



National **V**eterinary
Assay **L**aboratory
Ministry of **A**griculture,
Forestry and **F**isheries

VICH General Principles and
Harmonization of Criteria to Waive TABST for
Vaccines for veterinary Use

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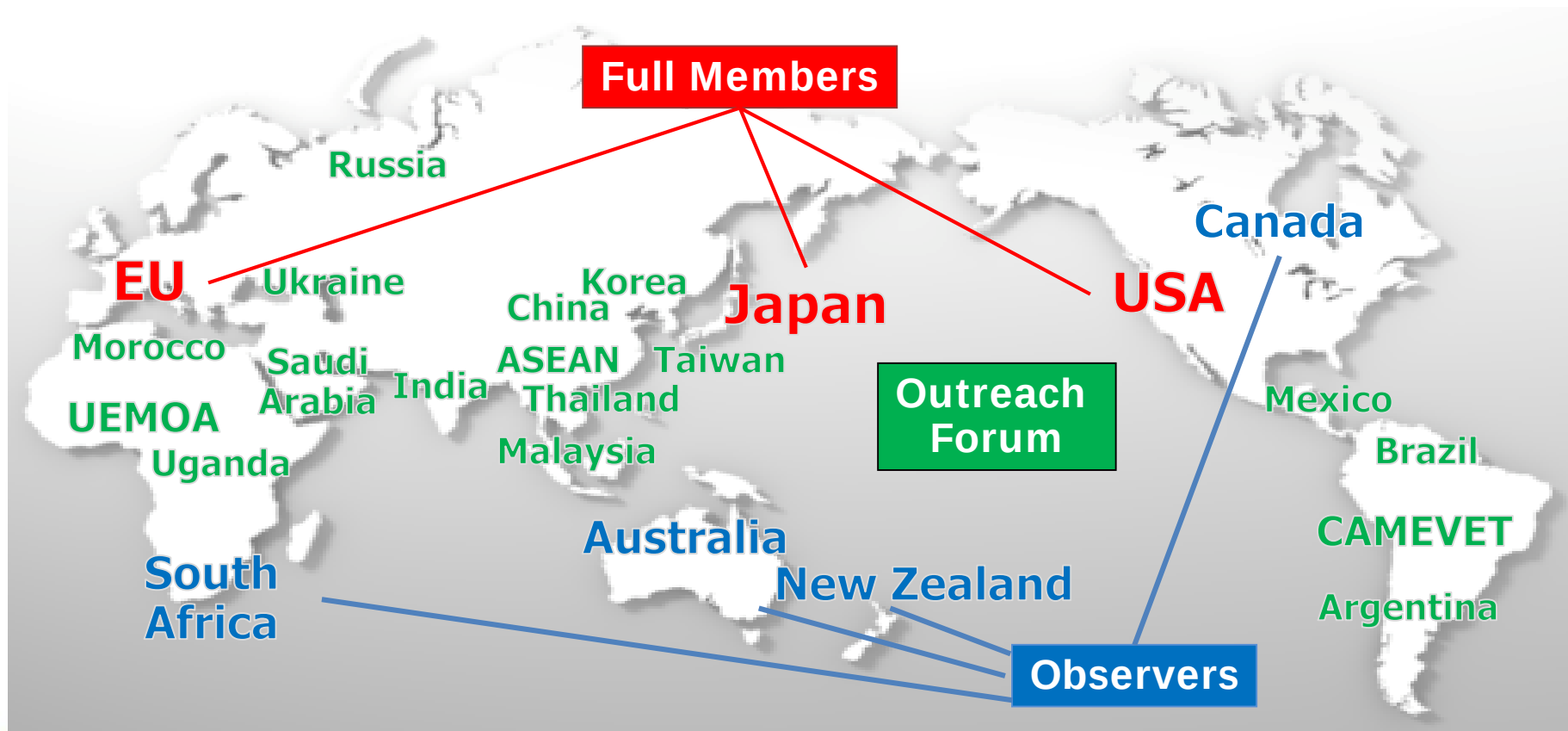


1. WHAT Is VICH?

VICH =



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



What is the role of VICH?



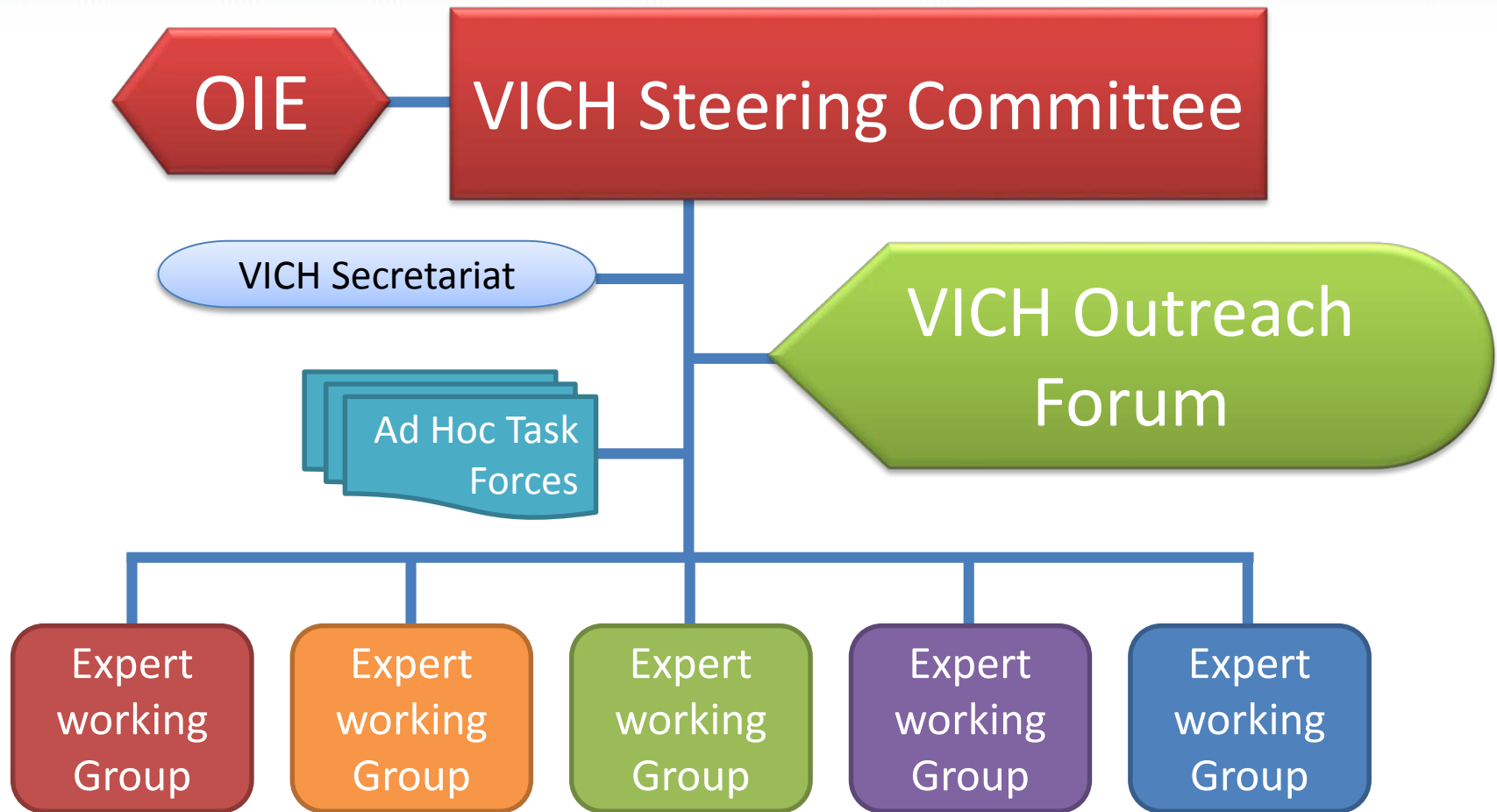
- To harmonise **technical** requirements for data necessary for registration
- To develop and implement VICH Guidelines
 - ✓ Study and testing methodology
 - Quality, safety and efficacy (including bioequivalence)
 - ✓ Post-marketing safety monitoring
 - Pharmacovigilance

VICH Guidelines



Category		GL numbers
Pharmaceuticals	Quality	1, 2, 3, 4, 5, 8, 10, 11, 17, 18(R)*, 39, 40, 45, 51
	Efficacy	7, 12, 13, 14, 15, 16, 19, 20, 21, 52
	Environmental Safety	6, 38
	Metabolism and Residue	46, 47, 48(R), 49(R)
	Toxicology	22, 23, 28, 31, 32, 33, 37
	Target Animal Safety	43
	Antimicrobial Safety	27, 36
Biologicals	Quality	34, 25, 26
	Target Animal Safety	41, 44, 50
General	GCP	9
	Pharmacovigilance	24, 29, 30, 35, 42
	Electronic file formats	53

VICH Structure



Steering Committee (SC)



Management of VICH

Status	Country/Region	Number of participants	
		Government	Industry
Full member	Japan	3	3
	EU	3	3
	USA	3	3
Observer	Australia	1	1
	New Zealand	1	1
	Canada	1	1
	South Africa	1	1



Expert Working Group (EWG)



- SC establishes EWG with a specific mandate
- Active EWGs



- Participants for each EWG

Country/Region	Number*	
	Government	Industry
Japan	1	1
EU	1	1
USA	1	1

*Each member may send one additional advisor when required.

Experts from observer or VOF countries may also be appointed or requested.

VICH guideline creation process



Step	Stage
1: SC agrees to start a topic and appoints an EWG 2: EWG elaborates a draft GL 3: SC approves the draft GL for public consultation	Drafting
4: Draft GL is circulated to stake holders and public 5: EWG prepares a revised GL 6: SC approves the revised GL	Fine-tuning
7: Final GL is circulated to authorities of VICH region 8: Final GL is implemented in VICH region	Publishing
9: SC monitors, maintains and reviews the GL	Maintenance

VICH -the History

Foundation & Expansion

1980's - 90's	First talks & Meetings on VMP harmonisation
1990 -	ICH (human medicines)
1994 - 95	OIE ad hoc Group on the VMP Harmonisation
1996 -	VICH
2011 -	VICH Outreach Forum (VOF)

International Meetings

33 Steering Committee meetings	Every 9 months
5 VOF meetings	
5 VICH Public Conferences	Every 3 to 5 years

2. WHY Participate in ?

Primary Benefits of VICH



- Use of Internationally harmonised guidelines to;
 - ✓ Ensure product quality, safety and efficacy
 - ✓ **Reduce animal testing and costs of development**
 - ✓ Accelerate the development and reviewing process
 - ✓ Increase availability of new VMPs
 - ✓ Contribute to animal/public health, environment
- Unique opportunity for;
 - ✓ Regulators and industry to discuss regulatory data requirements
 - ✓ Discussion between worldwide scientific experts

Secondary Benefits of VICH



- Better understanding of regulations and concerns in the other regions
- Opportunity to update regional regulations
- A basis for future global harmonisation of registration guidelines
- Opportunity to discuss emerging global issues and relevant science
- Contribute to the Global One Health approach

3. WAIVING TABST FOR VACCINES

What is TABST for IVMPs ?

- **TABST:** **Target Animal Batch Safety Test**; Safety test in target animals which is performed as a routine final product batch test for all immunological veterinary medicinal products (IVMPs) or a product group such as inactivated viral vaccines.
- **Target Animal:** The specific animal species, class and breed identified as the animal for which the IVMP is intended for use.

What is BST (batch safety test) ?

- Tests in laboratory and/or target animals
- For final product
- Considered as general safety tests
- Apply to a broad group of IVMPs
- should provide some assurance that the product will be safe in the target species

What is BST (batch safety test) ?

- BST should reveal
 - “abnormal local or systemic reactions”
(European Pharmacopoeia)
 - “unfavorable reactions attributable to the biological product ...”
(Title 9. United States Code of Federal Regulations)
 - “no abnormal changes”
(Minimum Requirements for Veterinary Biological Products under the Pharmaceutical Affairs Law in Japan).

Categories of BSTs

	Inactivated Vaccine	Live Vaccine
Laboratory Animals	Work in future?	Work in future?
Target Animals (TABST)	VICH-GL50*	Developing VICH-GL50**

*VICH-GL50

HARMONISATION OF CRITERIA TO WAIVE TARGET ANIMAL BATCH SAFETY TESTING FOR **INACTIVATED** VACCINES FOR VETERINARY USE

* * VICH-GL55

HARMONISATION OF CRITERIA TO WAIVE TARGET ANIMAL BATCH SAFETY TESTING FOR **LIVE** VACCINES FOR VETERINARY USE

Why BSTs for IVMPs has been necessary?

There are many concern about adverse reactions of IVMPs

Because of

In live vaccines

- Using live attenuated virus/bacteria,
→risk for reversion to virulent
- Using law material ; Cell, Embryonic Egg, Serum
→risk for contamination

In inactivated vaccines

- Using virulent(pathogenic) virus/bacteria,
→risk for insufficient inactivation
- Using Additives(ex;adjuvant)
→risk for local reaction

Are BSTs for IVMPs necessary?

Decreased concern about adverse reactions of IVMPs

by

Great improvements in manufacture of IVMPs

- Quality of raw materials
- Culture method
- Purification method
- Assay method



Great improvements of safety and quality of IVMPs
by introduction of GMP, GLP and Seed lot system

3Rs principle of VICH

- Statement of Principle for VICH - Alternatives to Animal Testing (VICH/07/038-Final; 18/09/2007)
- At its 19th meeting on 23-24 January 2007 in Washington D.C., USA, the VICH Steering Committee reiterated its ambition to minimise animal testing and specifically expressed its support for the 3Rs principle – replacement, refinement and reduction of animals in research.

Development of VICH GL50 - Harmonisation of criteria to waive Target Animal Batch Safety Testing (TABST) for inactivated vaccines for veterinary use

2008	Europe proposed to VICH to aim at harmonisation of general batch safety tests across the VICH regions Due to the great divergence in requirements between the regions it was concluded to adopt a phased approach and start with the TABST for inactivated vaccines
2009 - 2012	VICH Biologicals Quality Monitoring Expert Working Group – subgroup TABST elaborated the draft guideline
2012	VICH Steering Committee approved draft. Draft VICH GL50 underwent public consultation in the VICH regions, observer countries (Australia/New Zealand, Canada, South Africa) and associated members (OIE).
2013	Revised draft is approved by VICH and published, giving 1 year for implementation.
2014	VICH GL50 came into force

VICH-GL50

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- **2. GUIDELINE**
- ***2.1. Scope***
- This guideline is limited to the criteria on data requirements for waiving target animal batch safety tests (TABST) of inactivated immunological veterinary medicinal products.
- ***2.2. Regional Requirements***
- ***2.2.1. General batch safety testing***
- ***2.2.2. Other relevant requirements***
- ***2.2.2.1. Quality Systems***
- ***2.2.2.2. Pharmacovigilance***

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- ***2.3. Data requirements for waiving of target animal batch safety tests***
- ***2.3.1. Introduction***
- The TABST may be waived by the regulatory authority when a sufficient number of consecutive production batches have been produced and found to comply with the test, thus demonstrating consistency of the manufacturing process.

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- ***2.3.1.1. The characteristics of the product and its manufacture***
- The manufacturer should demonstrate that the product is manufactured following the quality principles, i.e. the product has been manufactured in a consistent and suitable manner.

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- ***2.3.1.2. Information available on the current batch safety test***
- The manufacturer should submit batch protocol data for **a sufficient number of consecutive batches** to demonstrate that safe and consistent production has been established.
- The conduct of the TABST shall be in accordance with the regional requirements in operation at the time when the tests were performed.

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- **2.3.1.3. Pharmacovigilance data**
- A pharmacovigilance system in accordance with the VICH Guidelines, where available, should have been in place over the period during which the batches for which data are submitted were on the market.

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- ***2.3.2. Procedure for waiving the target animal batch safety test***
- A report should provide an overall assessment of the consistency of the product's safety and would include taking into account the number of batches manufactured, the number of years the product has been on the market, the number of doses sold and the frequency and seriousness of any adverse reactions in the target species and any investigations into the likely causes of these events.

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- **3. GLOSSARY**
 - **Good Laboratory Practices (GLP)**
 - **Good Manufacturing Practices (GMP)**
 - **Immunological veterinary medicinal product (IVMP)**
 - **Production Batch**
 - **TABST**
 - **Target Animal**
- **4. REFERENCES**

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- Since the start of drafting this guideline, the requirements in Europe have changed. In 2012, the European Pharmacopoeia Commission has decided to progress from the possibility to waive the TABST to the implementation of its complete deletion as of 1st April 2013. This VICH guideline does not affect the current requirements in the EU.

How is GL50 implemented in Japan ?

- GL50 has been implemented in Japan from Feb. 2014.
- 1. Target IVMP
- The IVMP which is fulfilled all of following requirements.
 - (1) Inactivated vaccine for veterinary use.
 - (2) More than the last 10 batches were passed the TABST.
 - (3) Seed-lot product.
 - (4) Product which is not within the reexamination period.

How is GL50 implemented in Japan ?

- 2. Application Documents
- (1) Revised application dossier
- (2) Accompanying materials:
 - A. Manufacturing records (last 10 batches)
 - B. Batch release test data (last 10 batches)
 - C. Information on a defect batch (if any)
 - D. Revision history of the dossier
 - E. Rational explanation for waiving TABST
 - (from A-D)
 - F. Overall safety assessment (includ. PhV rec.)

Thank you very much for your attention.

