

EVALUATION REPORT OF THE UNIT
ISP - Infectiologie et Santé Publique

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Institut national de recherche pour l'agriculture,
l'alimentation et l'environnement - INRAE
Université de Tours

EVALUATION CAMPAIGN 2022-2023
GROUP C

Report published on September, 26 2023



In the name of the expert committee¹ :

Nicole Pavio, Chairwoman of the committee

For the Hcéres² :

Thierry Coulhon, President

Under the decree n° 2021-1536 of 29th November 2021:

¹ The evaluation reports "are signed by the chairperson of the expert committee". (Article 11, paragraph 2);

² The president of the Hcéres "countersigns the evaluation reports established by the expert committee and signed by their chairperson." (Article 8, paragraph 5).

This report is the result of the unit's evaluation by the expert committee, the composition of which is specified below. The appreciations it contains are the expression of the independent and collegial deliberation of this committee. The numbers in this report are the certified exact data extracted from the deposited files by the supervising body on behalf of the unit.

MEMBERS OF THE EXPERT COMMITTEE

Chairperson:

Ms Nicole Pavio, Anses, Maisons-Alfort

Experts:

Ms Sarah Bonnet, INRAE, Paris

Ms Priscille Brodin, Institut Pasteur, Lille

Ms Anne Caignard, Inserm, Paris

Mr Vincent Dupres, Université de Lille (representative of CNU)

Mr Alain Filloux, Nanyang Technological University, Singapore (vice-chairman)

Mr Patrick Linder, Professeur émérite, Suisse

Ms Pascale Pescher, Institut Pasteur, Paris (supporting personnel)

Ms Aurore Vidy-Roche, Université Paris-Cité/Institut Pasteur, Paris (representative of CSS INRAE)

HCÉRES REPRESENTATIVE

Ms Muriel Mercier-Bonin

CHARACTERISATION OF THE UNIT

- Name: Infectiologie et Santé Publique
- Acronym: ISP
- Label and number: UMR 1282
- Number of teams: 10
- Composition of the executive team: Ms Nathalie Winter

SCIENTIFIC PANELS OF THE UNIT

SVE4: Immunity, Infection and Immunotherapy

SVE3: Living Molecules, Integrative Biology (From Genes and Genomes to Systems), Cell and Development Biology for Animal Science

SVE2: Plan and Animal Production (Agronomy), Plant and Animal Biology, Biotechnology and Biosystems Engineering

THEMES OF THE UNIT

The main mission of the Jointed Research Unit (JRU) Infection and Public Health ("*Infectiologie et Santé Publique*" ISP), INRAE, University of Tours 1282, focuses on the understanding and control of infectious diseases important in human or animal health. The ISP unit is structured into 10 research teams with 2 supporting teams dedicated to imaging or bacterial collections, 1 administrative team and 1 team for the management. The 10 research teams work on bacterial, parasitic and viral diseases that are major health concerns. The studied diseases lead to major economic losses to the livestock industries and/or represent human health threats because of zoonotic agents involved or because the disease is a major public health problem (Covid-19 pandemic). The main research themes developed by the 10 scientific teams are following 3 axes: i) the host protective versus pathological responses, ii) the pathogen under constraint, iii) the integrated view of the infectious processes. These 3 axes contribute to the development of new tools to better diagnose infections, identify new drug targets or develop new/alternative control measures such as host-directed therapies to resist or clear infectious agents, or new vaccines (nasal air-spray vaccine for Covid-19). The unit's themes are perfectly in line with the "One Health" concept considering the interaction between pathogens and animals, humans and the environment.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The ISP unit was created in January 2012 (after a first evaluation by AERES, former Hcéres). It was reevaluated and renewed in January 2018 (after evaluation by Hcéres). The actual director (INRAE) was appointed in 2018 and has managed the unit, during the present evaluation period, with three co-directors from both supervising bodies (INRAE, University of Tours (UT)). ISP has a multi-site location with a total surface of approximately 7 000 m², including 1 350 m² of Bio Safety Level (BSL) 2 and 291 m² of BSL3 laboratories. The ISP unit spreads over four different locations: two main buildings on the INRAE campus, in Nouzilly, one building on the University of Tours "Grandmont" campus, close to the Sciences Department and the Pharmacy School and one on the University of Tours "Bretonneau" campus close to the Medical School. Nouzilly and Tours are approximately 25 km apart, with easy access through a highway. All sites are very well equipped with video and conference communication systems.

RESEARCH ENVIRONMENT OF THE UNIT

The ISP unit is under the supervision of two public governing bodies: the French National Research Institute for Agriculture, Food and Environment (INRAE) and the University of Tours (UT). ISP is affiliated to two INRAE divisions: "Animal Health" (SA for '*Santé Animale*') and "Microbiology and the Food Chain" (MiCA for '*Microbiologie de la Chaîne Alimentaire*').

The ISP unit has strong links with the local Infectious Diseases Experimental Platform (PFIE), Centre INRAE Val de Loire, labelled by the scientific interest group, GIS IBI SA, which carries out a selective national policy of labelling and support for biology, health and agronomy platforms and biological resource centres. The PFIE possesses BSL2 and BSL3 facilities able to host large farm animals.

Within ISP, the International Center for Microbial Resources for Pathogenic Bacteria (Team 12: CIRM-BP) is part of the national infrastructure RARE (Ressources Agronomiques pour la Recherche) labelled by the "Ministère de l'Enseignement Supérieur de la Recherche et de l'Innovation" (MESRI) and part of the pan-European distributed Microbial Resource Research Infrastructure (MIRRI, ESFRI landmark) for the preservation, systematic investigation, provision and valorisation of microbial resources and biodiversity. MIRRI has been granted the legal status of European Research Infrastructure Consortium (ERIC) by the European Commission (EC)".

Several teams are involved in four metaprograms launched by INRAE for favouring interdisciplinary approaches to solve the current challenges faced with emerging or re-emerging infectious diseases.

Three teams of ISP are partners of two LabEx structures. The team 5 is member (since 2020) of the French Alliance for Parasitology and Health Care (LabEx ParaFrap) and the teams 7 (since 2011) and 10 (since 2020) are members of the LabEx MablImprove, aiming at improving antibodies development and use. The ISP unit is part of the Infectious Diseases Research Federation (FéRI) of the Centre-Val de Loire county, led by University of Tours. This federation includes the universities of Tours, Orléans, Poitiers, Angers and Limoges. The director of ISP is also the co-head of the FéRI. This federation gives access to several experimental platforms certified by IBISA and high-tech centres. The FéRI is funded by Region Centre-Val de Loire. The two core facilities of ISP (Team 11 'Imagerie et infectiologie' IMI and Team 12 CIRM-BP) are involved in the federation. Within the UT, the ISP unit can rely on the doctoral school ED 549 in Life Sciences (Health, Biology and Biochemistry), section B "Infections, Immunology and Symbiosis" for the recruitment of PhD students.

UNIT WORKFORCE: in physical persons at 31/12/2021

Permanent personnel in active employment	
Professors and associate professors	8
Lecturer and associate lecturer	15
Senior scientist (Directeur de recherche, DR) and associate	11
Scientist (Chargé de recherche, CR) and associate	23
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	67
Subtotal permanent personnel in active employment	124
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	16
Post-docs	3
PhD Students	34
Subtotal non-permanent personnel	54
Total	178

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: NON-TUTORSHIP EMPLOYERS ARE GROUPED UNDER THE HEADING "OTHERS".

Employer	EC	C	PAR
INRAE	0	34	61
Université de Tours	22	0	5
CHRU Tours	1	0	1
Total	23	34	67

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	4 102
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP index, i-site, CPER, territorial authorities, etc.)	3 887

Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	2 465
Own resources obtained from international call for projects (total over 6 years of sums obtained)	1 532
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.)	1 780
Total in euros (k€)	13 766

GLOBAL ASSESSMENT

The global assessment of the ISP unit is excellent.

The ISP unit, and its 200 members, cover various research topics within the One Health concept. The unit addresses key questions regarding host-pathogen interactions with viruses, bacteria or parasites of major concern in animal health and/or zoonotic. In the last mandate, ISP has continued to achieve very good to excellent scientific productions, publishing original research articles in high profile journals in fields of animal health, veterinary science, infectious disease, immunology, microbiology and human health.

In France, the unit has a leading position in animal infectiology and zoonotic agents with a very good recognition at the European level. Research activities are guaranteed by excellent funding secured from regional, national and European public and private funding bodies. ISP is supported by technological platforms, including high-level imaging technology in whole animals, in BSL2/3 (unique in France) as well as the International Centre for Microbial Resources for Pathogenic Bacteria. Platforms are at the centre of collaborative works between the unit's teams and run by highly qualified personnel. ISP has created a task force in bioinformatics to level up its analytical competence in big data.

In addition to the relevant preclinical experimental models developed by ISP, scientists are promoting alternative models based on organoids (mini-organs in a dish) to fit with the 3R rules (Replacement, Reduction and Refinement).

Several ISP teams have established excellent connections to the socio-economic world, including the filing of several patents and licences, the establishment of productive partnerships with the industrial sector and the founding of 3 start-ups. ISP is an excellent centre for doctoral and undergraduate training. Particularly, ISP professors and assistant professors from UT created an international Master degree in One Health (IDOH+) with other European Universities (Universitat Autònoma de Barcelona and Hannover Medical School). Up to now, 160 undergraduates were trained to the One Health concept all over the world.

ISP scientists have very good recognition in their respective fields, participating to editorial boards of peer-reviewed scientific journals, organizing symposiums and congresses in their field of expertise. Several members obtained prizes and contribute to science assessment as scientific members of national and international funding bodies.

The unit is located in four different building, on two campuses 25 km apart (Nouzilly-Tours). The geographical distance between teams tends to decrease the feeling of belonging to the same unit. The direction team makes effort to create a sense of cohesiveness that must be continued. It was particularly important during the COVID-19 crisis that profoundly impacted the daily life during several months, and the direction team was keen to maintain this spirit of cohesion between the unit's members and teams. From the human resources point of view, higher transparency of decision-making processes and improvement of top-down communication by the direction team to the personnel (researchers, engineers, and technicians) is encouraged. Management by the direction team and team leaders, of permanent staff (researchers, engineers, technicians) regarding recruitment, carrier evolution and visibility, is expected to improve the unit's spirit.

Overall, the unit has achieved an excellent mandate.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

In the previous report, recommendations were addressed to the ISP unit and several measures were taken to improve all points raised, as detailed below.

First, after discussions with all ISP members, three major research axes were defined for all the unit. Consequently, common projects, including at least 2 teams within these three themes, have been developed and received financial support by the Region Centre-Val de Loire. Specific scientific animations were organized around the three scientific themes.

“One objective of the coming period should be to increase the proportion of publications in the upper journal groups and stimulate inter-team collaborations. Based on high quality results, ISP should also stimulate the groups to publish “big picture” papers rather than several smaller papers giving fragmented descriptions. While this may reduce the overall number of papers, it will improve the impact of the ISP scientific production”.

The impact of the ISP scientific production was improved by increasing the inter-teams collaborations, with 15% of the papers published, involving at least 2 teams. The number of papers with a higher impact, published in upper journal group, was also increased from 57% to 63%. The number of grant applications, grouping at least 2 teams, has reached 22%. Furthermore, papers with large impact were also published by association of teams' forces.

“There should be an effort to increase the funding, which includes interaction with private companies; this is also relevant to obtain funding for PhD projects. Members of ISP should ensure that, wherever possible, they aim to lead funding applications”.

The percentage of contracts with private companies and professional actors has increased from 16% to 23% compared to the last evaluation period. More PhD programs were supported by Cifre contracts (private actors).

“ISP has strong links with veterinary, food and animal health companies. Its platforms, scientific resources and topics are of clear interest for them and this translates into funding, contracts and service agreements. Most of the ISP teams obtained private contracts during the last 5 years and this communal effort and attractiveness can only be encouraged in the future as public funding is decreasing”.

ISP teams have maintained an excellent level of private funding (2 500 k€) as, indeed, public funding is decreasing.

“The good quality of the unit organization and life is a great strength and shall be carried on for the next 5-year period. To improve relationships between distant sites, the use of videoconferences should be increased, notably for the weekly scientific meetings, a bonus for ISP that must benefit to the whole JRU. Tools to facilitate the integration and life of foreign researchers and students have also to be set up to improve the international appeal of ISP especially in view of the recent creation of the International Master of sciences Erasmus Mundus “Infectious Diseases and One Health” (IDOH)”.

ISP pursued its organization as it was positively evaluated in the previous period. The video systems implemented have greatly gained in attendance during the COVID-19 pandemic and lockdowns. Furthermore ISP is still part of the International Master of sciences Erasmus Mundus “Infectious Diseases and One Health” (IDOH) and welcome foreign students.

“The relationships between students of the different teams from both sites should be increased. Efforts must be done to facilitate the attendance at the regular scientific meetings. A modification of the agenda could be helpful, with less meetings organized”.

As recommended, interactions between the students from teams located on different sites were improved by the organization of a PhDDay, where students present their work. All students, including graduates and undergraduates, and scientists are participating to this event. Furthermore, the periodicity of scientific animation was concentrated on one unique -Monday afternoon- presentation that is shorter. Students are encouraged to present their results.

“ISP should identify the relevant partners to develop research to link Human and animal health (One Health perspective)”.

As recommended, ISP strategy and the five-year plan were oriented toward the “One health” concept, as 7 teams work on zoonotic agents or agents with interest in both animal and human health. Similar approaches are developed for human, animal and zoonotic agents, in terms of control methods, resistance mechanism... One team coordinates a program within the European Joint Program One Health (OHEJP, H2020 EU work program).

"ISP should take more profit of the CIRMBP and its bacterial collection in future research. ISP also should identify partners to develop a few promising antimicrobial strategies. ISP is invited to establish contact with the PAI2B on the Nouzilly campus for its "omics" competence at least for proteomics approaches".

As suggested in the previous report, the core facility 'Centre International de Ressources Microbiennes-Bactéries Pathogènes' (CIRM-BP/Team 12) is playing a key role in the screening of antimicrobial drugs and is involved in several projects with private companies.

Regarding the proposition of collaborations with local platforms, such as PIXANIM ('Phénotypage par Imagerie in/eX vivo de l'ANIMAL à la Molécule'), 2 teams have developed proteomic studies with this core facility. Furthermore, ISP has developed new "omics" projects, using NGS technologies, RNAseq or metabolomics. Therefore, the ISP has set up a bioinformatics working group for the analysis of large datasets and statistical analyses.

B – EVALUATION AREAS

EVALUATION AREA 1: PROFILE, RESOURCES AND ORGANISATION OF THE UNIT

Assessment on the unit's resources

The unit resources are excellent with 126 permanent members including 58 researchers (46%) and 68 qualified technical staff (54%). Financial resources are excellent with near 70% resulting from success to competitive grant (national, international, public or private). The unit has two excellent core facilities and an excellent administrative support team.

Assessment on the scientific objectives of the unit

The scientific objectives are excellent. All projects developed in the unit are clearly in line with the One Health concept and the challenges of controlling infectious diseases in animal and/or human health. All teams fulfil at least 2 of the 3 axes of research defined collegially by the unit's members.

Assessment on the functioning of the unit

The functioning of the unit is very good. Several committees are in place for the good functioning of the unit: CoDir within the direction team weekly; CoISP with the direction team and team leaders, every other week; service board, every 3 months, with representative of each category of personnel. In fact, no representative of PhD and post-docs participated to the service board since the Covid-19 pandemics; once a year, a general assembly meeting, with all members is organized. The unit follows the rules regarding safe informatics data storage, environmental respect with recycling and energy saving and biosafety.

1/ The unit has resources that are suited to its activity profile and research environment.

Strengths and possibilities linked to the context

ISP is a very large unit of 200 persons including 126 permanent staff and around 80 personnel with fixed-term contracts (post-docs, PhD students, technical support). ISP is divided into 10 research teams, with 5 to 18 people per team, 2 core facilities (5 persons/facility), 1 team for administrative support (15 persons) and 1 team for the direction (4 persons). Near half of the staff are researchers (46%), the other half are technical personnel (54%) (17% engineers and 37% technicians). Except for two teams, the number of technical supports is excellent per team. The direction is concerned about the gender equality. The administrative team accomplished an important work during the mandate and is a great support to all members of the Unit.

Total resources of the unit are excellent with an increase during the 2016-2021 contract, with 69% from competitive grants (from 1.3 M€ to >2 M€/year), 26% from institutional resources and 5% for delivery of services. The rules for budget used per team and for mutualized cost are well established for the funds managed by INRAE. The unit has mutual budget for scientific animation (invited speakers, workshops linked to Topics

animation, team building activities, PhDDday) and promotes inter-team collaboration with an internal grant of 10 k€. Furthermore, the unit was successfully funded by the Region Centre-Val de Loire that supports inter-team programs (near 600 k€ over the evaluated period).

The ISP unit has two excellent core facilities ('Imagerie et infectiologie'-IMI, Team 11; 'Centre International de Ressources Microbiennes-Bactéries Pathogènes'-CIRM-BP, Team 12) that play important roles at the local and national levels. Especially, as equipment of Team 11 are located in BSL2 or BSL3 laboratories that can be used with infectious agents, which is expensive and not so frequent, many collaborations have been built at the national level with joint publications on the evaluated period. Team 12 is also a key actor, as it is part of a national network of INRAE laboratories (GIS CIRM: group of scientific interest including 5 centres of biological resources) and involved in the European network (H2020 IS-MIRRI-21: Implementation and Sustainability of Microbial Resource Research Infrastructure for the 21st Century). The CIRM-BP has the ISO 9001 certification and IBISA recognition. It provides bacterial strains or genomic DNA to academic or industrial partners.

Weaknesses and risks linked to the context

37 permanent staff will reach the retirement age during the next period and may leave the unit. Among these, 18 are researchers. Important topics may then be stopped.

Core facilities necessitate to have up to date instruments and/or specialized personnel to operate them. Future retirement of personnel and possible decrease of funding (15 grants of the unit will end in 2023) may compromise the excellent work of these 2 teams.

2/ The unit has set itself scientific objectives, including the forward-looking aspect of its policy.

Strengths and possibilities linked to the context

ISP has defined three main research axes and the 10 research teams develop projects within these three themes: axis 1 "The host protective versus pathological response" (Teams 1, 4, 5, 7, 8, 9 and 10); axis 2 "The pathogen under constraint" (Teams 2, 3, 4, 5, 6, 8 and 10) and axis 3 "Integrated view of the infectious process" (Teams 3, 4, 6 and 9). All topics are clearly in line with the One Health concept and the challenges of controlling infectious diseases, which is of major concern in animal and human health. The researches pursued by the teams aim at fighting against drug resistance, identifying new drug targets, designing new diagnostics tools using human or animal biomarkers signature, optimizing intestinal microbiota to resist to pathological events, developing vaccine-based approaches on protective immune responses or therapies based on immuno-stimulation for chronic diseases or at periods of life with increased susceptibility to infections. Furthermore, the unit is involved in the development of *ex vivo* and *in vitro* models as alternative to animal experimentation (3R rules).

The unit has excellent collaborations with both academic and private partners with possible applications (11 invention disclosures, 8 patents and 4 licences). The unit's research also meets societal concerns on emerging infectious diseases, as during the Covid-19 crisis and the development of an intra-nasal vaccine by Team 7 ('Agence Nationale de Recherche contre le Sida et les hépatites-Maladies Infectieuses Emergentes' (ANRS-MIE), 2.5 M€) or diagnostic tool by Team 10 (Theradiag). There are today major concerns on the use of antibiotics and their impact on the environment and biodiversity and the spreading of resistance. The unit is then deeply involved in finding alternative to xenobiotics. A collaboration with the Olmix company (ANR project ALGAHEALTH coordinated by Team 4) allowed the discovery in 2020 of 10 compounds derived from sea algae with antimicrobial activity (Teams 4, 5, 6, 9). New aspects of immunology are also investigated using single-cell analysis and the technique was implemented by the Team 11 with the purchase of Chromium® apparatus. To face the increasing amount of data generated by new technologies, the unit has also created a new Bioinformatics task force gathering 6 personnel from Teams 3, 4 and 6.

The research performed in the unit are totally in line with the policy of the two supervisory authorities, INRAE and UT. The unit meets the Scientific Priorities (SP) of INRAE planned until 2030. All teams are involved in at least one of these priorities:

- SP2 Accelerating agroecological and food transitions while answering socioeconomic challenges; SP 2.3. Farming transitions.

The unit aims at contributing to livestock systems that respect animal health, animal welfare and farmers and are also compatible with healthy food products.

- SP4 Promoting a holistic approach to health; SP 4.1. Emerging and re-emerging infectious diseases that move within and among environments, agricultural systems, and food production systems.

The unit also follows the INRAE policy regarding the contribution to major French university campuses, at the local level. As a JRU, ISP is strongly implicated in UT research and teaching activities. For UT, infectious diseases is one axis of excellence and some ISP researchers are involved in the coordination of the national and international masters' programs (Team 7). One future objective of the unit is to capitalize on the existing experience to create a Graduate School on the One Health concept.

For the next period, the unit will keep the same organization and number of teams and the three main axes will be continued toward the delivery of more finalized solutions.

Weaknesses and risks linked to the context

Since 37 permanent members of the unit, including 18 researchers, will reach the retirement age during the next period, the scientific objectives may be impacted and revised downwards.

Fifteen contracts will end in 2023 and only seven contracts (Teams 1, 5, 7, 10) are until 2024, one contract until 2025 (Teams 7 and 10), one until 2026 (Team 1). In this context, funding should be sought to support the ambitious objectives of the unit in the next mandate.

3/ The functioning of the unit complies with the regulations on human resources management, safety, the environment and the protection of scientific assets.

Strengths and possibilities linked to the context

The successful functioning of the unit is based on several committees.

The scientific committee, CoSP, meets once a month (first Tuesday). It is composed of the team leaders (12 persons) and the direction (4 persons). This committee discusses the scientific need of new positions to open. It determines ranking of staff members for promotions and decides on new expensive equipment acquisition or lab space attribution.

The Direction committee (CoDir), composed of the director and 3 co-directors, meets weekly and debates on organisation and management of the unit. All issues are considered by this committee, day-life difficulties, and strategic agendas and other topics related to current news and events.

The service board includes personnel from all categories (technicians, engineers, scientists, post-docs and graduate students) and discusses budget, maintenance, time management, application of administrative rules that always refer to the two supervising bodies. Once a year, a general assembly brings together all the personnel of the unit. The agenda of this general assembly includes interventions of the direction and other staff members. Review of scientific strategy, budget, building renovation programs, staff recruitment and departures, promotions, internal issues is presented with the next-year perspectives.

With regard to gender equality, the unit has a ratio in favour of women, in supporting activities (85%), and in favour of men in leadership positions (9 team leaders are men). However, it is balanced as the director and two deputies are women. One member of the unit (Team 4) is involved in the INRAE's actions for equality and diversity.

The unit supports its personnel career progression and, during the mandate, 56 agents obtained a promotion.

The information systems security policy is in accordance with the INRAE information systems (INRAE Cybersecurity - State's IS Policy (PSSIE)). All individual and team data are stored in the INRAE datacenter.

In terms of public purchasing, the national rules are applied with the support of the Centre Val de Loire. Criteria for selecting suppliers integrate elements of sustainable management of resources, eco-responsibility, and reduction of energy consumption. The unit has invested in an electric vehicle and bikes to reduce its carbon footprint. A shuttle bus is also available between the different sites and restaurant. The waste treatment and recycling are well organized in the unit: biological sector, chemical sector, paper and packaging.

Working conditions are excellent with sufficient lab spaces, equipment and funding for maintenance. Health and safety rules benefit from the involvement of 15 'Assistants de Prévention' staff members (technicians and engineers). They contribute to the working group "Preventing, Quality and Regulations (PQR)" that aims at preventing hazardous exposures, follow regulations on "MicroOrganisms and Toxins" usages from the "Agence Nationale de la Sécurité et des Médicaments", and implement security and safety rules.

Weaknesses and risks linked to the context

Despite several implications in committees (e.g. award attribution (Master 2, PhD Day, inter-teams grants), investment plan or scientific orientation of the unit), researchers without managing responsibility feel that they are not enough involved in decision instances and continuous communication from the management team is expected.

Due to the Covid-19 pandemic, less committees were organized and the situation is not back to normal. Representatives of PhD students and post-docs are missing in the service board committee.

Considering the high number of different infectious agents manipulated within the unit, a biosecurity manager heading a committee, which will analyse risks regarding possible miss use or dual-use of modified pathogens, is needed.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of the unit is excellent. Members of the unit were involved in the organization of national and international scientific congresses. The unit obtained the recruitment of 11 new scientists and 10 HDRs were defended. A total of 29 PhD students obtained their thesis in less than 40 months. Fifteen post-docs were hired. Members of the unit were successful to grant application, from both public competitive calls (ANR, H2020, Region Centre-Val de Loire...) and private partnership. The quality of the unit's major equipment is excellent. The unit possesses equipment for imaging of whole animals in BSL2 and BSL3 as well as a very large collection of pathogenic bacteria (risk classes 2 and 3), which can be used for human and veterinary research projects. This collection was a founding member of a larger European research infrastructure MIRRI ("Microbial Resources Research Infrastructure").

1/ The unit has an attractive scientific reputation and contributes to the construction of the European research area.

Strengths and possibilities linked to the context

The attractiveness of the unit at the national level in its various research fields is well demonstrated by the organization of national congresses/symposia, participation in scholarly societies, or the award of national distinctions.

At the international level, four teams have organized some international symposium/congresses during the reporting period, knowing that this activity has surely been greatly slowed by the Covid-19 pandemic. Team 3 organized the 8th edition of the international symposium on Antimicrobial Resistance in Animals and the Environment (ARAE); Team 4 organized an international symposium on *Salmonella* and salmonellosis; Team 5 the 7th International Giardia and Cryptosporidium Conference (IGCC); and Team 8 organized the 11th international symposium on Marek's disease.

Several members of the unit are associate editors or specialty chief editors for both specialized (e.g. *Frontiers in Microbiology*, *Veterinary Research*) and generalist journals (e.g. *PLoS One*).

In terms of recognition, the head of the unit was nominated "Chevalier de l'ordre du mérite agricole" (2017), the leader of Team 7 was nominated officer in "Ordre des palmes académiques" (2019), while one member of the same team was nominated "Chevalier de l'ordre des palmes académiques" (2021).

Weaknesses and risks linked to the context

There is a small imbalance between the teams concerning the organisation of international conferences and the participation in conferences as invited speakers.

2/ The unit is attractive for the quality of its staff hosting policy.

Strengths and possibilities linked to the context

During the reporting period, 29 PhD students have obtained their thesis and 33 are currently being trained (then 62 PhD students in total). All the students have obtained their PhD in less than 40 months, which is remarkable knowing that no PhD defence was allowed without at least one accepted publication as first author. The supervision of these students is ensured by a high number of researchers holding an HDR (40 scientists and 3 IR). During the evaluation period, 10 young scientists have obtained this accreditation. In order to facilitate and encourage young scientists to prepare their HDR, ISP offers the possibility for non-HDR holders to co-supervise a PhD thesis with one HDR holder scientist from the unit.

The unit is affiliated to the Doctoral School "Health, Biological Sciences and Life chemistry" (ED549, SSBCV), which is joint between University of Tours and University of Orléans. It is organized in 4 curricula and ISP belongs to the curriculum B "Infectiology, Vaccinology and Immunology", which is co-directed by a scientist of Team 4.

Several initiatives are offered to students during their training at ISP: Each student is followed by a member of ISP throughout the duration of his/her PhD thesis, which should allow for early detection of any problem. Each student also benefits from a scientific PhD committee, including at least two external experts in the field.

In addition to PhD students, ISP has hosted 394 short-term students during the reporting period, including 96 M2 students. Among them, more than 90% were affiliated to the Master Curriculum "*Infectiologie, Immunité, Vaccinologie et Biomédicaments*" headed by leader of Team 7. Eight internship subjects are funded each year by the unit through a selection by a dedicated committee.

Indicated as a setting-up project during the previous evaluation period, the International Master of Sciences Erasmus Mundus "Infectious Diseases and One Health" (IDOH) was awarded in July 2016 by the European commission and granted again in July 2019 (program IDOH+). Three European universities are involved in this Master: UT (coordination by a scientist of Team 7), Autonomous University of Barcelona (Spain) and the University of Hannover (Germany). 160 students from worldwide are planned to be trained under this program, which aims at educating students in the One Health concepts to fight against infectious diseases. Several members of ISP have been strongly involved in this IDOH Master: 4 MCU and 8 CR/DR were responsible for teaching units and 20 scientists regularly gave lectures.

Regarding the attractiveness of ISP for young researchers, it should be noted that eleven researchers have been recruited during the period (5 INRAE and 6 MCU UT).

Three foreign senior researchers have been hosted by ISP during the period: one member from "*Faculté de médecine vétérinaire*", "*Université de Montréal*" (Canada) for 5 months in Team 4; one member from Department of Infectious Diseases/University of Georgia (USA) and one member from Institute of Parasitology and Tropical Veterinary/Freie Universität Berlin (Germany) for one year and 6 months with Team 6, respectively.

Weaknesses and risks linked to the context

If the number of PhD students and trainees is remarkable, only 15 post-docs were present during the period, which seems relatively low compared to the number of teams and funding.

3/ The unit is attractive because of the recognition gained through its success in competitive calls for projects.

Strengths and possibilities linked to the context

The unit has demonstrated excellent capacities to secure funds from both public and private origins. ISP has signed 200 contracts for a total amount of about 11 000 k€. Over the previous reporting period, 178 contracts were awarded with a total of 8 800 k€ over 5 years, so the unit has slightly increased its funds. Over the 6 years of the reporting period, the annual amount has increased from 1 440 k€ in 2016 to 2 110 k€ in 2021.

Public funds represent almost 70% of the total amount. Main funders are local authorities (50 projects, 40 as leaders, 5 609 k€). Among them, the Region Centre-Val de Loire has granted 30 projects (25 as leaders) for a total of 3 886 k€. The unit has also obtained multiple grants from European funding (e.g. H2020, FEDER) for a total of 3 057 k€; 7 projects are led by the unit, the most important one being the FEDER project PSAT2 - IMAGISP 660 k€; also, the H2020 project VetBioNet is coordinated by the unit since 2017, and will go on thanks to the infrastructure project "Integrated Services for Infectious Diseases Outbreak REsearch/Isidore".

The unit has also obtained multiple grants from national sources (e.g. ANR): 33 contracts for a total amount of 1 221 k€ in diverse types of calls. The unit obtained 14 grants (221 k€ in total, leaders for BoNeutro and EPIC) from the Carnot program '*France Futur Elevage/F2E*'; it also obtained 5 grants (478 k€) from Era-Net programs INFECTERA, EMIDA and ANIHOWA dedicated to animal health and welfare (1 grant MADISUP as leader); finally the unit got 12 (7 as leaders) generic ANR grants on collaborative projects (PRC) and 2 grants awarded to young scientists (JCJC program). A two-year project (MUCOVID, '*Ministère de l'enseignement supérieur, de la recherche et de l'innovation*') was granted in 2021 for a total amount of 1 500 k€.

For 23 out of these public grants, the projects involve a collaboration between at least 2 teams of ISP.

Less important amounts of funds come from associations such as '*Ligue contre le Cancer*', '*Fonds Eperon*', '*Vaincre la Mucoviscidose*' (425 k€), INRAE metaprograms (149 k€) and LabEx programs.

Private funds represent 30% of the total amount with 4 447 k€ under 27 contracts. The main socio-economic partners are APIS-GENE (1 109 k€), Ceva (216 k€), Elanco (150 k€), Merial (511 k€), Olmix (189 k€), Phileo (423 k€), Zoetis (212 k€).

Weaknesses and risks linked to the context

The number and origin of grants are very large but there are no ERC grants.

4/ The unit is attractive for the quality of its major equipment and technological skills.

Strengths and possibilities linked to the context

The unit possesses two major technological assets making it a key player in the context of animal health and infectious diseases.

As the first asset, the unit offers unique and extensive BSL2 and BSL3 facilities allowing infectious experiments and which is at the origin of extensive European collaborations in the context of One Health.

Moreover, the unit and INRAE invested massively on live imaging devices within these BSL2 and BSL3 facilities in order to extend their competences. This will improve their performances in science as well as in ethics.

New investments are programmed to still increase capacities in terms of BSL2 and BSL3 laboratories, platforms for imaging, new equipment for cell sorting within BSL3 facilities and transcriptomic device.

As the second asset, the CIRM-BP possesses a very large collection of pathogenic bacteria (risk classes 2 and 3), which can be used for medical, veterinary or research projects. CIRM was a founding member of the European research infrastructure MIRRI ("Microbial Resources Research Infrastructure") that gathers more than 50 collections of microorganisms. It is also part of the "Integrated Services for Infectious Diseases Outbreak REsearch / Isidore" project and strongly contributes to the European visibility of the unit.

Weaknesses and risks linked to the context

None identified.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production of the unit is very good to excellent. The unit has published in well-respected international journals. Several papers correspond to collaborative work between, at least, 2 teams of the unit. Members of the unit are main authors in 50% of the original papers. All personnel, PhD students, technical staff are co-authors. The teams published in Open access journals and follow ethics and scientific integrity through the creation of a small working group deontology & scientific integrity scientific.

1/ The scientific production of the team meets quality criteria.

Strengths and possibilities linked to the context

During the reporting period, ISP produced a total of 541 publications. Among them, 415 were scientific original articles and reviews, which is of the same order of importance compared to the production reported in the previous period. 63 (15%) involved at least two teams of the unit (9% during the previous reporting period).

The scientific production represents 380 original articles among which 197 are signed by members of ISP as main authors (first, corresponding, last). Some of them have been published in excellent, well-respected international journals, such as *PLoS Pathogens* (8, 5 as leader), *PLoS Genetics* (2), *mBio* (2, 1 as leader), *Cell Reports* (1), *PNAS* (1) or *Clinical Cancer Research* (1). Many articles were published in multidisciplinary journals, such as *Scientific Reports* (17, 7 as leader) or *PLoS One* (15, 9 as leader). The most important fields of the specialized journals were *Microbiology* (17% of publications), *Infectious diseases* (10%), *Immunology* (9%), *Veterinary science* (9%), *Virology* (6%) and *Parasitology* (6%).

ISP published reviews in various journals covering the unit's topics, including *Frontiers in Microbiology* (4, 3 as leader), *Frontiers in Immunology* (1 as leader), *Frontiers in Oncology* (1 as leader), *Frontiers in Genetics* (1 as leader), *Frontiers in Cellular and Infection Microbiology* (1 as leader), *Trends in Parasitology* (2, 1 as leader), *Current Opinion in Oncology* (1 as leader) and *American Journal of Respiratory and Critical Care Medicine* (1 as leader).

Weaknesses and risks linked to the context

There are very few publications in the best specialized journals in microbiology, infectious diseases or immunology, or in outstanding multidisciplinary journals. In addition, in most cases, ISP members appear at intermediate positions in the authorship.

2/ Scientific production is proportionate to the research potential of the unit and shared out between its personnel.

Strengths and possibilities linked to the context

All the teams participate in the research outputs of the unit in relation to their research field and technical expertise.

The 29 PhD students who have been trained over the reporting period co-authored 103 publications or reviews, resulting in 3.5 manuscripts per student.

In several teams, the supporting personnel is leader on the publications.

Weaknesses and risks linked to the context

Given the outstanding translational realizations and the stunning number of research contracts, the impact of the scientific production is quite moderate.

3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science.

Strengths and possibilities linked to the context

A large number of publications are in Open Access journals.

The unit has created a small working group, DISC ("déontologie & intégrité scientifique") for ethics and scientific integrity.

All experiments are performed according to French and European legislation. 3R rules are applied wherever possible.

The management and use of laboratory notebooks are described in a dedicated procedure, which concerns the teams working on the INRAE campus. Staff is regularly made aware of the importance of the laboratory notebooks.

Weaknesses and risks linked to the context

None identified.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

Assessment on the inclusion of the unit's research in society

The inclusion of the unit's research in society is excellent. In veterinary science, the unit has established strong links with breeders and associations. In human health, the unit contributes to the production of guidelines and recommendations related to infectious diseases. The unit has obtained several contracts with companies (23% of the budget) including PhD grants (6 Cifre contracts). Members of the unit created 3 start-ups, owned 11 invention disclosures and 8 patents (4 licences). Members of the unit were strongly involved in interactions with the general public during the Covid-19 pandemics. Members of the unit regularly contribute to showcase INRAE and UT in press releases or at the international salon of agriculture for example.

1/ The unit stands out by the quality of its non-academic interactions.

Strengths and possibilities linked to the context

ISP has established strong links with breeders and their respective associations ("Institut Français du Cheval et de l'Equitation", "Institut technique des filières avicole, cunicole et piscicole", "Groupement de Défense Sanitaire de Bretagne") as well as syndicates ("Syndicat des Sélectionneurs Avicoles et Aquacoles Français") in the frame of networks (national poultry network, Team 4 and H2020 project VetBioNet, Team 9) or consortium (Healthycalf, Teams 1 and 5).

Two teams participated in the elaboration of guidelines and recommendations for health ("Haut Conseil de Santé Publique and Haute Autorité de Santé", Team 2) and certification (AFNOR, Team 6) agencies or for laboratory practices (REferentiel en MICrobiology, Team 2). Likewise, members of the ISP unit are solicited on

regular basis by national and international organizations and agencies to evaluate projects, unit activities, labellisation processes or research strategy in the field of veterinary infectious diseases (Teams 4 and 7). Several teams (e.g. Teams 3, 6, 7, 8, 9, 10) received funding from associations ("Association pour la Recherche sur le Cancer" (ARC), "Ligue contre le cancer Grand Ouest", INCa, "Fondation Hippolia") or patients' associations ("Vaincre la mucoviscidose").

Weaknesses and risks linked to the context

The contribution of ISP teams to non-academic interactions is uneven. Three teams of the unit (Teams 2, 7, and 8) do not report any interaction with actors from the livestock sector (e.g. breeders, associations and syndicates) whilst three teams (Teams 3, 8 and 10) are not implicated in other non-academic interactions (e.g. support to public policies or services corresponding to their field expertise).

2/ The unit develops products for the socio-economic world.

Strengths and possibilities linked to the context

The unit represents a hub for industrial partners involved in animal health and agro food sector. The presence in the same structure and same place of recognized experts on bacterial, viral and parasitic diseases is a real strength for industrial partnership.

ISP has trained 6 PhD students with a Cifre contract during the reporting period. This represents 15% of all the PhD students (5 times more than for the previous period).

ISP has produced 11 invention disclosure and 8 patents with 4 having been licenced to Kymeris Therapeutics, SAS McSAF.

The unit increased research contracts with companies up to 2 500 k€, which represents 23% of the budget. For instance the unit collaborates with Ceva Santé Animale through three projects (MARDISHED, HVYDTMR and MARDIVAC), Lesaffre, Nevia, Elanco, APIS-GENE, Olmix, Merial, MG2MIX, Virbac, Zoetis and Bpifrance.

The unit responded to the emerging infectious diseases with the creation of three start-ups LoValTech, Kymeris Santé and SPyDiag for the development of a nasal vaccine against Covid-19 and with serodiag licensing to Theradiag.

The unit implemented an ANR LabCom ALGAHEALTH project (2020-2023), coordinated by one unit's member and involving 4 teams, in collaboration with the company Olmix to develop sea algae-derived products. This allowed the discovery of 10 compounds.

Stemming from a long term collaboration and a patented "Automated Larval Migration Assay" (ALMA), the company INVENesis, a Swiss spin-off from Novartis, has located its incubator on the INRAE campus dedicated to high throughput drug screening on arthropods and macroparasites.

Weaknesses and risks linked to the context

None identified.

3/ The unit shares its knowledge with the general public and takes part in debates in society.

Strengths and possibilities linked to the context

Results from research teams are regularly published in press dossiers from INRAE.

Some ISP members participated to the "Salon de l'Agriculture" and are invited to exhibitions organized by INRAE. Most of the teams are involved in science popularization events like "La fête de la science".

Some members of the unit participate to articles in different press media, such as "la nouvelle république", "les Echos", take part to TV or radios shows dedicated to science and health (e.g. "Médiation scientifique" on France Culture, E=M6 on TV channel 6, "Allo Docteur" on channel 5).

The unit published numerous publications to all public audiences on SARS-CoV-2 and vaccination during the COVID-19 crisis.

The unit is strongly involved in education and training in infection and microbiology to diverse audiences. In particular, Team 2 participates in continuous training for high school teachers on food microbiology ('Maison pour la Science'), new technologies, microbiota, bacterial gene transfers and biofilm (Orléans/Tours academic district) and for hospital lab technicians, with the "BioFormation" and "Bio Médical Formation" institutes.

Weaknesses and risks linked to the context

The involvement of the unit in the interaction between science and society is rather disparate among teams.

Communication actions are more oriented towards the various professional sectors (veterinarians, doctors, agricultural professionals, etc.) than towards the general public.

C – RECOMMENDATIONS TO THE UNIT

Recommendations regarding the Evaluation Area 1: Profile, Resources and Organisation of the Unit

Collaborations between teams are effective and should be pursued in the next mandate.

Teams 8 and 10 are encouraged to share the development of new relevant models (keratinocytes, hair follicles or feather follicles) that could be used for both themes (viral persistence).

Considering the future departure of numerous staff members, it will be important to maintain effort towards the supervising bodies to optimize manpower/workforces in all teams. Both technical staff and researchers must be recruited to keep an efficient balance of workforces.

The unit was supported by numerous public and private grants during the last period, but several contracts will end in 2023, ISP is encouraged to maintain its momentum in securing funding for the next period.

The unit should reinforce support for personal career development plans of the permanent and non-permanent staff.

The unit is encouraged to support team leaders to develop skills in management and follow formations related to team building.

The unit should plan ahead and discuss with the supporting personnel in a bottom up and anticipated manner before making decision.

In the service council, all categories of personnel must be represented, especially PhD and post-docs.

All scientists are encouraged to create a committee to discuss scientific strategies, themes and new axes or technologies, or grant opportunities.

The direction needs to strengthen the dialogue within the unit to increase cohesion among members and the sense of belonging to a single entity. To this end, it is important to take care of communication at different levels (intra-team/inter-team), avoid top down and one way management. The use of tools like newsletters, introducing newcomers, is encouraged.

Since the unit has different locations, stronger links must be developed through scientific animations on both sites, with more participation of PhD students and post-docs. The unit should provide support to PhD students and post-docs for the organization of seminars with invited speakers. It would be in addition to the PhD Day, which must be maintained.

In the direction team, one of the deputy directors should be identified as a referent in case of intra-, inter-team conflict, with possible psychosocial risks. The direction needs to ask for tools from supervising bodies to address psychosocial risks.

Committees addressing questions relative to i) psychosocial risks of personnel other than PhD students ii) scientific strategies including all scientists would benefit to the well-being of the members of the unit.

In order to frame the handling of the various pathogens studied in the unit (i.e. viruses, bacteria and parasites), a biosecurity manager heading a committee that will analyse risks regarding possible miss use or dual-use of modified pathogens, is recommended.

Recommendations regarding the Evaluation Area 2: Attractiveness

The unit should increase its attractiveness towards post-docs, by offering contracts of 24 to 36 months through European grants or individuals with their own fellowships (EMBO, Marie Skłodowska-Curie actions, etc.). Work of post-docs should be associated to valorization (publications, patent filing) during their contract.

The unit should welcome visiting scientists and participate to programs with short-term or middle-term exchanges (e.g. 'Programme Hubert Curien', invited chair).

The unit should encourage scientific animations in both locations with invited speakers (other local laboratories, INSERM...).

The teams should keep the organization of workshops in their domain of expertise.

Teams and researchers should keep the leading position in ANR grants.

The unit should encourage the application to European grants.

The unit should consider establishing collaborations with veterinary schools (French or from abroad).

Teams and researchers should consider applying to ERC grants.

Recommendations regarding Evaluation Area 3: Scientific Production

The unit is encouraged to keep the high number of publications.

The productions of the 10 teams are heterogeneous, all teams are encouraged to valorize their results and go deeper into identification of molecular mechanisms. Such mechanistic approaches should increase the valorization into higher profile journals with generalist interest.

The unit and teams should take advantage of their relevant animal models, within the One Health concept, to publish in journals related to human health. They should keep persuading journal editors, without censorship, that animal health is as important as human health and contributes to understand universal biological mechanisms.

Recommendations regarding Evaluation Area 4: Contribution of Research Activities to Society

The unit has excellent social-economic partnerships, with the creation of three start-ups, and is encouraged to maintain this way of valorising their discoveries.

Communication toward the general public is heterogeneous between teams. Internal communication should emphasize outreach activities led by colleagues and encourage others to do so.

TEAM-BY-TEAM ASSESSMENT

Team 1: IBIR - Infections Bactériennes et Immunité des Ruminants
 Name of the supervisor: Mr Pierre Germon

THEMES OF THE TEAM

The team's research focuses on two bacterial diseases, bovine tuberculosis and mastitis. These two diseases are of major importance because they impose heavy economic costs on livestock farms but they also represent a threat to public health, particularly through the massive use of antibiotics. The objective of the work carried out by the team is to better understand the host-pathogen interactions associated with these two diseases in order to promote the development of new prophylactic measures, such as vaccines, immunomodulation or phenotypic assays.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

"Consideration should be given to integrating the host together with pathogen studies. Additionally, comparison and validation of cell and small animal models with studies in the natural whole animal host should be undertaken" and *"The team should develop links to improve their contribution to the One Health goal"*. Thanks to the recruitment of two young researchers during the period, the team has redefined its research themes along three axes that comply with the recommendations made in the previous evaluation. Nevertheless, the links with other teams allowing to better integrate the One Health concept into the team's studies are still to be developed.

"Although they are already excellent, the reputation and appeal of the team will benefit from its participation to a larger number of editorial boards of relevant journals. The same effort is required from team members to lead projects of WP. The international visibility of the team would be improved by attending some key conferences outside of the strict veterinary field (e.g. International Congress of Immunology)". Two members of the team are editorial board members (*PLoS One* academic editor for one member while the other one is assistant editor in *Frontiers in Immunology* and in *Frontiers in Microbiology* and editorial board member in *Infection and Immunity*). International visibility through invitations to international conferences was not really improved during the reporting period despite invitations in congresses in front of scientists in the veterinary immunology field, stakeholders or veterinary practitioners. During the same period, two young scientists of Team 1 successfully applied to ANR JCJC grants.

"The team should aim to increase their interactions with private companies – this is particularly relevant as the diseases studied are of strategic relevance to animal health and the goals are to develop correlates of protection/vaccines and diagnostics, which would be highly attractive to commercial companies. This could be an additional source of funding for PhD projects". During the reporting period, the team has developed non-academic interactions, highlighting the expertise acquired in recent years, especially for the quality of the experimental models developed. The team is thus involved in the NEOLAC project (consortium including the milk cooperative SODIAAL, the Biodevas laboratory and INRAE). Among the other projects in which the team was involved, one of them, the MASTICELLS project in collaboration with APIS-GENE society, allowed the recruitment of a Cifre PhD student.

"The team should increase the number of PhD students and thus the number of staff with HDR status". If only one PhD student has obtained her thesis during the reporting period, two are currently being trained (since 10/2019 and 10/2021 respectively). In the meantime, one member of the team has obtained his HDR diploma, thus bringing the number of HDR holders to three at the time of the report.

"The team should make efforts to increase the publication rate without compromising the drive to publish in high impact factor journals". During the reporting period, the team produced 48 scientific original articles and reviews. This is approximately the same number of publications as in the previous evaluation period.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	3
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	6
Subtotal permanent personnel in active employment	10
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1
Post-docs	0
PhD Students	2
Subtotal non-permanent personnel	3
Total	13

EVALUATION

Overall assessment of the team

The scientific production of the team is qualified as very good to excellent. Its attractiveness is very good to excellent regarding financial resources. Inclusion in society is very good. The overall assessment of the team is very good to excellent.

Strengths and possibilities linked to the context

The team is clearly well recognized for its expertise in bovine immunology and bacteriology applied to two major ruminant diseases: mastitis and bovine tuberculosis.

The team produced 41 scientific original articles with 18 as first, last or corresponding author and published in e.g. *Microbial Genomics* (2021), *mSphere* (2021), *Journal of Immunology* (2016), *Frontiers in Immunology* (2019, 2021). The team co-authored articles in specialized journals of solid reputation, such as *PLoS Pathogens* (2020), *NPJ Vaccines* (2020) or *Frontiers in Microbiology* (2019). The team also produced 7 reviews, all in leader position. Two scientists are involved in editorial boards (*Frontiers in Immunology*, *Frontiers in Microbiology*, *Infection and Immunity*, *PLoS One*) and the team's members have been solicited on several occasions for their expertise (PhD juries, evaluation of teams/units).

The team has strong relationships with stakeholders in the breeding sector with several projects funded during the reporting period (BOVIMUNE – PI – 2016-2019 – 271 k€, BovEpiSign – 2019-2020 – 195 k€, MASTICELLS – PI - 2019-2023 – 340 k€). Two young scientists successfully applied to ANR JCJC grants.

The team has significantly reinforced its international visibility during the period, notably through the coordination of the "Galactinnov" International Research Network and regular 'Partenariats Hubert Curien' (PHC) projects with the University College of Dublin (Ireland) and the University of Minas Gerais (Brazil).

Weaknesses and risks linked to the context

The number of articles in main positions remains moderate (around 44%) and the team has no high-profile publications.

With regard to attractiveness, only one PhD student has obtained her thesis during the period while there was only one post-doc who stayed less than one year.

The team does not develop significant collaborations with teams working on *M. tuberculosis* infections in humans.

RECOMMENDATIONS TO THE TEAM

The team should increase the proportion of original articles in leadership position.

It would be good to promote new collaborations (e.g. access to grants, new research hypotheses) with research teams studying tuberculosis in humans in a One Health context.

The team is encouraged to maintain the training of Master students and to supervise new PhD students.

The team should capitalize the outputs from ANR JCJC grants to set up collaborative projects.

Team 2: BRMF - Bactéries et Risque Materno-Foetal
 Name of the supervisor: Mr Laurent Mereghetti

THEMES OF THE TEAM

Team 2 works mainly on Streptococci of the group B, which cause severe neonatal infections and can also harm immunocompromised adults. The team aims at elucidating the adaptation of this pathogen to diverse environments, its metabolism and Zinc homeostasis. Another interesting and relevant topic is the analysis of virulence factors carried by bacteriophages.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

1 - Assessment of scientific quality and outputs

"The team is invited to reflect on how refocus on an original aspect of the project" and "Concerning the publication policy, the expert committee recommends to favour quality rather than quantity and to increase the part of publications belonging to the excellent and outstanding groups, and to improve impact and visibility".

The team publishes in general in medium-level journals, such as *Frontiers in Microbiology*, *Microorganisms*, but has also published work in high-standard journals, such as *Molecular Microbiology* or *Journal of Bacteriology*. The team has still several parallel topics (CcpA transcription factor, homeostasis of Zn, prophages and virulence, CRISPR Cas, sRNA and csRNA).

2 - Assessment of the team academic reputation and appeal

"The expert committee would recommend to the B5 team to increase its visibility at the European and international level. All the scientists of the team should be encouraged to present their results in congresses", "The results concerning S. agalactiae, presented as the main topic of the team should be more frequently presented orally in congresses", "Increasing the connections with other INRA teams working either with GBS or with mobile genetic elements would probably be beneficial" and "The investment of the members of the team in the search of contracts should be improved to support the project".

The team has international collaborations (University of Melbourne, Australia; University of Laval, Canada; University of Colorado, USA; University of Geneva, Switzerland). 20 out of 31 publications are from international collaborations.

3 - Assessment of the team interaction with the social, economic and cultural environment

"Team B5/BRMF could improve contacts enabling them to provide information and prevention actions towards hospital patients".

The team has published over 30 clinical articles as contribution to hospital care.

4 - Assessment of the team involvement in training through research

"According to its high PhD supervising capacity and its privileged access to many masters, team B5/BRMF should train more PhD students, privileging as possible the most promising master students. The experts committee encourages the team to do it and is satisfied to see that 4 PhDs are already in progress in the team".

The team is already highly involved in teaching duties and has trained 6 PhD students, 15 Master students and 63 other interns.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	3
Lecturer and associate lecturer	4
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0

Research supporting personnel (PAR)	3
Subtotal permanent personnel in active employment	11
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	0
Post-docs	1
PhD Students	4
Subtotal non-permanent personnel	6
Total	17

EVALUATION

Overall assessment of the team

The scientific production of the team is excellent. Without any competitive national grants, financial resources are qualified as good. Regarding the training of PhD students, attractiveness of the team is excellent. The inclusion in society is very good. The overall assessment of the team is very good to excellent.

Strengths and possibilities linked to the context

The research area of the team is timely and important. Adaptation of GBS (Group B Streptococci) to different environments and analysis of the virulence factors are very relevant.

Despite a heavy teaching activity, the team managed a steady publication output with 74 publications. Regarding basic research, publications are in journals such as *Frontiers in Microbiology*, *Journal of Infectious Diseases*, *Journal of Clinical Microbiology* and others, but also in high-standard bacteriology journals such as *Journal of Bacteriology* and *Molecular Microbiology*. Among them, 20 are signed as first author and 20 as last author (including one editorial with only one author). These publications with first and/or last author are mostly related to the main research topics of the team, e.g. (i) prophages and virulence, (ii) metabolism, competence, and adaptation, (iii) Zinc homeostasis and (iv) CRISPR. The study of prophages is important for understanding the evolution and virulence of *S. agalactiae*. Studies on metabolism and adaptation are part of fundamental research work in analysing competence and transporter encoding genes. Results on Zinc homeostasis contribute to the understanding of Zinc acquisition and growth adaptation in human tissues. The publications on CRISPR are mainly focused on the strain characterisations during carriage.

Other publications of Team 2 are more clinically oriented and often in collaboration with other teams from the unit (Teams 3 et 4) and other groups in France and abroad (University of Melbourne, Australia; University of Laval, Canada; University of Colorado, USA; University of Geneva, Switzerland), which reflects visibility and research quality.

The team is attractive and has trained 10 PhD students, of which 6 have defended their thesis during the reporting period. One assistant professor was recruited in 2019 and one member of the team defended her HDR in 2021.

Weaknesses and risks linked to the context

Members of the team have heavy pedagogical duties in different geographical sites.

The team has no publications in more generalist journals to strengthen in-depth research.

Overview articles are only from a part of the team working on small regulatory RNAs.

With only a partnership in a regional project supported by FéRI and support for a PhD thesis (Region Centre-Val de Loire), the team has no major national or international competitive grants.

RECOMMENDATIONS TO THE TEAM

To strengthen the impact of the team, it is suggested to focus on fewer research directions.

In view of the heavy teaching duties of most of the team's members, the team is encouraged to recruit another full-time researcher.

Although the quantity of research papers is excellent, the team should try to publish in more generalist journals.

Prophage biology and adaptation to human tissue may be good subjects for overview articles to gain better visibility.

The team should apply for competitive national grants to strengthen the fundamental-research oriented work. Moreover, possibilities to obtain grants based on the international collaborations should be explored, such as for example bi-national ANR grants. Additional funding could then be used to hire a post-doc to reinforce one of the research topics.

Team 3: PGBA - Plasticité Génomique, Biodiversité, Antibiorésistance
 Name of the supervisor: Mr Benoît Doublet

THEMES OF THE TEAM

Team 3 investigates genomic evolution on three families of bacteria i) *Enterobacteriaceae*; ii) *Brucellaceae* and iii) *Mycobacterium*. The team assembled more than 500 bacterial genomes that have been deposited in public databases. The major scientific achievements are i) in the field of antimicrobial resistance with the study of spread of the mobile genetic element *Salmonella* genomic island 1 (SGI1); ii) the exploration of *Brucella* diversity, which resulted in reassessment of the *Brucella* genus taxonomy and iii) the study of the spread of *Mycobacterium bovis* in cattle in France, together with the characterization of novel cell wall antigens (Map) and the role of amoebae in the transmission of paratuberculosis.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

"The team should establish collaboration with groups skilled in environmental microbial ecology and acquire more expertise in comparative genomics".

The team has acquired skills in comparative genomics, one member was sent for a one-year training at the INRAE bioinformatic platform MIGALE in Jouy-en-Josas. Of note, a member of Team 6 went to the Wellcome Sanger Institute for two years on a European mobility program (Agreenskills program) to acquire the necessary knowledge.

The skills in environmental microbial ecology remain limited. The scientific appeal of Team 3 resulted in the recruitment in 2018 of a senior scientist with high-level skills in genomic evolution, phylogeny, and bioinformatics.

"Based on its excellent scientific production, team B3/PGBA must now reach an international visibility by participating to collaborative projects and networks. Efforts should also be done to attend national and international research steering committees".

The team has gained on national and international visibility. It organized in 2019 in Tours the eighth edition of the international symposium on Antimicrobial Resistance in Animals and the Environment (ARAE), which gathered more than 150 scientists from all over the world interested in the spreading issue of antibiotic resistance under the One Health concept. The team was at the origin of this scientific event in 2005 and the congress has been reconducted every two years since then, with increasing numbers of participants (as indicated in the portfolio of Team 3). Team 3 obtained several ANR projects with the RESINFIT Inserm unit in Limoges (e.g. project PRE-EMPT, ANR 2020) to study and prevent antibiotic resistance via the environment. Some members of the team were associate editors and specialty chief editors for different journals (e.g. *Frontiers in Microbiology*).

The team participates to different national committees dedicated to the research on antibiotic resistance (ABRomics steering committee, French JPI-AMR working group at ANR, jury of French priority program on antibiotic resistance for junior/senior positions) and is member of different national groups dedicated to bovine tuberculosis and paratuberculosis "Réseau Français de la Santé Animale" (RFSA), "Agence Nationale de Sécurité sanitaire de l'alimentation, de l'environnement et du travail" (Anses), "Direction générale de l'alimentation" (DGAL).

"Team B3/PGBA should much more consider its actual contribution to interaction with the social, economic and cultural environment by enforcing its participation to committees of expertise".

Team 3 published 6 technical/professional articles in journals such as 'le point vétérinaire', 'Innovations agronomiques' that bring research works to different stakeholders (veterinarians, farmers). In addition, the team leader has been implicated in an INRAE press release for a general audience on the reduction of antibiotic usage in food-producing animals.

Scientists and PhD students regularly participate to 'La fête de la science' to bring research topics to a general audience in Tours each year. Moreover, 2 PhD students of the team have participated to the contest 'Ma thèse en 180 secondes' up to the regional (Centre Val-de-Loire) or national level (Lebanon). One PhD student has also been awarded the best poster prize at the MICROBES meeting of the French Society for Microbiology in 2019.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	3
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	6
Subtotal permanent personnel in active employment	10
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	6
Subtotal non-permanent personnel	6
Total	16

EVALUATION

Overall assessment of the team

The scientific production of the team is excellent. Attractiveness and inclusion in society are very good. The overall assessment of the team is excellent.

Strengths and possibilities linked to the context

The research themes of the team are of utmost importance in the field of veterinary medicine.

The team secured major funding during the reporting period (450 k€). It was involved in 5 national projects supported by the ANR-Astrid-Maturation (Microtype as coordinator (2014-2018) 197 k€), by the Ministry of Agriculture (FluGenAvi as coordinator (2018-2022) 85 k€, and Plasmequi as partner (2019-2022) 51 k€), by APIS-GENE, a society that brings together professionals from the ruminant sector (Genomap as coordinator (2019-2022) 5 k€) as well as 2 "Programmes d'investissements d'avenir" (PIA) ABROmics (2020-2025) and PROMISE (2021-2026) as partner. These two programs are national networks that tackle surveillance on antibioresistance. It is involved as partner in 2 European projects, Fullforce and CARE, from the CO-FUND OHEJP initiative (respectively of 69 k€ and 96 k€ with Team 4 and CIRM-BP).

The team published 62 articles, 4 editorial notes, 4 methodology papers and 1 book chapter during the reporting period with 30 being as first/last/corresponding author. For example, the team is first, last or corresponding author in articles published in journals of solid reputation, like *MSphere* and *Molecular Microbiology*, but also in *Scientific Reports*, *Frontiers in Microbiology* (10 manuscripts) and *Vaccines*.

The team is involved in teaching for Master students in Infectiology (national and Erasmus Mundus JMD IDOH) and at the Medical School of Tours.

The team trained 30 Master students and supervised 8 PhD students (with 2 foreign students from Lebanon and Hungary and 3 on-going with one student from Belgium). With 4 HDR holders, the team members were members of 18 PhD and HDR juries.

The team organized several international conferences: Antimicrobial Resistance in Animals and the Environment (ARAE); International symposium on *Salmonella* and Salmonellosis and the International Association for Paratuberculosis colloquium.

The team initiated the web interactive database (MAC-INMV-SSR) and developed a diagnostic tool for Multi Locus VNTR Analysis (MLVA) typing of *Brucella*. A patent was granted and licenced for this tool with Genoscreen and the "Institut de Biologie Intégrative de la Cellule" (I2BC).

The team has also a national recognition of its expertise by decision-making bodies. The team leader is involved in the ABRomics consortium steering committee, the French "Joint Programming Initiative on Antimicrobial Resistance" (JPIAMR) at ANR. One team member joined national groups dedicated to bovine tuberculosis and paratuberculosis studies "Réseau Français de la Santé Animale" (RFSA), "Agence Nationale de Sécurité sanitaire de l'alimentation, de l'environnement et du travail" (Anses), "Direction générale de l'alimentation" (DGAL). Two members of the team are associate editors in *Frontiers in Microbiology*.

Weaknesses and risks linked to the context

The team has no publication in high profile journals.

The team has little dissemination actions toward the general public.

RECOMMENDATIONS TO THE TEAM

The team should improve its publication impact by performing more basic research.

The team should contribute more to the dissemination of science with the general public.

Team 4: SPVB - Signalisation Portage et Virulence Bactérienne
 Name of the supervisor: Mr Philippe Velge

THEMES OF THE TEAM

The main theme of the team is to investigate *Salmonella* infections, including mechanisms involved in cell entry of this intracellular pathogen. The understanding of these mechanisms should lead to better control of chicken contamination, in which carriage is often asymptomatic, and transmission to human causing food poisoning, gastro-enteritis, or typhoid fever.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

“The three axes of the research project seem very diverse. Focusing on immune responses and/or microbiota impacts on Salmonella infection in chickens will improve the understanding of asymptomatic carrier”.

The team is focussing on *Salmonella* and host cell infection (notably invasion and entry), also emphasizing the role of microbiota and how it determines the super shedder phenotype in chicken. All of the research directions have been kept but the team has delivered and published on all of them.

“Members of team B4/SPVB should get more involved in scientific journals as editorial board members or reviewers. The senior researchers (CR1) should be more involved in scientific committees, scientific assessments of grant applications. In addition to their strong activity in international networking, the team should be more active in national grant applications (ANR, etc.)”.

The editorial or committee engagement has not been really addressed since only the PI of the team is an editor at *Frontiers in veterinary science*. The PI is also an INRAE expert for the European One Health EJP. However the funding has been addressed and notably through the obtaining of an ANR grant (running until 2025) and a H2020 which ended in 2021.

“As the team itself acknowledged, more emphasis should be placed on interacting with potential non-academic partners. In this respect, the team has important and original assets such as chicken models and germ-free chicks. Such approaches will open avenues to novel collaborations, not only with academic but also with industrial partners, who are increasingly interested in modulating microbiota to preserve the host from diseases. In addition, more efforts should be paid by the team to transfer its researches to a broader audience”.

This has been partly addressed by engaging with companies such as Adisseo and Phileo and coordinating an ANR LabCom ALGAHEALTH looking into molecules from algae for controlling infection in chicken.

“The team is invited to limit excessive thesis duration because this is a bad criterion for the evaluation of the doctoral school”.

There has been no excessive duration of PhD thesis over this period.

“There are clearly gaps in the understanding of the role of the microbiota on chicken immune responses in the context of Salmonella pathogenesis, colonization and persistence in vivo. The team should prioritize their research on this topic as it has a huge potential of discovery and application in disease control that will be an asset to attract private companies”.

As indicated, this is only partly addressed since all research directions have been kept.

“The team would benefit from internal collaborations with teams using similar or complementary tools that could be mutualized (microbiota analysis pipelines and germ-free chickens). Collaborations between teams are likely to lead to interesting results and communal publications”.

This is partly addressed since the team is now collaborating with 10 of the 12 teams and platforms of the unit, although it is not clear how many publications have been co-authored through these collaborations.

“Interaction with industrial partners, such as Lesaffre, is encouraging. However, contractual collaborations with companies should be concretized”.

As said above, this is partly addressed through engagement with Adisseo and Phileo.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	3
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	6
Subtotal permanent personnel in active employment	11
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	2
Post-docs	0
PhD Students	3
Subtotal non-permanent personnel	5
Total	16

EVALUATION

Overall assessment of the team

The team has a very good to excellent track record. Attractiveness is excellent with an increased portfolio of external funding in securing European and national grants. Inclusion in society is also excellent and has been starkly improved by attracting funding from non-academic partners. The overall assessment of the team is excellent.

Strengths and possibilities linked to the context

The team is rather homogeneous since most of the PIs are working on related scientific questions and thus co-authoring many of the papers published by the team.

The team has at least two rather original research directions, which include the role of outer membrane proteins (Rck or PagN) in the T3SS-independent invasion of *Salmonella* in cells. The other innovative aspect of the research is the characterization of super-shedders involved in transmission.

The number of publications, 57, is very significant for a team of this size (5 PIs).

External funding has also been substantial since there is one H2020 grant (PI - 2018-2021 - 250 k€- MoMIR PPC on zoonosis) and one ANR grant (PI - MOSSAIC - 2022-2025 - 250 k€) which are running. Other grants have terminated during the period, the main ones being another European grant that ended in 2018 (FP7, PROHEALTH), and 3 ANR grants that ended in 2018 (Antibiophage), 2020 (AWAP) and 2021 (Sal Host Trop). A number of other small grants from industry and the Region were also obtained during the period.

Funding has been attracted from non-academic partners, notably Phileo and Adisseo (>500 k€). Moreover, one PI of Team 4 (she joined Team 4 after the previous evaluation, and she was the lead PI of Team B6 'Pathogénie de Colibacillose aviaire' (PCA)) coordinates the ANR LabCom ALGAHEALTH project (started in January 2020), involving 3 other teams of ISP, and which aims at the assessment of algae-derived compounds to control infection in chicken.

There were 4 post-docs/engineers who stayed for most less than 2 years in the unit, which is on the high end when compared to other teams in the unit, although the team is willing to increase this even further, as indicated in its SWOT analysis.

Most of the PIs are known in their field and have regular invitations to give lectures, while one of them evaluated prestigious ERC advanced grants.

The team engaged with the public mostly about Salmonellosis in chicken, at the "Salon de l'Agriculture" (2019), and in the press, e.g. "Les Echos", "La Nouvelle République" or "La revue de l'industrie agroalimentaire".

The momentum of the team is excellent, although there have been departures of some key staff members (see weakness below), but others have joined the team. For the future, there is also guarantee from INRAE to recruit a DR (host side expertise and in prevision of the team PI retirement) and a young researcher (CR, microbiota) which will nicely reinforce two of the main axes.

Weaknesses and risks linked to the context

The team publications are for most in good, specialized journals but none in more generalist and high-profile reviews. Some of the breakthroughs on the T3SS-independent invasion are published in journals like for Rck in *Open biology* (2021), *Microbiology Spectrum* (2021); or for Pagn in *BMC Microbiology* (2021), whereas a recent review on super-shedders is in *Microorganisms* (2022).

The number of PhD students trained over the period is 6, which is on the low mark for 5 PIs.

The team is ongoing some restructuration with the departure of one key PI in 2021, who was lead author on many of the key publications.

The performance in securing grants, publishing and supervising PhD students is well spread across all team's PIs except for one, who also still needs to demonstrate leadership in authoring papers and giving lectures.

All PIs are INRAE and it may result in some lack of teaching and attractiveness for Masters and PhD students.

RECOMMENDATIONS TO THE TEAM

One main recommendation to the team is to expand the research towards mechanistic issues, such as could have been the case for the mechanisms of *Salmonella* entry and the variety of receptors and pathways. These had excellent potential for impactful fundamental research that could be published in more generalist journals. There is no specific reasons not to do that when the resources and manpower are there as it was the case.

The team can only be encouraged to carry on with this momentum in securing funding and in engaging with industrial partners. This should be possible considering the plans already in place for recruitment and the research project directions, which are timely and appealing both from fundamental and veterinary perspectives.

Team 5: AIM - Apicomplexes et Immunité Mucosale
 Name of the supervisor: Mr Fabrice Laurent

THEMES OF THE TEAM

Team 5 is conducting research on host-pathogen interactions and development of affordable solutions for controlling two protozoan diseases: coccidiosis affecting chicken, and cryptosporidiosis, a zoonotic disease affecting ruminants and young children and immunodeficient humans. The search for new methods of combating these infections is based both on the analysis of the innate immune response of the host at the intestinal level, and the search for new compounds capable of directly countering the virulence of the parasites.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

"Good review articles published in international peer-reviewed journals are, although tedious to write, a good way to make one's name more aware to the academic environment".
 This was done as three reviews were published over the reporting period.

"The team activities as reviewers of research papers are not evident, and they do not participate in scientific journals as editors or editorial board members".
 This was not improved in the reporting period.

"Since the topics that are being studied in these two pathogens are also different (virulence factors and drug targets in Eimeria and intestinal immunity in Cryptosporidium infections), focussing the research efforts might be considered as an option in the long term".

This recommendation has not been followed but the committee considers here that it would be detrimental to lose one of the two expertise, considering in addition that the number of people in the team is in agreement with the development of these two topics. In addition, very encouraging results were obtained over the reporting period concerning the two parasites: identification of a new target to control cryptosporidiosis (CPSF3), and the characterization of the first Rop-kinase on *E. tenella* that induces G0/G1 cell cycle arrest and inhibits host cell apoptosis, this corresponds to a new field of investigation to control this parasite.

"To diversify funding for more sustainable and free academic research, the group should try hard to obtain funding from the public domain".

The team's own resources have increased significantly since 2016 (292 to 428 k€) and have been diversified, notably by increasing the proportion of academic funds.

"To improve the supervising capacity of the team, the expert committee encouraged unqualified scientist to get a HDR".

This was not done during the reporting period.

"A stronger contribution of team members to teaching is expected".

This was done during the reporting period with a 33% increase in the number of teaching hours of the team's researchers. The team is involved in the I2VB and BMC Sorbonne national masters, the IDOH+ international master and manages a lecture and tutorials for the LabEx ParaFrap.

WORKFORCE OF THE TEAM:

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	4
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0

Research supporting personnel (PAR)	4
Subtotal permanent personnel in active employment	9
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	2
Post-docs	0
PhD Students	6
Subtotal non-permanent personnel	8
Total	17

EVALUATION

Overall assessment of the team

The production of the team is qualified as very good with a fairly average number of publications regarding the size of the team. The attractiveness of the team is qualified as excellent with obtaining several national and international grants but no implication in journal editorial boards, nor expertise activities or invited conference. The inclusion in society is good regarding the general public but excellent to outstanding regarding the professional sector. The overall assessment for the team is very good to excellent.

Strengths and possibilities linked to the context

The team is clearly well recognized for its expertise on the two studied parasites, knowing that these are difficult models to study and that this expertise is rare and valuable.

The team has very strong interactions with the professional world of breeding, and has benefited from 3 Cifre grants during the reporting period. In particular, an excellent achievement in the field is the coordination of the APIS-GENE project funded by the professional sector (297 k€), which brings together research units, an experimental unit, a reference centre, a veterinary sanitary defence group and breeders.

The team has completed 2 invention disclosures during the period.

The team produced 26 publications during the reporting period. The publication of 3 papers in high-profile journals is notable: one as co-corresponding author in *Science Translational Medicine*, two in intermediate author position in *PNAS* and *Gastroenterology*. The team's other papers were published in very good to excellent journals in the field of parasitology (e.g. *International Journal for Parasitology*, *Parasites and Vectors*, *Parasites*) or more generalist ones (*Cellular Microbiology*, *Frontiers in immunology*, *microorganisms*, *BMC Biology*). In addition, 75% of the team's publications involve intra-unit, national (e.g. "Unité Parasitologie moléculaire et Signalisation", Institut Pasteur), and international collaborations (e.g. Umea University, Sweden; Professorial Faculty Technical University of Munich, Germany).

Eight PhD students were trained during the reporting period with an average of 2 publications per student.

The team participates to the LabEx ParaFrap, a French Alliance for Parasitology and Health Care, coordinates an international contract (FORMAS CRYPTO, 2020-2023, 111 k€), and is involved as a partner in 4 other European projects.

Weaknesses and risks linked to the context

The published papers are in very good journals in the discipline but given the research potential of the team, the number of articles is limited, especially because only 50% of them involve a team's member as a main contributor to the publication.

The team is not implicated in journal editorial boards.

There are little communication with the general public and participation in social debates.

No post-doc was recruited during the reporting period.

RECOMMENDATIONS TO THE TEAM

Regarding the staff potential, the team should try to increase the number of scientific publications, especially in leader authorship.

It might be a good idea to encourage once again the two researchers in the team who have still not defended their HDR during the period, to get this accreditation.

Topics such as research work to reduce the use of antiparasitic component could be better communicated/promoted to the general public.

Team 6: MPN - Multirésistances et Pouvoir Pathogène des Nématodes
 Name of the supervisor: Mr Cédric Neveu

THEMES OF THE TEAM

The team develops novel approaches for the sustainable control of parasitic gastro-intestinal nematodes impacting ruminants and mono-gastric animals.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

"Increasing the number of HDRs within the team is indispensable especially since one of the two team HDRs is brought by an emeritus. The expert committee thus strongly encourage team executive members, CR and IR, to obtain HDRs".

"The team is invited to limit excessive thesis duration because this is a bad criterion for the evaluation of the doctoral school".

"Likewise, teaching master courses could be helpful to recruit students interested by the team research. In addition, recruitment of postdoctoral fellows would help in supervising students".

One HDR was defended in 2020, doubling the number of HDR holders in the team, but the overall number remains low.

The thesis duration issue has been addressed to allow an average duration closer to 3 years. (one student: started 01/10/2017, ended 16/12/2020); the 3 other PhD students started in October 2019 (2, not yet finished) and October 2020 (1).

Two postdoctoral fellows have been recruited.

"Each of the team's scientists (as well as the one who is already very active) should aim to be more pro-active and participate actively in reviewing papers for scientific journals and become members of the editorial boards of good journals, or get involved in assessments of grant applications. This is important to increase the academic profile, and this, although time-consuming, is a part of academic life".

No participation in editorial boards has been achieved.

"Since the focus of the research is gastrointestinal infection, one wonders why there is not a closer link to e.g. P1 and P3. P1 is looking at hallmarks of innate immunity in the gastrointestinal tract and the knowledge on innate immune responses could be possibly exploited in a nematode infection model as well".

"Sheeps are capable of developing protective immunity to H. contortus through repeated exposure to this parasite, and innate and adaptive immunity in the host animal is capable of controlling the infection. The group could exploit the close proximity to P1 and P3 to develop measures that could lead to immunological control of the infection, or could use tools developed by P3 as drug-delivery vehicles".

This was not done during the present period.

However, a new thematic direction has been chosen by the team. As a consequence, an inter-team rapprochement was made with the Team 7 on the study of the effects of antihelminthic drugs on arthropods of interest (lice).

"The group seems to have managed to maintain a good mixture between communication with academic and non-academic and professional partners, and this should be continued".

There is still a good mixture between communication with academic and socioeconomic partners.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0

Research supporting personnel (PAR)	7
Subtotal permanent personnel in active employment	9
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1
Post-docs	0
PhD Students	3
Subtotal non-permanent personnel	4
Total	13

EVALUATION

Overall assessment of the team

The scientific production of the team is excellent with a high level of publications regarding the low number of scientists. The attractiveness of the team is excellent with obtaining several research contracts with private partners. The inclusion in society is very good regarding the general public, and excellent to outstanding regarding the socio economic world. The overall assessment of the team is excellent.

Strengths and possibilities linked to the context

The team is well-known in the field of antihelminthic resistance. It regularly developed new models to study these issues. Aside the core expertise with antihelminthic resistance, the team has undertaken new valuable activities in the reporting period including:

- the use of NGS (omics) in order to investigate the role of climatic change in emergence and diffusion of antihelminthic resistance;
- a new research topic aiming at identifying parasiticide targets on arthropods;
- a new functional phenotypic assay based on automated larval migration assay;
- the use of the free-living nematode *C. elegans* as a model for parasitic species.

Despite the small number of scientists, Team 6 has an excellent publication record with 43 papers in journals of solid reputation, including *Nature Communications*, *International Journal for Parasitology*, *International Journal for Parasitology: Drugs and Drug Resistance*, *Molecular Pharmacology*, *PLoS Pathogens*, *Parasite & Vectors*, *Scientific Reports*, *BMC Genomics*, *British Journal of Pharmacology*. 24 of these articles are the result of international collaborations (Iowa State University USA; McGill University, Canada; Wellcome Sanger Institute, University of Glasgow UK; University of Lublin, Poland, University of Belgrade, Serbia...), illustrating the extensive collaborative networks of the team.

During the reporting period, 2 post-docs and 4 PhD students were supervised, 3 PhD students are still in the lab. The PhD student who completed his PhD during the period published 2 articles (both first-authorship) in well-known journals in the field (*PLoS Pathogens* and *British Journal of Pharmacology*).

The team has demonstrated excellent capacities to secure funds from non-academic origins (Zoetis 212 k€, Merial 536 k€, Elanco 156 k€, Olmix 135 k€, Bpifrance 308 k€). One collaboration has led to the industrialization of a novel technology ("ALMA" Automated Larval Migration Assay) developed with INVENesis for drug screening. 25 projects are funded by European/national/regional calls for a total of 876 k€. The team is leader for 7 of them. In addition, 9 projects are funded by the 'Institut français du cheval et de l'équitation' (IFCE) and the team's members are leaders for 3 of them. They are also leaders for two regional grants (out of 3 obtained) from Region Centre-Val de Loire. The team is leader for two projects funded by equine associations (foundation Hippolia and the 'Fonds Eperon').

The European Commission has also funded 2 AgreeSkills researcher mobility programs.

A new researcher CR has been recruited in 2021.

1 HDR was defended in 2020, doubling the number of HDR holders in the team.

Weaknesses and risks linked to the context

The number of researchers is still low even if a new scientist has joined the team. Thus, the number of HDR holders is low.

The topics are very diverse regarding the limited human resources and HDR holders. Indeed, the newly recruited researcher will bring her expertise on a new project on arthropods and in collaboration with Team 7. The team is only partner for one ANR project and it is not part of any European Commission's collaborative programs (H2020, Horizon Europe). There are only little communication with the general public and participation in social debates.

RECOMMENDATIONS TO THE TEAM

The team should try to increase the number of HDR holders and post-docs in order to be able to carry out the various projects in which it is engaged.

Given its recognized expertise, the team should apply more regularly as a leader to competitive academic calls like ANR or EU funding sources.

Worm treatments and helminth resistance are of great interest and could be better communicated/promoted to the general public.

Team 7: BioMAP - Biomédicaments Anti Parasitaires

Name of the supervisor: Ms Isabelle Dimier-Poisson

THEMES OF THE TEAM

The main themes of the team are the therapeutic and prophylactic approaches against several parasites and viruses, *Toxoplasma gondii*, the head louse *Pediculus humanus* and SARS-CoV-2 as well as the development of anti-cancer immunotherapy using *Neospora caninum*.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

"For the immunological aspects of the project, the recommendation is to link more closely with P1 and profit from the insights achieved from this group, especially with regard to intestinal immunity that is elicited early in infection" and "The expert committee would recommend that the team collaborate with team P1 when it comes to targeting the relevant immune cells for initiating the correct innate immune responses. The expertise of this group might be very useful for assessment of the relevant adjuvants. GPs might be useful, but other options should also be considered".

The team published one article with former Team P1 (now Team 5) in Medical Microbiology and Immunology in 2016 by showing that antigen-specific response to *Toxoplasma gondii* profilin, a TLR11/12 ligand, depends on its intrinsic adjuvant properties.

"To gain a higher visibility, the team members should be more proactive in joining editorial boards of scientific journals, or documenting their activities as peer reviewers in scientific journals and / or assessments of grant applications".

This point is no more relevant given the excellent output of the team during the reporting period.

"The group has taken up many additional responsibilities and it is hoped that this way of interaction with the economic and public sector can be maintained".

The team has numerous striking interactions with the socio-economic sector. It has created a start-up company Kymeris Santé.

"If possible, funding through companies for doing research that implies patent applications should be managed in a different way for PhD students, since this can obviously delay publications and PhD defences, which is not in the interest of the PhD student, except if the company plans to recruit the new doctor".

The team has trained 9 PhD students. The ones who have already defended their PhD thesis have all one article in first author at least.

"The fact that the approaches described are mainly targeting the tachyzoite stage is an important issue when considering a one-health approach and especially food security, and it will be important to develop a read-out that allows to assess the impact also on the cyst-forming bradyzoites, and possibly measures need to be developed to target also this stage more specifically".

During the reporting period, the team investigated its nasal *T. gondii* vaccine against murine chronic and congenital toxoplasmosis, ovine chronic and congenital toxoplasmosis and on captive saimiris in several French zoos, which fully answers to the suggestion raised.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	2
Lecturer and associate lecturer	7
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	3
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0

Research supporting personnel (PAR)	4
Subtotal permanent personnel in active employment	16
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	3
Post-docs	2
PhD Students	0
Subtotal non-permanent personnel	5
Total	21

EVALUATION

Overall assessment of the team

The scientific production of the team is very good to excellent. The attractiveness of the team is excellent with its outstanding implication in the European Erasmus Master on Infectious Diseases one Health and its ability to secure national and international grants. The inclusion in society is outstanding regarding the socio economic world with the creation of two start-ups and with its communication to the general public via numerous broadcasting on the development of nasal SARS-CoV-2 vaccine. The overall assessment of the team is excellent to outstanding.

Strengths and possibilities linked to the context

The team published 39 articles with 22 as first, last or corresponding author. Among these 22, publications are in *PLoS Pathogens* (2021), *Journal of Infectious Diseases* (2021), *International Journal of Parasitology* (2018), *Molecular Pharmacology* (2022) and *Frontiers journals*. The team co-authored articles in a large variety of *Journals: PloS genetics, Immunology Letters, Journal of Virology, International Journal of Pharmaceutics, Toxins, Bioconjugate Chemistry*.

The team trained 9 PhD students, 4 post-docs and more than 30 Master students.

The team interacts with several other teams in the unit, and in particular Team 6 for anti-Pediculus therapeutic intervention and Team 10 for nasal SARS-CoV-2 vaccine. It has an excellent national visibility and is member of the LabEx MablImprove.

The team secured 3 international grants from the British Society for Antimicrobial Chemotherapy (GA2016_020P as coordinator (19 k€)), from FEDER (ANIMALT and ADCITMER as coordinator (461 k€)). It also obtained 3 national grants, all as coordinator: DBAB-TOL, MUCOVAC from the MESRI (1500 k€), NANO-SARS-CoV-2 from ANR (36 k€). The team was supported by several regional grants as coordinator (BASTET (122 k€), BIOMEDICAMENT 2 (540 k€), BIOMEDICAMENT 2 BIOS (486 k€), MUCOVAC (200 k€), MUCOVAC (95 k€), NCIS (18 k€), VAB (134 k€)). It received financial support from the 'Ligue contre le cancer' with 6 different grants (42 k€).

The team has outstanding interactions with the socio-economic world. Two patents were granted and licenced with the University of Tours, Kymeris Therapeutics INC and INRAE (WO2018224656 Neospora for use in treating cancer and infectious diseases and WO2020240024A1). It has created the start-up Kymeris Santé. The team also developed an intranasal vaccine against SARS-CoV-2, which led to the creation of LoValTech, a DeepTech start-up labelled by Bpifrance. One patent has been at the origin of the collaboration with Vaxinano for the development of vaccine against toxoplasmosis.

The team coordinates the Master on 'Infectiologie, Immunité, Vaccinologie et Biomédicaments/I2VB' and the international EMJMD of Sciences "Infectious Diseases and One Health" (IDOH, 2017-2021; IDOH+, 2020-2025), with a total of 160 trained students from all over the world.

One team's member defended his HDR in 2017.

The team actively disseminates to the general public during the "Fête de la Science", "Journées Portes Ouvertes", "Forum de l'Étudiant". A large number of interviews were done on TV and radio regarding the IDOH Master, the lice project and the SARS-CoV-2 nasal vaccine.

Weaknesses and risks linked to the context

The team has limited technical staff.

The researcher staff is composed mainly of assistant professors with overloaded teaching duties.

RECOMMENDATIONS TO THE TEAM

The team has a unique niche in the breeding of *Pediculus*, which should be continued.

The work should be more valorised in high-profile journals.

The committee recommends to apply for larger EU funding.

The team's PI should be supported by supervising bodies to devote herself to her team and her teaching activities.

The committee recommends the team's members to document their activities as peer reviewers in scientific journals and/or assessments of grant applications.

Team 8: BioVA - Biologie des Virus Aviaires
 Name of the supervisor: Ms Caroline Denesvre

THEMES OF THE TEAM

Team 8 aims at understanding the physiopathology of Marek's disease, which is caused by Marek's disease virus (MDV, genus mardivirus) and induces lethal lymphoma in chicken. The vaccine protects against disease but not transmission, failing to eradicate the virus and allowing viral evolution.

Using *in vivo* and *in vitro* approaches, the team studies interactions between MDV and its host and develops novel vaccine vectors and antiviral therapies.

Regarding viral transmission, the team characterises host and viral factors that regulate mardivirus tropism, persistence and shedding in feathers.

The team also studies the effect of infection on lymphocytes biology, the role of extracellular vesicles in pathogenesis, and the effect of cellular stresses on MDV replication and reactivation.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

"The team is rather small needing to reach a significant critical mass (lack of supporting personnel)".

Since 2016, a new permanent engineer (IE) was recruited, which increased the critical mass of the team, and the two researchers got their HDR during the reporting period. Currently, one PhD student also works in the team.

"The team should publish more original and more impressive scientific stories in much prestigious journals", "it should cumulate the data it used to publish in several papers into a single paper".

The majority of the team's publications during the reporting period are in outstanding or excellent-reputation journals in the field of virology and veterinary research, including *Journal of General Virology* (1), *Journal of Virology* (2), *PLoS Pathogens* (2), *Viruses* (1), *Frontiers in Cellular and Infection Microbiology* (1).

This indicates an increase in the number of excellent publications per permanent researcher.

"Contracts with companies could be increased in order to build a bigger critical mass for the group".

The team has obtained 5 contracts during the reporting period with industrial partners: 3 with Ceva Santé animale, 1 with Olmix, 1 with Merial.

"The team should continue with the current method of engaging and training students".

This recommendation was followed: 2 PhD students graduated and another one is in training. In addition, 7 other students were trained by the team.

"Team BioVA should perhaps focus its project on the secretion of the virus", "targeting mechanisms studies should allow the team to publish in more prestigious journals".

At least 5 original publications of the team were related to this subject during the period (one third of the team's publications). Mechanistic aspects were indeed broached and published during the reporting period.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	3
Subtotal permanent personnel in active employment	6

Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	1
Subtotal non-permanent personnel	1
Total	7

EVALUATION

Overall assessment of the team

The scientific production of the team is excellent. Its attractiveness is very good to excellent. Inclusion in society is good regarding the general public but excellent regarding the socio-economic world. The overall assessment of the team is very good to excellent.

Strengths and possibilities linked to the context

Team 8 is still a rather small group focusing its research on the infection of chicken by Marek's disease virus (MDV). The three scientists of the group now have their HDR (+2 during the period). Moreover, the team size increased with the recruitment of a new engineer in 2019, specialized in 3D skin models, which increases the team's attractiveness thanks to this additional methodology useful to study Marek's disease physiopathology and transmission. This model also allows to reduce the number of chickens used for *in vivo* projects, in accordance with the 3R principle.

The team went on developing new solid and original methodologies and very diverse competences (e.g. skin model, chicken feather follicles culture *in vitro*, other original chicken cellular models like keratinocytes, new mutant viruses, *in vitro* and *in vivo* imaging technologies, infections in hypoxic conditions) to support its projects and collaborations. Significant progress was then achieved on the molecular mechanisms, the physiopathology, and the transmissibility of MDV.

The team produced 16 publications during the reporting period in the field of virology and veterinary research, among which 87% are in leader position. These articles were published in journals with excellent reputation, such as *Journal of General Virology* (1), *Journal of Virology* (2), *PLoS Pathogens* (2), *Viruses* (1), *Frontiers in Cellular and Infection Microbiology* (1).

The team develops fundamental and applied research with numerous academic partners and private companies. It succeeds well in combining partnerships with socio-economic partners and still conducting fundamental research of high quality in virology. It was then able to raise major funding from both public and private sources. In particular, it is coordinator of academic projects, notably the ERA-NET Aniwha MADISUP (140 k€) and the Institut Carnot "France Futur Elevage" MARDISHED (77 k€). It is also funded by extensive contracts with private companies (227 k€), like Merial (SANOFI, 1 contract), Ceva Santé animale (veterinary pharmaceutical group, 3 contracts) and the Olmix group (1 contract). These partnerships aim to improve vaccines as well as to test potential antiviral molecules.

The team is leader in the projects with its international partners and in particular the Freie Universität Berlin (Germany).

By organizing an international symposium (11th international Symposium on Marek's disease and avian Herpesviruses in 2016), the team was able to increase its already excellent international visibility and to begin new partnerships with the private sector, while contributing efficiently to train the next generation of researchers.

Weaknesses and risks linked to the context

No post-doctoral contract and few academic grants like ANR funding were obtained during the reporting period.

Very few communications/interactions with the general public were performed during the period.

RECOMMENDATIONS TO THE TEAM

The team developed a high diversity of skills and technical/methodological assets, and is encouraged to go on with the same dynamics (e.g. transcriptomic high-throughput technics).

Regarding the One Health concept, the team could collaborate more actively with other teams of the Unit. The team should apply for academic grants (e.g. ANR PRCI with its German partner), which would allow to recruit post-docs.

The reinforcement of the HDR holders in the team should allow to train an increased number of PhD students. The positive research dynamics (topics, methodological diversity, 3R principle, scientific production) should be maintained.

Team 9: 3IMo - Infections et Immunité Innée des Monogastriques
 Name of the supervisor: Mr Sascha Trapp

THEMES OF THE TEAM

Team 9 was created in January 2019 after several retirements, some departures for other functions and the merging of 2 teams ("*Pathologie et immunologie aviaire*" and "*Immunologie mucosale porcine*"). This team studies host-pathogen interactions for avian and porcine pathogens like avian influenza and African swine fever. It also studies the immune aspect of inflammatory diseases in pigs like cystic fibrosis. Moreover, it characterizes the impact of gut microbiota modifications and of treatments with bioactive compounds on the immune system of the host and on the pathology (often lethal) outcome.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Some recommendations (not detailed here) are not appropriate anymore after the fusion in 2019.

"The team is invited to consider whether they might achieve greater visibility by volunteering to serve as editors or on editorial boards. They might also promote their visibility by applying to more general basic science meetings".

Since 2019, the team published notably in *Frontiers in Microbiology*, *Frontiers in Immunology*, *PNAS* (intermediate position) and *PLoS Pathogens*. The fusion is too recent to evaluate the efficiency of the publication strategy of the new team.

Two scientists were actively involved in editorial boards (*Frontiers in Microbiology*, *Veterinary Research...*).

"The team is invited to consider whether they might extend their collaborations to groups outside of Europe and try publishing in general science journals".

"The team is invited to consider how they might engage more fully with their stakeholders, the press and the public".

About collaborations, 29 out of 63 publications of the period were in collaboration with international partners. Regarding interactions with private companies, in 2021, about 20% of funding came from industrial partners (valorisation/collaborations).

The team leader coordinates the EU Horizon 2020 project VetBioNet that seeks to strengthen European competences to meet the challenges of epizootic/zoonotic infectious disease outbreaks by establishing a network of organisations and institutes.

"The team is invited to consider whether they might extend their analyses with influenza to human cells."

The team did not seem to have extended its analyses with Influenza to human cells.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	5
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	4
Subtotal permanent personnel in active employment	9
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1

	Post-docs	0
	PhD Students	1
	Subtotal non-permanent personnel	2
	Total	11

EVALUATION

Overall assessment of the team

Considering the recent creation of the team, its scientific production and attractiveness are excellent. Inclusion in society is excellent to outstanding regarding interactions with the general public. The overall assessment of the team is excellent.

Strengths and possibilities linked to the context

There was a very active scientific production before the creation of the team in 2019, and a great effort has been done to maintain this dynamics.

Due to similar methodological approaches, and despite distinct research topics, all the researchers from the two previous teams already worked together before the fusion. This collaborative work went on efficiently in the new team.

Team 9 contributed to major advances:

- in immune mechanisms leading to inflammatory and/or infectious diseases in pigs;
- in immune response and viral escape mechanisms in chicken and their impact on influenza cellular tropism and pathogenicity (and host specificity);
- in the impact of gut microbiota on the development of immunity, especially in the respiratory tract of chicken.

The team developed new methodological approaches, which are shared in the context of the VetBioNet network. It also contributed to the research of new treatments with bioactive compounds (e.g. flagellin) to reduce pathogenicity of respiratory infections (in pigs).

The recent publications of the present scientists are well distributed among the team's projects. The quantitative analysis of the publications has no great significance due to the recent fusion and creation of the new team, but it must be noted that Team 9 published in *PLoS Pathogens*, *PNAS* (intermediate position), *Frontiers in Microbiology* and *Frontiers in Immunology*.

During the reporting period, 4 post-docs and 5 PhD students were supervised, 1 PhD student is still in the lab. Every PhD student who completed his/her PhD during the period published 2 to 5 articles (and at least 1 with first-authorship). The last post-doc (the only one in the new team) published 2 articles.

Team 9 has secured 3 major grants, in accordance with its major research themes: 2 from public sources (coordination of the EU Horizon 2020 project VetBioNet, 2017-2023, 391 k€), ANR JCJC grant (PIGIMMUNITY, 2019-2022, 240 k€) and 1 from private sources (coordination of the GUTMIVIR project funded by ADISSEO, 2021-2024).

The team is also partner in the ANR LabCom ALGAHEALTH project (coordinator in Team 4, 2020-2023), and in a EuroFéri project (2020-2023).

The team communicates very actively towards the general public, including 4 articles in *Biofutur* and "*Science et Pseudo-Science*", two interviews (radio and podcast), a live streamed discussion in YouTube, public lectures at the "*Salon de l'Agriculture*". INRAE press releases (5) and newspaper articles (6) were published about the team's work.

Weaknesses and risks linked to the context

None identified due to the recent creation of the team.

RECOMMENDATIONS TO THE TEAM

It would be relevant to reinforce the synergy within the team. Some transversal projects with common pathogens for poultry and pigs, like influenza virus, could represent a good opportunity for that.
The research of new private contracts or of public funding would permit to recruit post-docs for longer periods.
The team leader should defend his HDR to reinforce the PhD supervision potential.

Team 10: BIP - Biologie des Infections à Polyomavirus

Name of the supervisor: Mr Antoine Touzé

THEMES OF THE TEAM

The research activity of Team 10 is focused on human Polyomavirus infections. The research programs developed aimed at studying the association between MCPyV (Merkel cell Polyoma virus) with the Merkel cell carcinoma and the association of BKPyV (BK Polyoma virus) with BK nephropathy. For Merkel cell carcinoma, the team's aim is to identify diagnostic/prognostic tools to elaborate new treatments. A cognitive research program studies the histogenesis of Merkel carcinoma. For BKPyV, the team develops programs in collaboration with a start-up (SPyDiag) to elaborate new diagnostic tools and therapeutic solutions for BK-associated nephropathy.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

"Team V3/BIP is invited to consider whether they have been involved enough with the international research community for optimal progress".

The team was involved in the European project Summertime with the European Academy of Dermatology and Venereology (EADV) to test new diagnostic tools on MCC patients within all Europe. The team has strong collaborations with laboratories from Julius-Maximilian University of Wurzburg in Germany on MCPyV. The team also collaborates with Teams 9, 8 and 7 and should further strengthen such interactions to develop research programs on mechanisms and improve their international recognition.

"Team V3/BIP is invited to consider whether the discoveries that they have made from human oncogenic polyomaviruses have lessons to teach the wider world of basic science, which might raise the profile of the group".

Projects of the team include research on the host. Thus, the discoveries on MCPyV may have implications for other oncogenic various polyomaviruses and their mechanisms of infections in target cells. The team examines the host genetic and epigenetic events that impact of the development of MC carcinoma in collaboration with PRISM (INSERM U1192, Lille) and the Wurzburg University. The team studies epigenetics factors of HLA molecules in MCC to assess the role of the host immune system in cancer development.

"Team V3/BIP is invited to consider whether they might be more involved in leadership and organization".

The team is a key leader on Merkel cell polyomavirus and Merkel cell carcinoma. However, it is a small-sized team, composed of staff with hospital and/or teaching duties. The team is housed in the Faculty of Pharmacy. The team's programs focused on Polyoma virus in human are distinct from those of the other ISP teams devoted to animal health. These characteristics do not facilitate the team's involvement in the organization of the unit. However, the team's programs belong to the One Health One Medicine approach of ISP unit.

"Team V3/BIP is invited to consider whether they have been involved enough with the international research community for optimal recognition".

The team is extremely well connected with the European Academy of Dermatology and Venereology (EADV), notably through the European project Summertime (2019-2024). It has established collaborations with the University of Wurzburg. It published in the best scientific journals of the specialty (*Journal of Investigative Dermatology, British Journal of Dermatology*). One member is Associate editor for Clinical trials of *British Journal of Dermatology* since 2015. One member has responsibilities in Soc. of European Dermatology.

"Team V3/BIP is invited to consider whether they have been involved enough with the private sector, the press or the public for optimal progress and recognition".

During the reporting period, the team has conducted several actions related to reinforce the contribution of its research activities to society. Indeed, it has devoted its activity on the SARS-CoV-2 pandemic crisis and worked on diagnostic tool and vaccine candidates against the SARS-CoV-2 with Team 7. The team has transferred its specific technologies of detection of papillomavirus to Texinfine society (licence contract signed in 2018). The team has generated an antibody conjugates Adcitmer, deposited a patent (WO2021170961) to target MC carcinoma cells. The conjugate is evaluated in preclinical studies and supported by the regional Program ARD "Biomédicaments". In addition, the team has generated cross reacting mAbs against different BK virus genotypes, and this discovery was patented in December 2020. Members of the team have created SAS SPyDiag in 2020 for the development of early diagnosis assays for reaction of BKPyV in kidney transplanted patients, and they have obtained a contract BPI French tech Emergence. The clinical evaluation of the mAbs is programmed in 2023 with Amiens CHU.

"The team is invited to limit excessive thesis duration because this is a bad criterion for the evaluation of the doctoral school".

During the reporting period, the team has trained 2 PhD students. Their thesis lasted three years at most.

"Team V3/BIP is invited to explain how so few scientists hope to accomplish so much work. It looks like that a great part of the work will be done in collaboration".

The projects on MC PyV are performed with the team's collaborators from the lab from Wurzburg University. The publications of this program are signed by co-authors from the two labs. The team also collaborates with Team 7 on the projects devoted to translational research (development of mAbs).

"Team V3/BIP is invited to explain whether they have considered their MCC cohort for examination of other genetic and environmental predispositions towards MCC".

During the interview, the team has presented projects to evaluate the impact of immune genetic factors (HLA genes) in relation with the development of Merkel cell carcinoma, using the cohort.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	3
Lecturer and associate lecturer	2
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	7
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	3
Post-docs	0
PhD Students	2
Subtotal non-permanent personnel	5
Total	12

EVALUATION

Overall assessment of the team

The scientific production of the team is excellent. Its attractiveness is very good. The inclusion in society is good regarding the general public but excellent regarding the socio-economic world. The overall assessment of the team is excellent.

Strengths and possibilities linked to the context

Team 10 develops focused projects on two Polyomavirus that are associated with specific human diseases. During the reporting period, most of the works that have been valorised by publications concern MCPyV and Merkel disease.

The scientific production includes 97 publications with 41 clinical articles. Among the 56 articles from research activity, 25 publications involved PhD students and 21 out of 25 are signed as first author by students. The team also produced 10 reviews and synthesis from which 5 are signed as first or last author by members of the team. Some members also produced 12 professional and technical reviews (on buccal mucosa, Covid-19 pandemic, and hospital career attractiveness).

The team publishes original articles as leader in major journals of the specialty, like *Emerging microbes & infections*, *Journal of The American Academy of Dermatology*, *Journal of Investigative Dermatology*, *British Journal of Dermatology*, *European Journal of Dermatology*, *Modern Pathology*, *Frontiers in Cellular and Infection Microbiology*.

The collaborations (local, national and European) and networks established by the team favour its research activities despite its small size.

The team has ongoing established collaborations with European laboratories within the international consortium *Summertime* (2019-2024). It actively collaborates with the Julius-Maximilian Wurzburg University (Germany), with 17 co-authored publications and one joint PhD supervision.

External funding includes the *Summertime* European contract coordinated by a member of the team (EADV-PPRC; 100 k€) for 2019-2024, 1 PLBIO from INCa as participant, several regional contracts from C-VaLo with the BK STRIP project (100 k€), from the "Cancéropole Grand Ouest" with two projects DIACAN (35 k€) and POCAME (98 k€). The team is also partner for an ANR grant with Team 7 (MUCOVAC, 200 k€). It obtained regularly grants from associations, e.g. "Société Française de Dermatologie (SFD)" and "Ligue contre le Cancer".

The team has developed products with the creation of a start-up company SPyDiag with Tours University. The team has valorised its results by 2 patents in 2019 and 2020.

In collaboration with Team 7, Team 10 has reoriented its research activity to work on SARS-CoV-2 and produced nasal type vaccine. It has generated new sero-diagnostic tests of SARS-CoV-2 infection for which an invention disclosure was obtained in April 2020 and a contract for exclusive exploitation of the test in July 2020. In collaboration with Team 8, the team works on Marek disease virus in poultry to decipher the mechanisms of oncogenesis. Other products developed by the team include one cohort on Merkel carcinoma and one collection of tumours.

One member of the team is associate editor for Clinical trials topic of *British J. Dermatology* since 2015.

Members of the team have received national prizes (Prize of communication to "Congrès Annuel de Recherche Dermatologique CARD", prize from SFD, and "Ligue contre le Cancer"); one member received the Hugo Prize from hospitalo-university of Grand Ouest. Members of the team have responsibilities in scientific societies (SFD, Society of European Dermatology). They organized in 2016 the "Journées des infections Polyomavirus".

Weaknesses and risks linked to the context

Team 10 is a rather small team that mainly develops clinical research linked to the hospital activities of its members in a structure focused on veterinary research.

The human resources devoted to research are limited. The only full-time permanent researcher will retire during the next contract.

RECOMMENDATIONS TO THE TEAM

Regarding the One Health concept, the committee recommends to establish more active collaborations with other teams of the unit.

As the team suffers from a limited research workforce, the committee recommends to increase its attractiveness to young researchers. It should apply for EU grants for recruiting post-docs.

The team should increase the communication/promotion of its research activities to the general public.

CONDUCT OF THE INTERVIEWS

Dates

Start: 06 February 2023 at 09:00

End: 07 February 2023 at 17:00

Interview conducted: online

INTERVIEW SCHEDULE

Day 1 of the interview 6/02/2023

8:30-9:00	Hcéres Committee meeting <i>Closed-door meeting</i>
9:00-9:05	Hcéres rules and procedures by M. Mercier-Bonin <i>Public session (all unit members)</i>
9:05-9:55	Scientific and administrative presentation of the unit 30 min presentation + 20 min discussion N. Winter <i>Public session (all unit members)</i>
(9:55-15:30)	Scientific presentations by team leaders 10 min presentation + 10 min discussion <i>Public session (all unit members)</i>
9:55-10:15	Team n°1/IBIR (Infections Bactériennes et Immunité des Ruminants, P. Germon)
10:20-10:40	Team n°2/BRMF (Bactéries et Risque Materno-Fœtal, L. Mereghetti)
10:45-11:05	Team n°3/PGBA (Plasticité Génomique, Biodiversité, Antibiorésistance, B. Doublet)
11:10-11:30	Team n°4/SPVB (Signalisation Portage et Virulence Bactérienne, Ph. Velge)
11:35-11h55	Team n°7/BioMAP (Biomédicaments Anti Parasitaires, I. Dimier-Poisson)
11:55-12:30	Committee debriefing <i>Closed-door meeting</i>
12:30-13:30	Lunch break
13:30-13:50	Team n°6/MPN (Multirésistances et Pouvoir Pathogène des Nématodes, C. Neveu)
13:55-14:15	Team n°5/AIM (Apicomplexes et Immunité Mucosale, F. Laurent)
14:20-14:40	Team n°8/BioVA (Biologie des Virus Aviaires, C. Denesvre)
14:45-15:05	Team n°9/3IMo (Infections et Immunité Innée des Monogastriques, S. Trapp)
15:10-15:30	Team n°10/BIP (Biologie des Infections à Polyomavirus, S. Touzé)
15:30-16:05	Committee debriefing <i>Closed-door meeting</i>
16:05-16:15	Break
16:15-16:45	Meeting with ITAs <i>In the absence of any managing staff (director, team leaders)</i>
16:50-17:20	Meeting with researchers

In the absence of any managing staff (director, team leaders)

17:25-17:55 **Meeting with post-docs and students**
In the absence of any managing staff (director, team leaders)

17:55-18:15 **Committee debriefing**
Closed-door meeting

18:15 **End of the first day**

Day 2 of the interview 7/02/2023

9:00-9:30 **Committee debriefing**
Closed-door meeting

9:30-10:20 **Meeting with institution representatives: Université de Tours* & INRAE****
Closed-door meeting

10:20-10:40 **Committee debriefing**
Closed-door meeting

10:40-11:30 **Meeting with the Director**
Closed-door meeting

11:30-12:00 **Committee debriefing**
Closed-door meeting

12:00-13:00 **Lunch Break**

13:00-17:00 **Redaction of the final report**
Closed-door meeting

17:00 **End of the interview**

GENERAL OBSERVATIONS OF THE SUPERVISORS

Nathalie WINTER
Infectiologie et Sant  Publique
UMR 1282 INRAE Universit  de Tours
Centre Val de Loire
37380 NOUZILLY

To: HCERES committee for unit "Infectiologie et Sant  Publique" N 1282- UMR INRAE/UT
Object: Reply to observations 4 pages

Nouzilly June 19th, 2023

Dear HCERES committee members,

First of all, we would like to thank you all again for your time and expertise for the evaluation of ISP's SAD for the current contract.

We also thank you for the generally very positive comments on ISP's realizations and the insightful recommendations to the unit and the teams.

Unit's reply to the evaluation report

We would like to bring some points of clarification on the functioning of the unit. Indeed, we believe that some weaknesses that were mentioned in the report were not accurately assessed.

- Regarding biosafety practices, the committee wrote page 8 in § assessment of the functioning of the unit that "the unit follows rules regarding .../... biosafety and biosecurity rules" which does not seem compatible with the next sentence: "a biosafety committee is necessary". As this is a very serious matter for the ISP unit where biological risk is highly present, we would like to clarify some points for the committee.
 - As exposed on page 18 of ISP's SAD, we have set up the committee called "**PQR**" as a task force where **all questions regarding biosafety (and other hazards) are thoroughly examined and delt with**. All actions are coordinated in this task force which **regularly meets** every two months and can also be activated when specific issues are raised. We would also like to stress the point that ISP currently has a 15 staff members' team dedicating an important part of their time as "assistants de prevention" to deal with all biosafety issues. This, as we believe, represents one of the most important teams dedicated to biosafety issues, at least in the INRAE Centre Val de Loire. In January 2023, in reply to question N 21 from the committee, we also provided some more explanations on actions organized by the PQR i.e. ISP's biosafety committee.
 - Therefore, we do not agree with the rather strong statement page 8 that "a biosafety committee is necessary", unless the HCERES committee has a completely different definition of what this biosafety committee should be. In that case, we would appreciate an insight of what is expected from the unit for the next contract.
 - We think that the recommendation to the unit page 16 "in order to frame the handling of various pathogens studied in the unit.../... a biosecurity committee must be constituted with regular meetings" should also be revised, accordingly.
- Statement in § "assessment on the functioning of the unit " (page 8) that "committees addressing questions relative to i) psychosocial risks .../... are missing" is not accurate. As exposed in ISP's SAD (page 21) such committee has been put in place to accompany doctoral students whom we consider most at risk regarding this point. During the mandate, since our doctorate school proposed similar help (as we believed), a user survey was carried out and ISP's doctorate students decided that the ISP's committee was useful and helpful and should be kept.
- We disagree with the point raised in page 10: "researchers without managing responsibility are not included in decision instances". We would like the committee to consider the following examples disproving that this is the way the unit is managed. **i)** every year, the unit financially supports 8 internships for master 2 students. Each scientist willing to supervise a master student first addresses its master's project to an internal committee who ranks the 8 subjects that will be supported by the unit. This committee composed of 7 members is led by a scientist (team N 8)

Nathalie WINTER
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and involves 2 scientists (teams N 7 and 8) who **are not team leaders ii)** during the annual PhD day, a prize - financially supported by the unit- is awarded to the best two presentations given by students. Between half and the two thirds of the jury members (depending on the year) are **ISP researchers who are not team leaders iii)** as explained in ISP's SAD (§ "actions to promote inter-team's collaborations," page 13) ISP's direction has launched in 2019 the ISP specific scientific day ("Journ e de retraite scientifique") during which projects conducted by at least two ISP teams are presented. One project is awarded 2x10 k  on ISP internal funds. The jury awarding this prize is exclusively composed of **ISP researchers who are not team leaders iv)** as presented in page 15 of ISP's SAD, animation of ISP's three scientific topics during the mandate often led to the purchasing of some new pieces of equipment that could help ISP's scientists to run their research projects. Decisions to purchase such important pieces of common scientific equipment arose from **large consultations and not from some decisions-making bodies v)** last, but not least, the **construction of the unit's strategic plan for the next contract** was thoroughly carried out with **all the unit's members** via interactive discussions and surveys, which required implementation of new virtual communication tools during the COVID-19 sanitary crisis. This last yet important part of IPS's direction management actions to involve **all members of the unit in a shared vision of the future** was not exposed in ISP's SAD since the document was limited to ISP's realizations for the current contract.

These are some facts demonstrating, as we believe, that researchers working at ISP without managing responsibilities are largely involved in decisions. In light of this, we would like the committee to reconsider statements that, in our opinion, are not accurate such as page 10 (§ pointing weaknesses on functioning of the unit) "researchers without managing responsibility are not included in decision instances" ; page 8 (§ assessment of the functioning of the unit) "Committees addressing .../... scientific strategies with all scientists are missing". We would also appreciate if the committee could rephrase their recommendations to the unit regarding evaluation area 1 (page 16): "the direction needs to strengthen the dialogue .../... to this end it is important to .../... avoid top down and one way management" as we consider that considerable effort has been made during the mandate to encourage debate, shared vision and fair decisions' making. We agree that there is still room for improving the dialogue. However, the committee is probably well aware, that this is a big challenge in very large units such as ISP...

- More generally, we would also appreciate if the committee could think again about the impact that the COVID-19 crisis had on all staff that indeed profoundly impacted the sense of belonging to the same unit. We do not think this is unique to ISP. The situation regarding the sense of belonging to the same unit is not back to normal yet. May we suggest that some points or "issues" that were raised during consultations of the different staff members with the committee are examined again from this perspective?
- We noted that the committee did not make mention of the great support from our administrative team (N 13/SAR) in the report, even though our committee kindly shared with us their very positive appreciation of the quality of the SAD during their visit 06th and 07th of Feb. The quality of analyses of the realizations of the unit during the mandate that our committee noticed is only one example among many of what team N 13/SAR achieved during the mandate. We believe this team -whose work is really appreciated from all our unit's members- is a great strength of the unit. We would really appreciate if some mention of their important work could be added to the report.
- In assessment of the forward-looking aspect of the unit's policy (evaluation area 1, §2, page 10), we do not fully understand why the committee identified a weakness about the level of funding? As we only reported contracts **that took place or started between Jan. 1st, 2016 and Dec 31st 2021**, (evaluation period), the teams did not report all the contracts they currently have. Indeed, some new ones were signed from Jan. 1st 2022. Moreover, quite a number of applications are still under evaluation and ISP's scientists never slowed down on proposals' submission. So, we do not foresee a weakness in financing our ambitious objectives. Secured positions are another matter and we agree with the committee that there could be some difficulties, if ISP was not successful in recruiting enough new scientists, engineers and technicians.

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Teams' reply to evaluation report

Team N 5/AIM (Fabrice Laurent)

We thank the HCERES committee for its evaluation and time spent for helping us to improve our scientific production and define our future objectives. Based on the following facts, we would like to bring some additional information to reply to some comments.

1- *"No member of the team presented any invited conference in international congresses"*.

Regarding the team participation to international congresses as invited speakers, we apologize for not having indicated this information to the committee. Indeed, members of the team were invited to conferences during the evaluation period to present their work in plenary sessions in international congresses. See the list below :

- F. Bussi re. European Coccidiosis Group 17th, London, May 2018. Establishment of an in vitro chicken epithelial cell line model to investigate *Eimeria tenella* gamete development and the epithelial cell response to the infection.
- F. Laurent. Protective and deleterious intestinal immune responses: the case of protozoan infections. Advancia academy 2018 Dubrovnik, Croatia.
- F. Laurent. Calf care symposium. Overview of current knowledge on cryptosporidiosis: impact and therapeutic solutions, 12-14th November Nice 2019.
- F. Laurent. How innate immune responses shape *Cryptosporidium* infection? Seventh international Giardia and *Cryptosporidium* conference 23-26 June, Rouen, France 2019.
- F. Laurent. Current knowledge and toward new promising therapies to control cryptosporidiosis. 13th European Multicollloquium of Parasitology, which will take place in Belgrade, Serbia, October 12-16, 2021.

2- *"The team is not implicated in journal editorial boards, nor expertise activities"*.

- a. Until now, we were indeed not involved in journal editorial boards. So, we agree on this part of the sentence.
- b. Yet, it was not clear to us if expertise activities refer to (1) reviewing scientific manuscripts or grants ((ANR, ANSES, DIM1health, etc.), which we did regularly or to (2) participation in scientific councils (we participated in several scientific advisory boards (GIS IBISA, several platforms, vet School (ONIRIS, ENVA)) or to (3) conventional expertise's for agencies like ANSES which for now we didn't perform, although one of us participated in the COT of ANSES ("Animal health, nutrition and welfare") and in its international scientific board from 2023. So, we believe that teams members are indeed recognized as experts

3- *"one as first and last authors in Gastroenterology"* in the sake of fair evaluation, we would like to point that even though two of the team's researchers contributed to this beautiful study, none signed as first or last authors.

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Hoping that the points above shed some light, it would be greatly appreciated if the committee could reconsider its assessment of the functioning of the ISP unit. We would also appreciate if statements and recommendations on the points mentioned above were revised in the final report, accordingly.

Sincerely yours,

Muriel Vayssier -Taussat
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Santé Animale , INRAE



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