Virologie

Rapport Hcéres

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agence d'évaluation de la recherche
et de l'enseignement supérieur

Department for the evaluation of research units

AERES report on unit:

JRU VIROLOGY

VIRO

Under the supervision of the following institutions and research bodies:

École nationale vétérinaire d'Alfort

Agence Nationale de Sécurité Sanitaire de l'alimentation, de l'environnement et du travail - ANSES

Institut National de la Recherche Agronomique - INRA

January 2014

agence d'évaluation de la recherche
et de l'enseignement supérieur

Department for the evaluation of research units

On behalf of AERES, pursuant to the Decree of 3 november 2006[1]*,*

- Mr. Didier HOUSSIN, president
- Mr. Pierre GLAUDES, head of the evaluation of research units department

On behalf of the expert committee,

- Mr. Bruno LINA, chair of the committee

[1] The AERES President "signs [...], the evaluation reports, [...] countersigned for each department by the director concerned" (Article 9, paragraph 3 of the Decree n ° 2006-1334 of 3 November 2006, as amended).

Evaluation report

This report is the result of the evaluation by the experts committee, the composition of which is specified below.

The assessment contained herein are the expression of independent and collegial deliberation of the committee.

Unit name:	JRU VIROLOGY
Unit acronym:	VIRO
Label requested:	UMR ENVA-ANSES-INRA
Present no.:	1161
Name of Director (2013-2014):	Mr Stephan ZIENTARA
Name of Project Leader (2015-2019):	Mr Stephan ZIENTARA

Expert committee members

Chair:

Mr Bruno LINA, Université de Lyon

Experts:

Ms Luisa BARZON, University of Padova, Italy

Ms Ann Brigitte CAY, CODA CERVA, Uccle, Belgium

Mr Georg HERRLER, Zentrum für Infektionsmedizin Stiftung Tierärztliche Hochschule Hannover, Germany

Mr Michel PÉPIN, VetAgro Sup, Lyon

Mr Fréderic TANGY, Institut Pasteur, Paris

Mr Jean-François VAUTHEROT, Centre INRA du Val de Loire, Tours (representative of CSS INRA)

Scientific delegate representing the AERES:

Ms Catherine SCHUSTER

Representatives of the unit's supervising institutions and bodies:

Mr José COHEN (representative of Doctoral School n°402)

Ms Anne COLLIGNON (representative of Doctoral School n°425)

Mr André JESTIN, ANSES

Mr Thierry PINEAU, INRA

Mr Renaud TISSIER, ENVA

1 • Introduction

History and geographical location of the unit

The JRU unit research entity is the current UMR 1161 that was created in 2002. It is located at the French National Veterinary School at Maisons-Alfort. The former head of the research entity is the leader for this new 5 year contract proposal. Research pursued concerns three major strategic orientations, namely physiopathology of viral infections and notably cross-species transmission, detection and epidemiology of emerging and re-emerging viral infections and vaccine development. Research activities are supported by three institutional bodies, the French National Institute for Agricultural Research (INRA), the Veterinarian National School Alfort (ENVA) and the National Agency for Food, environmental and occupational health safety (ANSES).The former team 6 of the research entity is not part of the project, the team leader has implemented a start-up at Pasteur Institute, Paris, based on the skills developed on next generation sequencing (NGS). If the project fails, the team leader might reintegrate the research entity. During the intermediate period, interactions between the former team and the research entity will be maintained.

Management team

Director: Mr Stephan ZIENTARA

Deputy director: Ms Jennifer RICHARDSON

AERES nomenclature

SVE1_LS6, SVE1_LS7

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2 (0.45 FTE)	2 (0.45 FTE)
N2: Permanent researchers from Institutions and similar positions	7 (5.5 FTE)	9 (6.5)
N3: Other permanent staff (without research duties)	13 (7.05 FTE)	12 (6.25 FTE)
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	1	
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	4	
N6: Other contractual staff (without research duties)	3(2.2 FTE)	1 (0.5 FTE)
TOTAL N1 to N6	**30 (20.2 FTE)**	**24 (13.7 FTE)**

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	9	
Theses defended	9	
Postdoctoral students having spent at least 12 months in the unit*	4	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	5	7

2 • Assessment of the unit

Global assessment of the unit

The unit has a very good track record for publication and the scientific output is of very good quality, despite some discrepancies between the teams. The experts committee noticed that some of the team leaders are involved in internationally funded research programs and are regularly invited for lectures during international meetings. In addition to their research activities, 4 over the 5 teams are in charge of reference activities that are not always in the scope of their research programs. However, they are handling well this double role of reference and research activities. The head has presented a sound strategic plan for the coming years with the implementation of some transversal activities, and good connections between applied and research activities. The research entity has shown its excellent reactivity in the context of newly emerging viruses. Amongst the five teams, some display a weaker scientific output and five-year plan strategy. The committee noticed a relative lack of transfer activities, except for the implementation of a new diagnostic tool for the diagnosis of Schmallenberg infection. The translational research potential is very high but not developed by the research entity. Some of the teams of the research entity have a strong interaction with the social and economic sector and should be a driving force for transfer of technology.

Strengths and opportunities related to the context

Strong commitment of the lab into a large number of reference activities, with 7 National Reference Laboratories and 3 EU-Reference Laboratories. Some of these reference activities are fully accredited by COFRAC. The research entity is involved in numerous EU-funded research programs as well as in international networks. The head of the laboratory and some of the team leaders are internationally recognized and are amongst the best experts in their fields. In December 2013, a LABEX young team creation has been awarded to a member of the team EViR. This reflects the strength of the scientific output clearly improved in the last 5 years and the quality of the projects. The experts committee noticed also the strong support from the institutional bodies, even in the difficult context they are facing in 2014.

Weaknesses and threats related to the context

Some of the projects would benefit of a stronger interaction between the other teams of the unit. The teams tend to link their numerous reference activities to their research activities, leading to some dilution in the visibility of their research programs and difficulties to run collaborative projects between the different teams. The experts committee noticed the decrease of recurrent funding from one of the agencies and the large number of retirements in some of the teams that will need an effort of reorganization of the technical staff duties and definition of priorities in the research projects.

Recommendations

The LABEX young team headed by the former co-principal investigator of team EviR is an added value to the JRU. This new team (not presented in the project as a consequence of its very recent notification) should aim to support the different activities of all teams (mostly teams EViR, NVZ and VEBE). This new group will independently implement projects described in team EViR. The head of the unit should be careful that this will not drain off the research projects from the EViR team, and as a consequence, have a negative impact on the next scientific output of Team EViR.

Some projects should be cross-team projects, using the transversal skills of some teams (i.e. team VAV).The integration between research and reference activities should be maintained, but this does not mean that all reference activities have to be linked to research programs. In regard of their research workforces, the teams should select their best research programs and focus on a more limited number of projects. Collaborations outside of the research entity should be sleeked for some projects with limited human resources.

3 • Detailed assessments

Assessment of scientific quality and outputs

The scientific output of the research entity has been recognized as very good with 115 original publications in peer-reviewed journals (only 50 in the former period), and for 61 publications at least one team member is first or last author (18 J. Virol-IF 5.4, 2 Virology-IF 5.4, 5 Vet Microbiol-IF 3.5, 7 Vet Res-IF 4.1, 9 Plos One-IF 4.4, etc.). Since the last evaluation, the scientific output has markedly increased in the number of published papers, the mean IF (3.5) and their quality. Many publications were co-signed by members from two teams of the unit or more, highlighting the existence of transversal research projects inside the research entity. During the last five years, the research entity teams have been involved in internationally funded research projects (EU funded projects) and national project i.e. the network of excellence EPIZONE, EU-RAPIDIA-FIELD, FP7 projects PREDEMICS and MEDVETNET, AniBio Threat, EDENnext, EuroWestNile, ImproCon, Disconvac, Arbozoonet, and ANR and ANSES funding. This reflects the quality of the research carried out in the research entity. In addition, several teams have implemented and subsequently distributed new diagnostic tools, in the frame of their reference activities. In 2013, a LABEX young team was created, emerging from team EViR, meaning that the research program and outputs of this co-team leader is of excellent quality. This reflects the vivid research carried out.

Assessment of the unit's academic reputation and appeal

Individually, most of the team leaders are of international reputation in the field of veteran virology. They are involved in international experts groups (FAO, EU EFSA, EU project DISCONTOOLS, DEFRA and BBSRC (UK), IZSLER (I)) and national councils. All team leaders but one are responsible for one or several national and sometime European-Reference Laboratories. This strongly supports their international recognition. In the context of its reference laboratory activities, the research entity frequently hosts foreign students and is clearly identified as a training site. They also promote and take part in some international events (meetings). The research entity attracted a senior scientist who will integrate research entity this year and develop a new aspect of animal virology.

Assessment of the unit's interaction with the social, economic and cultural environment

As responsible for reference laboratories, the team leaders are involved in the writing of expert group documents for the community. They are frequently asked to explain emerging situation to policy makers from the Ministry of Agriculture. In that context, they have to implement and disseminate new diagnostic tools. However, despite their strong commitment in the development and dissemination of new diagnostic tools or new strategies for the Control of emerging viruses, the research entity members do not interact with industry, and do not report of any patent filing (a result of the ANSES policy regarding patents in association with industrial partners). In their reference activities, they have implemented quality insurance systems and some of their techniques are accredited by COFRAC. The team leaders are involved in the publication of official reports concerning the pathogens for which they are internationally recognized as experts. They transmit regularly their knowledge to the veterinarian community.

Assessment of the unit's organization and life

The global organization of the research entity is very good, with mutualization of resources. The structure for unit management is clear and is supported by the staff. The five proposed teams have their specific projects that might be shared by two or three teams. This kind of interaction might benefit from some reinforcement especially for the human resource-limited teams, or by reducing the number of teams. This year the research unit awarded a LABEX young team for a junior researcher of team EViR. This reflects that the research entity head promotes his researchers, allowing them to become scientifically independent. The premises is providing the structures and platforms required to carry out the research program.

Assessment of the unit's involvement in training through research

The research entity hosts a very large number of students coming from various French regions or foreign countries. This reflects the scientific visibility of the research entity and its capacity in training. Over the period, the research entity hosted 5 masters, 9 PhD students defended their PhD, and 9 PhD students are already on site. PhD students belong to three different doctoral schools (ED 402, ED 425 and ED516). This situation is a rather peculiar since mostly one unit hosts PhD students belonging to one single doctoral school. The chairs of the three doctoral schools are aware of this situation and fully support this multiplicity of doctoral schools for the students of the research entity. The training and supervision of the students is of very good quality, PhD mid-term committees are performed and duration of the thesis are in accord with the doctoral school's rules. All the students published papers and could attend international meetings. Some unit team leaders are involved in the training programs for the Master degrees at University of Tours and of Saint-Quentin en Yvelines and in the frame of the doctoral schools.

Assessment of the strategy and the five-year plan

The strategy for the next five years is clear and is built on the outputs of the past period. The major topic concerns the emergence of new diseases, and the investigation of the factors that may result in the transmission of animal pathogens to the human population, and the different means to avoid such transmission. The proposed work program focuses on the understanding of the pathogenesis, the epidemiology of the diseases and the development of vaccination approaches. The research priorities are well defined, and ask clear (but may be to many in regard of the workforces) questions about the interaction between the viruses and the infected cell or host. The research program will be carried out in parallel with the reference activities of the research unit. It will use the platforms (infectiology, interactomic) available on site or in the frame of already existing collaborations. The project wishes to reinforce some of the research themes that emerged during the last contract. Among them, some will be surly successful. However, the head of the research entity may anticipate that others will fail and the project leaders should be cautious to avoid implementation of too many new themes, even if they are in the remit of the surveillance/reference duties of the research entity. However, the project is of very good quality, and the feasibility has been estimated as excellent by the experts committee.

4 • Team-by-team analysis

Team 1: Biology of Picornavirus (BIOPIC)

Name of team leader: Mr Labib BAKKALI KASSIMI

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1 (0.7 FTE)	1 (0.7 FTE)
N3: Other permanent staff (without research duties)	4 (1.4 FTE)	4 (1.4 FTE)
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**7 (4.1 FTE)**	**5 (2.1 FTE)**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The research activity output is mainly focused on two viruses EMCV and FMDV. It includes all aspects of basic and clinical virology, i.e., investigation of pathogenicity mechanisms, viral persistence and evasion from host immunity, development of sub-viral particles- and DNA-.based vaccines, development of new serological and molecular methods for diagnosis, and molecular epidemiology. This indicates the very good interdisciplinarity of the team, but reflects also a too large number of subjects in regard of the workforces in the team. Moreover the team

supports duties in reference activities requiring emergency diagnostic services in case of FMDV outbreaks. The large number of themes reflects the role of the team in reference activities (NRL for FMDV and related disease) where the lab has to perform diagnostic services in emergency in case of outbreaks.

Most of the publications reflect research activities in the FMDV and EMCV fields. Nine research articles have been published in scientific journal on virology with good impact factor in the field (mean IF 3.2, 1 J. Virol IF 5.4, 1 Vaccine IF 3.5, 1 J Gen Virol IF 3.3, etc) which is a good rate for a team counting only 0.7 FTE researcher and 1.4 FTE technical staff. The main topic is about the persistence of FMDV in animals. They try to decipher the mechanisms that allow the persistence of the virus in cattle for more than 2 years. The team also reports vaccine development in FMDV with different approaches. For the molecular epidemiology study, BIOPIC has established several collaborations with FMDV endemic countries in Africa and Asia which provided interesting data.

Assessment of the unit's academic reputation and appeal

The research team has been involved in several EU-projects (EPIZONE, RAPIDIA-FIELD, Disconvac, AniBio Threat). During the last five years, the team hosted 2 PhD students, and has trained technicians from different countries. They have been requested for the training of European, African and Middle East technicians. This reflects their expertise in the FMDV reference activities.

Assessment of the unit's interaction with the social, economic and cultural environment

The team is in charge of three National Reference Laboratories (FMDV, SVD, VS). Members of the team are involved in international EU and FAO committees. They also have close connections with the French public veterinary authorities. They transfer knowledge, and provide technical support and training in their reference activities.

Assessment of the unit's involvement in training through research

The research team has trained 2 PhD students and 11 students from foreign countries and conducted training missions in different countries in West Africa, North Africa, and Middle East. The PhD students belong to doctoral school ED 516 Biochimie, Biothérapies, Biologie moléculaire, Infectiologie (B3MI).

Assessment of the strategy and the five-year plan

The research team proposes to continue the ongoing activity and strengthen international collaborations. They acknowledge that they conducted research in a too large number of subjects, in regard on their workforces dedicated to research activities. They propose to focus on FMDV only, with a special emphasis on the understanding of the mechanisms of “persistence”. Although this is a highly relevant topic and a sound choice for the next years, the experts committee noticed that they did not provide a convincing strategy for the development of this research program. On the other hand, all the translational studies are excellent, and provide data of interest.

Conclusion

- **Strengths and opportunities:**

The BIOPIC team is involved in numerous EU projects. The large international network connected to this team is an added value to all the epidemiological studies carried out on FMDV and has been considered as strength by the experts committee. The attractiveness of the team is also reflected by the large number of trainees coming from FMDV endemic foreign countries. The focus on FMDV for the next 5 years is an excellent choice, with a balanced mixture of translational and basic research. This team has provided kits with an internal quality control to other labs. Opportunities are the connection with the newly implemented LABEX young team structure emerging from the research entity and the strong commitment to reference activities (National Laboratories of Reference) for FMDV, VS and EMCV.

- **Weaknesses and threats:**

Important changes in the team composition due to a large number of retired staff may threaten the research programs; however the reconstruction of team is ongoing. The research programs on the FMDV “persistence” or long-term carriage in cattle need to be matured.

- **Recommendations:**

The expert committee recommends focusing their research program on FMDV, by combining epidemiology, translational and basic scientific approaches. The committee felt that the team should promote the connection with the LABEX young team group, and other groups within the research entity to maintain the level and quality of the scientific production in this "reconstruction" period.

Team 2: Viral emergence in ruminants(EViR)

Name of team leader: Mr Stephan ZIENTARA

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2 (1.3 FTE)	2 (1.3 FTE)
N3: Other permanent staff (without research duties)	3 (1.3 FTE)	3 (1.3 FTE)
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	
N6: Other contractual staff (without research duties)	1 (0.7)	
TOTAL N1 to N6	**8 (5.3 FTE)**	**5 (2.6 FTE)**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

- Detailed assessments

Assessment of scientific quality and outputs

The EViR team (previously ORBI team) includes 4 permanent scientists (2.1 FTE) and 1 permanent technician (0.4 ETP). This team is dedicated to investigate the pathophysiology of Orbiviruses and Schmallenberg Virus-SBV. Beside the fundamental research performed on these viruses, applied research is performed in line with the reference tasks the team has to perform in his mandate as French reference laboratory for Bluetongue-BTV, African horse Sickness virus-AHSV and Epizootic Hemorrhagic Disease of Deer-EHDV. The overall scientific activity over the period has been considered as excellent in the research domain. A total of 52 peer-reviewed international publications of which 20 where the first or last author belonged to the EViR team and 68 publications in national papers. The average IF is around 3.25 (7 J. Virol IF 5.4, 2 Virology IF 5.4, 4 Vet Microbiol IF 3.5, 4 Vet Res IF 4.1, 2 Plos One IF 4.4, etc.), which is an excellent score in the field of veterinarian medicine and veterinarian virology.

Assessment of the unit's academic reputation and appeal

The EViR team has an excellent academic reputation. The excellent reputation is also supported by the expertise activities of the team members in French instances as ANSES and INRA and in international organizations like EFSA (European Food Safety Agency), FAO, DEFRA (United Kingdom Ministry of Agriculture), OIE (Animal Health world Organization). The recognition of the team is further supported by the number of national and international invitations to conferences (n=43), and the fact that they act as referees for peer-review journals including Emerging infectious Diseases, Journal of Virology, PloS One. Members of the team are also regularly member of PhD thesis committees for various faculties in France and European countries. The reputation of excellent research is also supported by the involvement of the team as partner in many European projects (Orbivac, NADIR, RAPIDIA-FIELD, ORBINET, SBV-DG Sanco, etc) during the period and also for the next years (Vmerge, ISCOM).

Assessment of the unit's interaction with the social, economic and cultural environment

The overall EViR's interaction with the social, economic and cultural environment is very good. The team has regular contacts with different French public veterinary authorities and associations in the frame of his mandate as national reference laboratory. During the emergence of Bluetongue Virus and Schmallenberg Virus the team transferred their knowledge to the veterinary services regarding tools for disease control and tools for diagnosis to the departmental laboratories. The team achieved the expression of the VP7 proteins of Bluetongue Virus and Epizootic Hemorrhagic Disease of Deer Virus in baculovirus. These proteins were transferred to a private company which used them for the development of diagnostic tools. Their excellent reactivity in the treatment of viral emergence was demonstrated in front of the Schmallenberg Virus emergence, e.g. transfer of a kit ELISA to a commercial company for the serology of Schmallenberg Virus infection just or 4 months only after the first outbreak in France in January 2012. Team's members also gave seminars at different universities and for veterinarians.

Assessment of the unit's involvement in training through research

The overall EViR's involvement in training through research is very good. The team is strongly involved in training through research with 7 PhD students (3 PhD thesis defended in the last five years and 4 PhD are in progress). PhD students belong to the Doctoral Schools ED 425 « Innovation thérapeutique » and ED 402 « Sciences de la Vie et de la Santé ». Team members are teaching in several universities in different degree programs and organize profession trainings (CIRAD, Vet Schools, etc).

Assessment of the strategy and the five-year plan

Overall, the EViR's strategy and five-year plan is very good. The team will concentrate his research activities on diagnosis, epidemiology, physiopathology and prevention on the three viruses of which a very good expertise has been built during the evaluated period.

Some of their research projects are in continuity with the past period as the research on innate immunity. This project has been retained to be a full project of the highly competitive LABEX EBEID lead by Pasteur Institute to which belongs the emerging LABEX young team; this project is not only included in the five-year plan of the team but may also contribute as a transversal project for the unit as other viruses are included (FMD virus - team BIOPIC, HEV-team VEBE). Another research axis will focus on the determination of the virulence for BTV and SBV by exploring the interactome of some BTV and SBV proteins. The EViR's team tries to have a good balance between fundamental and applied research. The applied research will contain topics from the mandate as reference laboratory. This implies that new diagnostic methods will be developed and validated such as multiplex detection method based on Luminex technology for simultaneous detection of different serotypes of BTV, EHDV or AHSV.

Conclusion

- **Strengths and opportunities:**

The research program is focused on two important animal viruses, Bluetongue virus-BTV and Schmallenberg virus -SBV and is corroborated with the strong commitment of the team to reference activities (National Reference Laboratories) for both viruses, reference activities which are fully accredited by COFRAC (norm ISO 17025). The team has an excellent record of publications and has during the past demonstrated its ability to react to the emergence of new viral diseases.

The experts committee noticed that the excellent national and international reputation of the team leader allows fund raising, point which is emphasized by the high number of European and national grants obtained over the period and for the future projects. The strong involvement of the team in training through research allows recruitment of highly motivated PhD students who contribute to the workforces dedicated to research. The experts committee noticed an excellent working atmosphere in the team which is considered as strength.

The future program aims to:

I) initiate an original and more fundamental research program on modulation of innate immunity by these viruses;

II) develop and master tools like reverse genetics;

III) take the opportunity to initiate a new project on seadornaviruses (zoonotic viruses) through the recruitment of a new senior scientist in September 2014.

- **Weaknesses and threats:**

The experts committee noticed a marked decrease of the financial support of one of the institutional partners and expects as well a decrease in European Union funding since the Horizon 2020 program leaves not much place to animal health programs.

The implementation of the LABEX young team from the EVIR team will result into the split of both the workforces and research program. Hence, the remaining subgroup of EVIR will have to rethink ots research program, and/or implement very strong collaboration with the new team research program of the EViR team.

- **Recommendations:**

The committee makes them aware that the connections and collaborations between the newly created LABEX young team and EViR are clarified soon to avoid a draining of the research subjects from team EViR to the LABEX structure. The experts highly recommend to maintain the integration between reference and research activities which is considered as an opportunity and a force.

Team 3: Neuro-Virology of Zoonoses (NVZ)

Name of team leader: Ms Muriel COULPIER and Ms Sophie LECOLLINET

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2 (1.6 FTE)	2 (1.6 FTE)
N3: Other permanent staff (without research duties)	3 (2.05 FTE)	3 (2.05 FTE)
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	1 (0.5 FTE)	1 (0.5 FTE)
TOTAL N1 to N6	**6 (4.15 FTE)**	**6 (4.15 FTE)**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions		1

- Detailed assessments

Assessment of scientific quality and outputs

Research activity of the team (3 scientists (1.9 FTE), 1 engineer (0.9 FTE) and 2 technicians (1.35 FTE)) is focused on equine neurotropic viruses with zoonotic potential (i.e, Borna disease virus - BDV, and West Nile virus - WNV). Research activities on BDV include investigation of pathogenesis and epidemiology, i.e., the study of the effects of viral infection and viral proteins on neurogenesis in cell cultures and the development of RT-PCR methods for the detection of the virus and its application to the study of horses with neurological symptoms. Research activity on WNV includes studies on virulence determinants (i.e. NS3 protein variants), host susceptibility (in birds and mice), epidemiology in Europe, and vaccine development. The results of the research on WNV have been published in good quality journals, 11 articles in international scientific journals with medium IF, including epidemiology and pathogenesis studies among them 4 with first or last author from the team (1 emerging infect diseases, IF 6; 2 Plos One IF 4.4) as well as 1 relevant publication on BDV published in Journal of Virology (IF 5.4). For pathogenesis and

epidemiology studies on BDV, the team has established collaborations with other centers in France. Research activity on WNV leads to more publications and has been funded by EU FP7 projects.

Assessment of the unit's academic reputation and appeal

The team was partner in two projects funded by the European Union, the EU-projects EUROWESTNILE and EPIZONE and is involved in international PhD and post-doctoral programs and expert meeting activities.

Assessment of the unit's interaction with the social, economic and cultural environment

The team is in charge of two National Reference Laboratories (WNV and AHSV) and two EU reference laboratories (WNV, exotic equine encephalitis viruses) and provides assistance and expertise to French and EU public veterinary authorities and associations.

Assessment of the unit's involvement in training through research

The research team has trained several PhD students and master degree students over the period. The students belong to the doctoral school ED 425 Innovation thérapeutique.

Assessment of the strategy and the five-year plan

The research team proposes to perform –omics analyses (transcripts, miRNAs, epigenetics) in BDV infected neural progenitor cells and to continue the ongoing epidemiological studies. Future research on WNV will included in vivo studies on innate immunity in birds, early events in viral replication capacity, and molecular identification of virulence for European strains. These research activities are in line with the programs and goals of the Institutions.

Conclusion

- **Strengths and opportunities:**

The team displays a very good level of publications in their field of research. The research committee noticed an excellent balance between applied and fundamental research activities for the WNV project. The project is in line with some of the objectives of the National Reference laboratory hosted by the team. The team and his leaders are internationally recognized experts. The vaccine development in link with the WNV research can lead to interaction with the industry. Implementation of collaborations with relevant laboratories for the newly emerging activity regarding BDV appeared as an opportunity to the expert committee.

- **Weaknesses and threats:**

Unbalanced output of the two projects (WNV and BDV) might be a weakness in regard to the size of the team. The BDV project is at risk as assessed by the limited number of publications, despite the implementation of high level collaborations. Although the 2 team leaders synergized their efforts on WNV studies, which led to 2 publications on WNV physiopathology, the committee regretted the absence of a stronger link between the two themes of the team.

- **Recommendations:**

The “omics” approaches described should be carried out in close collaboration with the LABEX young team of the research entity. The committee feels that the epidemiological studies should be one of the objectives and would be of help to show some scientific output in short terms.

Team 4: Enteric Virus and Species Barrier (VEBE)

Name of team leader: Ms Nicole PAVIO and Ms Sophie LE PODER

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1 (0.4 FTE)	1 (0.4 FTE)
N2: Permanent EPST or EPIC researchers and similar positions	1 (0.5 FTE)	2 (1.5 FTE)
N3: Other permanent staff (without research duties)	2 (1.3)	1 (0.5)
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**5 (3.2 FTE)**	**4 (2.4 FTE)**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	2

• Detailed assessments

Assessment of scientific quality and outputs

VEBE is a rather small team (2 principal investigators and a recently recruited research associate – CR2 INRA corresponding to 1.9 FTE and two part time technicians 1.3 FTE), with interest focused on two positive strand RNA viruses, hepatitis E virus (HEV) and Canine/Feline Coronaviruses (CCoV and FCoV), which both may cross the species barrier. These viruses cause extremely different pathologies and show a different degree of species barrier crossing, HEV being largely distributed in human and several mammalian species whereas carnivores coronaviruses seem to be more restricted to feline/canine species and possibly to pigs. However, there are common tools and strategies, regarding the molecular epidemiology and development of new cellular models. A number of 22 articles (15 with first or last author from the team) were published over the period including: 1 AIDS IF 6.3, 1 J. Virol IF 5.4, 1 J Gen Virol IF 3.3, 1 J Clinical Virology IF 3.9. The work on HEV appears to be highly pertinent regarding the mandatory missions of ANSES institution on the control of food born infections. Indeed, according to all epidemiological studies performed by VEBE, human hepatitis E cases in France are related to the consumption of contaminated meat/animal products,

mostly of porcine origin. The publication activity is very successful with a good number of original publications in the best journals of the discipline and an increase over time in the number of papers as first or senior authors.

The work on CCoV/FCoV is supervised by an associate professor having a high load of teaching and performed by a technician (INRA – retiring) and a PhD student. Epidemiological studies are of great interest as they are essential in getting information on circulating strains in the different animal species concerned. The quality of the results is illustrated by the integration of this small group in a larger ANR project (EPICOREM). As outlined in the former AERES report, the publication rhythm and level is however low compared to the HEV group due at least in part on the teaching duties of the leader.

Assessment of the unit's academic reputation and appeal

The molecular epidemiology work was and is already supported by ANR grants (2008-2010 and 2011-2014), moreover the VEBE team leader was the coordinator of the 2008-2010 grant. This illustrates how efficiently this task was achieved, raising adequate collaborations in France and Europe. The small CCoV/FCoV group is integrated in a large ANR project (EPICOREM). The HEV team leader gave lectures in international meetings and is internationally recognized.

Assessment of the unit's interaction with the social, economic and cultural environment

The HEV subgroup is very active in the field of communication with the social and economic environment. They produced official documents on HEV. They are also involved in field analysis. The team leader on HEV is an expert for committees in ANSES. This team leader has implemented meetings in collaboration with the industry in the frame of the research entity.

Assessment of the unit's involvement in training through research

The VEBE team trained 2 PhD students over the period (1 PhD defence, a 2nd ongoing). They contributed to teaching in Master courses and in professional training courses. Training courses were also implemented for the detection of canine coronaviruses. The PhD students belong to the doctoral school ED 425, Innovation thérapeutique.

Assessment of the strategy and the five-year plan

In the future, the team will contribute to a better understanding of HEV ecology, gaining access to information on circulating viruses in several species. Species barrier crossing studies are of special interest in the context of molecular epidemiology and High Throughput Sequencing has elegantly been used as a tool to ascertain the origin of human contamination and study the evolution of the viruses in their hosts. VEBE has developed a promising approach for studying viral replication in differentiated cell-lines. This allows further developments in the fields of reverse genetics for HEV and of pathophysiology. The recruitment of a research associate to develop the pathophysiology models *in vitro* should consolidate the team and allow a real progress in the knowledge about HEV interactions with the host.

Further studies on the impact of recombination/presence of additional ORFs on the pathogenicity of FCoV and CCoV should be conducted in collaboration with teams currently handling a reverse genetic system (RGS). If grouping both research axis in a single team corresponded to a logical organization one may now question the persistence of fundamental studies on Coronaviruses, as research activities on HEV are progressing very fast and as the replacement of the technician (for the CCoV/FCoV project) is not yet acquired.

Conclusion

- **Strengths and opportunities:**

Both groups have a very good experience and usage of sequence analysis and molecular epidemiology, strain isolation and study on species barrier trespassing. Both groups are well integrated in national and international (HEV) networks and the HEV team leader is an internationally recognized expert in the field. The team has developed for both viruses interesting cellular models, a difficult task in hepatovirology and the HEV group is ready for pathophysiology (see above and below) studies, including the use of reverse genetics studies for the evaluation of the impact of viral genes on cell and immune functions. Although the clinical cases are not very frequent in humans, HEV

is a concern in public health and a better knowledge on the ecology and evolution of the virus(es) is of great importance. The HEV group displays a very good publication rate and the program proposed for the next period of time is based on well mastered techniques for molecular epidemiology and on an enlargement of the field of investigations toward viral pathophysiology.

- **Weaknesses and threats:**

The CCoV/FCoV group appears to be more fragile as it might lose its unique technical help, while the project leader is involved in heavy teaching duties. Due to the difficulties of the model and to the small size of the group, the publication rhythm and quality are not as good as for HEV.

For the HEV group the pathophysiology studies in cellular context might be hampered by the low efficiency of those cellular systems to replicate HEV.

- **Recommendations:**

The scientist and the team leader could, at the end of the on-going thesis project in CoV group, consider a reorganization of the group, either by reinforcing the group or by re-examining the persistence of studies on coronaviruses in regard of the size of the team.

Team 5: Adenovirus-based Vectors and Vaccines (VAV)

Name of team leader: Ms Jennifer RICHARDSON and Mr Bernard KLONJKOWSKI

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1 (0.05 FTE)	1 (0.05 FTE)
N2: Permanent EPST or EPIC researchers and similar positions	2 (1.4 FTE)	2 (1.4 FTE)
N3: Other permanent staff (without research duties)	1 (1 FTE)	1 (1 FTE)
N4: Other professors (PREM, ECC, etc.)	1	
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**5 (3.45 FTE)**	**4 (2.45 FTE)**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

This is a small team with 4 permanent staff including 3 scientists (1.45 FTE and one technician) and a PhD student. A post-doctoral fellow recently left the team. The team develops improved vaccines for domestic animals, mostly based on adenoviral vectors. They developed in the past a canine adenoviral vector (CAV-2) which was successfully used to immunize mice and sheep against rabies. Adapted to feline immunodeficiency virus, this vector enhanced infection in an antigen-specific manner, similarly to what was observed with Ad5-HIV in humans. A porcine CAV-2 vaccine against Footh and Mouth Disease (FMD) was also developed. Concerning Bluetongue Disease (BT), the sole expression of VP7 in CAV-2 did not protect sheep from homologous or heterologous challenge. The team also evaluated the activity of adenoviral vectors on DCs (mouse DC with Ad5, ovine DC with CAV-2 and ruminant DC with Ad5). The projects for the next period are in continuation with these studies. The number of publications during the

last five years is correct, 17 publications with an average IF of 3.99 (1 J Emerging Disease IF 6.5, 2 J. Virol IF 5.4, J Gen Virol IF 3.4, 3 Plos One IF 4.4), for 8 publications one team member was first or last author.

Assessment of the unit's academic reputation and appeal

The team is part of an FP7 research program. The only PhD student of the team is funded by a CIFRE contract.

Assessment of the unit's interaction with the social, economic and cultural environment

Owing to excellent knowledge in vaccine development, this team has received a CIFRE doctoral fellowship (2013-2015) and accompanying research contract with a company involved in development of vaccine adjuvants. The VAV team has expertise, but in contrast with the other teams, no reference activities.

Assessment of the unit's involvement in training through research

The team is reporting four PhD students over the period. The PhD students of the team belong to the doctoral schools ED 402 Sciences de la Vie et de la Santé or ED 516 Biochimie, Biothérapies, Biologie moléculaire, Infectiologie (B3MI), which is quite unusual.

Assessment of the strategy and the five-year plan

The projects for the next period are in continuation with the studies that have been carried out in the last years. There is no specific development of a five-year plan in the project presented, but the willingness to continue the development and evaluation of prototypic vaccines, and the exploration of the molecular and cellular mechanisms that underlie the induction of immune response by Adenoviral-based vaccines was emphasized. The team leaders think that this evaluation/exploration of prototypic vaccines and immune responses will provide new insights for the development of a next generation of Adenoviral-based vaccines against animal diseases.

Conclusion

- **Strengths and opportunities:**

The number of publications during the last five years is correct (20 publications with an average IF of 3.99). The committee noticed the participation in different collaborative programs. The team leaders have tried to address comments from the previous evaluation by developing a more integrative research project they entitled: from vaccines to vaccination.

- **Weaknesses and threats:**

In contrast with the other teams, the VAV team has no reference or expertise activities. There is no staff from ANSES as, according to the team's leaders, the team's activities on CAV-2 as a vaccine vector are not priorities for the agency. The team has no connection with industrial partners working on vaccine development except a CIFRE fellowship and a research contract with a company working in the field of adjuvants. Their vector strategy did not result in large trials or applications. The project aiming to identify tick molecules that contribute to transmission of tick-borne pathogens should be clarified as it looks a bit far from the general topic of the team.

- **Recommendations:**

The skills of the team are important and may be used to support research activities of the four other teams of the research entity. If the vaccine projects are maintained, connections with the industry should be implemented to foster the research and translational activities.

5 • Conduct of the visit

Visit date:

Start:	January 28th 2014 at 8:00 am
End:	January 28th 2014 at 7:30 pm
Institution:	ANSES
Address:	Salle du Conseil
	ANSES – Laboratoire de santé animale de Maisons-Alfort
	23 avenue du Général de Gaulle
	94706 MAISONS-ALFORT CEDEX

Conduct or programme of visit:

January 27th 2014

Experts committee closed-door meeting (30 min)

January 28th 2014

Welcome

Unit presentation: key achievements and projects (presentation - discussion)

BIOPIC team presentation (presentation - discussion)

EViR team presentation (presentation - discussion)

NVZ team presentation (presentation - discussion)

VEBE team presentation (presentation - discussion)

Adenovirus-vaccine team presentation (presentation - discussion)

Pathogen discovery team presentation (presentation - discussion)

Meeting with institutions representatives ENVA, ANSES, INRA

Meeting with the doctoral schools N°402 and 425 representatives

Meeting with staff scientists

Meeting with technical staff

Meeting with PhD students and post-docs

Individual meeting with team leaders

Meeting with unit director

Closed door meeting of the experts committee –pre-writing of the report

End of the visit at 7:30 pm

6 • Supervising bodies' general comments

EnvA
École nationale vétérinaire d'Alfort

Ministère de l'Agriculture, de l'Agroalimentaire et de la Forêt

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n° MG/CF/103-2014

AERES
Section des Unités
20, rue Vivienne

75002 PARIS

Maisons-Alfort, le 18 avril 2014

Objet : **S2PUR150008251 - UMR1161 Virologie - 0940608A**

Madame, Monsieur,

En tant que directeur de l'EnvA, je souhaite vous transmettre les éléments suivants concernant le rapport d'évaluation de l'Unité "Virologie".

En vous remerciant, je vous prie de croire, Madame, Monsieur, en l'expression de mes salutations très distinguées.

Le Directeur,
Professeur Marc Gogny

UMR 1161 de VIROLOGIE

Professor Bruno Lina
Chair of the expert committee

Maisons-Alfort, 10th of April 2014

As regards Evaluation : S2PUR150008251 - UMR1161 Virologie - 0940608A

Dear Sir,

I would like to thank you for the report of your committee. However, I think one point could be underscored if you agree.

Many thanks again to you and your colleagues for your report.

Kind regards

Stéphan Zientara

Team 4 VEBE :
In the context of viral emergence of highly virulent MERS CoV, the activities on CoVs are extremely important. Feline and canine coronaviruses provide excellent natural models of pathogenicity and interspecies transmission of CoVs. The team is presently involved in an ANR program until 2017 to characterize molecular determinants of host species, through molecular epidemiology. To carry out the different projects and develop new studies on viral determinants of host barrier crossing, the replacement of the technician on the verge of retirement is crucial.

Fait à Maisons-Alfort,
Dr Stéphan Zientara, DVM, PhD
Directeur UMR ANSES/INRA/ENVA

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