OVERVIEW OF COMMENTS RECEIVED ON
VICH GUIDELINE ON HARMONIZATION OF CRITERIA TO WAIVE TARGET ANIMAL BATCH SAFETY TESTING FOR INACTIVATED VACCINES FOR VETERINARY USE (GL50)

	Name of non-VICH country/organization that commented on Draft VICH GL on VICH GUIDELINE ON HARMONIZATION OF CRITERIA TO WAIVE TARGET ANIMAL BATCH SAFETY TESTING FOR INACTIVATED VACCINES FOR VETERINARY USE (GL50)
1	Dr Mbi Makungu Norbert (Congo) – O.I.E.
2	Dr Doshima Kwange (Nigeria) – O.I.E.
3	International Council on Animal Protection in Pharmaceutical Programmes (ICAPPP, USA)
4	People for the Ethical Treatment of Animals (PETA, USA)

Discussion of comments

GENERAL COMMENTS - OVERVIEW

Nigeria:
The GLs are suitable and can be followed by the institute.

PETA
The use of TABST was called into question during the 1990s and scientific and animal welfare concerns led the European Centre for the Validation of Alternative Methods (ECVAM) to focus on TABST. In 1997, ECVAM convened the Advisory Group on Alternatives to Animal Testing in Immunobiologicals to perform a study on the relevance of TABST. Results of this study included data from official medicines control laboratories (OMCLs) within the European Union as well as from private industry. Throughout the period 1994 to 1997, OMCLs tested 11,185 vaccine batches and fourteen manufacturers submitted data from 11,386 batches for the period between 1997 and 1999. The study's findings resoundingly illustrated that TABST, as a routine part of batch testing, was no longer relevant to ensure safety due to the increased rigor and quality control introduced by Good Laboratory Practices and Good Manufacturing Practices. The advisory group recommended that TABST be omitted from routine testing requirements, with the exception of new products or for vaccines that had been recently licensed.
The advisory group further recommended that the TABST requirement be immediately deleted from Ph. Eur. monographs (except in specific cases where it is considered necessary e.g., for novel products and for vaccines that cause major pharmacovigilance issues) and that the Committee for Veterinary Medicinal Products (CVMP) of the European Medicines Agency (EMA) revise its guidance for immunobiologicals to reflect this recommended change. Harmonization between Ph. Eur. and E.U. guidance was also a priority in the 2002 "Statement of the Relevance of the Target Animal Safety Test for Batch Safety Testing of Vaccines for Veterinary Use" published by ECVAM.
Our experience in the United Kingdom (UK) leads us to request 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 TABSTs. Prior to PETA and PETA UK's concerted efforts, 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.
Because TABST is no longer considered to be a valuable or useful aspect of vaccine safety testing, we are hopeful that VICH's waiver harmonisation is only a first step to the complete elimination of the use of TABST.

ICAPPP
The ICAPPP strongly welcomes the creation of this guideline. It provides both internationally harmonised recommendations for criteria to waive target animal batch safety testing (TABST) of inactivated immunological veterinary medicinal products (inactivated IVMPs), and encourages global implementation to reduce the use of animals.
The guideline relates specifically to waiving 'target' animal batch safety tests. However, as the guideline describes, non-target (laboratory) animals are also used in general batch safety tests of IVMPs in some VICH regions. The requirements for these additional safety tests have been almost completely removed in the EU (i.e. in the European Pharmacopeia) for the reasons outlined in section 1.1.1. ICAPPP urges VICH to clarify that the scope of the waiving can also apply to these non-target animal tests and to modify the text accordingly.

SPECIFIC COMMENTS ON TEXT

SECTION: Guidance title		
Paragraph no.	**Comment and Rationale**	**Proposal for consideration**
Title	*PETA* Given that there are no scientific reasons preventing the waiver from being used for live virus vaccines, we request that the title of the guidance be changed to "Testing Harmonisation of Criteria to Waive Target Animal Batch Safety Testing."	VICH intends to widen the scope in a stepwise approach, and work has been initiated. Rationale for the phased approach is given in the "Introduction": *Submission of batch safety test data from target or laboratory animals is a requirement for batch release of immunological veterinary medicinal products (IVMPs) in the regions participating in the VICH. The VICH Steering Committee has decided to aim at harmonization of the batch safety tests across the regions in order to minimize the need to perform separate studies for regulatory authorities of different countries. However, due to the great divergence in requirements between the regions it was concluded to adopt a phased approach with the first step to harmonize the criteria on data requirements for waiving of the target animal batch safety test (TABST) for inactivated vaccines in regions where it is required.*
SECTION: 1		
Paragraph no.	**Comment and Rationale**	**Proposal for consideration**
1 & 1.1	*PETA* PETA urges VICH to take a stronger role in encouraging complete implementation of the TABST waiver and apply it to those batches that are produced for local as well as for international distribution.	Noted by the VICH Steering Committee. Matter to be considered by the local regulatory authorities.
1 & 1.1	*ICAPPP* The guideline relates specifically to waiving 'target' animal batch safety tests. However, as the guideline describes, non-target (laboratory) animals are also used in general batch safety tests of IVMPs in some VICH regions. The requirements for these additional safety tests have been almost completely removed in the EU (i.e. in the European Pharmacopeia) for the reasons outlined in section 1.1.1. ICAPPP urges	VICH intends to widen the scope in a stepwise approach, and work on this has been initiated Rationale for the phased approach is given in the "Introduction", see above

	VICH to clarify that the scope of the waiving can also apply to these non-target animal tests and to modify the text accordingly.	
1.1.1	*ICAPPP* Correct "Coopers" to "Cooper"	Done
1.1.1	*PETA* Given the large body of scientific data collected and analyzed by ECVAM's Advisory Group on Alternatives to Animal Testing in Immunobiologicals (with data on both live and inactivated vaccine batches) and the acknowledgement that TABST does not result in rejected vaccine batches, PETA recommends the expansion of this draft guidance to include both live and inactivated vaccines in the waiver of TABST. We recommend that the last sentence in section 1.1.1, paragraph 4, be replaced with, "The scope of the guidance document is valid for both inactivated as well as for live virus vaccines."	See above. Rationale for the phased approach is given in the "Introduction", see above
1.1.1	*ICAPPP* The ICAPPP encourages VICH to extend the scope of this guideline to live IVMPs as a matter of priority. This should be regardless of the success of a guideline for inactivated IVMPs for two reasons: • Firstly, TABSTs of live vaccines are of particular concern due to the welfare implications associated with the large injection volumes often involved (Cooper, 2008. Batch safety testing of veterinary vaccines – potential welfare implications of injection volumes. ATLA 36 685-694). • Secondly, implementation of the guideline for inactivated IVMPs may be hampered by the Ph.Eur. requirement for extraneous agents testing of inactivated viral vaccines to be combined with the TABST (see EMA/675371/2011 for further discussion). However, no such barriers exist for live vaccines and so implementation of a waiver of the TABST of live vaccines could be more widespread than for inactivated IVMPs. **Proposed change to wording of the last sentence of 1.1.1:** ~~It is foreseen that should this prove successful t~~ The scope ~~may~~ will be extended to live vaccines in the future	The proposed change has been discussed by the VICH Steering Committee and the scope will be extended in the future. This sentence has been removed to avoid updating the Guideline in the future.

SECTION: 2		
Paragraph no.	**Comment and Rationale**	**Proposal for consideration**
2.2.2.1	*PETA* As was found throughout ECVAM's large-scale study, use of Good Manufacturing Practices (GMP) have resulted in extremely reliable vaccine batch safety. The scientific need for TABST no longer exists as both GMP as well as sensitive analytical methods have replaced the use of animals for these purposes. The ethical imperative to remove routine TABST requirements remains.	No amendments necessary.
2.3.1.1	*O.I.E – Nigeria* "For those circumstances when *in vivo* batch tests are conducted in target animals for reasons other than the target animal safety test (e.g. potency tests) and these tests include the collection of safety information (e.g. on mortality), it is recommended that manufacturers use these tests to gain additional data of the safety of the vaccine in the target species." Comment on "(e.g. on mortality)" - *Adverse product reactions maybe due to handling, storage problems etc rather than quality issues during manufacturing. There should be a way to distinguish between the two.*	No amendments necessary.
2.3.1.2	*O.I.E - Congo* … informations disponibles sur le test de securité lot courant, j'estime que les données d'essai de 10 lots consecutifs n'est pas suffisant il serait mieux de tester 100 lots consecutifs sur une période échellonnée pour un résultat plus credible, le reste du texte est bon. (Information on 10 consecutive lots might not suffice, it might be better to increase the lot number to 100 over a certain period. This would make the result more credible.)	No amendments necessary. GL50 states "Without prejudice to the decision of the competent authority …", i.e. competent authorities can set the number of batches needed for a given vaccines.
	PETA The suggestion to use existing data for a TABST waiver should be emphasized and should appear in section 2.3.1.2 in addition to the introductory section (2.3.1).	This is covered by the wording used in the paragraph is "information available". No amendments necessary.
2.3.1.3	*O.I.E – Nigeria*	

	"Available pharmacovigilance data to demonstrate the consistent safe performance of the vaccine in the field should be provided using recent Periodic Safety Update Reports for the relevant time period." Comment on "available": *In many developing countries, pharmacovigilance system is not in place for veterinary products so such data will invariably be absent.*	The term "available" already implies that there might be no pharmacovigilance data available.
2.3.2	*PETA* In describing the procedure for a TABST waiver, VICH should again specify that retrospective analyses and data from previously-manufactured batches are preferred and that no new data are likely to be required.	No amendment necessary.
SECTION: 4		
Paragraph no.	**Comment and Rationale**	**Proposal for consideration**
Reference Coopers	ICAPPP An author name has been misspelt. Coopers should be corrected to Cooper.	Done