# VIM - Virologie et immunologie moléculaires

Rapport Hcéres

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

Department for the evaluation of research units

# AERES report on unit:

## Virologie et Immunologie moléculaires

## VIM

# Under the supervision of the following institutions and research bodies:

## Institut National de la Recherche Agronomique - INRA

February 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 Alain VANDERPLASSCHEN, 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: | Virologie et Immunologie moléculaires |
| Unit acronym: | VIM |
| Label requested: | UR INRA |
| Present no.: | UR 892 INRA |
| Name of Director (2013-2014): | Mr Bernard DELMAS |
| Name of Project Leader (2015-2019): | M$^{me}$ Sabine RIFFAULT |

# Expert committee members

**Chair:** Mr Alain VANDERPLASSCHEN, University of Liège, Belgium

**Experts:**

Mr Philippe DERREUMAUX, Université Paris 7

Mr Daniel DESMECHT, University of Liège, Belgium

Mr Benjamin DEWALS, University of Liège, Belgium

Mr Dieter STEINHAGEN, University of Veterinary Medicine Hanover, Germany

Mr Thierry VAN DEN BERG, University of Liège, Belgium

## Scientific delegate representing the AERES:

Mr Daniel OLIVE

## Representatives of the unit's supervising institutions and bodies:

Mr Bernard MIGNOTTE (director of the Doctoral School "Des Génomes aux Organismes")

Mr Thierry PINEAU, INRA

# 1 • Introduction

## History and geographical location of the unit

The "Virologie et Immunologie moléculaires (VIM)" research unit is located on the INRA Campus of Jouy-en-Josas and belongs to the INRA Animal Health Division (AHD). The VIM unit was created in 1988 and located in a new building called "Bâtiment des Biotechnologies". VIM has remained at this location for nearly three decades and experienced several thematic evolutions over the years.

## Management team

The VIM unit comprises 6 research teams, for a total of 24 scientists, an administrative staff and shared services.

- Macroassemblages Protéiques et Maladies à Prions (MAP2): Mr Vincent BERINGUE and Mr Human REZAEI;

- Biologie Moléculaire des Paramyxovirus (BMP): Mr Jean-François ELEOUËT;

- Vaccin et Immunité Antivirale chez les Mammifères (VIAM): Ms Isabelle SCHWARTZ-CORNIL;

- Infection et Immunité des Poissons (IIP): Mr Pierre BOUDINOT and Mr Eric DUCHAUD;

- Virologie Moléculaire des Poissons (VMP): Mr Michel BREMONT;

- Virus Influenza (FLU): Mr Bernard DELMAS.

## AERES nomenclature

SVE1_LS6 Immunologie, microbiologie, virologie, parasitologie

## Unit workforce

| Unit workforce | Number as at 30/06/2013 | Number as at 01/01/2015 |
|---|---|---|
| **N1**: Permanent professors and similar positions | | |
| **N2**: Permanent researchers from Institutions and similar positions | 24 | 24 |
| **N3**: Other permanent staff (without research duties) | 29 | 29 |
| **N4**: Other professors (Emeritus Professor, on-contract Professor, etc.) | | |
| **N5**: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.) | 7 | ND |
| **N6**: Other contractual staff (without research duties) | 3 | ND |
| **TOTAL N1 to N6** | **63** | **>53** |

ND: not determined

| Unit workforce | Number as at 30/06/2013 | Number as at 01/01/2015 |
|---|---|---|
| Doctoral students | 11 | |
| Theses defended | 23 | |
| Postdoctoral students having spent at least 12 months in the unit* | 23 | |
| Number of Research Supervisor Qualifications (HDR) taken | 4 | |
| Qualified research supervisors (with an HDR) or similar positions | 14 | 16 |

# 2 • Assessment of the unit

The main scientific fields investigated by VIM scientists are related to pathogens affecting animal and/or human health (concept of ONE HEALTH), with special emphasis on RNA viruses, prions and the host response to the infection in these models. The scientific research project of VIM falls within the strategic orientations of INRA and its Animal Health Division (AHD) as defined for 2011-2015, namely:

- thematic field 1 – Pathogens characterization;

- thematic field 2 – Host responses to infection and modulation of the host response by the pathogen;

- thematic field 3 – Epidemiology.

The investigated biological questions are: the structure-function relationships of viral proteins, prions and their macro-molecular assemblies, the virulence factors and the adaptation mechanisms to the host responses, the host response and its plasticity during ontogenesis as well as evolution and all aspects related to anti-pathogen strategies (diagnosis, vaccination to therapeutic approaches).

## Strengths and opportunities related to the context

VIM unit is quite remarkable for the reasons listed below. Firstly, its structure allows the complete and synergistic study of all topics related to the themes presently targetted by INRA. The expertises present in the unit, not only allow to address the present topics at a competitive international level, but it also allow to study any emergent diseases that could occur in the future. The present structure seems adequate, both the size of the teams and their research topic justify to keep the present structure. Secondly, while the structure consisting of independent teams, the management at the level of the unit is well organised; it involves the management of financial ressources, human ressources, platforms, scientific seminars. Thirdly, the scientific production of VIM is remarkable for its quality, quantity and diversity (applied and fundamental researches, publications for scientists but also for the public). Importantly, the unit has been at the origin of several scientific breakthroughs over the reviewed period. All teams have an international visibility and “no weakest link” team can be identified in the unit. Fourthly, since 2008, the balance of scientists between INRA recruitments (+7), arrivals of INSERM scientists (+2) with leaving persons (mainly retirements) (-10) is stable. Taking into account the general reduction of founding at the european level, the stability of VIM human resources should be seen as a success. Fifth, for the same reason, the ability of the unit to acquire or upgrade important equipments (L3 and L3+ laboratories, imaging and cell sorter and a platform for protein purification) during the reviewed period should also been as an important achievement. Sixth, the program of the visit allowed the experts committee to interact with all categories of personnel. Systematically, the experts committee observed that VIM employees consider that they are happy and lucky to work at VIM. While events are organised based on various human ressource regroupments (team, PhD, ITA, etc), it has to be noted that people declare and appreciate that they have the chance to interact with people at all levels.

## Weaknesses and threats related to the context

The experts committee observed a slow decline in the number of technical staff. Together with the evolution of biosafety rules over the last few years that increased the amount of work, the manpower of the technical staff will be reaching a critical stage. The turnover of the assistant engineers, technicians and technical assistants is an important issue to maintain high technical competencies or operationnal functions of the unit. Especially, some key persons are close to retirement and there is no clear strategy for follow-up and transfer of knowledge, responsabilities and skills. A similar threat exists at the management level in some teams where the leader is close to retirement and there is no clear plan for the follow-up. The attractiveness for young scientists for PhD is too passive and does not follow a real strategy. The recurrent budget allocated steadily decreases and represents a real threat for the unit. This is, at the moment, largely compensated by external funds but there are no sufficient guarantees for sustainability. The possibilities of non-extendable support have also declined and might hopefully be replaced by other fundings.

## Recommendations

The strategy and five-year plan should be more elaborated, especially at the individual unit level. Although very well elaborated and ambitious at VIM's level, the programs represent more a continuum of opportunities than clear visions for the future in several teams. There is often no real SWOT analysis and the general feasibility is sometimes underestimated. Considering the big challenges for the future and the highly competitive context for fund raising (particularly the unsecure economical context and the progressive globalisation of research activities), the international position of VIM should be increased and consolidated in the near future. This should not only give access to additional funding but also guarantee VIM's long-term attractiveness for junior and senior scientists. More attention should also be paid to some managerial issues. On one hand, the attractiveness for young scientist should be more structured (notably by the organisation of trainings) and, on the other hand, the risk of gap between generations in several units as well as in the administrative and technical staff (ITA) should be anticipated.

# 3 • Detailed assessments

## Assessment of scientific quality and outputs

The scientific production of VIM has been analyzed globally. Over the 2008-2013 period, VIM scientists produced a total amount of 233 articles, among them 217 articles indexed in Web of Sciences, 18 reviews and 63 articles in journals with a IF>5. The top five among these publications are Science (2x), J. Exp. Med. (1x) and PLoS Pathog. (2x), each representing a remarquable breakthrough in the related field of research. Additional remarkable publications include 6 PloS Pathog., 3 PNAS and 3 Immunological reviews. Half of VIM publications (49 %) are with VIM scientists as major author (first, last, or corresponding) and 14 % are publications involving VIM scientists from more than one team (collaboration intra-VIM). Overall, more than 80 % of VIM publications involve a partnership (59 % a national collaboration, 27 % a European collaboration and 9 % another international collaboration). The quality of the publications increases regularly since 2008 up to 2012 with nearly 80 % in the categories from “outstanding” to “excellent”. Besides, 75 % of VIM publications are ranked in Tops ESI (Essential Science Indicators): all disciplinary fields and all years included, 39 % belongs to the 50 % most cited papers, 17 % to the 20 % most cited papers, 18 % to the 10 % most cited papers and nearly 1 % to the 1 % most cited papers (more than 60 citations).

## Assessment of the unit's academic reputation and appeal

VIM’s reputation and appeal goes from leader in the field to important challenger/outsider. VIM scientists were also successful in obtaining funding at national (ANR, FUI, Investissement d’avenir and ICSA) and European calls (Eranet EMIDA, ERC, ITN). In 2012, 80 % of the VIM operating budget was based on external funding. For the 2008-2012 period, 12 ANR projects were granted, 7 of them as coordinator (FluNucleoVir, Phylogen-DC, TRIGNOSTUMOR, BRONCHIOLITEASER, DCskinVacFlu, RiftVac, RSV-NanoViaSkin). In addition, VIM organised an international symposium, 3 workshops and obtained a four-year INRA “Package” fellowship. Finally, last but not least, VIM is Editor of the Veterinary Research journal, ranked first in Veterinary Sciences. The impressive evolution of this journal over the last few years must be correlated with the work of some VIM members.

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

A considerable amount of patents have been submitted by VIM members (they are listed below for each team). Importantly, all scientists consider that the structure of INRA dealing with intellectual properties issues is extremelly efficient when filling patent but also for research of a licensee. VIM scientists were successful in obtaining private funding. VIM members have contacts with professionnal organisations and do their best to solve some of their problems. VIM contributes to information of the public by various actions: publications, media, meetings.

## Assessment of the unit's organisation and life

Mutualization is the key word for the general functioning of the VIM unit. A substantial proportion of the funds obtained by grants are attributed to the overall functioning of the laboratory. This means that a large proportion of the products are indistinctively used for all the research projects carried out in VIM and all the equipments are accessible to everybody. This allows young scientists to develop new fields of research and to devote most of their time to research, promoting new research axes and supporting scientific topics that have not been sufficiently granted for one year. This is quite remarkable and unique. This ethic for work is also observed in the organisation of collective tasks and shared approach regarding GLPs and biosafety. Seminars and journal clubs are organized on a regular basis. In addition, much attention is paid to social activities in order to maintain a positive team spirit in the VIM unit. Importantly as indicated above, these events involved all VIM members indipendently of their function or team.

## Assessment of the unit's involvement in training through research

There are 13 scientists with HDR at VIM, 34 PhD students and 32 M2 students were trained at VIM during the evaluation period and a M2 module « Circulation of pathogenic agents » was organized at Université de Versailles Saint-Quentin en Yvelines. The École Doctorale n° 423 "Des Génomes aux Organismes" is the main partner of VIM.

## Assessment of the strategy and the five-year plan

The strong specificity of VIM is the continuum of scientific projects from the molecular level to the animal level, with both fundamental and applied goals. This ability to achieve this continuum is reinforced by the diversity of pathogens (viruses, prions and fish bacteria) and the diversity of host models (model species like rodent or zebrafish and target species like swine, calf, trout, etc) studied. This dynamics creates synergies between teams involved in the characterization of the pathogens and those studying the host response to the pathogen. Another feature of the scientific dynamics is the integration of veterinary and human health issues by targeting zoonotic pathogens (prions, influenza and rift valley viruses) or family of viruses that cause the same disease in their respective host (for instance respiratory syncytial viruses in human and calves). Moreover veterinary species are studied for their relevance to human as preclinical models (for instance swine to develop skin vaccine for human). The VIM project 2014-2019 aims at strengthening these dynamics, and will meet new scientific challenges in three major axes:

- axis 1 - Understanding pathogens at the molecular level: their genome, their proteins and their interaction with host cellular factors;

- axis 2 - Understanding host responses to infection from high-throughput signatures to in vivo-imaging;

- axis 3 - Innovative strategies to fight infectious diseases: implementation of sustained partnership with industry.

The context behind the programs is well identified, with, on one hand, a sustained demand for research in a field covering major threats for livestock production, major zoonotic risks, growing needs for veterinary vaccines and a major need for translational models for human health and, on the other hand, an increasing impact of new factors related to bioethics, biosecurity, sustainability of husbandry practice and social acceptance of vaccination. However, this strategic plan remains much theoretical, addressing opportunities more than risks or threats. For instance, emerging issues are considered as a must although they could also jeopardize VIM's basic missions. Similarly, heavy investments in high level biosecurity facilities are also considered as a necessity although they can have a strong impact on the budgets and workload of the staff. In summary, a solid SWOT analysis is missing in the presented strategy and perspectives.

# 4 • Team-by-team analysis

**Team 1 :** Team MAP2

Name of team leader: Mr Vincent BÉRINGUE and Mr Human REZAEI

## 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 | 7 | 7 |
| **N3**: Other permanent staff (without research duties) | 5 | 5 |
| **N4**: Other professors (PREM, ECC, etc.) | | |
| **N5**: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) | 4 | 2 |
| **N6**: Other contractual staff (without research duties) | | |
| **TOTAL N1 to N6** | **16** | **14** |

| Team workforce | Number as at 30/06/2013 | Number as at 01/01/2015 |
|---|---|---|
| Doctoral students | 2 | |
| Theses defended | 10 | |
| Postdoctoral students having spent at least 12 months in the unit | 4 | |
| Number of Research Supervisor Qualifications (HDR) taken | | |
| Qualified research supervisors (with an HDR) or similar positions | 3 | 4 |

# • Detailed assessments

### Assessment of scientific quality and outputs

The team MAP2 includes 7 permanent scientists (2 DR2, 4CR1 with 2 from INSERM) and 5 permanent ITA. This team is dedicated to fundamental studies on prion diseases and its main fields of investigation focus on the relationship between protein structural information transparency and prion propagation and neurotoxicity.

The overall scientific activity in the 2009-2013 period is outstanding, with 87 peer-reviewed publications. 36 publications are signed as first or last author by one member of the team, 14 publications are signed by only the members of the team and 72 result from national and international collaborations. Among the 36 publications signed as a first author or last author, the most significant include one Science 2012, 4 JBC, 3 Plos Pathog, 3 FASEB J, 1 Nucleic Acid Res. 1 Path BioL, and 3 J. Virol. Other publications where the team was partner, include Plos Genetics, Brain Path, J Neuroscience, Prion and Plos One, among others.

At the scientific level, the Science 2012 publication represents a real breakthrough in our knowledge of prion diseases by demonstrating for the first time that prion species barriers is tissue-dependent within the same infected host species. Other results of significant importance involve the identification of the C-terminal H2-H3 two-helix bundle (2 JBC,1 FASEB J and 1 J Virol) responsible for PrP conversion, and the discovery that discrete oligomers and the smallest PrP oligomers are the most toxic species (Plos Pathog), a clear analogy with what has been found for Alzheimer's disesase, although toxicity is still a subject of debate in Alzheimer's.

The outstanding quality of the work is also supported by an European patent in 2010 "Compositions for use in the treatments or diagnosis of prion diseases", not licenced however.

## Assessment of the unit's academic reputation and appeal

The overall academic reputation and appeal of the team are outstanding. At the national level, team members have coordinated 1 ANR and participated in three other ANR, have coordinated 5 regional Ile de France projects from the DIM MALINF and have coordinated 7 projects of the French "Fondation Alliance Biosecure". At the international level, the team has coordinated one DEFRA (Department for Environment Food and Rural Affairs) project funded by UK and is one of the partners of one ERC coordinated, however, by an INRA researcher of the INRA center of Jouy-en-Jossas.

The academic reputation of the team is also supported by the activities of the team members in many french evalution comittees: ANSES, INRA, INSERM, AERES, in international instances: NIH and MRC and by the nomination of one member of the team as the TSE expert at AFSAA/ANSES and at ANSM. The team is also participating to the French National de Reference on ANTC (prions). The recognition of the team is further supported by the number of national and international invitations to conferences (20), and the fact they act as referees for peer-review journals including Science, Nature and Plos Pathog (100 papers reviewed), PhD and HDR committies. One of the team's member is also a Scientific editor of Plos One.

Finally, the team has developed a number of tools (cell lines, transgenic mouse models and protocols) that have been distributed in 30 laboratories world-wide. The team has also obtained a four-year INRA contract to host a renowned british expert in NMR studies of amyloids.

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

The overall team's interaction with the social, economic and cultural environment are excellent. The team has industrial colloborations and contracts with various biotechnology and pharmaceutical companies. These interactions mainly concern decontamination procedures for the safety of blood products. Two postdoctoral fellows and one PhD student are currently funded by these collaborations. There is also one European patent.

The team has held a stand at the Salon de l'Agriculture (2009, 2011) and given seminars at the open days of the INRA research center (2009, 2010) and Fête de la Science (2008-2010). The appeal of the team is also supported by the organization of two-day workshop through a GDR. Team members also give a few seminars at the Université du Temps libre de l'Université d'Evry-Essone and students from 2$^{nd}$ et 1$^{e}$ du Lycée Eliot (ZEP, Epinay sous-Sénart).

## Assessment of the unit's organisation and life

There is no evaluation at the team's level, but at the unit level.

## Assessment of the unit's involvement in training through research

The overall team's involvement in training through research is very good. During the period, the team had 5 PhD students, and 5 shared PhD students ("en cotutelle"), and 5 five M1/M2 students from France and abroad, Canada, Spain, United Kingdom, Italy and Germany.

## Assessment of the strategy and the five-year plan

Overall, the team's strategy and five-year plan are excellent. The team has a clear vision of the field of prion and their seven main reasearch axes are original at the national and international levels. Some of their research plans are in continuity of the past period and involve a better understanding of the molecular basis of PrP structural diversity in relation with strain phenomenom, the structural mutation during prion conversion, tissue/cell selectivity of prion replication and toxicity, and the interaction of PrP with cellular partners. Other new projects include the role of fragmentation in the prion conversion process, prion phenomenom involved in regulatory system: Structural Epigenetic. The latter topic is highly original. All these studies will be performed with the aim to extend our knowledge of protein misfolding in neurodegenerative studies. However, the general feasibility of this plan could have been better explained.

## Conclusion

- **Strengths and opportunities:**

The subjects of research are strategic and pertinent at the interface between biology, chemistry, biophysics and computer simulations. The laboratory has a strong expertise in prion diseases. He has an excellent productivity in terms of quality and quantity, a good visibility and has a rich network of national and international collaborations. The number of departures has been compensated by new arrivals and the five-year plan is based on the continuity of current projects and the introduction of new exciting subjects.

- **Weaknesses and threats:**

The number of six subjects of research might be too high for a number of seven scientists to achieve a top or higher international visibility although the team has a high number of external collaborations. However, the experts commitee is convinced that the team will, after an explorary phase of all six subjects, focus on the most promissing ones.

- **Recommendations:**

The recommendations below are advices that must be taken into account based on the excellent report made above. Efforts should be made to attract more PhD students and postdoctoral fellows through applications to national (LABEX) and international grants (European Union, and the PhD grants available in many countries to get their PhD abroad). The implication in teaching and master's training programs could be also substantially improved even though this is not anymore synonymous of the obtention of PhD grants from École Doctorale. There are also possibilities to improve the international visibility of the unit by the number of invited conferences and to obtain international fundings. Despite their rather specific topic, the team should improve their interactions with the other teams of the unit. Developping and exploiting the intellectual property associated with their research could also be improved.

**Team 2:** Team BMP

Name of team leader: Mr Jean-François ELÉOUËT

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 | 2 |
| **N3**: Other permanent staff (without research duties) | 2 | 2 |
| **N4**: Other professors (PREM, ECC, etc.) | | |
| **N5**: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) | 1 | 1 |
| **N6**: Other contractual staff (without research duties) | 1 | 1 |
| **TOTAL N1 to N6** | **6** | **6** |

| Team workforce | Number as at 30/06/2013 | Number as at 01/01/2015 |
|---|---|---|
| Doctoral students | 2 | |
| Theses defended | 1 | |
| 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 team BMP is one of the smallest within VIM (see table workforce) and includes only 2 permanent researchers (1 DR2 and 1 CR2), and 1 technician. The main purpose of the team is to study the functioning and the structure of the RNA polymerase complex of respiratory syncytial virus. They also developed a powerful reverse genetics system, identify targets for antivirals and collaborate with immunologists (from VIM and from other labs) to develop new vaccine strategies using recombinant proteins.

Considering the small size of the team, the overall scientific activity over the 2009-2013 period is very good, with 20 peer-reviewed publications and 3 patents (2 active, 1 withdrawn). Among those, 7 publications are signed as first or last author by one member of the team, 13 publications are signed by members of the team as co-author, and result from national and international collaborations. Instead of quantity, publications are of high quality: among the

7 publications signed as a first author or last author, the most significant ones include J. Virol, Vaccine and Plos Pathogens. Other publications where the team was partner, include Science, Plos One, Vet Research among others.

At the scientific level, the science 2009 publication represents a real breakthrough in the knowledge of paramyxoviruses structure and function, by establishing the atomic structure resolution of the RSV nucleoprotein. The structure revealed that the RNA wraps around the protein ring, running in a basic groove, with seven nucleotides contacting each N protomer, what distinguishes RSV from other paramyxoviruses for which 6 nucleotides contact with each N protomer. Other results of significant importance involve the localization of a P-binding domain on N, representing a target for anti-RSV drugs, structure-function studies on M2-1 and studies on the large polymerase L subunit.

Finally, the team jumped into the SBV emergence. In collaboration with ANSES Maisons-Alfort, it produced recombinant proteins that were produced to develop an ELISA test. Unfortunately, in April 2012, an ELISA test based on the N protein was sold by ID.vet, which prevented the BMP team from exploiting their work.

## Assessment of the unit's academic reputation and appeal

The overall BMP's academic reputation and appeal is excellent. The team has 7 research projects, among which they coordinate 4 of them. BMP is coordinator of an « ANR blanc international 2013 - project », which aims to identify cellular partners of the RSV RNA polymerase complex in collaboration with Saõ Paulo University, Institut Pasteur and CNRS (Gif-sur-Yvette), is also coordinator of an « ANR blanc 2011 – BRONCHIOLITEASER » project, which aims to characterize the structure and function of the RSV RNA polymerase complex in collaboration with Institut Pasteur and CNRS (Gif-sur-Yvette), of a franco-Brazilian project 2013-2015, which aims to identify cellular partners for RSV and financed by the « CAPES-COFECUB » and of a national project « Prévalo INRA 2010 » on Respiratory Syncytial Inhibitors. In addition, BMP participate to an « ANR RPIB (2013-2015) » project, which aims to demonstrate the efficiency of N rings as epicutaneous vaccine in pre-clinical tests in collaboration with DBV technologies, to an EMIDA project "Development and comparative evaluation of three new generation BRSV DIVA vaccines and a corresponding DIVA test" in collaboration with the Institute for Animal Health, Compton, and the Swedish University of Agricultural Sciences (2012-2014) and to the national project « Prévalo INRA 2009 »: Nanneau-M2.

The academic reputation of the team is also illustrated by collaborations with the Institut Pasteur to study RSV infected cells by super resolution microscopy and atomic structure resolution of RSV N and L; the MRC in Glasgow for electron microscopy of RdRp molecules; the University of Leeds for crystallographic structure of M2-1; the University of Liverpool for proteomics of RSV, Institut Pasteur, the CNRS Gif for NMR studies, the Uppsala university and Compton for bovine vaccination, the University of Saõ Paulo for virus-cell interactions; the HSE-SO, Valais, Swiss for peptide inhibitors for RSV, and the UVSQ for reverse genetics.

The international recognition of the team is further supported by invitations to conferences (3), reviewing of articles (9) and expertises for academic instances: evaluation of projects for ANSES, CIRAD, Welcome Trust and recruitments or promotions of staff for French instances.

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

The overall BMP's interaction with the social, economic and cultural environment is excellent. The team has industrial collaborations and contracts with a pharmaceutical company for drug design and a biotechnology company for vaccination using transcutaneous route (patches). Especially, this latter project: (600 k€) entitled "Innovative Epicutaneous Sub-unit RSV Vaccine strategy for infants : Pre-clinical proof of concept" is particularly promising and was emphasized by a press release by INRA and was widely relayed by the French press. In addition, an ELISA kit based on the SBV N protein was developed and is now marketed by a third company.

## Assessment of the unit's organisation and life

There is no evaluation at the team's level, but at the unit level.

## Assessment of the unit's involvement in training through research

The overall BMP's involvement in training through research is very good. During the period, the team contributed to one completed PhD thesis and to 4 ongoing PhD theses. This involvment is reasonable considering the size of the team.

## Assessment of the strategy and the five-year plan

Actually, the strategy and five-year plan was not described in the report but was developed during the presentation. The team has a very good, although very (too) ambitious vision of their future research. Some of the prospects are the continuation of the running projects: RSV interactomes studies (ANR blanc grant France – Brazil 2014-2018) and vaccination strategies (ANR grant RPIB 2013-2015 on transcutaneous vaccination; EMIDA project and future participation in an Horizon2020 project submission). Another axis will further study the RSV Polymerase and represents the basis for 2 PhD programs: expression of the large protein in baculovirus and functional studies of M2-1. A third axis will further investigate the therapeutic potential of RSV antivirals in a mice model. This prospect will go in line with the adaptation of RSV to mice by using and improving the in-house reverse genetics system. Finally, a new aspect, namely the role of the SH glycoprotein in inflammation, will be addressed but has not been described during the visit. All these studies will be performed with the main goal to extend the knowledge of the structure and function of the RSV RdRp complex in order to use several domains as potential target for antiviral or vaccine strategies.

## Conclusion

- **Strengths and opportunities:**

Despite the small size of the BMP team, excellent basic research on structure/function of the RSV polymerase complex has been achieved, giving an international recognition and visibility to the team in its field of research. This led to very innovative applications of the obtained results. Indeed, the development of new drugs and vaccines against RSV are clearly needed and represent strong opportunities. The interactions with the VIAM, MAP2 and FLU teams are very strong.

- **Weaknesses and threats:**

The report as presented is scientifically sound but is incomplete and has many inconsistencies. Those were partly clarified during the presentation and the interviews. This might denote some overload. The five-year plan is based on the continuity of current projects and the introduction of new subjects. The number of six subjects of research, although closely related, might be too important for the two permanent senior scientists to achieve a top and/or higher international visibility. The five-year plan described during the visit (it was absent in the pre-report) lacks of priority and the general feasibility of this plan remained very theoretical. RSV remains poorly studied in France and Europe and the network of collaborations should be further expanded, especially outside Europe.

- **Recommendations:**

The team is small and sometimes scattered. For instance, the strategy regarding the antiviral developments should be consolidated by stronger interactions with pharmaceutical research groups or companies that are specialized in drug design and synthesis. This could be achieved jointly with the other VIM units. In this context, better knowledge and protection of IP rights should also be encouraged. Also, the implication in emerging diseases (like SBV) should be reconsidered. Efforts should also be made to improve the international visibility of the unit by the number of invitations to conferences and international funding.

**Team 3:** Team VIAM

Name of team leader: Ms Isabelle SCHWARTZ-CORNIL

## 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 | 4 | 4 |
| **N3**: Other permanent staff (without research duties) | 3 | 3 |
| **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 | 1 |
| **TOTAL N1 to N6** | **8** | **8** |

| Team workforce | Number as at 30/06/2013 | Number as at 01/01/2015 |
|---|---|---|
| Doctoral students | 1 | |
| Theses defended | 5 | |
| Postdoctoral students having spent at least 12 months in the unit | 3 | |
| Number of Research Supervisor Qualifications (HDR) taken | 1 | |
| Qualified research supervisors (with an HDR) or similar positions | 4 | 3 |

## • Detailed assessments

### Assessment of scientific quality and outputs

The team included during the 5-year period 5 permanent scientists (1DRE – retired in 2013, 1 DR1, 1 DR2, 2 CR1 one of them retired in 2013) and 3 permanent ITA. The research developed by this team is dedicated to study the immune responses induced by viral responses in domestic animals (ruminants and pigs) with the focus on intervention and vaccine strategies against three main viral infections with public health and/or socio-economical importance (Repiratory Syncitial virus- RSV, Bluetongue virus-BTV, Influenza virus-IV, Rift Valley Fever virus).

The overall scientific activity in the 2009-2013 period is excellent, with 36 peer-reviewed original publications with IF ranging from 2.2 to 13.85. The team is also at the origin of 3 active patents. 19 publications were signed as first or last author by one member of the team. Among the 19 publications signed as a first author or last author, the most significant include 1 J Immunol 2010, 1 J Virol 2012, 1 Eur J Immunol, 2 PLoS ONE. Other publications where

the team was partner, include J Exp Med, PNAS, J Virol, J Immunol, Eur J Immunol, Vaccine, Vet Res, PLoS ONE, Vet Immunol Immunopathol, among others.

At the scientific level, this team is one of the leading groups in the field of comparative immunology focusing on dendritic cell subsets characterization and function in ruminants and pigs, in particular in the context of viral infection. In addition to its strong fundamental reseach the team, is also developping vaccination strategies. The results obtained and published during the period 2009-2013 have given good hope for the development of an effective RSV vaccine, in particular using the "nanoring" strategy developed by another team of the unit (BMP). Another result of functional significance is the development of the "Vaccibodies" and "Vaccicomplexes" by using XCL1-antigen complexes to target XCR1 expressing DCs and enhance vaccine effectivity against IV and Rift Valley Fever Virus infections.

## Assessment of the unit's academic reputation and appeal

The overall team's academic reputation and appeal is outstanding. At the national level, VIAM's members have coordinated 5 ANR and participated to 2 other ANR, have coordinated 1 AVIESAN, 2 ICSA (Institut Carnot), 1 AFSSA-INRA, and one DIM Malinf contract. At the international level, the team has coordinated one ERANET-EMIDA project, 2 transnational access FP7 – Capacity NADIR project and collaborated on 2 FP6/FP7 projects of the EU.

The academic reputation of the team is also supported by the activities of the team members in many evaluation instances (AERES and evaluation of foreign laboratory structures (Belgium, Spain, Sweden), and evaluation of research projects (DIM Malinf, ANR, ISC). The recognition of the team is further supported by the number of national and international invitations to conferences (29), and the organization during the period of 3 national workshops. The team is currently coordinating the submission of a H2020 grant.

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

The overall team's interaction with the social, economic and cultural environment is excellent. The team has 5 industrial contracts (bio)technology and pharmaceutical companies. These concern essentially vaccination improvement technologies. The team has 3 active patents but no license.

The team has held a stand at the Salon de l'Agriculture (2011) and given seminars at the open days of the research center Jouy (2010) and Fête de la Science (2009). More than 50 press releases (national and international) on the objectives of an ANR RPIB 2012 project on Innovative Epicutaneous sub-unit RSV vaccine for infants have been made to the large audience.

## Assessment of the unit's organisation and life

There is no evaluation at the team's level, but at the unit level.

## Assessment of the unit's involvement in training through research

The overall team's involvement in training through research is excellent. During the period, the team had 5 PhD thesis completed, 3 postdoctoral fellows and 8 M1/M2 students from France and abroad (Brazil, Iran, Romania and Tunisia). Three of the PhD students obtained competitive Doctoral School contracts (ED GAO Versailles, ABIES Paris) and one obtained a highly competitive INRA young scientist contract. All PhD students were offered at least one international meeting and one national meeting attendance and they were encouraged to apply for travel grant support. All PhD benefited from thesis committees with local, national and sometimes foreign pertinent researchers. Three students wrote and/or defended their thesis in English. All PhD completed their thesis in <3 years 1/2 and published from 2 to 8 papers with the team. All PhD and postdoctoral fellows found employment when leaving the team, most often with the VIAM support.

The 3 project leaders are involved in recurrent teaching activities at the M1 and M2 levels (about 15-20 h/year) at the Université de Versailles Saint-Quentin en Yvelines (UVSQ), the Université de Tours, and AgroParisTech.

All VIAM scientists-have been involved in PhD jury (26) and HDR jury (8) during the period.

## Assessment of the strategy and the five-year plan

Overall, the team strategy and five-year plan is very good. Some sections of the proposed plan are of excellent originality, such as for example addressing the respective roles of immune cell vs epithelial cell during viral infection. DC subset characterization and physiology in ruminants and pigs has come near to an end and though some new data on DCs in chicken is a new asset to the team, it appears that the results confirm previous data of the team. The team wishes to further develop DC-integrated strategies in vaccination against viral infections, in particular Influenza and Rift Valley Fever viruses. Contracts are currently funding these projects but the five-year plan is not sufficiently detailed and the general feasibility of this plan could have been better explained. Overall, there is a relative lack of originality and the perspectives are mostly based on the on-going work, though some interesting and innovative ideas are briefly presented.

## Conclusion

- **Strengths and opportunities:**

The subjects of research are strategic and pertinent in the context of vaccine developments against virus infection having highly significant public health and socio-economical impacts. The laboratory is one of the international leading team on DC subset characterization, migration and pathophysiology during viral infections, using small ruminants and pigs as model to tackle key questions on the induction and enhancement of protective immune responses (during primary infection and after vaccination). The team has an excellent productivity in terms of quality and quantity, a good visibility and has a rich network of national and international collaborations. The team has also shown its high flexibility and reactivity potential in terms of subjects by switching from BTV to Rift Valley Fever virus infection studies to adapt itself to financial supports.

- **Weaknesses and threats:**

The DC subset characterization across mammals has somehow come to a relative end and though new data are apparently available for chicken, the team will have to focus on the use of this knowledge in the development of new innovative vaccination strategies.

- **Recommendations:**

Efforts could be made to attract more PhD students and postdoctoral fellows through applications to national (LABEX) and international grants (European community, and the PhD grants available in many countries to get their PhD abroad). The implication in teaching and master's training programs could be also substantially improved.

**Team 4:** Team IIP

Name of team leader: Mr Pierre BOUDINOT and Mr Eric DUCHAUD

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 | 4 | 4 |
| **N3**: Other permanent staff (without research duties) | 6 | 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) | 2 | |
| **TOTAL N1 to N6** | **13** | **9** |

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

## • Detailed assessments

### Assessment of scientific quality and outputs

The team includes 4 permanent scientists (2 DR2, 1 IR1, 1 IR2) and 6 permanent ITA. This team dedicated to fundamental studies on virus/ host interactions in fish as well as functional genomics of fish pathogenic Flavobacteria. The main fields of investigation are the deciphering of interferon type I immune responses, the identification of the B and T cell repertoire in rainbow trout during virus infection and the analysis of genes associated with virulent traits in the genome of fish pathogenic bacteria from the genus *Flavobacterium*.

The overall scientific activity during 2009 and 2013 is excellent, with 43 peer reviewed articles, from with 25 publication are signed as first or last author by one member of the team and 41 implicate national and international cooperations. Among the 25 articles with one member of the team as first or last author, the most significant included one Plos Pathog, 1 BMC Biol, 1 J Virol, 4 Plos one, 2 Appl Environ Microbiol and 4 Dev Comp

Immunol. Other publications where a member of the team was co-author include Science, Immunological Reviews, J Exp Med, Plos Pathogens, J Immunol among others. The team has so far not been submitted patent application.

At the scientific level, the publication in Plos Pathogens 2013 provides a breakthrough in our understanding of adaptive immune responses in fish by demonstrating for the first time that fish mount complex clonal IgM and IgT responses to virus infections. Other results of significant importance are the genome characteristion of Flavobacteria, analysis of the population structure of this bacterium in river models, a transcriptional analysis of immune responses of susceptible and resistant fish clones to the bacterium *Flavobacterium psychrophilum* (Appl Microbiol, J Bacteriol, Plos one, Vet Res.) and the identification and functional characterisation ISGs and of TRIM genes in fish.

## Assessment of the unit's academic reputation and appeal

The overall academic reputation and appeal of the IIP team is outstanding. The members of the unit were able to obtain grants for a total amount of more than 2 Million Euro. At the national level, the members of the team coordinated 1 ANR project and were involved 4 additional ANR projects. At the international level, team members coordinate an EMIDA ERA Net and participated in 3 EU FP 7 projects and an EU initial training network (FishForPharma). In addtion, the unit obtained funding for novel infrastructure (two-photon-confocal microscope).

The academic reputation of the team is also supported by a high number of collaborations with laboratories at the national level (including other institutes of INRA, CNRS, IFREMER, Institut Pasteur and universities) as well as at the international level including laboratories from Belgium, the Netherlands, Japan, Spain, Germany, United Kingdom and USA. Three members of the team act as editors of various scientific journals, including J System Evol Microbiol, Dev. Comp Immunol, Fish Shellfish Immunol, Plos One. The academic reputation of the team is further supported by a number of invitations of team members to international conferences or workshops (arround 8 for the reviewed period).

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

The overall interaction of team members with the social, economic and cultural environment is very good. The team is member of a network for supporting fish farms with respect to veterinary and epidemiologcal issues which directly allows to disseminate findings from the fundamental research of the unit into practical work with fish diseases. The team has industrial cooperation and contact with 7 companies dealing with the development of biological diagnostics and vaccines for fish.

Team members also disseminated their knowledge on fish pathogens and fish immune responses by publications directed towards the general public.

## Assessment of the unit's organisation and life

There is no evaluation of this point at the team level, but at the unit level.

## Assessment of the unit's involvement in training through research

The overall involvement of the team in training through research is very good. During the evaluation period, the team has been training 8 PhD students including 3 international students, 4 post doctoral researcher (2 international) and 2 M2 students from France. Three PhD theses have been finalised during the reviewed period. The international students/ scientists were attracted from Estonia, the Netherlands, Italy and Spain. Members of the team also participate in international training events (Fish Immunology Workshop, NL, doctoral course in Estonia).

## Assessment of the strategy and the five-year plan

Overall, the team's strategy and five-year plan are excellent. The team's scientific research perspective in fish immunology as well as in genomics of Flavobacteria are original both at the national and international level. The research plans are in continuation with the past period and aim in the field of fish immunology at an understanding of the spatial and temporal structure of INF-responses at various life stages of Zebrafish, taking advantage of the genetic tools available in the group and the newly acquired *in vivo* imaging tools. On the field of *Flavobacterium* genomics, the plans aim at a better understanding of the population structure of this bacterium as a tool for an improved management in fish farms and deciphering of genetic traits for pathogenicity by comparative and functional genetic approaches. All these studies will be performed with the aim of a better understanding of fish pathogen interactions by using concepts and methods from both areas of work.

## Conclusion

- **Strengths and opportunities:**

The planned research is well considered and significant. The work is at the interface of infection biology, functional genomics and biomathematics (handling of large data sets). The laboratory has a strong reputation in fish immunology and bacteriology. It has an excellent productivity, both in quality and quantity, it is highly visible and a well extended network of national and international collaborations. This is in particular reflected by the high number of international grants that the team managed to obtain. The number of departures has been largely compensated by new arrivals and the five years plan included the continuation of current projects, takes advantages of developed tools and introduces new and exciting visions.

- **Weaknesses and threats:**

The two lines of research (fish immunology, bacterial genomics) were developed largely independent from each other, which might interfere with the achievement of top visibility of the team, even though the team members working in both areas have a high number of collaborations. Even though there are active collaborations with the VMP unit, their number and goals are rather limited. The unit has not generated intellectual properties despite working in a field propitious to applied sciences.

- **Recommendations:**

Efforts should be made to further strenghten the collaboration between the two research lines. The involvement in teaching at local universities in training programmes at the master level could be improved in order to attract more PhD students and post doctoral fellows, even though it is anticipated that efforts in teaching not always guarantee the obtention of PhD grants from national resources. Collaborations with team 5 should be increased. The team should be sensitized to the importance of intellectual property.

**Team 5:** Team VMP

Name of team leader: Mr Michel BRÉMONT

## 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 | 2 |
| **N3**: Other permanent staff (without research duties) | 3 | 3 |
| **N4**: Other professors (PREM, ECC, etc.) | | |
| **N5**: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) | 1 | 1 |
| **N6**: Other contractual staff (without research duties) | | |
| **TOTAL N1 to N6** | **6** | **6** |

| Team workforce | Number as at 30/06/2013 | Number as at 01/01/2015 |
|---|---|---|
| Doctoral students | 1 | |
| Theses defended | | |
| 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

The team VMP includes 2 permanent scientists (1 DR1, 1 CR1), 1 enginieer assistant, 2 technicians (working part time, 80 %), one post-doc and 1 PhD student. It is one the smallest teams of VIM.

This team is dedicated to the study of fish viral diseases, that cause important financial losses to the aquacultural industry. It is studying established diseases such as VHSV, IHNV, IPNV but also emerging diseases such as SDV, SPDV, ISAV. The general strategy of the group is to develop methods to allow viral genome mutagenesis in order:

I) to generate live attenuated vaccines to be used by bath immersion;

II) to identifiy the virulent factors encoded by these viruses;

III) to investigate the potential of fish virus as gene vectors for fish but also for warm blood vertebrates (includind mammals);

IV) to use these viruses as models to study the anti-viral innate immune responses (RIG-1, MAVS, Sting proteins).

The strategy of the team is to develop both fundamental and applied researches.

The overall scientific activity during 2009 and 2013 is very good to excellent, with 18 peer reviewed articles, from with 7 publications are signed as first or last author by one member of the team. Most of the publications signed by the team as first or last author are in very good journals (3 J. Virol, 1 J gen Virol, 1 Plos One, 1 Vet res). The co-author publication list demonstrates the implication of the team in national and international cooperations. Most of the co-author publications are also in very good journals (1 Plos Pathogen, 2 J Virol, 1 Plos one, 1 Fish Shelfish Immunol, 2 J Fish Diseases, 1 Immunol immunopath). Importantly, the team is at the origin of 5 active patents, one has lead to an important license while the 4 remaining ones are currently subject of license options.

At the scientific level, the main results of the team can be summarised as follows. Firstly, the reserve genetic systems developed by the team and the derived applications represent real breakthroughs. Secondly, the unexpected discovery that Novirhabdovirus can be used as a vaccine delivery platform for warm blood animals is quite remarkable. Thirdly, the team demonstrated that fish encode orthologues of RIG-1, MAVS and Sting. These studies represent a significant contribution to our understanding of fish innate immunity.

In addition to their main topics, the activities of the team performed during the last 5 years demonstrated their willingness to respond positively to external request as demonstrated by the studies of the team on brown muscle disease in clams and trout alphavirus as a model for muscular lesions following natural alphavirus infection.

## Assessment of the unit's academic reputation and appeal

The overall academic reputation and appeal of the team is excellent. The team members were able to obtain grants from various resources (National and International) including from private companies (license and sale of product). At the national level, the team members acted as coordinator or participant in 4 national grants (2 ANR, 1PTR and 1 INRA). At the international level, team members initiated the formation of ERA-NET EMIDA consortium which was unfortunately not funded. However, despite being not funded, this network seems to be active.

The team is frequently visited by foreign scientists aiming to acquire the know-how of the team in reverse genetics. Its academic reputation is further supported by the implication of its members in PhD thesis committee (at both national and international levels), as invited speakers in international meetings, as organisers of meetings and participation to reviewing activities for funding agencies (national and international) and virology journals.

Importantly, the team is playing a strategic role in the editorial of the Veterinary Research journal (editor in chief). It is important to note that the progression of this journal has been quite spectacular over the last few years laeding to submission of two manuscripts per day. One member of the team will remain the editor in chief of the journal for the next 5 years .

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

The overall interaction of team members with the social, economic and cultural environment is outstanding. The team is at the origin of numerous patents that have lead to license (three years R and D program on west nile, dengue and respiratory syncytial virus vaccine development using the Novirhabdovirus as a delivery plateform), research grants and product sale. VMP members also disseminated their knowledge on fundamental and applied researches by publications directed towards the scientific community (book chapters) but also to the general public. One member of the team has been strongly involved in the organization of a stand at the“salon de l’agriculture” 2012.

## Assessment of the unit's organisation and life

There is no evaluation of this point at the level of the team, but at the unit level.

## Assessment of the unit's involvement in training through research

The overall involvement of VMP in training through research is very good. As mentioned above, the team is frequently hosting international scientists aiming to acquire a know-how in the reverse genetics systems developed by the team. However, no PhD thesis has been completed during the reviewed periode and only PhD thesis is going on at the moment.

## Assessment of the strategy and the five-year plan

Overall, VMP's strategy and five-year plan is very good to excellent.

The team's scientific research perspective relies mainly on the data they obtained over the last 5 years. Their goal is to pursue the difficult challenge to develop in parallel fundamental and applied researches. While the plan described in the team report is rather synthetic, the team described their strategy in more details during the interview and convinced the experts committee that their strategy was sound, original and rational. In general their overall strategy to identify genes involved in innate immune responses of fish against viruses is important. Their applied research on attenuated live vectors and identification of virulent factors encoded by these viruses is in line with their overall strategy.

## Conclusion

- **Strengths and opportunities:**

The planned research is well considered and significant. Its is build on the know-how acquired by the team and based on the original data they obtained and protected (intellectual property). The laboratory has a strong reputation in fish virology. The role of the team in the editorial board of the Veterinary Journal represents a key and main function for the person in charge.

- **Weaknesses and threats:**

The team did not produce any PhD thesis over the reviewed period. The role of the main investigator of the team as editor in chief of Veterinary Research represents an important function that is time consuming. Since the size of the team is rather limited, this important and time consuming function could have a negative impact on the scientific production and/or management of the team when considered on the long term. While existing, the collaborations with team 4 are too limited.

- **Recommendations:**

Team members should develop strategies to attract PhD students and to support them financially. The key role played by the team's principal investigator in the editorial board of the Veterinary Research Journal should be compensated in the man power of this team. Some concerns were raised about the future retirement of the principal investigator of the team. A progressive transfert of the responsibility in the team to promising scientists should be discussed. As mentioned for the team, while existing, the collaborations between teams 4 and 5 are rather limited while their complementary expertises should lead to synergistic and original collaborations.

**Team 6:** Team FLU

Name of team leader: Mr Bernard DELMAS

## 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 | 5 | 5 |
| **N3**: Other permanent staff (without research duties) | 5 | 5 |
| **N4**: Other professors (PREM, ECC, etc.) | | |
| **N5**: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) | | |
| **N6**: Other contractual staff (without research duties) | | |
| **TOTAL N1 to N6** | **10** | **10** |

| Team workforce | Number as at 30/06/2013 | Number as at 01/01/2015 |
|---|---|---|
| Doctoral students | 1 | |
| Theses defended | 4 | |
| Postdoctoral students having spent at least 12 months in the unit | 5 | |
| Number of Research Supervisor Qualifications (HDR) taken | | |
| Qualified research supervisors (with an HDR) or similar positions | 3 | 4 |

## • Detailed assessments

### Assessment of scientific quality and outputs

The team « FLU » includes 5 permanent scientists and 5 permanent ITAs (2 engineers and 3 technicians). The team's efforts are dedicated to host-influenza interactions in general. On the virus side, the main efforts are focused on the biochemical and biophysical characterization of 2 influenza A virus proteins: NP and PB1-F2. The fundamental works on NP aims at generating sufficient theoretical and material resources for innovating in the field of antivirals. On the host side, the team focuses on the delineation of the status of the PB1-F2 polypeptide as a key virulence factor, with efforts to establish the specific impact of its expression on cytokine/chemokine transcripts expression patterns and clinical disease severity, along with an attempt to identify the transcriptional factors involved.

The overall scientific activity over the 2009-2013 period is excellent, with 34 peer-reviewed publications signed as first or last author by one member of the team (in a total of 56 publications). Among these, the most significant include PNAS, PLoS Pathogens, J. Immunol., JBC, J. Virol. and Am. J. Respir. Cell Mol. Biol. Overall, the team's permanent scientists thus published 1 scientific publication as first/last author per year over the reviewed period. This is excellent although improving this average in the future seems possible.

## Assessment of the unit's academic reputation and appeal

The overall academic reputation and appeal of the team is very good. At the national level, the team coordinated 2 ANR projects and participated to 2 additional projects (ICSA & ITMO). At the international level, the team participated to 2 EU projects, of which 1 IP and 1 Marie-Curie. Besides, team members delivered 4 invited talks, 1 in France, 2 in Germany and 1 in China. The academic reputation of the team is also supported by its designation to evaluate a Wellcome Trust project.

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

The overall team's interaction with the social, economic and cultural environment is very good. The team has an industrial collaboration with a company for screening the antiviral properties of drug panels. There is no patent, but 3 active PCTs. None of them has been licensed so far. The team participated to the « Salon de l'Agriculture (2011, 2013), to the « Fête de la science » (2009) and to the « Open day of the Jouy-en-Josas Research Center » (2010). The team also signed posters at « Journée de Lyon Biopôle » in 2011 and 2012. Overall, we noticed that the « patenting culture » is present, which is likely to be promising.

## Assessment of the team's organisation and life

Not applicable. The unit was evaluated in this respect, not the team.

## Assessment of the unit's involvement in training through research

The overall team's involvement in training through research is very good. During the period, the team trained 5 postdoctoral fellows and supervised 2 completed and 1 ongoing PhD theses. In addition, one member of the team co-supervised two completed theses. The team is also involved in teaching, about 15 h/year, at the M1/M2 levels at local universities and AgroParisTech.

## Assessment of the strategy and the five-year plan

Overall, the team's strategy and five-year plan are rather disappointing. For example, there is no SWOT analysis available, no definition of new targets and no clear biological questions to be answered. The future is seen as a continuation of the past and the projects intended typically to address very broad themes that are descriptive in nature. The team's strategy consists in continuing the structural and functional characterization of the PB1-F2 protein on the one hand and in developing compounds targeting the influenza virus nucleoprotein on the other. It is not clear what is meant by « developing compounds », i.e. « synthesizing and testing » or « testing compounds generated by others » ? The strategy and the five-year plan elaborated for the announced 10 permanent positions (5 scientists and 5 ITAs) are explained in 19 lines in all. This unit should revisit its strategy and five-year plan.

## Conclusion

- **Strengths and opportunities:**

The « FLU » team significantly contributes to the world scientific driving force in influenza biology; this is very important because influenza viruses will stay a top priority for public health policies in the future decades. Indeed, according to the FAO, OIE and WHO the most significant global trend for the next 40 years will be the rise of monogastric species intensive breeding, i.e. pig, poultry and fish. Of which 2 are the most important bioamplificators of influenza viruses. The FLU team has the know-how to play a key role in the research related to this topic.

- **Weaknesses and threats:**

The fact that no serious five-year action plan has been worked out yet is a critical weakness. About half of the activities foreseen consist in competing with the big pharmaceutical companies to identify and develop new antivirals dedicated to the human species. This is a tough challenge and we feel great respect for this ambition. However, it is likely that the resources invested in such a project by both parties are so disproportionate that a favourable outcome for the team is unlikely. In comparison, the team displays few efforts to improve our global understanding of the biology of influenza viruses in nature and in farms, which information is critical for governmental authorities to improve prevention policies at the national/EU level. This is, at least partly, the consequence of the criteria used to evaluate/compare scientific teams (IF, citation index, etc.). However, a disinvestment in this area could threaten the sustainability of the team in the medium term, especially if the new antiviral intended are finally not identified.

- **Recommendations:**

Efforts should be urgently made to elaborate a long term strategy and a five-year plan. The team needs to diversify its scientific activities, including subjects that are critical for sanitary policy makers and for developing innovative prevention strategies (new vaccines, genetic selection, management practices, knowledge on reservoir species, monitoring of circulating strains and virulence markers, etc.). The team should also define quantitative objectives in terms of publications as first/last author and in terms of PhDs. There is also some margin of progression for increasing international partnerships and for improving the international visibility of the team by increasing the number of invited conferences and by obtaining international fundings.

# 5 • Conduct of the visit

## Visit dates:

Start: 23 january 2014, at 08.30 am

End: 24 january 2014, at 03.00 pm

Visit site: UR892 VIM

Institution: INRA

Address: F-78350 Jouy-en-Josas

## Specific premises visited:

None, the visit was restricted to the open hall and to one auditorium.

## Conduct or programme of visit:

AERES scientific advisor (DS): Mr Olive DANIEL

| Day one – 01/23/2014 |
|---|

**The activities below are public unless specified (indicated as closed-door)**

| | |
|---|---|
| 09.00-09.30 am | Welcome (closed-door) experts committee with the DS (the roles and procedures of AERES) |
| 09.30-10.30 am | Director of the unit (presentation, discussion): presentation of past activities and projects |
| 10.30-10.50 am | Coffee break |
| 10.50-11.30 am | Team MAP2 (talk + discussion) |
| 11.30-12.10 pm | Team BMP (talk + discussion) |
| 12.10-12.20 pm | Closed-door discussion with the group leader of team 1 |
| 12.20-12.30 pm | Closed-door discussion with the group leader of team 2 |
| 12.30-01.10 pm | Lunch |
| 01.10-01.50 pm | Team VIAM (talk + discussion) |
| 01.50-02.30 pm | Team IIP (talk + discussion) |
| 02.30-02.40 pm | Closed-door discussion with the group leader of team 3 |
| 02.40-02.50 pm | Closed-door discussion with the group leader of team 4 |
| 02.50-03.30 pm | Coffee break |
| 03.30-04.10 pm | Team VMP (talk + discussion) |
| 04.10-04.50 pm | Team FLU (talk + discussion) |
| 04.50-05.00 pm | Closed-door discussion with the group leader of team 5 |
| 05.00-05.10 pm | Closed-door discussion with the group leader of team 6 |
| 05.15 pm | Debriefing on team presentations |

| Day two – 01/24/2014 | |
|---|---|
| 09.00 am | Meetings with personnel (closed-door) |
| 09.00-09.45 am | Discussion with engineers, technicians, administrative |
| 09.45-10.30 am | Discussion with staff scientists |
| 10.30-11.15 am | Discussion with students and post-docs |
| 11.15-11.30 am | Coffee break |
| 11.30-12.30 pm | Discussion with the representatives of the managing bodies (INRA, université, École Doctorale) |
| 12.30-01.10 pm | Lunch |
| 01.10 pm | Possibility of private meeting with the experts committee (in presence of the DS). Any person who would like to talk to the experts committee in private should request it to Mr Daniel OLIVE during day one. |
| 02.10 pm | Discussion with the head of the unit and/or team leaders |
| 03.00 pm | End of the visit |

## 6 • Supervising bodies general comments

REPUBLIQUE FRANCAISE
Etablissement public à Caractère Scientifique et Technologique
placé sous la tutelle conjointe des ministres
chargés de la recherche et de l'agriculture

Unité de Virologie
et Immunologie Moléculaires

Ref : ***S2PUR150007950 –***
***Virologie et Immunologie Moléculaires (VIM) –***
***0755361V***

Jouy-en-Josas, march, 28th 2014

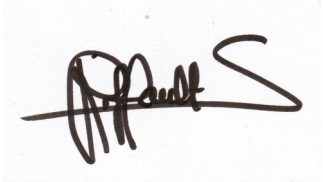
**To the AERES evaluation committee**

We would like to thank you for the accuracy of your report. We collectively appreciated the positive assessments we viewed as a general encouragement to make sound science. The recommendations made by the visiting committee are seriously taken into consideration.

In reply to the recurring comment that projects and SWOT analyses were not sufficiently detailed for all teams, we must say that we followed AERES guidelines. We have chosen to explain the scientific strategy for 2015-2019 at the level of our research unit and same for the SWOT analysis. Nevertheless all teams presented their project during the visit.

We hope to keep up the current pace of our research activities.

Yours sincerely,



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