International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products

VICH/12/056
FINAL

PUBLIC CONSULTATION AT STEP 4 OF THE VICH PROCEDURE
OVERVIEW OF COMMENTS RECEIVED

VICH draft Guideline GL50R on Harmonization of criteria to waive target animal batch safety testing for inactivated vaccines for veterinary use

VICH EWG: BIOLOGICALS QUALITY MONITORING

Name & Country of individual, organisation, or VICH delegation that commented

Comment n°	Name - Country
1	International Council on Animal Protection in Pharmaceutical Programmes (ICAPPP, USA)
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Discussion of comments

GENERAL COMMENTS – OVERVIEW		
Comment N°	**Comment received**	**Outcome of consideration**
1	**General comment:** The ICAPPP welcomes an update to this guideline, which is now in line with recent changes to target animal batch safety test (TABST) requirements in Europe. The proposed text of the guideline does not make clear the extent to which further harmonisation between the VICH regions has been achieved since the guideline was first created in 2011. The text implies that the US and Japan will consider waiving if 10 (or 5 over 3 years) consecutive batches have been tested successfully. However, the table does not suggest this. We request that this is clarified and encourage the US and Japan to work towards harmonisation with Europe as much as possible, with the global deletion of the TABST being the ultimate objective. The proposed text specifies that the guideline's aim is to harmonize TABST waiver policies in VICH-participating regions, but omits information that would assist OIE member countries – which are encouraged by OIE to use VICH guidelines – in adopting harmonized policies.	The VICH EWG BQM acknowledges these general comments. Table 1 has been updated in the light of the specific comments 1-4, see below. The guideline does not address the degree to which harmonisation has already been achieved as this is not its aim. Rather, it summarises the current requirements and describes a harmonised approach for future waiving of the TABST. Gathering information on TABST requirements for all OIE member countries would be a major undertaking, would greatly delay implementation of the guideline and is not necessary to allow its use in OIE member countries. Furthermore, opportunities (in particular through the VICH Outreach Forum) exist through which non-VICH countries can seek clarification on any issues relating to VICH guidelines. VICH secretariat to advice on acceptability of proposed reply.

SPECIFIC COMMENTS ON THE TEXT OF THE GUIDELINE

SECTION 2			
Paragraph	**Comment N°**	**Comment received and rationale; proposed change**	**Outcome of consideration**

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2.2.1 Table 1 – Row Europe	1	According to the guideline, Table 1 is supposed to contain a list of testing procedures that are “required for batch safety testing of inactivated veterinary vaccines”. It therefore seems inappropriate to continue to include reference to the TABST in the ‘requirements’ or ‘remarks’ section of the table for Europe. Since the test has been deleted, it is no longer a requirement in Europe and this must be made clear. If the historical/background information surrounding the deletion of the test must be included in the guideline, it should instead be moved to a footnote so as not to allow for any confusion or misinterpretation. Proposed change (if any): We suggest that the text in both the ‘requirements’ and ‘remarks’ sections of Table 1 for Europe be deleted or moved to a footnote.	Row "Europe" now only includes a sentence on deletion of the TABST in 2013. Information of waiving possibility is now moved to a footnote.
2.2.1 Table 1 – Rows USA and Japan	2	**2.2 Table 1: USA and Japan** We are disappointed that the testing requirements in Table 1 for the US and Japan remain unchanged from the previous version of guideline. Both the text and the table need to accurately and fully reflect the requirements and waiving options. The table omits reference to the current US Department of Agriculture (USDA) Center for Veterinary Biologics (CVB) policy that allows licensed firms to seek waivers from TABST for inactivated veterinary vaccines. This policy, outlined in Veterinary Services memorandum 800.116, specifically references its consistency with VICH GL 50 (see https://ntp.niehs.nih.gov/iccvam/suppdocs/feddocs/usda/vsmemo-800-116-508.pdf). It is as yet unclear whether USDA has granted any TABST waivers since the introduction of this policy. The revised text should reflect current status of this USDA policy and the extent to which USDA has allowed licensed firms to implement it. According to the Japanese Ministry of Agriculture, Forestry and Fisheries (JMAFF), Japan has also been implementing the latest version of VICH GL50 and allowing waivers based on certain criteria, including 10 consistent batches (see JMAFF presentation at http://slideplayer.com/slide/10232852/).	These comments have been considered and the following amendments made: **Table 1** now only lists the requirements for the target animal batch safety testing and includes in the column "Remarks" a) for the USA, a reference to Veterinary Services Memorandum 800.116, and b) for Japan, a reference to the notice from director general of the National Veterinary Assay Laboratory, No.3000. Feb. 28 2014. The guideline does not address the degree to which TABST waivers have already been granted as this is not its aim. Rather, it summarises the current requirements and describes a harmonised approach for future waiving of the TABST. VICH secretariat to advice on acceptability of the proposed highlighted text.

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		We understand that considering the participation of OIE in VICH, a list of TABST testing requirements for OIE member countries would be helpful for regulatory authorities in those countries seeking to use this guideline. Proposed change (if any): Include reference to USDA VS memo 800.116. Include the following text in the 'remarks' section for both the USA and Japan: "Can be waived provided that at least 10 consecutive batches from separate final bulks had been tested and product complies with test". Alternatively, delete the 'remarks' column so that there is no confusion over whether waiving is an EU option and not a US or Japanese one but is in fact now harmonised. We prefer the former option.	Gathering information on TABST requirements for all OIE member countries would be a major undertaking, would greatly delay implementation of the guideline and is not necessary to allow its use in OIE member countries. Furthermore, opportunities (in particular through the VICH Outreach Forum) exist through which non-VICH countries can seek clarification on any issues relating to VICH guidelines. See above reply to the general comment.
2.2.1 Table 1 – row USA	3	It is not clear if the requirement in USA is for tests in both mice and guinea pigs. Furthermore, the justification for tests in both species is not given. Since the EU no longer requires any animal testing it is not clear why the USA would require tests in two species. Experience in other regions is that these tests do not add confidence in the safety of batches of product and they therefore represent an additional burden for industry (over and above other regions) and unnecessary use of animals. Therefore, these requirements should be deleted as a matter of urgency. Proposed change (if any): Clarify the requirement for mice and guinea pig in the 'requirement' section of Table 1 for USA. Provide justification for tests in both species. Consider deleting this requirement.	The guideline no longer lists the requirements for the safety tests in laboratory animals. Note that VICH is working on a guideline on harmonisation of criteria to waive the laboratory animal batch safety test for veterinary vaccines.
2.2.1 Table 1 – row Japan	4	The requirement in Japan for abnormal toxicity tests and toxicity limit tests is superfluous. Experience in other regions is that these tests do not add confidence in the safety of batches of product and they therefore represent an additional burden for industry (over and above other regions) and	The guideline no longer lists the requirements for the safety tests in laboratory animals. Note that VICH is working on a guideline on harmonisation of criteria to waive the laboratory animal batch safety test for

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		unnecessary use of animals. Therefore, these requirements should be deleted as a matter of urgency. Proposed change (if any): Remove the abnormal toxicity test and toxicity limit test from the 'requirement' section of Table 1 for Japan.	veterinary vaccines.
2.3	5	This guideline gives no recommendation to regulatory authorities on best practices for encouraging implementation of TABST waivers. Experience in the United Kingdom (UK) suggests that such recommendations are needed. Prior to concerted efforts of ICAPPP members, there was no oversight of the use of the waivers in the UK and use of the waiver was low. Once barriers – including fees – to the use of the waiver were removed and oversight was put in place to ensure that TABST was avoided where possible, implementation increased to maximum levels. Proposed change (if any): The guideline should specify that no fees be applied to the waiver process and that each country implementing the waiver system appoint an agency official to oversee the process in order to ensure that waivers are used whenever possible so that the largest number of animals are saved from TABST.	VICH provides technical guidance. The proposed change is outside of the remits of VICH. No amendments necessary.