Research evaluation

EVALUATION REPORT OF THE UNIT

IAME - Infection, Antimicrobien, Modélisation, Evolution

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université Paris Cité

Institut national de la santé et de la recherche médicale - Inserm

Université Sorbonne Paris Nord

EVALUATION CAMPAIGN 2023-2024
GROUP D

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High Council for evaluation of research and highter education

In the name of the expert committee :

Alain Filloux, chairman of the committee

For the Hcéres :

Stéphane Le Bouler, acting president

In accordance with articles R. 114-15 and R. 114-10 of the Research Code, evaluation reports are signed by the chair of the expert committee and countersigned by the Hcéres chair.

To make the document easier to read, the names used in this report to designate functions, professions or responsibilities (expert, researcher, teacher-researcher, professor, lecturer, engineer, technician, director, doctoral student, etc.) are used in a generic sense and have a neutral value.

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

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Mr Pierre-Emmanuel Rautou, UFR de médecine, Université Paris Cité
Mr Matthieu Resche-Rigon, Faculté de Santé, Université Paris Cité

CHARACTERISATION OF THE UNIT

- Name: Infection, Anti-microbien, Modélisation, Evolution
- Acronym: IAME
- Label and number: UMR 1137
- Composition of the executive team: Mr Erick Denamur (director) and Ms France Mentré (deputy director)

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement
SVE4 Immunité, infection et immunothérapie

SVE7 Prévention, diagnostic et traitement des maladies humaines

THEMES OF THE UNIT

The unit's main theme is the understanding, prevention and control of infectious diseases. Emphasis for bacteria is on *Escherichia coli*, enterobacteriales, mycobacteria, while emphasis on viral diseases is on HIV, HCV, HPV, Ebola, Zika and SARS-CoV-2.

In the last few years, lot of efforts have been put on SARS-CoV-2 because of the urgent threat associated with this pandemic.

The unit is at the interface between basic and clinical research, with a multidisciplinary approach from basic microbiology and genetics, to ecology, epidemiology, evolution and adaptation, including biostatistical modelling and clinical investigation.

Some of the sub-themes that are prominent in the unit are the control and transmission of antimicrobial resistance.

The outcome of the research performed in IAME is highly relevant in terms of decision-making process for prevention, control and care of the above-named infectious diseases.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

IAME was created in 2014 upon assembly of groups working on infectious diseases on the Université Paris Cité/Bichat Medical School campus.

The unit is hosted in the UFR of Medicine of the Health faculty (laboratories 3rd floor, offices on -1, 2nd and 4th floors) and the connected building is the Bichat Hospital.

IAME now spreads broadly across Paris, and has connection with eight hospitals from Université Paris Cité and Université Sorbonne Paris-Nord. All hospitals are university hospitals, so connecting tightly clinical and basic research and education.

Today most personnel is based at Bichat with some prints at the Bobigny Campus of Université Sorbonne Paris Nord (USPN) (mainly office rooms and since November 2023 a wet-lab).

This set up is likely to change with the new campus planned to be constructed in Saint-Ouen (by 2028), and called the Saint Ouen Grand Paris Nord University Hospital campus.

RESEARCH ENVIRONMENT OF THE UNIT

IAME is mainly based on the Bichat campus, where three other UMR units are also based. These are 'Centre de Recherche sur l'Inflammation' (CRI), Physiopathology and Epidemiology of Respiratory Diseases (PHERE) and Laboratory for Vascular Translational Science (LVTS), and although there is no formal research federation grouping these units, there are multiple scientific connections that result in a good number of co-authored publications (46 from the last mandate).

The unit is structured in four distinct teams called QEM (Evolutionary microbiology), EVRest (Ecology, evolution of resistant bacteria), BIPID (Biostatistical modelling in infectious diseases) and DeSCID (Infectious disease prevention, control and care), with BIPID and DeSCID strongly connected with clinical research.

The unit has two bound service/platform. One called wetlab includes biosafety level 2 and 3 laboratories, sequencing, flow cytometry, microscopy, as well as many small equipment. The other is an IT platform called CATIBioMed, hosted in IAME since 2016, but providing service to all units on the campus. This facility has excellent capacity with 13 calculation clusters, 356 To high-speed storage, 368 CPU and 3.6 To RAM. From 2022, CATIBioMed has been associated with the research federation in multimodal imaging (FRIM-UMS 34).

IAME is bound to clinical research services and notably, the Centre of Clinical Investigation (CIC) and the Methodological and Management Centre (CMG). This connection provides access to clinical investigations, patients' cohorts and clinical trials.

IAME has also collaboration with medical foundation such as IMEA ('Institut de Médecine et d'Épidémiologie Appliquée').

IAME staff members are leading associated National Reference Centres e.g. for *E. coli*, non-tuberculosis mycobacteria (NTM) and HIV.

IAME is affiliated with 3 doctoral schools, ED 562: BioSPC; ED 393: "Épidémiologie et Sciences de 'Information Biomédicale"; ED 146: "Sciences, Technologie, Santé".

IAME manpower in 2022 is 170 individuals with 95 full-time equivalent (FTE). There is a representation of staff from Inserm and Universities, however the majority are hospital-university teaching researchers.

UNIT WORKFORCE: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	29
Maîtres de conférences et assimilés	15
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	5
Praticiens hospitaliers	28
Personnels d'appui à la recherche	19
Sous-total personnels permanents en activité	**98**
Enseignants-chercheurs et chercheurs non permanents et assimilés	21
Personnels d'appui non permanents	17
Post-doctorants	10
Doctorants	34
Sous-total personnels non permanents en activité	**70**
Total personnels	**168**

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: in physical persons at 31/12/2022. Non-tutorship employers are grouped under the heading "others".

Nom de l'employeur	EC	C	PAR
Université Paris Cité	36	0	3
Inserm	0	6	6
Université Sorbonne Paris Nord	5	0	0
Autres	3	1	10
Total personnels	**44**	**7**	**19**

GLOBAL ASSESSMENT

IAME strength relies on a unique interface between academics and clinicians, through the tight interconnection of University hospitals across Paris while the main campus is at Bichat.

IAME has visibility and recognition in the field of infectious diseases and notably some specific pathogens, bacterial or viral, including *E. coli* or HIV, HCV and HPV.

The productivity of the unit in terms of publications is remarkable and outstanding with a total of 2,042 articles published over the reporting period, including 45 highly-cited papers. It spreads across clinical to basic research and with a very significant component in mathematical modelling and implications it has in monitoring evolution and epidemiology. The balance between clinical, translational and basic publications is in favour of the former, with 47.7%, 34.7% and 17.6%, in these respective categories. Yet the quality of a majority of papers is not undermined, with impactful papers published in influential journals, both clinical, such as in the Lancet series, and basic research, either general (e.g. PNAS, Nat. Commun.) or specialized (Nat. Microbiol.). Highlights from the unit could be flagged in two of the main research directions that were conducted over the reporting period, including research on Covid-19 and on *E. coli* genomics. In the former, IAME reported and detailed clinical and virological data of first cases of Covid-19 in Europe; in the latter, IAME described the phylogeny of *E. coli* isolates in bloodstream infection using their unique collection of strains.

The unit has scientists with international and national visibility in the field of microbial infections, and this has been even further highlighted in the Covid-19 crisis during which IAME response has been exemplary by both its contribution to governmental advices and its participation to European efforts. Notably members of the unit were appointed to advise the French Minister of Health during the crisis, and other members contributed to the EU response through programmes such as Discovery (antiviral treatment).

IAME has attracted a very significant level of funding, 16.6 M€, mostly from national (10.6 M€ including ANR) and regional (500 k€) sources. IAME could further assert its leadership by securing additional European grants, as leader and not only partner, such as the ERC Consolidator grant (GENPHEBACT, 1.1 M€) obtained by the leader of QEM team.

Because the unit is at the forefront of clinical research on several infectious diseases, it is key to involve industrial and pharmaceutical partners, which IAME has to some extent (e.g. Roche and Sanofi) as well as reaching to the public to generate even further societal impact. Initiatives, like Microb'UP linking Université Paris Cité and Institut Pasteur, or the educational tool "BacteriaGame" to initiate the grand public to infectious diseases emergence and spread, are excellent. The societal impact can be strengthened through more perennial links with industrial partners and planning further public engagement for infectious diseases comparable to what was done during the Covid-19 crisis.

Training and well-being in the unit are excellent. All personnel from students to PIs and from administrative to technical staff, unanimously recognized the leadership provided by the director over the years. The unit was driven, both from a scientific and human perspective, in a very coherent and inclusive manner. These traits should be capitalized on to attract even more PhD students, potentially international, while the creation of an "École Universitaire de Recherche" on emerging Infectious diseases could be a vector for this. IAME should also capitalise on its visibility and unique set up in Paris to attract further post-doctoral scientists. The current infrastructure, notably on the Bichat campus, appears sufficient for the unit to deliver on its objectives, although office space is limited considering that a large part of the work is not wet lab. Yet for the data handling and storage, IAME has excellent resources through the platform CATIBioMed.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The unit was encouraged to host visits of foreign scientists to strengthen internationalisation and visibility. This has been addressed to some extent although the number, frequency and duration of the visits can still be improved. The unit was also encouraged to organize international meetings, which was done on two occasions, in 2018 with the "Stan Workshop on pharmacokinetics" and in 2019 with the 4th viral dynamic meeting. It is clear overall that the SARS-CoV-2 pandemic has made visits and conferences difficult to arrange post 2019.

On the comment about creating a SAB, the unit has responded very positively. This was done only recently, in 2022 (with the first meeting held in March 2023), and the SAB is composed of renowned international scientist experts in the field of infectious diseases, and includes French (Lyon, Poitiers) as well as international experts from Portugal, The Netherlands, Spain and the UK.

Another recommendation was to engage further with industries, policy makers, and the general public. This has been done and facilitated by the strong response of the unit to the Covid-19 crisis, but should be furthered to cover globally all of the topics conducted in the unit.

Finally, the unit was encouraged to increase the number of PhD students, including international students. The unit was also encouraged to increase the number of students involved in basic research as compared to clinical research. As it stands, only 14% of the PhD students are involved in clinical research while 41% are involved in basics research. The other students (45%) are involved in translational research and that is linked to many Cifre studentships. Of note, there is the securing in 2022 of a EUR ('École Universitaire de Recherche') on emerging infectious diseases, which would increase student attractiveness for IAME.

B - EVALUATION AREAS

Considering the references defined in the unit's evaluation guidelines, the committee ensures that a distinction is made on the outstanding elements for strengths or weaknesses. Each point is documented by observable facts including the elements from the portfolio. The committee assesses if the unit's results are consistent with its activity profile.

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

Assessment on the scientific objectives of the unit

The scientific objectives of the unit are outstanding. Developing strategies to prevent and control infectious diseases is more than timely. This is demonstrated by the recent SARS-CoV-2 pandemic and the rise of antimicrobial resistance to critical level. The coherence of the unit's research program on a subset of selected pathogens is well supported by the expertise of the scientists and clinicians on these diseases. The benefit of the unit's research for human health and well-being and more generally for our society is clear and needed.

Assessment on the unit's resources

The unit's resources are excellent. The research program is well balanced and not overambitious and matches the manpower and infrastructure context, notably through the exceptional links with many Parisian hospitals. This tight connection gives access to patients' cohorts and clinical trials.

Assessment on the functioning of the unit

The functioning of the unit is excellent. The executive team led by the director and the deputy director conveys the laboratory council once every 2 months. The structure of the council is perfectly inclusive of all personnel categories and all four teams in the unit. The management of the director is exemplary at all levels and praised by all staff and institutions involved. The regrouping on one single campus planned in 2028 on the new Saint Ouen campus could be an excellent reorganisation, despite the disruption caused by the move.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The unit's objective to design multidisciplinary approach to understand microbial adaptation, evolution, virulence and antimicrobial resistance is at the interface of basic and clinical research and is ideally supported by expert scientists in tight connection with clinicians and hospitals.

The connectivity with statistical and modelling approaches is extremely good, quite unique to the unit, and provides a lot of capabilities for prevention, control and care of infectious diseases.

The work performed in the unit could be used to guide decision makers in a timely context of emergence of disease or pandemic X. In such a context, the response provided by the unit to the Covid-19 crisis has been really impressive.

Weaknesses and risks linked to the context

The response to the Covid-19 crisis was exemplary and may have tweaked the focus of the unit for a couple of years. Such strong response should be applied to other diseases.

The immersion of the unit within university and hospitals deserves the purpose of the mission to tackle infectious diseases, but the connectivity between the different sites could be stronger. The grouping of IAME on one single site in 2028 is promising but the move and reorganization can be challenging.

There is an obvious shortage in terms of human resources staff as compared to the size of the unit.

The unit members are mostly on the Bichat campus but in connection with many hospitals in Paris as well as on the Bobigny Campus of Université Sorbonne Paris Nord. Some of the personnel working in the various hospitals there is a very limited time to be spent on the Bichat campus.

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

Strengths and possibilities linked to the context

The tight integration of the unit with clinicians and hospitals gives access to patients' cohorts and clinical trials.
External funding of the unit over the reporting period is about eight times more than the core funding from the supporting institutions (16.6 M€ vs 2.2 M€). This funding arises both from industry and public calls (national or international).
The number of staff (total) in IAME has remarkably increased over the years reaching 170 in 2022.

Weaknesses and risks linked to the context

The coherence and share between basic and clinical research could be hard to maintain and may suffer from the low number of researchers from Inserm, compared to hospital-university personnel.
The manpower and resources may seem unevenly distributed across the four teams, notably on the low end for QEM, but that may correspond to this team moving to Institut Cochin since 2022 and therefore for the next mandate.
It seems that the resources in terms of bioinformaticians technical staff is rather limited.

3/ The unit's practices comply with the rules and directives laid down by its supervisory bodies in terms of human resources management, safety, environment, ethical protocols and protection of data and scientific heritage.

Strengths and possibilities linked to the context

The unit has a proper laboratory council in place that addresses all matters regarding unit's operations and infrastructures.
The management of the director is exemplary at all levels and praised by all staff and institutions involved.
The unit is making all efforts to support environment sustainability including shared equipment or train travel when appropriate.
Regarding the gender balance, the Male/Female ratio is 0.76 and is trending towards 1 over the years.
Students and post-docs are provided with dedicated support to organize events and develop their skills and responsibilities at an early career stage.
All ethical approvals are in place and properly controlled including for clinical trials.

Weaknesses and risks linked to the context

Mentoring of PhD students and post-docs for preparing their future career could be developed more formally, together with a record made available of where previous students/post-docs from IAME are now based. Alumni culture could be important as well.
There are only 6 IAME seminars per year, which is on the low end and could be brought to one per month and include profile speakers.
IAME has a huge set of data to store and protect because of the nature of the work at the interface with clinical and industrial partnerships. All necessary measures have to be thoroughly monitored.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness is excellent. IAME has a strong visibility in the field of infectious diseases. One member has co-chaired the prestigious Gordon Research Conference on Molecular mechanisms in evolution (2021). The unit has been very successful in attracting funding, and this has peaked during the Covid-19 pandemic. Funding came largely from national instances. There is as much as 26 ANR grants (5 as PI) and 36 ANRS contracts (7 as leader). IAME has also secured European funds notably through an ERC Consolidator grant. The unit has an excellent training record for PhD students (86) but far less success in attracting post-doctoral researchers (10). The technological capabilities of the unit are excellent, including data handling and storage through the CATIBioMed platform, which is a significant part of IAME research with its involvement in mathematical and statistical modelling.

1/ The unit has an attractive scientific reputation and is part of the European research area.

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

3/ The unit is attractive through its success in competitive calls for projects.

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

Strengths and possibilities linked to the context for the four references above

The visibility of IAME scientists can be seen through the number of invitations to speak at international conferences, about 27 invitations per year, across all teams between 2017 and 2022. The involvement in organizing international conferences is also significant, including co-chairing in 2021 (and automatically chairing in 2023) the prestigious Gordon Research Conference on Molecular mechanisms in evolution.

The unit has been very successful in attracting national funds from ANR (26 grants; 5 as PI, e.g. DREAM for 815 k€), ANRS (37 grants; 7 as PI, e.g. ANRS CO5 VIH-2 'Coordination virologique Cohorte' for 330 k€), PHRC (19 grants as PI for a total amount of 12 M€) and FRM (11 grants; 3 as PI). The unit has also attracted significant European funding, and this has arisen from all four teams in IAME. It includes four contracts as PI (total of 1.5 M€, mostly the ERC Consolidator grant of 1.1 M€) and 15 as collaborators for a total of 4.07 M€. There are some additional non-EU but international funding resources, although limited, that came from NIH, FDA, Bill and Melinda Gates foundation or MRC.

IAME scientists are part of European and worldwide bodies as member or chair, including European Society of Clinical Microbiology and Infectious Diseases (ESCMID), World Health Organisation (WHO), (International Antiviral Society (IAS), European AIDS Clinical Society (EACS).

The unit has trained 86 PhD students and obtained a EUR ('École Universitaire de Recherche' "One Health in Emerging Infectious Diseases" (1H-EID)) in 2022, which should increase attractiveness for students in the infectious diseases field.

The facilities available to IAME to conduct and deliver on its mission are appropriate and include most expected facilities based on the Bichat campus (sequencing, microscopy, animal facilities, safety laboratories etc.) but also a very significant power for data storage and exploitation through CATIBioMed.

Weaknesses and risks linked to the context for the four references above

The main European contracts in which IAME is leader are ERC GENPHENBACT (QEM team, 1.1 M€ ended in 2020); IDEAL_GA (BIPID team, 197 k€ ended 2018); GA 115156-DDMORE (BIPID team, 55 k€, ended 2017); and EU response (DeSCID team, 72 k€, will end in 2025). Except for the ERC Consolidator grant, these contracts are limited in funds and most of them have now ended.

Large part of the funding, including European funds, has been leveraged through the Covid-19 crisis and one should make sure not to lose this funding dynamic post-Covid.

The number of post-docs attracted in the unit as for 2022 is low, 10, and most are not international.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production is outstanding, with publications in top-ranked journals like Lancet Infectious Diseases or Nature Microbiology. The publication synergy between IAME teams is a real asset and the proportion of publications from each team reflects on their available FTEs. There is a bias toward clinical journals, given the nature of IAME work, but the proportion between clinical and basic research publications is overall balanced and reflects the proportion of academics affiliated to hospitals, university or Inserm.

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

2/ The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.

3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.

Strengths and possibilities linked to the context for the three references above

The number of publications for the unit during the reporting period is outstanding with 2,042 papers.

The publications are well spread across the four IAME teams and team members with 4 publications/year/FTE and none of the scientists can be flagged as non-publisher.

The quality of the papers published is high, including 45 highly-cited papers, although many are Covid-related (27) which has naturally attracted more attention during the Covid-19 pandemic. For the period 2020-2022, there has been 338 publications on Covid-19. As such, there is a slight bias towards DeSCID publications (total of 752 with no other IAME co-authors).

Many publications are in clinical journals, some amongst the best ones, but also in high-profile generalist journals. This includes Lancet Infect Dis, Lancet HIV, Nat. Microbiol., Nat. Commun., Science Advances, PNAS, PLoS Genet. or Cell Reports, in which unit's members are in leading position.

There is a clear publication synergy between the IAME teams and 17% of the papers are co-authored by members of at least two teams.

The choice and presentation of the key publications are very informative and show clearly where IAME had an impact over the last six years.

The publication strategy is very inclusive and supports PhD students' first authorship as well as including technical staff members who contributed.

The unit wrote a clear statement about and against predatory journals policies.

Weaknesses and risks linked to the context for the three references above

There is a bias towards publication in clinical journals and that may be at the expenses of high-profile publications in generalist journals, including Nature and Science, even though timing would obviously be longer from discovery/observation to publication.

Some of the teams published fewer papers as compared to others. Notably QEM team has a record of 169, although many with high profile, versus 712, 589 and 993 for EVRest, BIPID and DeSCID teams, respectively. However, this is likely due to the fewer QEM team members.

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 to outstanding. The IAME position at the interface between clinical and basic research is excellent. The unit has tight connections with pharmaceutical industries (e.g. Sanofi, Servier, Astrazeneca, Roche, Merck) and this interaction should result in further applied outcomes including validation and IP on drugs or their applications. The societal engagement of the unit has been outstanding through the Covid-19 pandemic; key members in IAME were called onto various governmental instances. This is an indication that it could be maintained and enlarged to all the other diseases and medical issues (e.g. AMR) that are core to IAME research.

1/ The unit stands out for the quality and the amount of its interactions with the non-academic world.

2/ The unit develops products for the cultural, economic and social world.

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

Strengths and possibilities linked to the context for the three references above

The implication of IAME through the clinical sector has been very strong during the Covid-19 crisis. Notably, contribution to major projects includes the French Covid cohort (4,000 patients), H2020 EU response for coordinated repurposing of drugs against Covid, or Covidicus as a clinical trial with Intensive Care Units (ICUs) patients.

The partnership of the unit with industry provides PhD students and early career scientists a broader perspective in terms of their employability.

Several IAME members have been called on governmental crisis cells during the Covid-19 crisis,, including at the Minister of Health. Others were appointed at key position in national instances like ANRS/MIE (Inserm agency) created in 2021 as part of the Covid response.

Several IAME members were involved in Covid-related public debates in various media, including France 5, RMC or Radio France.

An educational tool "BacteriaGame" has been developed to initiate the grand public to infectious diseases emergence and spread.

Weaknesses and risks linked to the context for the three references above

IAME work is ideally positioned at the interface with medical applications and diagnosis, yet there are only a few patents in the planning, mostly one about RT-PCR for detection of HIV DNA. Since there have been several partnerships with pharmaceutical industries (e.g. Sanofi, Servier, Astrazeneca, Roche or Merck), IAME IP strategy could have been more prominent.

The level of funds from Industry is rather low with only 1.4 M€ out of the total 16.6 M€. This does not necessarily reflect the direct implication of IAME research for the medical and pharmaceutical sectors. Moreover, all contracts with industrial partners have now ended, so there is a need to expand on this.

IAME is heavily involved in bioinformatics modelling and analysis, and although developing a few software (e.g. NONMEM and MONOLIX) there might be room to do far more in this area.

Besides Covid intervention, the presence in the media and through book publications is limited to a couple of books on antibiotics or ancient *E. coli*, as well as the educational tool BacteriaGame.

Reaching out to the public and peers through social media has been launched with the @IAME_Center Twitter account since 2020, but the number of followers is low, 547, for such a large structure and which has such a huge societal impact.

ANALYSIS OF THE UNIT'S TRAJECTORY

The unit trajectory has already been impacted by the departure of the QEM leaders to Institut Cochin and the redistribution of other QEM members in the EVRest team, as for effect in June 2023.

The next term (2025-2029) will further refine the new organisation in three teams and will also see the change in the leadership, the current director being replaced by the current deputy director who will then be replaced in this position by a new PI. There will also be a new secretary general to help the directors.

During the visit, the committee has also learned that a PU-PH from the BIPID team has obtained an "ATIP-Avenir" and as such will start a new team in April 2024 called EPIC and addressing the burden of pneumococcal disease in children. The deputy director for the next mandate has obtained a 'Contrat d'interface pour Hospitaliers', this will also start in April 2024 and that would relieve him from some clinical duties, thus allowing to commit even further to his new managerial role within IAME.

The three teams in the next term will then be EVRest, while DeSCID and BIPID will make few more changes and the new teams will be called PreVIST and MOCLID, respectively.

The mission and objectives of the new version of IAME are well in line with the previous focus with no major modifications. EVRest focus is on *E. coli* related diseases (gut and Urinary Tract Infection (UTI)) with emphasis on AMR genes transmission, transition from commensalism to virulence and drug development, including use of bacteriophages. PreVIST will continue to study major viral diseases, including SARS-CoV-2 and mpox. A theme on perinatality for pregnant women infected by viral pathogens combined with preventive and therapeutic approaches will be implemented. MOCLID will continue the work on infection, prevention and control supported by innovative methodologies in statistics and mathematical modelling.

One major event that would happen by the end of the next term is the move of IAME on a new campus at Saint Ouen (2028) and such planning may cause some organisational disruption although it is a source of excitement and motivation to work in a fully renovated environment.

Overall, the current director leaves a very solid and strong unit, and he has been praised by all members of the unit for his charisma and leadership. Yet it appears clear that the new management team for the next mandate is receiving full back up from the unit's members and their work has already taken effect and shown they have clear vision and leadership as well.

RECOMMENDATIONS TO THE UNIT

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

The connection between basic and clinical research is what makes IAME so successful and unique, and this should be pursued. There is no question that the clinical research is outstanding and on a great trajectory. Yet the balance should not be pushed at the expense of basic research, which is always key to unfold major discoveries. The departure of the QEM team, which was one of the strongest branches of basic research in IAME, should thus be considered and pondered with care. There is a clear path and connectivity, which is kept with IAME and the members of the ex-QEM team (now at Institut Cochin), but this should be assessed on the long term and potential alternatives, or complementary solutions, should be considered. The new direction is confident that with the recruitment of new academics, including an already filled, 'maître de conférences' position, the unit is slightly drifting and adapting to the departure of the QEM team, but is not shifting to a clinical "alone" research.

There is a clear need for bioinformatics support, including to maintain the full exploitation of the CATIBioMed platform, and as such recruitment of engineers with this expertise should considered and is encouraged. It is important also to make sure that the platform, created by the previous and next IAME directors, which is now under the umbrella of the research federation in multimodal imaging (FRIM-UMS 34), keeps being an asset for IAME research.

Among the scientific objectives for the unit, one involves focussing on Tuberculosis research. This is probably legitimate considering the impact of the disease within this area of Paris. Yet it should be considered with care, what will be the questions addressed and how coherent they are regarding the people involved in this sub-project.

It is clear to this committee that the previous director has grown the unit with a superb working and social atmosphere and made IAME a great place to work in. This should be maintained, and it requires full transparency and communications at all levels with the IAME staff and with the supporting Institutions. It is clear that some misunderstandings, such as what are the HR resources available (e.g. support in budgeting grants), or what are the immediate needs in technical support (e.g. bioinformatics) or academic recruitment for IAME, can only benefit from regular and open discussions. These discussions should start immediately including the recruitment of two Inserm candidates that the unit has nurtured and wish to present in 2024 (CSS5, 6 or 7). It is also important to flag that the administrative support for a unit of 175 members is very limited and the unit should engage discussion on whether they could use HR resources that are not necessarily within IAME but bound to the university.

Discussion with the supporting institutions should also be coordinated, with Inserm, Université Sorbonne Paris Nord and Université Paris Cité, but also with AP-HP, to clearly structure the connectivity between all partners and make IAME strategically unavoidable in the infectious diseases field.

Recommendations regarding the Evaluation Area 2: Attractiveness

The unit has a visible and unique interface between basic, clinical and applied research and should capitalize on this to attract students but more particularly post-docs. This could be supported by increased communication towards the public, national and international institutions, and agencies, by using promotional material such as corporate video and social media activity.

The success in funding is clear, although on many of the grants the budget is limited and IAME members are not leading. Considering the excellence of the IAME members, it is always possible to improve leadership, and that should be pushed particularly in the context of prestigious grants, such as European grants and notably ERC. So far only one IAME member has secured an ERC grant but has now left the unit.

IAME visibility could also be improved by presenting a structured description of international partnerships, and by clarifying IAME position within the Parisian landscape on infectious diseases research.

Recommendations regarding Evaluation Area 3: Scientific Production

IAME scientific production has been outstanding, and the unit should maintain this high level and high impact in every domain, from basic to clinic and considering translational outcomes.

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

Due to the very nature of IAME scientific objectives to support human health, there should be a natural incentive to engage with the public and with the industrial/pharmaceutical sector. As for the former communications through various supports, including books, could be further considered, but one shall also acknowledge the very large success of a bacterial game, which has been developed in the unit and which is widely distributed. For the latter many of the current industrial grants have ended, and most of the industrial partnership goes through the award of Cifre studentships. This should be considered cautiously. It appears that recent engagement, in 2023, notably with MSD Avenir, is in place, and this should be capitalised upon.

With respect to the above, IAME should strengthen its desire to develop IP and patents, although the remit of the unit is to benefit society and not necessarily to make profit.

It is also clear that considering the prominent component in clinical research within IAME, further engagements with patients' associations should be carefully considered.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: QEM : Quantitative Evolutionary Microbiology

Mr Olivier Tenaillon & Ms Mathilde Lescat

THEMES OF THE TEAM

The theme of the team concerns the multiple facets of microbial evolution with a particular emphasis on the model species *Escherichia coli*, using a multidisciplinary approach. During the reporting period, the team has adapted its approaches, including the use of higher-throughput data and the development of new methods.

The team focuses its work on *E. coli* as a model species, which is both the most characterized bacterium and a major public health problem due to its virulence and increasing resistance to antibiotics. To do this, the team uses a combination of theoretical studies with high-throughput methods to provide a quantitative understanding of bacterial adaptation, which makes it unique.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team made an effort to take into account the recommendations of the previous report. More specifically, the team:

- has taken the means to attract more national or international PhD students (5) and post-doctoral fellows (3), and has made an effort to recruit scientists and increase the number of HDR holders (2) to supervise research. The increase in visibility of the team is mainly due to the presentation of scientific results at international conferences (6).

- has tried to strengthen scientific animation and create working conditions where the different team members can regularly exchange (one lab meeting every two weeks, one-day team meeting each year). A difficulty is linked to the fact that the team is made up of a significant proportion of hospital-university staff.

- has obtained funding for all the projects conducted by the team despite an overall project that seemed ambitious.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	4
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Praticiens hospitaliers	1
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**9**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	1
Doctorants	1
Sous-total personnels non permanents en activité	**4**
Total personnels	**13**

EVALUATION

Overall assessment of the team

The overall assessment is excellent to outstanding.
The scientific production is excellent to outstanding with publications in high-profile journals (e.g. Nat. Commun., Sci. Adv., PNAS). The attractiveness is outstanding with a strong reputation in the field (e.g. 6 invitations at international conferences, chair at a Gordon Conference). The team has secured significant funding with prestigious grants (2 ERC grants, 1 as PI; FRM team label, 3 ANR grants, 1 as PI). Numerous young investigators (5 PhD students and 3 post-docs) were successfully trained by the team. The contribution to society is very good to excellent. Team members have participated in the development of the educational tool "BacteriaGame" that is used for medical training by the "Société Française de Microbiologie". They were also involved in educational innovation and participated to the foundation of the MICROB'UP "off-wall" Institute.

Strengths and possibilities linked to the context

The scientific project is solid and relevant, taking into account new technologies in the approaches used (e.g. development of high-throughput strategies, genome sequencing, Tn-seq strategy, coupled with validation using *in vivo* models). The association between clinicians and scientists provides an integrated approach to issues concerning bacterial adaptation.

The team produced 169 publications during the reporting period, including significant articles in notorious journals (e.g. 3 in Nat. Commun., 2 in PNAS, and 1 in Sci. Adv.). Among these, 110 are signed in first, last, and/or corresponding author position by a team member, and 114 involve researchers from two teams of the unit. 49 publications are co-signed by a PhD student, including 33 in first author position.

The team co-leader was invited at international conferences (6 in The Netherlands, India, Austria, USA…). The team participated to the organization of scientific events (1 Gordon conference (2017), 2 meetings on Evolutionary System Biology, four meetings of the Evolution Paris Network, and 1 workshop of the European Society Topic Network), and was involved in ANR evaluation panels (CES35).

The team secured significant funding for a total amount of 3 615 k€, from diverse sources at the national and European levels (e.g. 2 ERC grants, 1 as PI; 3 ANR grants, 1 as PI) and received the prestigious FRM team label (2019).

The team has an excellent policy in terms of human resources, scientific leadership and vision in terms of training and recruitment. Five members defended their PhD thesis and the team hosted three post-docs over the reporting period. Two former PhD students were recruited as CR Inserm and MCU-PH, and 1 former post-doc was recruited as CR CNRS. Three scientists visited the lab for few weeks or months to learn more about the methods developed by the team.

The team participated to the board of 'Société Française de Microbiologie', particularly in the setting up of meeting sessions and working groups on innovative pedagogies). They co-supervised the Microb'UP "off-wall" Institute.

The team developed the educational tool "BacteriaGame" that is used for training medical students and laboratory staff (800 copies sold). This led to communication actions towards non-specialized audiences (podcast, 'Quotidien du pharmacien').

Weaknesses and risks linked to the context

Although all the projects conducted by the team were funded, the overall project was large, which limits the possibility of focusing on the most important themes. For instance, the SARS-CoV-2 project was probably not necessary, given the core area of expertise of the team, namely the evolution of E. coli.

The major part of the team (including the two co-leaders) has left the unit to join the Cochin Institute, and the other part of the team (5 members) has joined the EVRest team. This new organization has been well anticipated and the ongoing collaborations between both teams mitigate the risk for such an evolution.

Analysis of the team's trajectory

As the team is leaving the unit for the next contract, no analysis of the trajectory was provided.

RECOMMENDATIONS TO THE TEAM

As the team is leaving the unit for the next contract, no recommendations were provided.

Team 2:	EVRest: Ecology, Evolution and Therapeutic of Virulence and Resistance in Bacteria
Name of the supervisors:	Mr Erick Denamur & Mr Etienne Ruppé

THEMES OF THE TEAM

The research activities are mainly focused on Escherichia coli with a first axis dealing with the emergence of virulence and antibiotic resistance in the frame of the One Health concept. A wide variety of isolates (pathogenic and commensal strains from humans, animals and environment) is analysed to study the adaptation of E. coli to various niches and the transition from commensalism to pathogenicity. A second axis deals with the development of new therapeutic approaches, and the adaptation of old approaches. Besides the activity on E. coli, another theme deals with the epidemiology of Mycobacterium tuberculosis.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The main recommendations of the previous report were the following.

1) To publish in high impact generalist journals (rather than specialist journals). Thanks to large cohorts/collections analysed in collaboration with partners, going from epidemiology to molecular mechanisms, the team has published 34 articles in notorious journals including The Lancet, Lancet Respiratory Medicine, Lancet Infectious Diseases, Lancet Microbe, Lancet Child and Adolescent Health, Nature Microbiology.

2) To recruit more students with a scientific rather than a medical background. The team increased the number of non-medical students by training three PhD and six master students. Finally, several PhD and Master fellowships were supported by the 'Année Recherche', FRM and Erasmus program.

3) To develop some high-risk / high-gain projects. The team obtained grants for ambitious projects such as ANORUTI (Priority Plan on AMR), EFAR (Priority Plan on AMR, Junior Chair) and BLA-IMPACT (ANR grant as a PI). The team is also strongly involved in the ERC EVE project, other projects funded in the Priority Plan on AMR (DYASPEO, DREAM, NASPEC, NAIL'R) and projects EMBARK (JPIAMR) and NETESE (JPIAMR grant as a PI). The team has also expanded the scope of its research (i.e. new topic on antibiotic tolerance).

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	11
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Praticiens hospitaliers	11
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	**29**
Enseignants-chercheurs et chercheurs non permanents et assimilés	7
Personnels d'appui non permanents	5
Post-doctorants	2
Doctorants	9
Sous-total personnels non permanents en activité	**20**
Total personnels	**49**

EVALUATION

Overall assessment of the team

The overall assessment is excellent to outstanding.
The research projects conducted by the team are highly relevant and tightly connected to clinical activities. The scientific production is outstanding, with a large publication record including articles in notorious journals (e.g. The Lancet, Lancet Respiratory Medicine, Lancet Infectious Diseases, Lancet Microbe, Lancet Child and Adolescent Health, Nature Microbiology). The attractiveness is excellent to outstanding with numerous national and international communications. The fundraising capacities are high with ANR grants (7, 2 as PI), a bilateral French-German ANR grant (1), JPIAMR grants (3, 1 as PI), AMR French Priority Plan (3, 1 as PI) and several clinical research grants (3 as PI). The team has an excellent network of interactions with other unit's teams and external partners. The contribution to society is very good to excellent (e.g. teaching and national reference activities, book for a general audience).
The committee would like to express its warmest congratulations to the leader of the team, Professor Erick Denamur, for his scientific career and outstanding contribution to the understanding of *E. coli* evolution and adaptation to various lifestyles.

Strengths and possibilities linked to the context

The scientific objectives dealing with *E. coli* and *Mycobacterium* are ambitious and highly relevant given the importance of community and hospital-acquired *E. coli* infections, highest incidence of tuberculosis in Northern Paris, and therapeutical failures caused by antimicrobial resistance. The team has a strong connection with eight AP-HP hospitals. The use of multidisciplinary approaches (i.e. population genetics, evolutionary and ecological studies) represents a fertile environment and makes of EVRest an original team in the French academic landscape.

A large number of articles (711) were published during the reporting period (one third with a leading position). One third was realised in collaboration with other unit's teams. 34 articles were published in notorious journals (e.g. The Lancet, Lancet Respiratory Medicine, Lancet Infectious Diseases, Lancet Microbe, Lancet Child and Adolescent Health, Nature Microbiology). The team also published an invited review in Nature Reviews Microbiology.

The team gave a high number of invited talks (44) at international conferences, mostly by the two PIs. Team members participated to various scientific committees for research evaluation and funding (e.g. 'Fondation pour la Recherche Médicale' [FRM], Hcéres, Inserm CSS) and to the organization of national and international meetings (e.g. International Conference on Clinical Metagenomics [ICCMg], 'Réunion Interdisciplinaire de Chimiothérapie Antiifectieuse' [RICAI], 'Journées Claude Bernard', European Congress on Clinical Microbiology and Infectious Diseases [ECCMID], and Congress of the French Society of Internal Medicine).

The team secured a high funding level, including several grants from ANR (7, 2 as PI), JPIAMR (3, 1 as PI), a bilateral French-German ANR grant (1), AMR French Priority Plan (3, 1 as PI) and several clinical research grants (3 as PI). The team also received funding related to their labelling by FRM (467 k€, 2016-2019) and association with Fribourg University as a European Associated Laboratory on antibiotic-resistance (2017-2020). Finally, several PhD fellowships were supported by the 'Année Recherche', FRM and Erasmus program.

The team has a good staff hosting policy. Parity is good among PIs (8 female and 9 male scientists) and scientific animation is excellent (1 meeting taking place once a week, with team members and external speakers). Several full-time and part-time researchers were recruited (1 CRCN Inserm; 2 associate professors; 1 junior chair professor, 1 civil servant IPEF). Several members were also promoted (1 IE, 3 full professors). A total of 16 students defended their PhD thesis, and 8 are still ongoing.

The team follows the HRS4R"Human Resources Strategy for Researchers". Procedures are in compliance with regulations regarding bio-safety, *in vivo* experiments and clinical trials. Data are well protected and secured, and a data management plan was established. The dedicated infrastructure CATIBioMed hosted in the unit is an asset for the team (i.e. use of computational cluster for genomic and metagenomic analyses).

The team disseminated some of the acquired knowledge to the general public (communication on a mummy's DNA, book entitled "Les antibiotiques : c'est la panique !" (2018), one-week event "La bio au labo" and discovery internships for third-grade students).

Weaknesses and risks linked to the context

A large part of the staff has clinical responsibilities, the number of full-time researchers and post-doctoral fellows (e.g., Marie Sklodowska-Curie fellowships) is low. Departure of QEM team to the Cochin Institute might also weaken some collaborations on population genetics.

Translation of the results from research activities to the development of novel technologies/therapies in collaboration with the industry was limited.

The retirement of the team co-leader in 2024 could be seen as a risk. However, it should be noted that he will continue for 3 years as an Emeritus professor, allowing transfer of his expertise and leadership.

Analysis of the team's trajectory

The team will develop three axes, led by three different pairs of PIs, and aiming at developing knowledge, new methods and new therapies (immunotherapy, vaccines).

Axis 1. Evolution and determinants of virulence and antibiotic resistance.

The analysis of evolutionary processes underlying changes in commensal, pathogenic and multi-drug resistant Enterobacterales will be continued by addressing evolutionary dynamics both *in vitro* and *in vivo* within humans (through longitudinal sampling) or mice. Pathogenic *E. coli* clones will mainly originate from urinary tract infections, neonatal meningitis and bloodstream infections.

The large collections of the team will represent an asset for this work, and new sets of strains will be collected from various cohorts (healthy volunteers, patients, children in the community…). Mechanistic aspects of resistance evolution will be studied in order to understand and predict the emergence of clinical resistance. Complex environments and intestinal microbiota (mini-bioreactor array) will be considered. The evolution of resistance-associated plasmids and associated fitness cost will also be studied, as well as the phylogenetic barriers to transfer of resistance genes.

In addition to Enterobacterales, comparative genomics in Mycobacteria will be performed with a focus on specific forms of tuberculosis (targeting organs other than the respiratory tract), and newly described *M. tuberculosis* lineages or non-tuberculosis mycobacteria.

Axis 2. Determinants of antibiotic response in individual cells and microbial communities.

This axis will include a new topic for the team: the tolerance and persistence mechanisms allowing bacterial survival upon antibiotic exposure. The relationship between antibiotics, chemotherapy, diet, microbiota and infections or resistance will be explored. This will involve Tn-seq single-cells experiments, evolutionary experiments, pharmacokinetics, physiology and *in vivo* models. Various microbiota will be considered (intestinal, vaginal, oropharyngeal, or faecal transplant communities). The impact of microbiota on either the course of infections or the carriage/clearance of multi-drug resistant Enterobacterales will be explored.

Axis 3. Antibiotic repurposing and phage therapy.

The team will use two preclinical models they have developed (peritonitis and UTI) to optimize the pharmacokinetics characteristics of antimicrobials. The efficacy of antibacterial peptides and phages will also be evaluated as innovative therapies. In the case of phages, a new method based on mathematical decision-making algorithm will be developed and tested in the context of pneumonia, in order to identify the most appropriate phages to be used as treatments against *E. coli* infections. The performance of a pharmacometric model developed in the team will be further improved and evaluated using other phage-bacteria pairs. Finally, a software integrating various parameters (such as phage resistance mechanisms and pharmacological parameters) will be developed to facilitate the selection of phages targeting a bacterial strain.

The team possesses all the necessary expertise and networks to achieve this. Many collaborations, linked to funded projects, are planned (e.g. unit's teams, Cochin Institute, Pasteur Institute, Ecole Nationale Supérieure de Paris, University Bourgogne-Franche-Comté, University of Nantes, National Reference Centres, ACTIV association, reference laboratories in Africa).

RECOMMENDATIONS TO THE TEAM

The team should maintain their excellent level of scientific production, fundraising and network of collaborations with unit's teams, national reference centres and external partners. They should also continue their ongoing efforts to promote mechanistic studies. The expansion of the scope of their research (i.e. antibiotic tolerance, impact of microbiota, new treatments as alternatives to antibiotics) is also highly relevant and promising, and should thus be continued.

Attractiveness towards post-doctoral fellows and full-time researchers should be increased to propel specific projects. More team members should seek invitations to give communications; this recommendation includes young researchers and last-year PhD students. More team members should also participate to editorial responsibilities in national/international journals or collections.

Team 3:	BIPID : Biostatistical Modelling, Pharmacometrics and Clinical Investigation in Infectious Diseases
Name of the supervisors:	Mme France Mentré & M. Jérémie Guedj

THEMES OF THE TEAM

The team's research is organized according to four main axes. The first axis focuses on the development of new methodologies in pharmacometrics, in particular for nonlinear mixed-effects models and design optimization. The team makes open-access software available to the scientific community. A second axis focuses on mathematical modelling of viral dynamics and host-pathogen interactions. A third axis focuses on clinical trial methodologies for severe or emerging infections. It also provides methodological support for the design and analysis of clinical trials. The final axis deals with infections during pregnancy and childhood, with a particular focus on HIV and cytomegalovirus infections, and antibiotic prescribing in paediatrics.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has satisfactorily addressed the main recommendations of the previous report, which were the following:

1) to increase the number of HDRs and international post-docs.

Three team members have defended their HDR, which facilitates the supervision of PhD students. Three international post-docs were recruited over the reporting period.

2) to recruit statisticians and engineers to develop software.

The team has recruited an Inserm research engineer to develop PFIM (Population Fisher Information Matrix) software and the R npde package.

3) to ensure proper integration of the new axis 4 (prenatal and paediatric infections).

Axis 4 "infections and anti-infective agents in pregnancy and childhood" has been integrated via co-direction with members involved in other axes. The scientific production in connection with this axis has been of a high standard, both quantitatively and qualitatively.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	5
Maîtres de conférences et assimilés	4
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Praticiens hospitaliers	3
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	**18**
Enseignants-chercheurs et chercheurs non permanents et assimilés	8
Personnels d'appui non permanents	3
Post-doctorants	4
Doctorants	13
Sous-total personnels non permanents en activité	**23**
Total personnels	**41**

EVALUATION

Overall assessment of the team

The overall assessment is outstanding.
The scientific production of the team is outstanding, with methodological and clinical articles published in high-profile journals (e.g. Nat. Commun., PNAS, CPT Pharmacometrics Syst. Pharmacol, Lancet Infect. Dis.). The attractiveness is outstanding with a strong national and international reputation in their field. The team has secured significant funding with international contracts outside Europe (NIH, FDA, Bill & Melinda Gates Foundation as PI), European grants (FP7 and H2020, 2 as PI) and national grants (ANR and ANRS). The team has trained numerous young researchers (5 post-docs and 14 PhD students). The contribution to society is excellent with an active industrial partnership (e.g. Sanofi-Aventis, Institut Roche, AstraZeneca) including five Cifre contracts. Their involvement in the Covid-19 crisis was very strong with notably the contribution to setting up the French cohorts.

Strengths and possibilities linked to the context

The team provides the scientific community with new methods in pharmacometrics, which are implemented in software for wide academic and industrial use. The unit's environment offers numerous opportunities for preclinical and clinical studies, allowing it to be at the cutting edge of clinical research and virological data analysis. The CATIBioMed infrastructure, of which one team co-leader is the scientific manager, provides the team with strong computing, storage and data protection capabilities.

The team has published 587 methodological and clinical articles appearing in high-profile journals in their field (e.g. CPT Pharmacometrics Syst. Pharmacol., PLoS Med., Nat. Commun., PNAS, Lancet Infect Dis., Statistics in Medicine, Statistical Methods in Medical Research). Team members are first, last or corresponding author in around one third of these articles. Around 30% of these articles were published in collaboration with other teams in the unit.

The team enjoys a strong reputation, both nationally and internationally, in academic, institutional and industrial networks. Team members were invited for 43 oral presentations at international pharmacometric (PAGE), biostatistics (ISCB) or clinical (ECCMID) conferences. They are involved in the REACTing (REsearch and ACTion targeting emerging infectious diseases) Methodology Centre, which specializes in methodology for emerging infections. One team co-leader has been awarded an Inserm 2020 research prize.

The team had an average annual budget of 520 k€ over the reporting period. They have been awarded five international contracts outside Europe (NIH, FDA, Bill & Melinda Gates Foundation), all as PI. They participated in nine European consortia (FP7, H2020), two as PI, eleven national consortia (5 ANR grants, 2 ANRS grants).

The team has trained numerous young researchers (5 post-docs and 14 PhD students). The team has recruited an Inserm research engineer to develop software and the R packages.

The team is working with FDA on the methodology of bioequivalence studies and contributes to the drafting of guidelines for obtaining marketing authorization for drugs at international level. The team collaborates with the pharmaceutical industry and has obtained eleven industrial contracts (e.g. Sanofi-Aventis, Institut Roche, AstraZeneca), five Cifre contracts and three service contracts. The availability of software, e.g. PFIM, saemix and npde packages for R, contributes to the dissemination of the methodologies developed. The team analysed data from the Discovery study, a major European academic trial evaluating antivirals in Covid-19.

The team's involvement in the Covid-19 crisis was very strong and exemplary. For instance, several members were involved in setting up the French cohorts during the pandemic. The team has also participated in the popularization and dissemination of scientific knowledge, for example one team member took part in a TV show ('C'est à vous').

Weaknesses and risks linked to the context

The team has no leadership in current European projects, although it leads work packages in these projects (e.g. UNDINE project or Orchestra cohort for Covid).

The fact that the team has no wetlab of its own makes it dependent on collaborations for preclinical studies. Belonging to the unit mitigates this risk, but links need to be actively maintained.

Analysis of the team's trajectory

For the next contract, the BIPID team will become the MOCLID team. Eight permanent academic members will join the team, while four will leave, for a total of 17 permanent academic members. The MOCLID team was initially intended to comprise 5 axes, but the "paediatrics" axis, which was initially part of MOCLID team, will form an independent team (EPIC) following the award of ATIP-Avenir funding by Inserm.

The evolution of the team's first 3 axes is logical and should be a continuation of current work. Axis 1 will continue to develop pharmacometric methods, with a focus on estimating uncertainties, developing joint models and studying genetic biomarkers predictive of drug response.

Axis 2 will strengthen the link between viral dynamics models and epidemiological, pharmacological, bioinformatics and immunological models.

Axis 3, focusing on the methodology of clinical trials in severe and emerging infections, will be carried out on long Covid studies, and the experience acquired with Covid will be extended to other pathogens (e.g. human Monkeypox).

The fourth axis was not part of BIPID team's research activities, it will focus on the prevention and control of infections, particularly nosocomial infections caused by multi-resistant bacteria. This axis is an extension of the first three ones and should fit in well with the topics of MOCLID team. This inclusion will require the implementation of modelling for the analysis, prediction and implementation of new strategies in ICU patients. In particular, host-pathogen and epidemiological models can be coupled to assess hospital transmission dynamics. Extending the models used in the first 3 axes to this axis should not be seen as a critical issue, given the team's expertise.

RECOMMENDATIONS TO THE TEAM

The efforts to train junior staff and recruit top-level scientists should be maintained.

More formalised team meetings on issues related to research and the organization of team life could further increase the involvement of researchers in the team's overall research strategy.

Given the broad range of topics addressed by the team, it is advisable to focus on the main objectives and avoid dispersing oneself by responding to too many requests.

The team's themes are promising, and should offer funding opportunities in the years to come.

Team 4:	DeSCID : Decision Sciences in Infectious Disease Prevention, Control and Care
Name of the supervisor:	Ms Sylvie Deuffic-Burban & Ms Diane Descamps

THEMES OF THE TEAM

The teams DeSCID and STAR merged in 2019. The new team DeSCID aims at evaluating interventions designed for prevention, control and care of infectious diseases. In axis 1, the team studies chronic (molecular diversity and epidemiology of resistance to antiretroviral drugs of HIV-1 and HIV-2; HCV infection; STIs including HPV infection) and emerging viruses. In axis 2, the focus is on healthcare-associated infections and antimicrobial resistance (epidemiology and control of healthcare associated infections in the intensive care unit; epidemiology and control of antimicrobial resistance; modelling the spread of multi-resistant bacteria).

The team addresses basic research topics and translational questions of relevance to physicians, patients and also policy makers.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team DeSCID comprises previous teams STAR and DeSCID. The recommendations of the previous report were the following:

1) The team STAR was recommended to develop a detailed plan for recruitment of more PhD students, including non-medical. Two non-medical PhD students were recruited and the number of researchers with HDR was increased to have the possibility to enlarge the overall number of recruited PhD students.

2) The previous evaluation suggested that both teams should increase the number of non-medical researchers. This recommendation was partially addressed through the recruitment of two non-medical PhD students. However, recruitment of non-medical researchers is difficult in the Paris area.

3) It was recommended that the interactions between the DeSCID and STAR teams should be further developed and that the STAR team should develop more interactions with fundamental scientists. This recommendation has been implemented through the merge of the DeSCID and STAR teams; several additional collaborations were developed with ENS Paris Saclay, CRI (Inserm/CNRS) and Institut Cochin.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	12
Maîtres de conférences et assimilés	4
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Praticiens hospitaliers	13
Personnels d'appui à la recherche	9
Sous-total personnels permanents en activité	**39**
Enseignants-chercheurs et chercheurs non permanents et assimilés	6
Personnels d'appui non permanents	2
Post-doctorants	3
Doctorants	11
Sous-total personnels non permanents en activité	**22**
Total personnels	**61**

EVALUATION

Overall assessment of the team

The overall assessment is outstanding.
With a large number of relevant articles published in high-profile journals (e.g. Lancet, NEJM), the scientific production is outstanding. The attractiveness is outstanding with numerous invitations to international conferences and high fundraising capacities at the national (40 contracts with 11 as PI from e.g. ANR and ANRS) and international (e.g. EU-RESPONSE contract as PI) levels. A large number of young investigators (e.g. 17 PhD students) were successfully trained by the team. The contribution to society is outstanding. The research conducted by the team has an important economic and societal impact (e.g. web-based tool for therapeutic decision-making in antibiotic therapy). The team was actively mobilized during the Covid-19 pandemic and several members were nominated by the French President to be part of French Covid-19 scientific council.

Strengths and possibilities linked to the context

DeSCID work has important economic and societal impact, including the development of an independent web-based tool for therapeutic decision-making in antibiotic therapy, a large observational study showing that on demand PrEP was associated with low HIV incidence (Lancet HIV 2022) and studies on impact of Covid-19 crisis on children mental health.

Both axes published several high-quality articles. Team members were involved in 992 publications (242 in collaboration with other IAME teams), many of them published in high- profile journals (as examples Lancet HIV 2022, 2019; Clin. Infect. Dis. 2018, 2019, 2021; J. Hepatol. 2018; Gut 2021; J. Hepatol. 2023; Lancet Infect. Dis. 2020, 2022; Lancet Respir. Med. 2022; NEJM 2022; Nat. Med. 2022; Crit. Care 2022). Team's members were in prominent position in 21% of the publications. Important publications are highlighted in the portfolio, e.g. the prevalence of HPV, HIV and other STIs reported among MSM in Togo (Clin. Infect. Dis. 2019); presentation of clinical and virological data of first cases of Covid-19 in Europe (Lancet Infect. Dis. 2020); prediction of EBSL-Enterobacterales ventilator-associated pneumonia (Intensive Care Med. 2020). There is a high level of international interactions (MRC Clinical Trials Unit, UCL, UK; AIN Shams University, Cairo, Egypt; 'Université de Lome', Togo).

Team members were invited to 70 international conferences and organized 13 scientific events (e.g. AFRAVIH 2018 and 2022, 1500 participants per year). Several team members participated in journal editorial boards (e.g. PloS One, Vaccines). Members are implicated in institutional commissions (e.g. ANRS MIE sectorial committees 11, 13, 14, 17) and are well represented in national and international committees.

The number and amount of research contracts gained by the team are high. This comprises international contracts including five EU grants for a total of 2.135 M€ and one MRC grant for 30 k€; the team is the PI of the EU-RESPONSE contract that will run until 2025. A total of 40 contracts (11 as main contractor) was obtained from French funding authorities: five from ANR (1.208 M€) 33 from ANRS (2.804 M€) and two from Inserm (67 k€).

Quality of staff host policy is very attractive; an Inserm engineer research (2021) and three teachers-researchers-hospital practitioners (2020, 2021, 2022) were recruited. Several members were promoted to PU-PH and MCU-PH. 17 PhD students graduated during the reporting period and have progressed with their academic/hospital careers; PhD students and post-docs published as first author on their main project. The team hosted several international students, post-docs and scientists (from Tunisia, Chile, Burkina Faso, Gabon, Switzerland and French Guinea).

Team members were mobilized during the Covid-19 pandemic and several nominated by the French President to be part of French Covid-19 scientific council; for this work they received prizes and medals (OPECST-Inserm prize; "Chevalier de la Légion d'Honneur" by the French government).

Team members were involved in various partnerships including COREVIH IDF Nord, COREVIH and ANRS MIE. They participated in public debates, especially during the Covid-19 crisis. In 2021 a patent was granted on new highly sensitive real-time PCR to quantify Group A and Group B HIV-2 DNA.

The team participated in graduate school for "Emerging infectious diseases" led by Université Paris Cité.

Team members gather regularly in scientific meetings involving the whole staff or scientists at different career levels. The team follows HRS4R "Human resources strategy for researchers"; there is a good gender balance among permanent members (40% women and 60% men) and young investigators (48% women and 52% men). Strategies are implemented for Data and IP protection, bio-security and safety and reduction of carbon footprint.

Weaknesses and risks linked to the context

Several of the researchers operating in the team have a clinical background; clinical assignments may hamper the research activity of university-hospital members.

In view of the competitive research areas in which the team is operating, it may be difficult for PhD students to publish two articles during their PhD studies.

The number of HDR is not enough given the number of permanent researchers.

Analysis of the team's trajectory

The team's future work represents a logical continuation of its previously conducted research activities. The topics that will be addressed have the likelihood of generating novel knowledge.

The team will change name to PreVIST: pathogenesis, treatment and prevention strategies of viral infections and sexually transmitted infections. The new name well summarizes the focus of the five axes which will be included:

Axis 1: HIV and STIs including HPV (analyses of defective HIV viruses in reservoir according to the duration of virological suppression of participants in the previous LAMIDOL study; characterization of the evolution of the HIV reservoir composition in a trial of dual long-acting cART; study of a new resistance pathway to integrase inhibitors in HIV-2 infected patients; study of HIV-2 resistance to the new ARV drugs; follow-up studies in the previously established cohort of 3000 PrEP users, also with focus on microbiota; study of markers of evolution of HPV-induced high-grade lesions to anal cancer).

Axis 2: emerging viral diseases and respiratory viruses (use of the French cohort bio-bank established in 2020 and comprising 4000 individuals to identify biological markers, which could be associated with PACS; conduct vaccination studies in individuals recently exposed to mpox virus; assess RSV genetic diversity).

Axis 3: perinatology (distribution of ART through the placenta and its potential accumulation and toxicity; investigation of factors associated with antibiotic exposure during pregnancy).

Axis 4: strategies for access to prevention and treatment of viral infections: decision support (extension of a previous model that evaluated the potential impact of HCV screening and treatment strategies to include HIV exposed and infected children; use of mathematical modelling to evaluate the long-term clinical benefit of achieving HBV cure; simulation of the incidence and outcome of cutaneous infections in cohorts of IDU frequenting HR centre in France; evaluation of the cost-effectiveness of LAI PrEP in MSM; new STI testing strategies in MSM receiving PrEP; assessment of the medico-economic burden of SARS-CoV-2 infections).

Axis 5: poverty/primary care (quantification of precariousness of the PLHIV and integration of a precariousness score; vulnerability studies focusing on immigrant women and inmate populations).

Studies will involve collaborations with national and international research groups.

The trajectory described has the potential to generate high-quality science and training for young investigators. The work of the team will be built on the possibility of obtaining patients' specimens from relevant cohorts already established or in the process to be established. The work will be both basic and translational and gives the opportunity to knowledge important in the clinical settings.

Moments of risk for the future is to gain enough grants to support all important planned projects; not all axes to be part of the future PreVIST team may be funded at the same level.

RECOMMENDATIONS TO THE TEAM

The strong link with the clinic and its opportunities should be maintained, as it has been the driving force behind excellent translational research.

The participation of team members in European projects as PI could be further increased.

In view of the topics studied by the team, it should be possible to attract the interest of pharma companies for collaborative studies and grants.

The recruitment of several post-docs to the team would be important to further consolidate laboratory-based research efforts.

CONDUCT OF THE INTERVIEWS

Dates

Start: 20 December 2023 at 08:30

End: 21 December 2023 at 18:00

Interview conducted: on-site

INTERVIEW SCHEDULE

Day 1 of the interview 20/12/2023

8:45-9:10	**Hcéres committee meeting** *Closed-door meeting*
9:15-9:20	**Hcéres rules and procedures *by M. Mercier-Bonin*** *Public session (all unit members)*
9:20-10:10	**Scientific and administrative presentation of the unit** 30 min presentation (including unit's trajectory) + 20 min discussion *Erick Denamur, France Mentré & Etienne Ruppé* *Public session (all unit members)*
10:15-10:40	**Committee debriefing** *Closed-door meeting*
10:40-11:00	**Coffee break**
(11:00-12:15)	**Scientific presentations by team leaders and members 1/2** 30 min presentation (including team's trajectory) + 10 min discussion *(note: for Team QEM, no trajectory presentation so 20 min presentation + 10 min discussion)* *Public session (all unit members)*
11:00-11:30	**Team QEM** "Quantitative Evolutionary Microbiology" (leaders: Olivier Tenaillon & Mathilde Lescat)
11:35-12:15	**Team EVRest** "Ecology, Evolution and Therapeutic of Virulence and Resistance in Bacteria" (leaders: Erick Denamur & Etienne Ruppé)
12:20-13:30	**Lunch break & committee debriefing** *Closed-door meeting*
(13:35-15:00)	**Scientific presentations by team leaders 2/2** 30 min presentation (including team's trajectory) + 10 min discussion *Public session (all unit members)*
13:35-14:15	**Team BIPID** "Biostatistical Modelling, Pharmacometrics and Clinical Investigation in Infectious Diseases" (leaders: France Mentré & Jérémie Guedj)

14:20-15:00	**Team DeSCID** "Decision Sciences in Infectious Disease Prevention, Control and Care" (leaders: Sylvie Deuffic-Burban & Diane Descamps)
15:05-15:30	**Committee debriefing** *Closed-door meeting*
15:30-16:10	**Visit of the unit**
16:10-16:30	**Coffee break**

Committee splitting in three sub-groups for collective meetings with staff

16:30-17:30	**Meeting with ITAs (in French)** *In the absence of any managing staff (director, team leaders)*
16:30-17:30	**Meeting with researchers** *In the absence of any managing staff (director, team leaders)*
16:30-17:30	**Meeting with post-docs and students** *In the absence of any managing staff (director, team leaders)*
17:30-18:00	**Committee debriefing** *Closed-door meeting*
18:00	**End of the first day**

Day 2 of the interview 21/12/2023

8:30-9:00	**Committee debriefing** *Closed-door meeting*
9:00-09:50	**Meeting with institutions' representatives: Université Paris Cité, Université Sorbonne Paris Nord & Inserm** *Closed-door meeting*
9:50-10:10	**Committee debriefing** *Closed-door meeting*
10:10-11:00	**Meeting with the Director & Deputy Directors of the unit** *Closed-door meeting*
11:00-12:00	**Committee debriefing & Redaction of the final report 1/2** *Closed-door meeting*
12:00-13:00	**Lunch break**
13:00-16:00	**Redaction of the final report 2/2** *Closed-door meeting*
16:00	**End of the interview**

GENERAL OBSERVATIONS OF THE SUPERVISORS

Université Paris Cité

Le Président

Paris, le 19 février 2024

HCERES
2 rue Albert Einstein
75013 Paris

Objet : Rapport d'évaluation de l'unité **DER-PUR250024172 – IAME – Infection, anti-microbien, modélisation, évolution.**

Madame, Monsieur,

L'Université Paris Cité (UPCité) a pris connaissance du rapport d'évaluation de l'Unité de Recherche **IAME – Infection, anti-microbien, modélisation, évolution.**

Ce rapport a été lu avec attention par la direction de l'unité, de la part de laquelle vous trouverez un courrier en annexe signalant des erreurs factuelles, en particulier sur les effectifs qui sont à corriger, par le vice-doyen Recherche et le doyen de la Faculté de Santé d'UPCité, par la vice-présidente Recherche d'UPCité et par moi-même.

Le Doyen de la Faculté de Santé et moi-même souhaitons souligner que l'unité IAME se focalise sur la compréhension, la prévention et le contrôle de certaines maladies infectieuses d'origine virales ou bactériennes, grâce à des approches pluridisciplinaires adossées aux services cliniques et incluant un fort pôle d'analyses biostatistiques. L'unité IAME, soutenue par l'ensemble des tutelles (UPCité, USPN, INSERM) constitue une unité d'excellence dans cette thématique dans le paysage d'UPCité en général, et de la Faculté de Santé en particulier. Accompagnée par les tutelles, cette unité se re-structurera au prochain quinquennat et est destinée à terme à intégrer le futur campus hospitalo-universitaire de Saint-Ouen Grand Paris Nord.

Je vous prie d'agréer, Madame, Monsieur, l'expression de ma considération distinguée.

Édouard Kaminski

Présidence

Référence
Pr/DGDRIVE/2023

Affaire suivie par
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Paris, February 8, 2024

Object: General observations on the HCERES evaluation report of IAME

First, we want to express our deepest gratitude to the members of the Committee for their significant work and thorough examination of the IAME production.

We would like to thank the Committee for the very positive assessment of the unit and the teams. Notably, we are delighted to note that the Committee stressed the originality of the unit with mixing infectious diseases and statistical and modeling approaches, as it strongly supports the very core of IAME since its creation in 2014 and which is an alliance between clinical, translational and fundamental research.

We largely agree with the committee's recommendations that will help us to further improve the unit during the next term. In particular, we fully endorse its opinion on the shortage of supporting staff in human resources and bioinformatics, and this is something that we will discuss with our supporting institutions.

Erick Denamur (current Director)
France Mentré (current deputy Director and proposed Director for the next term)
Etienne Ruppé (proposed deputy Director for the next term)



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