World Organisation for Animal Health

Patrizia Cavadini - - ITALY

WOAH Reference Laboratory Reports Activities 2024

This report has been submitted: 24 janvier 2025 11:18

LABORATORY INFORMATION

***Name of disease (or topic) for which you are a designated WOAH Reference Laboratory:**	Rabbit haemorrhagic disease
***Address of laboratory:**	Via Antonio Bianchi 7/9, 25124 Brescia (Italy)
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Website:	https://www.izsler.it/chi-siamo/per-chi-e-con-chi-lavoriamo/centri-direferenza/internazionali/oie-reference-laboratory-for-rabbit-haemorrhagic-disease/
***Name (including Title) of Head of Laboratory (Responsible Official):**	Dr. Giorgio Varisco (DVM, General Director of IZSLER)
***Name (including Title and Position) of WOAH Reference Expert:**	Dr. Patrizia Cavadini (PhD)
***Which of the following defines your laboratory? Check all that apply:**	Governmental

TOR1: DIAGNOSTIC METHODS

1. Did your laboratory perform diagnostic tests for the specified disease/topic for purposes such as disease diagnosis, screening of animals for export, surveillance, etc.? (Not for quality control, proficiency testing or staff training)

Yes

Diagnostic Test	Indicated in WOAH Manual (Yes/No)	Total number of test performed last year	
Indirect diagnostic tests		Nationally	Internationally
RHDV Competition ELISA	Yes	530	60
RHDV2 Competition ELISA	Yes	645	1081
EBHSV Competition ELISA	Yes	563	0
RHDV IgG Isotype ELISA	Yes	4	

			919
RHDV IgM Isotype ELISA	Yes	11	2
RHDV IgA Isotype ELISA	Yes	11	2
Direct diagnostic tests		Nationally	Internationally
RT-PCR EBHSV	Yes	4	0
Genome sequencing	No	33	0
RT-PCR RHDV/RHDV2	Yes	20	1
RHDVs/EBHSV Sandwich ELISA	Yes	386	1
RHDVs Sandwich ELISA	Yes	84	0
EBHSV Sandwich ELISA	Yes	77	0
RT-PCR lagovirus	Yes	126	0

TOR2: REFERENCE MATERIAL

2. Did your laboratory produce or supply imported standard reference reagents officially recognised by WOAH?

No

3. Did your laboratory supply standard reference reagents (nonWOAH-approved) and/or other diagnostic reagents to WOAH Members?

Yes

Type of reagent available	Related diagnostic test	Produced/ provide	Amount supplied nationally (ml, mg)	Amount supplied internationally (ml, mg)	No. of recipient WOAH Member Countries	Country of recipients
RHDV serological kit	cELISA	Produced	1 kit	13 kits	5	AUSTRALIA, CANADA, INDONESIA, SINGAPORE, UNITED STATES OF AMERICA,
EBHSV serological kit	cELISA	Produced	3 kits	1 kit	1	POLAND,
RHDV2 serological kit	cELISA	Produced	1 kit	14 kits	6	AUSTRALIA, CANADA, FRANCE, POLAND, SINGAPORE, UNITED STATES OF AMERICA,
RHDV/RHDV2 Differential kit	MAbs sandwich ELISA	Produced	0	2 kits	1	POLAND,
RHDV/EBHSV virological ki	MAbs sandwich ELISA	Produced	14 kits	13 kits	3	GERMANY, POLAND, UNITED STATES OF

						AMERICA,
Reference positive and negative materials (liver homogenates)	ELISA and RT - PCR	Provided	0	1 panel	1	UNITED STATES OF AMERICA,
MAbs specific to RHDV or RHDV2	In vivo escape mutants	Produced	0	3ML	1	AUSTRALIA,

4. Did your laboratory produce vaccines?

Yes

5. Did your laboratory supply vaccines to WOAH Members?

No

TOR3: NEW PROCEDURES

6. Did your laboratory develop new diagnostic methods for the designated pathogen or disease?

No

7. Did your laboratory validate diagnostic methods according to WOAH Standards for the designated pathogen or disease?

No

8. Did your laboratory develop new vaccines for the designated pathogen or disease?

No

9. Did your laboratory validate vaccines according to WOAH Standards for the designated pathogen or disease?

No

TOR4: DIAGNOSTIC TESTING FACILITIES

10. Did your laboratory carry out diagnostic testing for other WOAH Members?

Yes

Name of WOAH Member Country seeking assistance	Date	Which diagnostic test used	No. samples received for provision of diagnostic support	No. samples received for provision of confirmatory diagnoses
COSTA RICA	2024-07-16	cELISA RHDV, cELISA RHDV2	2	0
FRANCE	2024-03-14	cELISA RHDV2	108	0
JAPAN	2024-11-16	cELISA RHDV, cELISA RHDV2	1	0
SPAIN	2024-04-11	cELISA RHDV2, ELISA IgG RHDV2	878	0
HONG KONG	2024-12-26	cELISA RHDV, cELISA RHDV2, ELISA IgG RHDV, ELISA IgA RHDV, ELISA IgM RHDV	1	0
UNITED STATES OF AMERICA	2024-12-15	cELISA RHDV, cELISA RHDV2	51	0

NEW CALEDONIA	2024-10-17	cELISA RHDV, cELISA RHDV2, ELISA IgG RHDV, ELISA IgA RHDV, ELISA IgM RHDV	1	0
THE NETHERLANDS	2024-12-23	cELISA RHDV2, ELISA IgG RHDV	35	0
SWEDEN	2024-10-16	cELISA RHDV, cELISA RHDV2, ELISA IgG RHDV	4	0

11. Did your laboratory provide expert advice in technical consultancies on the request of an WOAH Member?

Yes

Name of the WOAH Member Country receiving a technical consultancy	Purpose	How the advice was provided
ARGENTINA	Provision of the protocol for RNA extraction and RT-PCR amplification of lagoviruses	Emails
SOUTH AFRICA	Scientific opinion regardind the ability of Trizol reagent to incativate RHDV2.	Emails
ALGERIA	Consulting on the development of a surveillance plan for lagomorph diseases in Algeria	Emails

TOR5: COLLABORATIVE SCIENTIFIC AND TECHNICAL STUDIES

12. Did your laboratory participate in international scientific studies in collaboration with WOAH Members other than the own?

Yes

Title of the study	Duration	Purpose of the study	Partners (Institutions)	WOAH Member Countries involved other than your country
Study of the health status of wild and domestic lagomorphs in the Iberian Peninsula from a One Health approach (Iber-LagoHealth)	3 years	To advance the knowledge of health status of wild and domestic lagomorphs in the Iberian Peninsula from a One Health perspective	1.CIBIO/InBIO-UP Portugal 2.Universidad de Córdoba Spain3. Universidad Autonoma de Barcelona	PORTUGAL SPAIN
Enfermedades infecciosas y parasitarias de una especie invasora, la liebre europea (Lepus europaeus), a lo largo de un gradiente ambiental y de usos del suelo en Argentina	2 years	To study the health status of brown hare, an invasive species, in Argentina	El Instituto de las Ciencias de la Tierra y Ambientales de La Pampa (INCITAP),UniversidaAutónoma de Madrid. Universidad de Córdoba (España). Universidade Veterinaria de Vienna	ARGENTINA

Central				
European partnership on animal health and welfare (EUPAHW)	3 years	SOA12: BETO - Better tools for diagnosis of infectious diseases. Task 2: Faster, closer and across: Tools for early and rapid detection, as well as screening and monitoring	ANSES, CIRAD, CSIC, DEFR, DTU, EULS, FLI, INIAV, INRAE, ISS, IZSLER, IZSLT, IZS-Teramo, NVI, PIWET, RIVM, Ruokavirasto, Sciensano, SLA, SLU, SSI, SURREY, SVA, UAB, UCPH, UGent, UNIPD, UNITO, WR	BELGIUM DENMARK ESTONIA FINLAND FRANCE GEORGIA GERMANY ITALY NORWAY POLAND PORTUGAL SPAIN THE NETHERLANDS UNITED KINGDOM
Scientific collaboration aimed at a PhD thesis by an Algerian student.	2 years	Diagnosis of lagomorph diseases, with particular emphasis on viral diseases.	ENSV (Alger)	ALGERIA
Scientific collaboration aimed at a PhD thesis by an Spanish student.	2 years	Pathological and serological insights into Lagovirus diseases dynamics in the European brown hare (Lepus europaeus) in the northeast of the Iberian Peninsula	Universidad Autonoma de Barcelona	SPAIN
Scientific collaboration	2 years	Testing Norwegian hares for lagovirus infection (serological and virological approach)	Norwegian Veterinary Institute	NORWAY
Collaboration project between Cuba and Italy	6 months	1.- To characterise by electron microscopy the VLPs produced by the yeast Komagataella pastoris (Pichia pastoris) developed at the CIclassical RHDV and RHDV2 reference strains infection and disease development in rabbits vaccinated with VLPs and challenged against reference strains of classical RHDV and RHDV2.	Centre for Genetic Engineering and Biotechnology (CIGB, Havana, Cuba)	CUBA
JOINT LABORATORY ON RABBIT HEMORRHAGIC DISEASE	Not defined	Promote the cooperation of Joint Laboratory on genetic and antigenic variability and evolutionary trends of Rabbit hemorrhagic disease viruses: basis for	JIANGSU ACADEMY OF AGRICULTURAL SCIENCES (JAAS)	CHINA (PEOPLE'S REP. OF)

		the development of improved diagnostic methods and new subunit vaccines		

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

No

TOR6: EPIZOOLOGICAL DATA

14. Did your Laboratory collect epidemiological data relevant to international disease control?

Yes

If the answer is yes, please provide details of the data collected:
We analyse the genomic and antigenic characteristics of the different pathogenic and non-pathogenic lagovirus strains identified in rabbits, hares and cottontails, mainly in European countries but also in some other parts of the world. The studies are aimed at achieving data on the presence and distribution of lagoviruses strains infecting lagomorph species as target species or even as spillover hosts.

15. Did your laboratory disseminate epidemiological data that had been processed and analysed?

Yes

If the answer is yes, please provide details of the data collected:
Epidemiological data obtained from the examination of samples received from member countries are usually organized and elaborated in communications at meetings and conferences and for the preparation of scientific papers. Indeed, participation in international projects and established collaborations, also characterized by the exchange of reagents and materials, contribute to acquiring and exchanging data and information.

16. What method of dissemination of information is most often used by your laboratory? (Indicate in the appropriate box the number by category and list the details in the box)

a) Articles published in peer-reviewed journals:

5

1. Almeida T, Lopes AM, Estruch J, Rouco C, Cavadini P, Neimanis A, Gavier-Widén D, Le Gall-Reculé G, Velarde R, Abrantes J. A new HaCV-EBHSV recombinant lagovirus circulating in European brown hares (Lepus europaeus) from Catalonia, Spain. Sci Rep. 2024 Feb 4;14(1):2872. doi: 10.1038/s41598-024-53201-1. PMID: 38311618; PMCID: PMC10838927.

2. Riva F, Draghi S, Inglesi A, Filipe J, Cremonesi P, Lavazza A, Cavadini P,

Vigo D, Agradi S, Menchetti L, Di Giancamillo A, Aidos L, Modina SC, Fehri NE, Pastorelli G, Serra V, Balzaretti CM, Castrica M, Severgnini M, Brecchia G, Curone G. Bovine Colostrum Supplementation in Rabbit Diet Modulates Gene Expression of Cytokines, Gut-Vascular Barrier, and Red-Ox-Related Molecules in the Gut Wall. Animals (Basel). 2024 Mar 4;14(5):800. doi: 10.3390/ani14050800. PMID: 38473185; PMCID: PMC10930591.

3. Abrantes J, Bertagnoli S, Cavadini P, Esteves PJ, Gavier-Widén D, Hall RN, Lavazza A, Le Gall-Reculé G, Mahar JE, Marchandeau S, Lopes AM. Comment on Shah et al. Genetic Characteristics and Phylogeographic Dynamics of Lagoviruses, 1988-2021. Viruses 2023, 15, 815. Viruses. 2024 Jun 7;16(6):927. doi: 10.3390/v16060927. PMID: 38932219; PMCID: PMC11209181.

4. Urbinati C, Pezzoni G, Cavadini P, Giovanni VD, Capucci L, Rusnati M. Validation of plasmonic-based biosensors for rapid and in depth characterization of monoclonal antibodies directed against rabbit haemorrhagic and foot-and-mouth disease viruses in biological samples. Methods. 2024 Dec 9;234:85-92. doi: 10.1016/j.ymeth.2024.12.003. Epub ahead of print. PMID: 39653303.

5. Patrizia C, Vismarra A, Merzoni F, Di Giovanni V, Boniotti MB, Capucci L, Lavazza A. Two decades of occurrence of non-pathogenic rabbit lagoviruses in Italy and their genomic characterization. Sci Rep. 2024 Nov 25;14(1):29234. doi: 10.1038/s41598-024-79670-y. PMID: 39587141; PMCID: PMC11589700.

b) International conferences:

4

1. Cavadini° P, Vismarra° A, Merzoni° F, Mugetti° D, Di_Giovanni° V, Boniotti° B, Schiavitto M, Lavazza° A, Capucci° L
Occurrence and characterization of rabbit calicivirus (RCV) strains in Italy over 20 years
13th World rabbit congress : 2-4 October, 2024, Tarragona, Spain : book of abstracts . - [s.l. : s.n. , 2024] . - p 557-560
2. Defilippo° F, Merzoni° F, Di_Giovanni° V, Lavazza° A, Cavadini° P
Role of filies in the transmission of RHDV2 : a study of contamination in Lucilla sericata (diptera : callipohoridae)
13th World rabbit congress : 2-4 October, 2024, Tarragona, Spain : book of abstracts . - [s.l. : s.n. , 2024] . - p 569-512.
3. Di Giovanni° V, Bertasio° C, Lavazza° A, Capucci° L, Cavadini° P
Occurrence and characterization of RHDVA strains in Italy over 10 years
Ital J Food Safety 13 s1 (2024) . - p 82-83.
Congress of the European Association of Veterinary Laboratory Diagnosticians (EAVLD) (7th : Padua, Italy : 21st-23rd October 2024)
4. Di_Giovanni° V, Gratta F, Lavazza° A, Cavadini° P, Capucci° L
Passive protection from RHD : The role of immunoglobulins in milk
13th World rabbit congress : 2-4 October, 2024, Tarragona, Spain : book of abstracts . - [s.l. : s.n. , 2024] . - p 561-564.

c) National conferences:

1

Webinar organized by the National Reference Center entitled: "UPDATES ON VIRAL DISEASES OF LAGOMORPHS" March 19, 2024.
Speakers:
-Recombination as an evolutionary phenomenon of lagoviruses (P. Cavadini);

-Immunity of maternal origin for RHDV (V. Di Giovanni);
-Effects in the rabbit sector resulting from the application of the DLGS 136/2022 Modes of control of RHD (A. Lavazza);

d) Other (Provide website address or link to appropriate information):

TOR7: SCIENTIFIC AND TECHNICAL TRAINING

17. Did your laboratory provide scientific and technical training to laboratory personnel from other WOAH Members?

Yes

a) Technical visit : 2

b) Seminars : 0

c) Hands-on training courses: 0

d) Internships (>1 month) 0

Type of technical training provided (a, b, c or d)	Country of origin of the expert(s) provided with training	No. participants from the corresponding country
A	INDONESIA	1
A	CHINA (PEOPLE'S REP. OF)	11

TOR8: QUALITY ASSURANCE

18. Does your laboratory have a Quality Management System?

Yes

Quality management system adopted	Certificate scan (PDF, JPG, PNG format)	
UNI CEI ENISO/IEC 1702	PDF	certificato-148-L-rev.6.pdf

19. Is your quality management system accredited?

Yes

Test for which your laboratory is accredited	Accreditation body
RT_PCR	ILAC MRA , ACCREDIA
Serological Competitive RHDV-ELISA	ILAC MRA , ACCREDIA
Serological Competitive RHDV2-ELISA	ILAC MRA , ACCREDIA
Virological sandwich MAbs RHDV/EBHSV-ELISA	ILAC MRA , ACCREDIA
Immunohistochemistry	ILAC MRA , ACCREDIA
Electron Microscopy negative staining methods	ILAC MRA , ACCREDIA

20. Does your laboratory maintain a “biorisk management system” for the pathogen and the disease concerned?

Yes

The laboratory works according to the Manual of Diagnostic Tests and Vaccines for Terrestrial Animals, Chapter 1.1.4, and the WAHO Laboratory Biosafety Manual. A risk analysis approach was adopted to manage the biological risks of specific agents aimed at biosecurity in veterinary laboratories and animal facilities. As a result of this process, the assignment of RHDV to the risk group (BLS2) relevant to the country was defined and the consequent steps were taken to work in laboratory facilities defined by containment levels appropriate to the types of risks identified.

TOR9: SCIENTIFIC MEETINGS

21. Did your laboratory organise scientific meetings related to the pathogen in question on behalf of WOAH?

No

22. Did your laboratory participate in scientific meetings related to the pathogen in question on behalf of WOAH?

No

TOR10: NETWORK WITH WOAH REFERENCE LABORATORIES

23. Did your laboratory exchange information with other WOAH Reference Laboratories designated for the same pathogen or disease?

Not applicable (only WOAH Reference Laboratory designated for the disease

24. Do you network (collaborate or share information) with other WOAH Reference Laboratories designated for the same pathogen?

Not applicable (only WOAH Reference Laboratory designated for the disease

25. Did you organise or participate in inter-laboratory proficiency tests with WOAH Reference Laboratories designated for the same pathogen during the past 2 years?

Not applicable (Only WOAH Reference Laboratory designated for the disease)

Not applicable

26. Did your laboratory collaborate with other WOAH Reference Laboratories for the same disease on scientific research projects for the diagnosis or control of the pathogen of interest?

Not applicable (only WOAH Reference Laboratory designated for the disease

TOR11: OTHER INTERLABORATORY PROFICIENCY TESTING

27. Did your laboratory organise or participate in inter-laboratory proficiency tests with laboratories other than WOAH Reference Laboratories for the same pathogen during the past 2 years?

Yes

Purpose for inter-laboratory test comparisons1	Role of your reference laboratory (organizer/participant)	No. participating laboratories	Name of the test	WOAH Member Countries
We prepared and distributed a panel of positive samples (antigen positive extracts) to be used by recipients for the validation of their analytical performances	Organizer	1	ELISA and RT-qPCR	UNITED STATES OF AMERICA,

TOR12: EXPERT CONSULTANTS

28. Did your laboratory place expert consultants at the disposal of WOAH?

Yes

Kind of consultancy	Location	Subject (facultative)
Last review of the the Chapter of the Manual was completed on 2022 and approved and published on 2023.	On site, by email	We changes Table 1 to make it coherent with the "RHD case definition". Then we included some other changes in the chapter originating from the latest data and information from scientific literature i.e., species susceptibility to RHD/RHDV2 and new biotechnological vaccines.

29. Additional comments regarding your report:

Yes

During 2024 the laboratory has applied both nationally and internationally the specific direct and indirect tests (MAbsELISA and RT PCR for antigen detection, cELISA and
isotype_ELISAs for antibody detection) specifically developed for RHDV2.
Following the epidemic occurrence of RHDV2 in North and Central America, we continued to collaborate and support American colleagues in the detection of the virus in
wild and domestic lagomorphs.
Even more information on pathogenic and non-pathogenic lagoviruses' spread, host susceptibility, and antigenic and genomic characteristics were acquired thanks to the
scientific collaboration and research projects with colleagues from various member Countries.
Technical support, including training and visiting periods, was given to different WOAH member countries, mainly on diagnostic activity and providing of reagents and materials.