWP/192228/2017)

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

Stakeholder no.	Name of organisation or individual
1	Vaccines Europe
2	The European Association of Hospital Pharmacists (EAHP)



1. General comments – overview

Stakeholder no.	General comment	Outcome (if applicable)
2	EAHP welcomes the evidence presented in the questions & answers document that will encourage the use of vaccines by clearly communication of the purity of the product.	

2. Specific comments on text

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
47	1	<p>Comment: What is the “mandatory TSE guideline”? Is it EMA 410/01 rev 3?</p> <p>Proposed change: Make reference to the considered guideline.</p>	<p>Not accepted.</p> <p>Footnote 3 gives a clear reference.</p>
97-100	1	<p>Comment: Add human TSE diseases.</p> <p>Proposed change: They include classical (or sporadic) Creutzfeldt-Jakob Disease (CJD/sCJD), variant CJD (vCJD), Kuru (transmission via cannibalism in Papua New Guinea), and fatal familial insomnia (familial or sporadic), and Gerstmann–Sträussler–Scheinker syndrome.</p>	Accepted.
104	1	<p>Comment: The reference “Lancet, 1996, 347: 921-925” does not mention the author. Also, why not presenting it in the footnote as for other references.</p> <p>Proposed change: Will et al., Lancet, 1996, 347: 921-925, https://doi.org/10.1016/S0140-6736(96)91412-9</p>	Accepted to add complete reference, and hyperlink. Moved to footnotes.
123-124	1	<p>Comment: To add info to the sentence “chemical conditions which would normally kill bacteria and viruses”.</p> <p>Could there be some references to detail which conditions are effective?</p>	<p>Partially accepted.</p> <p>The following sentence was added to the end of the paragraph</p> <p>They can be destroyed using heat or chemical conditions which are more rigorous than are required for bacteria and viruses.</p>

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		Proposed change: Insert one or more references to effective conditions to destroy prions.	No reference is required as this is a very general statement, and the document is not intended to be a "how to" manual.
139	1	Comment: "EMA has been advised by a panel of international experts". Is there a link to a report from these experts panel? Proposed change: Insert a reference and/or a link to a report from the experts.	Not accepted. The report is no longer available.
167-168	1	Comment: Modification of the sentence "vaccine are then diluted to the desired strength and prepared into a finished product" Proposed change: "vaccine are then diluted to the desired composition or concentration and formulated strength and prepared into a finished product".	Partially accepted. The sentence was replaced as follows: The bacterial or viral components of the vaccine are then formulated into the finished product.
170	1	Comment: modification of the sentence " [...] vaccines are given in defined doses which are proven to be safe." Proposed change: "vaccines are given in defined doses which have been are proven to be safe."	Accepted.
173-175	1	Comment: For clarity, to introduce other uses of animal derived material (ADM) and to remind that majority of new vaccines are not using ADM anymore, modification of sentences "Bovine derived materials are used at some stages in the manufacture of some,	Partially accepted. The current sentence is clear and accurate. Other uses (e.g. gelatine as excipient) are mentioned elsewhere.

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		<p>but not of all vaccines. These bovine materials are one source of nutrients and growth factors for the growth of bacteria or for the cells used to grow viruses. These elements are essentially provided from materials of animal origin."</p> <p>Proposed change: "Even if main new vaccine produced in process free of material of animal origin are being now developed and authorized, bovine derived materials are still used at some stages in the manufacture of some marketed vaccines, but not of all vaccines. These bovine materials are mainly one sources of nutrients and growth factors for the growth of bacteria or for the cells used to grow viruses. These elements are still essentially provided from materials of animal origin, They can also act as excipient (i.e Gelatine)."</p>	<p>The sentence 'These elements are essentially provided from materials of animal origin,' has however been deleted since it is clear that bovine materials are of animal origin.</p>
176-178	1	<p>Comment: Same as above, modification of sentence "Generally they are used only in the early stages of the manufacturing process of the vaccine component(s), and then they are reduced to trace amounts during the further purification and dilution steps."</p> <p>Proposed change: "Generally When they are used only in the early stages of the manufacturing process of the vaccine component(s), and then they are reduced to trace amounts during the further purification and dilution steps."</p>	Accepted.

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208	1	<p>Comment: Add reference (6) WHO tables on infectivity distribution in TSE in the sentence “BSE infectivity has never been detected in bovine skin³.”</p> <p>Proposed change: “BSE infectivity has never been detected in bovine skin³⁻⁶.”</p>	<p>Not accepted.</p> <p>Refer to EU/EMA documents where available. We already refer to the TSE guideline and this is sufficient.</p>
217	1	<p>Comment: “The following measures are taken into account to ensure the safety of serum”.</p> <p>The fact that BSE prions has not been conclusively detected in the blood of cattle (line 226) is not a decided measure. It is a fact.</p> <p>Proposed change: The following measures factors (or aspects) are taken into account to ensure the safety of serum”</p>	<p>Accepted.</p> <p>The word “factors” was used instead of measures.</p>
230	1	<p>Comment: “Within the limits of experimental testing, BSE prion has not been detected in the milk”</p> <p>Why mentioning the experimental limit for milk and not for the serum for example?</p> <p>Is there any specific detection issue in the milk?</p> <p>Proposed change: Harmonize and not mention experimental testing limits specifically for milk (unless there is a specific issue with detecting Prion in milk).</p>	<p>Partially accepted.</p> <p>The sentence has been deleted as follows:</p> <ul style="list-style-type: none"> - Bovine milk has always been considered as non-infectious, regardless of the country of origin. Within the limits of experimental testing, BSE prion has not been detected in the milk of cattle which are sick or incubating the disease⁹.

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230-231	1	<p>Comment: Change of the references in the sentence “BSE prion has not been detected in the milk of cattle which are sick or incubating the disease ⁹”</p> <p>Proposed change: “BSE prion has not been detected in the milk of cattle which are sick or incubating the disease ^{3,6}”</p>	The sentence and the reference have been deleted as well as the sentence above.
236-237	1	<p>Comment: Add WHO reference (6) in the sentence “All of the tissues from which meat extracts are derived are classified in the no or low risk categories by the WHO³”</p> <p>Proposed change: All of the tissues from which meat extracts are derived are classified in the no or low risk categories by the WHO^{3,6}</p>	<p>Not accepted.</p> <p>Refer to EU/EMA documents where available. We already refer to the TSE guideline and this is sufficient.</p>
293	1	<p>Comment: “and so the agent that causes BSE <u>could not have been present</u> in the doses of vaccine”.</p> <p>Due to long incubation period for prions, this affirmative statement may not be true.</p> <p>Proposed change: “and so the agent that causes BSE is considered very unlikely could not have been present in the doses of vaccine”</p>	<p>Accepted.</p> <p>It is conceivable that prions could have been present but pre-symptomatic in cattle when these vaccine were made, however unlikely.</p> <p>Changed to:</p> <p>Thus, the vaccines used to immunise children who developed vCJD in later life had been produced in the years before the BSE epidemic and so the agent that causes BSE is very unlikely to could not have been present in the doses of vaccine given to these children.</p>

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301-303	1	<p>Comment: Sentence long and in the end unclear "To date there are no indications that vCJD is linked to the use of any vaccines, and that the risk posed by the use of bovine materials is very remote as substantiated by the experience to date."</p> <p>Proposed change: split the sentence.</p> <p>"To date there are no indications that vCJD is linked to the use of any vaccines and that. The risk posed by the use of bovine materials is very remote as substantiated by the experience to date."</p>	Accepted.
304-305	1	<p>Comment: Redundant sentence with line 301-303.</p> <p>Proposed change: remove sentence</p> <p>"To date, there are no indications that vCJD is linked to the use of any vaccines, and that the risk posed by the use of bovine materials is very remote as substantiated by the experience to date"</p>	<p>Accepted.</p> <p>The final paragraph was removed which was a duplicate of the previous sentence.</p>