World Organisation for Animal Health

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WOAH Collaborative Centre Reports Activities 2024

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CENTRE INFORMATION

***Title of WOAH Collaborating Centre**	Diagnostic Test Validation Science in the Asia-Pacific Region
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***Name Director of Institute (Responsible Official):**	Dr Debbie Eagles
***Name (including Title and Position) of Head of the Collaborating Centre (WOAH Contact Point):**	Dr Axel Colling
***Name of the writer:**	Dr Axel Colling

TOR 1 AND 2: SERVICES PROVIDED

1. Activities as a centre of research, expertise, standardisation and dissemination of techniques within the remit of the mandate given by WOAH

Category	Title of activity	Scope
		The CC is an international scientific

Diagnostic test validation sccience (true)	Diagnostic test validation science	consortium made of the Australian Centre for Disease Preparedness (ACDP, CSIRO), Faculty of Veterinary and Agriculture Science, Uni Melbourne (FVAS) and EpiCentre at Massey University, NZ and experts from other national and international research organisations, which combines expertise in the development and validation of diagnostic test validation, epidemiology and disease control and prevention. The Centre's mission is to generate new knowledge and techniques that improve the use and interpretation of diagnostic tests used in human and animal health and to promote dissemination of that knowledge to the wider medical and veterinary communities.
1) Chapter 2.2.1.Validation of Ab detection tests (true)	1) Chapter 2.2.1.Validation of Ab detection tests	Chapter reviewed and updated with new WOAH validation standard 2021, updated references and cross-referenced with WOAH validation standard 2021
2) Chapter 2.2.2.Validation of Ag detection tests (true)	2) Chapter 2.2.2.Validation of Ag detection tests	Chapter reviewed and updated with new WOAH validation standard 2021, updated references and cross-referenced with WOAH validation standard 2021
3) Chapter 2.2.3.Validation of NAD tests (true)	3) Chapter 2.2.3.Validation of NAD tests	Chapter reviewed and updated with new WOAH validation standard 2021, updated references and cross-referenced with WOAH validation standard 2021
4) Chapter 2.2.4.Measurement uncertainty (true)	4) Chapter 2.2.4.Measurement uncertainty	Chapter reviewed and updated with new WOAH validation standard 2021, updated references and cross-referenced with WOAH validation standard 2021
5) Chapter 2.2.5. Statistical Methods for test validation (true)	5) Chapter 2.2.5. Statistical Methods for test validation	Chapter reviewed and updated with new WOAH validation standard 2021, updated references and cross-referenced with WOAH validation standard 2021
		Chapter reviewed and updated with

6) Chapter 2.2.6. Selection and use of reference samples and panels (true)	6) Chapter 2.2.6. Selection and use of reference samples and panels	new WOAH validation standard 2021, updated references and cross-referenced with WOAH validation standard 2021
7) Chapter 2.2.7. Validation of tests for wildlife (true)	7) Chapter 2.2.7. Validation of tests for wildlife	Chapter reviewed and updated with new WOAH validation standard 2021, updated references and cross-referenced with WOAH validation standard 2021
8) Chapter 2.2.8. Comparability studies (true)	8) Chapter 2.2.8. Comparability studies	Chapter reviewed and updated with new WOAH validation standard 2021, updated references and cross-referenced with WOAH validation standard 2021
9) Validation of diagnostic tests for diseases of aquatic animals (true)	9) Validation of diagnostic tests for diseases of aquatic animals	In preparation / under review
10) Validation of point of care tests (true)	10) Validation of point of care tests	In preparation
11) Validation of biomarkers (true)	11) Validation of biomarkers	In preparation
12)_Validation of eDNA and e RNA tests (true)	12)_Validation of eDNA and e RNA tests	Under investigation
13) Review and test and comment on new WOAH validation template (true)	13) Review and test and comment on new WOAH validation template	Completed
14) Verification of diagnostic tests (true)	14) Verification of diagnostic tests	Proposed for consideration (new)

TOR 3: HARMONISATION OF STANDARDS

2. Proposal or development of any procedure that will facilitate harmonisation of international regulations applicable to the main fucus area for which you were designated

Proposal title	Scope/Content	Applicable Area
Items under 1-14 in Table 1 are already or will be published in the Manual and therefore will facilitate the harmonisation of science-based validation methods	Development of science-based validation methods for diagnostic test	Laboratory Expertise Training and Education

3. In exercising your activities, have you identified any regulatory research needs* relevant for WOAH?

Yes

Research need 1

Please type the Research need: • There is a pressing need for continued research of science-based validation and verification of purpose-oriented application of modern diagnostic methods such as point-of-care tests, NGS, biomarker assays, e-dna and e-rna methods and multiplex technologies. • Increasing computational capacities allow for more complex and faster calculations from which more complex and realistic mathematical models benefit. • Understanding and applying the WOAH validation pathway is a challenge for test developer and continuous updating by training and workshops is a key activity to achieve a harmonized validation and verification approach based on WOAH best practice. • The WOAH validation, certification and registration pathway is under review and put on halt until 2026. The CC is a multidisciplinary, international consortium of experts who have the experience and knowledge to assist WOAH in reviewing and improving this unique process. In fact the CC has succesfully reviewed a number of validation dossiers for inclusion in the WOAH manual of diagnostic tests for the diagnosis of diseases of terrestrial and mammal animals. We would like to propose the development of procedures which would assist in the harmonisation of verification information available which would be added to the WOAH terrestrial manual. Experiences from the last two verification training courses in Vietnam could serve as a start.

Relevance for WOAH Disease Control, Capacity Building, Other, Standard Setting, Animal Welfare, Facilitation of international collaboration,

Relevance for the Code or Manual Code, Manual,

Field Epidemiology and Surveillance, Diagnostics, Vaccines, Therapeutics,

Animal Category Terrestrial, Aquatic,

Disease:

Kind of disease (Zoonosis, Transboundary diseases) Zoonosis, Transboundary diseases,

If any, please specify relevance for Codes or Manual, chapter and title

(e.g. Terrestrial Manual Chapter 2.3.5 - Minimum requirements for aseptic production in vaccine manufacture)

Answer: Terrestrial Manual Chapter existing chapters; 1.1.6, 2.2.1, 2.2.2., 2.2.3., 2.2.4., 2.2.5., 2.2.6., 2.2.7., 2.2.8., new chapters # Validation of point of care tests, # Validation of biomarkers, # validation of eDNA and e RNA tests, Validation of NGS, Verification of diagnostic tests; Aquatic Manual Chapter: # Validation of diagnostic tests for diseases of aquatic animals; Review, test and comment on new WOAH validation template (will facilitate a more efficient use of valdation templates by kit producer submitter and subsequent assessment by expert group

Notes:

Answer: Diagnostic test validation is a key element in the effective detection and control of infectious animal diseases. etection and control of infectious animal diseases. The quality of diagnostic test validation studies for infectious diseases of animals has continued to improve owing to international educational efforts, the use of design and reporting standards to guide researchers and test developers, and the acceptance of the use of latent class models for statistical analysis of test validation data, when the true infection status of animals that are sampled in a validation study is unknown. The primary goal of these chapters (new and old) is to provide an up-to-date compilation of the relevant standards (OIE and non-OIE) and guidance documents for all stages of diagnostic test (traditional, e.g. ELISA, PCR and modern, e.g. NGS, biomarkers, eDNA/eRNA etc. validation and proficiency testing, including design, analysis as well as clear, complete and transparent reporting of validation studies in the peer-reviewed literature. Examples and case studies were used to help to guide readers in practical aspects of the validation process. During the review of existing and edition of new chapters particular attention and was given to the WOAH special issue "Diagnostic test validation science" Vol. 40 (1), 2021 by providing frequent references where applicable.

4. Did your Collaborating Centre maintain a network with other WOAH Collaborating Centres (CC), Reference Laboratories (RL), or organisations designated for the same specialty, to coordinate scientific and technical studies?

Yes

Name of WOAH CC/RL/other organisation(s)	Location	Region of networking Centre	Purpose
Sustainable Animal Health Laboratory Network in Southeast Asia and the Pacific through targeted technical laboratory twinning engagement (Laboratory Network Twinning).	Not defined	Asia y el Pacífico	Twinning laboratory arrangements supported by Australian Department of Foreign Affairs and Trade (DFAT), for the purpose of strengthening the capacity and creating a Sustainable Animal Health Laboratory Network in Southeast Asia and the Pacific through targeted technical laboratory twinning engagement (Laboratory Network Twinning) for review.
Several countries in Southeast Asia		Asia y el Pacífico	Hosting of visiting scientists,

(focus).	Not defined		scholars and fellows, through various funding sources.
The Asia Pacific consortium of Veterinary Epidemiology (APCOVE).	Not defined	Asia y el Pacífico	Support of APCOVE Fellows.
The ASEAN laboratory technical advisory group (labtag).	Not defined	Asia y el Pacífico	Provision of technical advice.
Pacific Heads of Veterinary and Animal Production services (PHOVAPS) and the secretariat (SPC) on laboratory and diagnostics.	Not defined	Asia y el Pacífico	Technical support.

TOR 4 AND 5: NETWORKING AND COLLABORATION

5. Did your Collaborating Centre maintain a network with other WOAH Collaborating Centres, Reference laboratories, or organisations in other disciplines, to coordinate scientific and technical studies?

Yes

Name of WOAH CC/RL/other organisation(s)	Location	Region of networking Centre	Purpose
Australian Government HPAI Taskforce Department of Agriculture, Fisheries and Forestry Agriculture House, 70 Canberra ACT 2601 Australia (AI)	Canberra, Australia	Asia and Pacific	Developing validation methods for new diagnostic platforms such as such as point-of-care tests for AI.
AVR, Agriculture Victoria Department of Jobs, Precincts and Regions Adjunct Professor in Animal and Veterinary Bioscience, La Trobe University AgriBio (AI)	Victoria, Australia	Asia and Pacific	Developing validation methods for new diagnostic platforms such as such as point-of-care tests for AI. Validation/verification of non-structural FMD ELISA for ovine and caprine sera.
	Queensland,	Asia and Pacific	Developing and validation of point-of-care tests for early

BSL Queensland, Australia (ASF)	Australia		detection of ASF in pigs.
chool of Veterinary Science (SVS) and School of Environment (SENV) The University of Queensland (HeV)	Queensland, Australia	Asia and Pacific	Developing and validation of point-of-care tests for early detection of Hendra virus in horses.
University of Canberra	Canberra, Australia	Asia and Pacific	Validation of e-DNA methods.
Faculty of Veterinary and Agricultural Sciences (FVAS) The University of Melbourne Parkville, Victoria 3010, Australia Tel: +61 3 9035 4114 Fax: +61 3 8344 7374 mark.stevenson1@unimelb.edu.au URL:http://fvas.unimelb.edu.au	Melbourne, Autralia	Africa Americas Asia and Pacific Europe Middle East	Quantitative and spatial epidemiology, modelling of infectious diseases and analysis of complex datasets including the use and development of latent class models to validate diagnostics for a range of endemic pathogens.
EpiCentre, Institute of Veterinary and Biomedical Sciences (called EpiCentre throughout the document) Massey University Private Bag 11-222 Palmerston North 4412, New Zealand Tel: +64 6 350 5270 Fax: +64 6 355 7955 E.Vallee@massey.ac.nz URL:http://epicentre.massey.ac.nz	Palmerston North, NZL	Africa Americas Asia and Pacific Europe Middle East	Veterinary epidemiology, statistics and test validation.
Atlantic Veterinary College, University of Prince Edward Island 50 University Ave. Charlottetown, Prince Edward Island, C1A 4P3 iagardner@upei.ca; Mobile: 902-394-6823	Prince Edward Island, Canada	Africa Americas Asia and Pacific Europe Middle East	Veterinary aquatic epidemiology, statistics and test validation. Review of chapters 1.1.6., 2.2.1.-2.2.8. Produce a new chapter titled: “Diagnostic validation of point-of-care (PoC) tests for WOAH-listed viral diseases using field samples” and submitt to WOAH for review. Review of WOAH’s validation, certification and registration process.

UC Irvine Department of Statistics Irvine 92697, California, USA 2232 Bren Hall wjohnson@uci.edu Location Irvine, California, USA	Irvine, California, USA	Africa Americas Asia and Pacific Europe Middle East	Bayesian Latent Class models applicable for test validation of diagnostic tests in wildlife. Bayesian latent class models and validation standard.
School of Animal and Veterinary Sciences The University of Adelaide, Roseworthy Campus, Roseworthy, South Australia, 5371, Australia +61-8-8313 1245 charles.caraguel@adelaide.edu.au	Adelaide, Australia	Asia and Pacific	Veterinary and aquatic epidemiology, statistics and test validation
WOAH Headquarters	Paris, France	Africa Americas Asia and Pacific Europe Middle East	Discuss review of validation chapters in terrestrial manual and WOAH process for validation, certification and registration of diagnostic kits Review WOAH validation template including a practice run with Bluetongue Ref labs using molecular data
IAEA Headquarters and Seibersdorf laboratory	Vienna/Seibersdorf, Austria	Africa Americas Asia and Pacific Europe Middle East	Workshops on diagnostic test validation and result interpretation - Production of guidelines and training for verification of test performance - Production of guidelines and training for production of secondary standards for molecular and serological methods - Review of chapter 2.2.1..

TOR 6: EXPERT CONSULTANTS

6. Did your Collaborating Centre place expert consultants at the disposal of WOAH?

Yes

Name of expert	Kind of consultancy	Subject
Axel Colling Nagendra Singanallur Tristan Reid Carryl Waugh		

Jianning Wang Matthew Neave Andrea Certoma Kim Newberry Shafi Sahibzada Dwane O'Brien Vilna Voslo James Watson Kristen McAuley Mark Ford Megan Poon Carlie Soul Andrew Keyburn Liza Cabuang Monica Reising Nick Mody Lenny Izzard David Williams John Hoad	Review chapters 2.2.1.-2.2.8. and produce drafts for new ones (POC, NGS, biomarker, edna/erna)	See 1 and 2 Service provided

TOR 7: SCIENTIFIC AND TECHNICAL TRAINING

7. Did your Collaborating Centre provide advice/services to requests from Members in your main focus area?

Yes

Evaluation of a POC for HeV, Lyndal Hulse, Qld, Australia, benefit to Australian equine vet practitioners

Evaluation of multiplex POCT PCR assay for PCV2, ASF and CSF EMAI, NSW Peter Kirkland (ongoing) benefit to early detection of exotic disease incursions

Evaluation and comparison of 7 serological tests for Brucellosis using BLCM, Elaine Dorneles, Universidade Federal de Lavras, Brazil (ongoing), expected benefit will be a more efficient use of serological tests for the effective detection of infected animals

Validation of biomarkers for Paratuberculosis, Cameron Stewart, Health + Biosecurity, ACDP, expected benefit will be a more efficient use of serological tests for the effective detection of infected animals

Validation of biomarkers for M. bovis, Cameron Stewart, Health + Biosecurity, ACDP, expected benefit will be a more efficient use of serological tests for the effective detection of infected animals

Validation of a new CSFV (Classical Swine Fever Virus) Antigen ELISA Kit and are seeking validation to ensure its accuracy and reliability, Ishaan Bhandari CEO of Mizala Biovet, India. Expected benefit will be a more efficient use of diagnostic tests for the effective detection of infected animals

LOD determination for RRT-PCR for AIV and referring to chapters 1.1.6. and 2.2.3. in WOAH's Terrestrial Manual, Etienne van Zyl, South Africa. Expected benefit will be a more efficient use of limit of detection experiments in validation studies.

8. Did your Collaborating Centre provide scientific and technical training, within the remit of the mandate given by WOAH, to personnel from WOAH Members?

Yes

a) Technical visit : 3

b) Seminars : 1

c) Hands-on training courses: 3

d) Internships (>1 month) : 6

Type of technical training provided (a, b, c or d)	Content	Country of origin of the expert(s) provided with training	No. participants from the corresponding country
A	A+ C, Preparation of quality assured positive control material for progressive monitoring of diagnostic assays for FMD and LSD (PCR and ELISA)	Indonesia	22
A	A+C, Verification training course: theory based. 1 week course at RAH06. Participants included 6 from Ho Chi Mihn, RAH06 and 2 from Hanoi, NCVD	Vietnam	8
A	A+C, Verification training course: practical based. 2-week training course to produce verification report for ASF IFAT at RAH06. Participants included 7 from Ho Chi Mihn, RAH06 and 3 from Hanoi, NCVD.	Vietnam	10
D	Internships provide last year vet students with introduction and overview of WOAH test validation pathway incl practical examples and exercises	Australia	6
B	Introduction to principles of test validation for biomarker POC assay for early detection of Paratuberculosis in cattle	Australia	25

TOR 8: SCIENTIFIC MEETINGS

9. Did your Collaborating Centre organise or participate in the organisation of scientific meetings related to your main focus area on behalf of WOAH?

Yes

National/International	Title of event	Co-organiser	Date	Location	No. Participants
	"Introduction to test validation" and "How				

Internationally	to select a kit?" Diagnostics presentation: 4th Regional Meeting for WOAH Reference Centres in Asia Pacific, 18+19 July 2024, Hybrid	WOAH, regional office Japan	2024-07-18	Japan	60
Internationally	"Submission of samples to WOAH reference labs?" Diagnostics presentation: 4th Regional Meeting for WOAH Reference Centres in Asia Pacific, 19 July 2024, Hybrid	WOAH, regional office Japan	2024-07-19	Japan	60

TOR 9: DATA AND INFORMATION DISSEMINATION

10. Publication and dissemination of any information within the remit of the mandate given by WOAH that may be useful to Members of WOAH

a) Articles published in peer-reviewed journals:

2

In preparation!

Proof of Concept: Comparative Assessment of QDAF Point of Care Molecular Tests (LAMP and qPCR) for Lumpy Skin Disease, Kelly Stanger (in preparation)

Validation of two commercial FMD NSP ELISA assays for use in small ruminants (sheep and goats) Nagendra Singanallur Balasubramanian (in preparation)

b) International conferences:

2

WOAH Veterinary Laboratories Focal Point Meeting 16-18 July (face to face 16-17 July, hybrid 18 July) back to back with WOAH Reference Centres Meeting on 19 July (hybrid meeting). https://rr.asia.woah.org/

FAO-EuFMD Open Session of the EuFMD Standing Technical Committee, 29-31 October 2024, Alcalá de Henares, Spain

c) National conferences:

4

Subcommittee of Animal Health Laboratory Standards (SCAHLS), Discussion of a generic diagnostic test validation and approval process and specific requirements for validation and approval of POC tests followed by establishing a national work group.

Emerging animal diseases (EAD) symposium 30-31 October 2024 (~180 participants)

Australian Association for Veterinary Laboratory Diagnosticians, 21 & 22 November 2024, ACDP, Geelong, Australia

30 years Hendra conference Development and validation of a serological DIVA ELISA for the diagnosis of Hendra virus infected and vaccinated horses 8-11 December 2024, ACDP, Geelong, Australia (Hendra Virus International Conference 2024)

d) Other (Provide website address or link to appropriate information):
6
Webpages for OIE Collaborative Centre for Test Validation Science South Pacific:

https://www.woah.org/fileadmin/Home/eng/Health_standards/tahm/2.02.00_INTRODUCTION.pdf authors (woah.org)

http://fvas.unimelb.edu.au/research/research-centres/oie-dx/contact - Webpage for epidemiology teaching tools, including Beta buster, sample size estimator and other tools for diagnostic test evaluation studies.

http://fvas.unimelb.edu.au/research/research-areas/veterinary-epidemiology-melbourne/resources epiR statistical library for the R statistical package, including functions for epidemiological calculations such as those required for or diagnostic test evaluation studies: https://cran.r-project.org/web/packages/epiR/index.html

http://252s-weblive.vet.unimelb.edu.au:3838/users/epi/epi.predvals/

http://www.massey.ac.nz/massey/learning/departments/centres-research/epicentre/post-graduate-study/teaching-tools/teaching-tools_home.cfm

11. What have you done in the past year to advance your area of focus, e.g. updated technology?
The CC has initiated the preparation of new validation chapters such as for diagnosis of infectious diseases of aquatic animals, POC tests, biomarkers and e-dna and e-rna.

Two staff participated in 0ne week workshop about use of BLCM in R at ISVEE conference in Sydney 11-15 November17th International Symposium on Veterinary Epidemiology and Economics | 11 - 15 November 2024

Current discovery HTS workflows are not standardised through quality assured frameworks and rigorous controls have not been developed. These shortcomings are leading to claims of pathogen discovery that are questionable, potentially impacting on claims of freedom from exotic pathogens, market access and trade.The combination of reduced HTS costs and a significant surge in demand underscores the need to develop standardised workflows to enable discovery HTS to operate within a quality assured framework, which is an objective of the CC (see also 2016 (van Borm et al 2016). These data will be used to integrate spatio-temporal assessments incl wind dispersion to better understand the unfolding of an outbreak and develop suitable biosecurity measures to control it. The findings from this project are crucial for confidently interpreting infectious agent (including pathogen) hits in HTS data. The project's focus includes guaranteeing freedom from laboratory contamination (that can lead to misinterpretation of results), maintaining an appropriate level of sensitivity, and ensuring the use of a suitable kit and workflow for a diverse range of pathogens. Accurate interpretation of HTS results is vital to prevent trade implications and safeguard specific disease-free status.

Since 2021 ACDP has been developing advanced analytics tools that facilitate mining of diagnostic testing data to assist in diagnostic test validation. Utilising the Elastic® platform, ACDP is now able to seamlessly interrogate over 15 years of diagnostic test results and associated metadata and perform stratified analyses that allow data-driven assessments of diagnostic test performance. This has been particularly effective for estimating diagnostic specificity of assays for exotic diseases in the relevant target population of interest where there is a known, demonstrated history of disease freedom. For example, ACDP has used this system to interrogate thousands of historical

records of serological testing for Foot-and-mouth disease in Australian ruminants to generate highly relevant and accurate DSp estimates, which have subsequently been used to inform test interpretation. Furthermore, the system has been used to perform nuanced analyses such as assessing variations in test performance between sample types. Such analyses performed during the initial stages of Australia's 2022 Japanese encephalitis outbreak helped identify the most appropriate sample types for diagnostic testing, while analyses of Hendra virus testing results have provided deeper insights into the relative sensitivities of various assays. ACDP is continuing to explore new opportunities and novel approaches to test validation using this Big Data approach, including potential for real-time computation of diagnostic test performance characteristics that incorporates new data from testing as it becomes available.

12. Additional comments regarding your report:
In 2024 the CC focussed on the finalization of pending and preparation of new validation chapters in the terrestrial and aquatic manual.