

## EVALUATION REPORT OF THE UNIT

MAVIVH - Morphogenèse et Antigénicité du VIH  
et des Virus des Hépatites

### UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université de Tours

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

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**EVALUATION CAMPAIGN 2022-2023**  
GROUP C

Report published on July, 17 2023



In the name of the expert committee<sup>1</sup> :

Francesca Chiodi, Chairwoman of the committee

For the Hcéres<sup>2</sup> :

Thierry Coulhon, President

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

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

<sup>2</sup> 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

<b>Chairperson:</b>	Ms Francesca Chiodi, Karolinska Institutet, Sweden
	Ms Filomena Conti, Sorbonne Universités (representative of CNU)
	Mr Slim Fourati, Université Paris-Est Créteil Val de Marne (representative of CSS Inserm)
<b>Experts :</b>	Ms Christine Goffinet, Charité - Universitätsmedizin Berlin, Germany
	Ms Jennifer Molle, Inserm, Lyon (supporting personnel)

## HCÉRES REPRESENTATIVE

Ms Birke Bartosch

## CHARACTERISATION OF THE UNIT

- Name: Morphogenèse et Antigénicité du VIH et des Virus des Hépatites
- Acronym: MAVIVH
- Label and number: U1259
- Composition of the executive team: Mr Philippe Roingeard

## SCIENTIFIC PANELS OF THE UNIT

SVE4 Immunité, infection et immunothérapie

## THEMES OF THE UNIT

The research of the unit is multidisciplinary with researchers specialized in virology, biochemistry, cell biology and public health. The unit comprises both pre-clinical researchers and hospital practitioners ensuring a strong link with the hospital and the development of translational medicine. The central research theme of "Infectiology" (Infectious diseases) of this research unit is in line with priorities set by some of the stakeholders (university, hospital, medical school, Inserm). The focus is on basic and translational research concerning intracellular traffic and morphogenesis of HIV-1, Hepatitis B Virus (HBV), Hepatitis C Virus (HCV) and Hepatitis E Virus (HEV), pathogenic viruses that cause chronic infections; more recently, studies on emerging viruses have also been initiated at the unit. The topic of research spans from pathogenesis of viral infections, genomic variability of viruses, viral escape mechanisms to immune responses, resistance to antiviral treatment to development of vaccines based on sub-viral particles. The recent recruitment to the unit of an Inserm researcher director (Fabrizio Mammano) will broaden the scientific interests of the unit to HIV infectious cycle and HIV evolution under immune response constraints.

## HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The MAVIVH unit was created in January 2006, underwent two positive evaluations in 2009 and 2012 before its recreation in 2018. The work of the unit on hepatitis viruses and HIV has national and international recognition. The first HBV vaccine was developed by this team several decades ago. The unit hosted a national reference center for HIV created in 2002 and directed by Francis Barin, member of the unit until 2020. As the diagnosis of new HIV infections remains highly relevant, and the unit has accumulated important knowledge in the field of HIV infection, MAVIVH has been commissioned to run one of the three HIV NRC associated laboratories in France. The unit is located at the Faculty of Medicine, Campus of the University of Tours.

## RESEARCH ENVIRONMENT OF THE UNIT

The unit has strong links with the Federative Research Structure in Infectious Diseases (FED 4225), the National Research Institute on Agronomy, the Regional Thematic Research Network in Infectious Diseases (with universities in Orléans, Angers, Poitiers and Limoges), research in Infectious Diseases at the University of Tours and the university hospital. The Regional Thematic Research Network provides funding for seminars, conferences and workshops in a One Health perspective to which well-renewed scientists are invited; funding for training and scientific cooperation at the international level are also provided by this organization.

The MAVIVH unit is composed by 20 researchers and teacher-researchers (11 with HDR), one university-hospital assistant, 4 post-docs, 6 PhD students, 1 secretary and 1 research technician.

Several of the MAVIVH members are involved in research training by participation in the management of the Master program "Cellular and Molecular Infectiology" and active teaching in different modules of this program. MAVIVH also initiated in 2016 the project of an Erasmus Mundus Joint Master Degree in Infectious diseases and one health which was selected for funding by the EACEA with 2.76 million euros. This project comprises 34 partners world-wide and was renewed in 2020.

MAVIVH has a strong involvement in technical platforms, especially the electron microscopy facility which is headed by one of MAVIVH investigators and plays an essential role for MAVIVH projects on viral morphogenesis. The unit expertise in virology and electron microscopy renders MAVIVH a preferred partner for several universities (including Pasteur Institutes of Paris and Lille) and industrial partners (Texcell, Clean Cell, Sanofi Pasteur, Replicor, BICE SARL, total of 540 k€) in France.

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

<b>Permanent personnel in active employment</b>	
Professors and associate professors	5
Lecturer and associate lecturer	7
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)	8
<b>Subtotal permanent personnel in active employment</b>	<b>22</b>
Non-permanent teacher-researchers, researchers and associates	4
Non-permanent research supporting personnel (PAR)	0
Post-docs	5
PhD Students	6
<b>Subtotal non-permanent personnel</b>	<b>15</b>
<b>Total</b>	<b>37</b>

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

Employer	EC	C	PAR
Université de Tours	12	0	5
Inserm	0	2	3
<b>Total</b>	<b>12</b>	<b>2</b>	<b>8</b>

## UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	653
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	2 390
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	1 567
Own resources obtained from international call for projects (total over 6 years of sums obtained)	0
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.)	547
<b>Total in euros (k€)</b>	<b>5 157</b>

## GLOBAL ASSESSMENT

The overall assessment of the unit is that they have performed at excellent/outstanding level during the reporting period.

The unit has an excellent and well niched focus prioritizing research on intracellular traffic and morphogenesis of HIV-1 and hepatitis viruses HBV, HCV, HEV. In view of the recent SARS-CoV-2 pandemic the unit took the opportunity to devote part of their work on different aspects of SARS CoV-2 virology, structural aspects and epidemiology. The unit has evolved and currently works around excellent technical platforms, especially the electron microscopy facility, which is pivotal for MAVIVH projects on viral morphogenesis; this platform has allowed several collaborations with academic and industrial partners. A BSL-3 laboratory, central to the work of the unit, needs further support to be developed optimally. A SARS-CoV-2 sequencing platform has also been developed.

The research focus of the MAVIVH unit is well embedded in the area of excellence of Tours University, University Hospital and the regional research network in infectious diseases. The activities are sponsored through funding agencies focused on infectious diseases ANRS-MIE and Inserm.

The unit has produced an excellent/outstanding level of peer-reviewed articles (with an average of 24 publications per/year). The majority of members of the units, both established researchers and PhD students, are part of these publications.

The unit successfully attracted funding from national agencies (66 contracts for a total of 5 259 k€ from ANRS, ANR, Region Centre Val de Loire, Ligue contre le Cancer; Future Investments Programmes), and co-coordinates the Erasmus Mundus Joint Master Degree on "Infectious diseases and one health"). The unit has gained many grants at the national level but emphasis should be placed on attracting international research grants.

The organization of the unit is outstanding and transpires a generous attitude in relation to the working conditions of established researchers and PhD students; training on scientific integrity should be mentioned as important for the culture present in this unit. With 14 PhD defences for 11 HDRs, the unit has outstanding teaching activities. MAVIVH collaborated with several companies (MabSilico, ViroCoVax); they have developed a concept of bivalent HBV-HCV vaccine which they are in the process of developing with the US based Celdara Medical. In addition, MAVIVH works actively on commercialization of research and has issued three patents related to their work. The unit has established fee for service contracts with several companies (Texcell, Clean Cell, Sanofi Pasteur, Replicor, BICE Sarl). In collaboration with Santé Publique France, and as an associate National Reference Center for HIV, MAVIVH has developed several tools for surveillance of dynamics of HIV infection, including subtyping serological assays.

The recommendation provided in the previous evaluation campaign 2016-2017 were optimally addressed.

## DETAILED EVALUATION OF THE UNIT

### A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The following recommendations were provided in the previous evaluation which were all addressed by the unit.

- 1) "Productivity in terms of number of papers per year is good, but could be improved." The number of articles has increased from 15/year to 24/year and so has the overall quality.
- 2) "The unit should be more active at the international level, e.g. by looking for more EU funding. The expert committee recommends to continue to recruit (permanent) researchers without major teaching or clinical duties. The unit should take advantage of the recently secured ERASMUS MUNDUS master 2 program to recruit the next generation of talented international PhD students. There could be possibilities to extend their "savoir faire" to other important human pathogens, but on the other hand the focus should be maintained." International collaborations have been strengthened with Ghent University and with the recruitment of a DR Inserm; two international PhD students have been recruited; viral models have been diversified to include emerging and re-emerging viruses.
- 3) "The expert committee recommends to maintain important local, regional and national tasks, but invest in better international exposure: e.g. by acquisition of foreign students and post-docs and the initiation of strategic international collaborations with top HBV-HIV-HCV research groups." The unit has recruited international PhD students (two) and post-docs (two).
- 4) "The expert committee recommends to continue the dynamic participation of students to the life of the unit. Development of clinical devices and vaccines are attractive topics for the future recruitment of students in infectiology research. Links between clinical hospital staff and basic research are to be reinforced. Erasmus mundus formation should help for external recruitments of students. An incentive to do more science activities in English is recommended by the expert committee such that students are better equipped to go for a post-doctoral position in countries other than France and Canada." As the unit has recruited young international collaborators, laboratory meetings are now held in English. The unit has reinforced its connection with the hospital through the tenured recruitment of young hospital practitioners who also operate as teachers and scientists.
- 5) "As the unit members indicated, the total program seems a bit fragmented due to the high number of different subprojects. It is therefore advised, especially for the weaker and riskier parts of the proposal, to introduce early go, no-go decisions to divert resources to other projects with a greater potential for success. It is encouraging to know that the team members are aware of this and will adapt projects when necessary." The unit implemented the suggested "go, no go decision" and too risky or not promising projects were abandoned.

### B - EVALUATION AREAS

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

##### Assessment on the unit's resources

The assessment on the unit's resource is excellent; MAVIVH has a complete, efficient and emerging research activity thanks to a very adapted and dynamic team. This team managed to obtain resources that allow them to finance even emerging projects, such as several projects on SARS CoV-2.

##### Assessment on the scientific objectives of the unit

The assessment on the unit's scientific objectives is excellent. Actually, MAVIVH develops research on HIV and viral hepatitis and new programs on emerging viruses, which are the areas of excellence of the Tours University Hospital, but also in line with Inserm research evolution. Research on bivalent HBV-HCV vaccine candidate could constitute a major advance in public health.

## Assessment on the functioning of the unit

The functioning of the unit is outstanding. Biosafety for the BSL-2, BSL3 laboratories is secured with great vigilance and annual controls by the health services are perfectly respected. The committee was impressed by the outstanding atmosphere reported by all groups of personnel within the unit.

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

### Strengths and possibilities linked to the context

MAVIVH has an important activity in research and student training, and interacts with the authorities, the socio-economic world and the general public. The team will benefit from an additional position and researchers look for additional funds (more than 5 million€ have been obtained). MAVIVH supports, when necessary, the financing of projects lacking funding, particularly if emerging and innovative. In 2020, the unit benefited from completely renovated premises, and has an access to technical platforms (EM, mass spectrometry, proteomics, NGS...) necessary for its research activities. The future change of director is carefully planned, since the present management will continue to be present during the next contract, to ensure a smooth transition.

The unit has links with the Federative Research Structure in Infectious Diseases (FED 4225), the National Research Institute on Agronomy, the Regional Thematic Research Network in Infectious Diseases (with universities in Angers, Poitiers and Limoges), research in Infectious Diseases at the University of Tours and the university hospital. The unit has collaboration with infectious diseases department of the university hospital.

The unit's expertise renders MAVIVH a partner for several universities (including Pasteur Institutes of Paris and Lille) and industrial partners (Texcell, Clean Cell, Sanofi Pasteur) in France.

The research focus of the MAVIVH unit is well embedded in the area of excellence of Tours University, University Hospital and the regional research network in infectious diseases. The activities are sponsored through funding agencies focused on infectious diseases ANRS-MIE and Inserm.

MAVIVH collaborated also with several companies (MabSilico, ViroCoVax, US based Celdara Medical).

### Weaknesses and risks linked to the context

MAVIVH develops multiple missions and risks a lack of staff to support all of them. There is an acute shortage of space in the BSL3 laboratory. In view of the intense activities within the BSL3 larger and better equipment within the BSL3 is needed.

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

### Strengths and possibilities linked to the context

The unit develops research on infectious diseases which is the area of excellence of the university and Tours hospital. The thematic evolution of MAVIVH, which continues with HIV and viral hepatitis research, with new programs focused on emerging viruses, is in line with Inserm research evolution and its funding agency on infectious diseases, the ANRS-MIE.

The research is balanced between fundamental and applied research, particularly in relation to the University Hospital. The applied research aims at improving the diagnosis and follow-up of patients of CHU of Tours, and at national surveillance of HIV infection, via the HIV NRC and Santé Publique France. Research on vaccines, (bivalent HBV-HCV vaccine candidate) could constitute an advance in public health; despite the availability of efficient direct-antiviral agents, this vaccine could further protect against two infectious agents that cause liver disease and cancer worldwide.

### Weaknesses and risks linked to the context

None.



### 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

Biosafety for the BSL-2, BSL3 laboratories is maintained with great vigilance. The entry process in these sensitive rooms is exemplary. The staff is tested once a year for HIV, HBV, HCV. The implementation of annual controls by the occupational health services is perfectly respected.

The unit also has a green lab perspective, for an eco-responsible and ecological approach. This includes raising awareness regarding waste management, recycling and discussion among the staff on the use of their facilities and equipment. The health safety officers are very involved in the proper functioning of the laboratory with a quality health and safety perspective. They train new members upon their arrival by giving them general security instructions.

#### Weaknesses and risks linked to the context

None.

## EVALUATION AREA 2: ATTRACTIVENESS

### Assessment on the attractiveness of the unit

The unit has an excellent level of attractiveness.

### 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 unit has attracted two Inserm staff, including an Inserm research director. The work of the unit is regularly presented at national and international meetings (between 2016-2021 members of MAVIVH were invited to 12 international meetings and 15 national meetings; 43 abstracts were presented in national/international meetings and 40 posters in international meetings), and the unit is involved in organizing international and national meetings (2 reported; as example the "International symposium on infectious diseases and one health. From concept to action in industry). Unit members participate in editorial boards of scientific journals (*PLoS ONE*, *Scientific Reports*, *Frontiers in Microbiology* and *Frontiers in Immunology*), and are well represented in steering committees (ANRS, National University Council, Sidaction, ANR, Carnot Institute). Regarding participation in national committees the unit director is vice-president of the CSS12 "Basic Research on viral hepatitis" of ANRS, president of the National University Council in medical disciplines for Cell Biology and former vice-president of the Tours University. He is a full member of the Inserm CSS5 "Immunology, microbiology, infection" for the period 2022-2026. Additional members of the unit participated in the steering committee Carnot Institute for Animal Health (ICSA), the Experimental Infectiology platform of INRAe, scientific council of Sidaction, AC33 "Medical Virology of hepatitis" of ANRS, ANR committee CE 18 Biomedical innovation, etc. Thus many members of the unit, and not only the director, are involved in participation in national committees.

In terms of international funding, the unit has managed to secure a second funding period for an Erasmus Mundus Joint Master Degree (EMJMD) IDOH ("Infectious diseases and one health"). This Erasmus Mundus Joint Master Degree in Infectious diseases and one health was initiated in 2016 by- and co-coordinated from MAVIVH; the project received 2.76 million euros funding by the EACEA. This project comprises 34 partners world-wide and was renewed in 2020 (3.3 million € / 5 years). Due to the Brexit situation the UK partner University of Edinburgh in Scotland) was replaced by Hannover Medical School.

The members of the unit received prizes from the National Academy of Medicine, the Foundation of France, the National Academy of Pharmacy, and from the ANRS on the topic of HBV entry.

## Weaknesses and risks linked to the context

Besides the Erasmus program, the unit does not participate in international/ European networks.

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

## Strengths and possibilities linked to the context

The unit has elaborated on careful onboarding strategies and members obtain training on scientific integrity. The mentoring and supervision of PhD students seems to be carefully done, as no PhD student dropped out, and all have published at least one paper as first author. Almost all of the PhD students who have defended their thesis over the last contract (14) are continuing in academia. With 11 HDRs within the unit (as of December 2021), student supervision is considered optimal; students can meet their supervisors at any time. Students are encouraged to attend national and international conferences for scientific discussion and networking. The unit increased its efforts to increase the internationality by recruiting four non-French members (two PhD students, two postdocs). Meetings are held in English which is a great advantage to allow everyone to participate to scientific and organizational discussion and to prepare unit members for an international career.

## Weaknesses and risks linked to the context

The percentage of international unit members, particularly at the permanent level, could be improved.

### *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 been very successfully attracting national funding in the context of different calls (ANRS, ANR, Region Centre Val de Loire, Ligue contre le Cancer), and managed to renew the Erasmus Mondus Joint Master Degree (EMJMD) IDOH ("Infectious diseases and one health"). The unit is involved in structures and projects funded by the Future Investments Programmes (PIA).

During the reporting period MAVIVH received a global recurrent core funding of 47 K Euros from Inserm and 40 K from the University of Tours, per year. MAVIVH has in addition received 66 public research contracts (Region CVL, Inserm, Sidaction ANRS, Ligue Cancer, etc.) for a total of 5 259 K Euros. Unit members were leaders on these grants.

## Weaknesses and risks linked to the context

International/ European funding is underrepresented, despite the unit clearly being competitive enough to apply. Based on the size of the unit in terms of number of researchers, there is room for further increase of third party funding acquisition.

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

## Strengths and possibilities linked to the context

The unit is very well equipped in terms of different technologies and infrastructures. It is heading the IBISA EM platform and is in charge of the Covid-19 sequencing platform that could be further used in the future for molecular surveillance of emerging viruses. It has access to its own BSI3 lab. These infrastructures and equipment of the labs are maintained regularly and machines are renewed where/when necessary. The costly EM maintenance in particular is being financed from private contracts with industry.

## Weaknesses and risks linked to the context

No weaknesses identified.

## EVALUATION AREA 3: SCIENTIFIC PRODUCTION

### Assessment on the scientific production of the unit

Overall, the scientific production of the unit is excellent and has been improved over the period 2016-2021.

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

##### Strengths and possibilities linked to the context

The scientific production has been focused on the expertise of the unit on morphogenesis, viral diversity/adaptation of HIV, and viral hepatitis. The unit has started to collaborate on SARS CoV-2 in several aspects including epidemiological, virological and structural aspects. In this respect, the team took the opportunity to transpose concepts/methodological approaches from the HIV/hepatitis fields to SARS CoV-2.

The number of publications of the unit (n=145; 40% of which correspond to a work fully or mainly performed in the unit) and their quality have increased over the last evaluation period.

Some major outstanding publications of the unit include (i) an establishment of a relevant HCV cell culture model (*Hepatology* 2021) that mimics the native intracellular HCV life cycle (ii) studies on HBV core morphogenesis describing the effect of two families of antiviral compounds on HBV capsid (*Antiviral Res* 2019 ; *Antimicrobial Agents Chemother* 2020, a collaboration with Emory University Center for AIDS Research); (iii) the expertise in viral morphogenesis allowed for describing several feature steps of SARS COV-2 life cycle upon infection (factories consisting of double-membrane vesicles (DMVs); the identification of defective virion assembly pathways at late stages of the cycle)(*Cell Mol Life Sci* 2021).

Overall, the team has produced 56 papers from work fully (or mainly) performed in the unit among which 7 reviews and two editorials (the director of the unit is the main scientist writing review articles or editorials in high level international specialized journals (*Gut, Hepatology, Rev Med Virol*)).

In addition, over a half of the scientific production of the unit takes the form of co-publications with partners of highest national (e.g. Inserm UMR 944, Centre de Recherche en Cancérologie de Lyon U1052; and Pasteur Institut- Virus and Immunity groups) and international level (e.g. FDA, Emory University Center for AIDS Research and Ghent University), some are published in high level journals (examples: *Nature Medicine, NAR, Nat Com*).

##### Weaknesses and risks linked to the context

The multidisciplinary of the team involving researchers, hospital teachers-researchers in virology, biochemistry and cell biology should enable more translational publications linking the research unit and the university hospital. The members of the unit have published in high profile, topic specific journals but it should be possible to generate some publications in journals of general interest.

#### *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

The unit has produced an average of 24 publications per year in high quality peer-reviewed articles.

The majority of researchers, teacher-researchers and the research engineer of the unit with a tenure position have produced at least one international peer-reviewed publication during the contract.

All 14 PhD students who have defended their thesis in the last 6 years have published at least one article as first author in international peer-reviewed journals.

Among the four post-docs at the unit, one has published 3 papers (1 as first author, 1 as last author and 1 as co-author); one additional post-doc has a paper in revision as first author in a peer-reviewed journal.

##### Weaknesses and risks linked to the context

Due to important teaching missions, one permanent researcher has only one publication (3<sup>rd</sup> position) during the contract. Two of the post-docs present at the unit have not yet published.

### *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

The unit has implemented several internal directives to guarantee the traceability and reproducibility of the results published: data are recorded and stored in digital laboratory notebooks, reproducibility of the data is ensured by senior researchers before publication. No predatory journals are used for publication. For human research, an internal ethics committee is consulted (within the university hospital). The preclinical models are conducted according to protocols following European Directive and approved by Agro-Bio Ethics Committee.

#### Weaknesses and risks linked to the context

No real weaknesses were identified.

## EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The unit has an excellent to outstanding interaction with the environment.

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

#### Strengths and possibilities linked to the context

A collaborative project was established with Ghent University to develop a vaccine concept against HEV; experiments were conducted for proof-of-concept in preclinical models which showed promising results; a collaborative patent is currently been prepared.

In collaboration with Santé Publique France, MAVIVH has developed several tools for surveillance of dynamics of HIV infection, including subtyping serological assays. Through the development of an automated surveillance model MAVIVH was able to estimate the incidence of HIV infection in individuals using HIV pre-exposure prophylaxis (PrEP).

A member of the unit during his Inserm fellowship was selected by Inserm for a crowdfunding campaign which resulted in collection of funds (12.000 euros) to support research on HBV treatment failures and the publication of two articles in Antiviral Research.

#### Weaknesses and risks linked to the context

No real weaknesses were identified. However, considering the specialized knowledge of MAVIVH in the fields of electron microscopy and virology it should be possible to develop collaborations with several industrial partners, for example in the field of antivirals. These potential activities could also include PhD grants in collaboration with industry.

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

#### Strengths and possibilities linked to the context

MAVIVH collaborates with the company MabSilico to develop highly efficient anti-SARS-CoV-2 neutralizing antibodies with the help of artificial intelligence.

The unit has also developed a novel concept of bivalent HBV-HCV vaccine and the start-up company ViroCoVax was created around this concept for fundraising aimed at production of GMP vaccine particles. Although this start-up company did not manage to raise funds, the HBV-HCV vaccine concept has attracted interest from the US based company Celdara Medical. Celdara Medical is specialized in investment in early-stage academic innovations and is actively working in the US to attract NIH funds to further develop the HBV-HCV vaccine and to elaborate an investigational New Drug application for the FDA. This will possibly lead to a Phase I trial of the vaccine in healthy volunteers.

The patent "new immunogenic compositions and their use in the preparation of hepatitis C vaccines" was published in 2020 by MAVIVH following a patent filed in 2009 on the same topic.

An additional three patents were published in 2020 and 2021 by the future unit director recently recruited to MAVIVH.

During the reporting period the unit received 540 K Euros from industrial contracts (Texcell, CleanCells, Sanofi Pasteur, BICE SARL, Replicor) including fee for service EM analyses (Texcell, clean Cell, Sanofi Pasteur), analysis of antiviral molecules on HBV morphogenesis (Replicor) or analysis of UV inactivation of SARS-CoV-2 (BICE SARL).

#### Weaknesses and risks linked to the context

None

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

#### Strengths and possibilities linked to the context

MAVIVH has the tradition of participating in the Science Festival for the diffusion of scientific knowledge to the general public. Spread of scientific culture is also ensured through workshops and radio programs; a total of 42 actions have been conducted in this context between 2016-2021. The unit has developed a panel exhibition on viruses and vaccines which is regularly used by high schools in the Centre Val de Loire region and other parts of France.

The unit has actively participated in outreach activities through TV programs, radio and videos on viral hepatitis, conferences and newspapers. For instance, the unit also participated in the development of television information programs with AIDES.

The unit has a twitter-account which is regularly used to address the general public and the scientific community. Activities have been conducted by the unit with schoolchildren through visits to the laboratory, one-week stage at MAVIVH; these activities are aimed at introducing the young public to the field of virology.

The unit actively participates in dissemination of knowledge in virology to socio-economic actors through the organization of an annual virology meeting, participation in scientific committee of the *Virologie* journal; MAVIVH also published several reviews in scientific journals edited in French (*Virologie*, *Médecine/Sciences*).

#### Weaknesses and risks linked to the contextt

None.

## C - RECOMMENDATIONS TO THE UNIT

### Recommendations regarding the Evaluation Area 1: Profile, resources and organisation of the unit

The BSL-3 laboratory is central to the unit's activity and for its attractiveness. Accordingly, it should be enlarged and be further equipped for example, to ensure the possibility of advanced imaging.

### Recommendations regarding the Evaluation Area 2: Attractiveness

The unit should continue its work in internationalisation of its research by attracting personnel at all levels including visiting researchers from abroad. The unit should focus on attracting international grants (possibly larger grants), especially from the EU.

### Recommendations regarding Evaluation Area 3: Scientific Production

In view of the very important work that the unit conducts, it should be possible to publish in more prestigious general journals. The unit publications would gain visibility if data are pre-published using preprint services (e.g. medRxiv, bioRxiv).

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

In view of the specific scientific niche of MAVIVH which, in addition to its scientific value is also important for the development of anti-viral therapies, the collaboration with industrial companies could be further developed by recruitment of PhD students working in between MAVIVH and industrial companies. Enhanced visibility should lead to several additional industrial collaborations.

## CONDUCT OF THE INTERVIEWS

### Date

**Start:** 30 January 2023 at 8:30

**End:** 30 January 2023 at 18:00

**Interview conducted: online**

### INTERVIEW SCHEDULE

- 8:30-8:40**      **Hcéres Rules and procedures by B. Bartosch**  
*Public Session (all unit members)*
- 8:40-10:40**      **Administrative and Scientific presentations of the unit**  
Philippe Roingeard, overall presentation of the unit (15' talk + 10' discussion)  
Martine Braibant, HIV diversity (12' + 8' discussion)  
Hugues de Rocquigny, HIV & HBV morphogenesis (12' + 8' discussion)  
Philippe Roingeard, HCV morphogenesis/vaccine (12' + 8' discussion)  
Catherine Gaudy-Graffin, Medical virology/translational research (12' + 8' discussion)  
Fabrizio Mammano, arrival & integration in the unit (8' + 7' discussion)  
*Public Session (all unit members)*
- 10:40-11:00**      **Debriefing committee and break** *(closed door meeting)*
- 11:00-11:20**      **Meeting with ITAs (in French)**  
*In the absence of any managing staff*
- 11:25-11:45**      **Meeting with researchers**  
*In the absence of any managing staff*
- 11:50-12:10**      **Meeting with post-docs and students**  
*In the absence of any managing staff*
- 13:15-13:45**      **Meeting with institution representatives: Inserm/University of Tours**  
*(closed door meeting)*
- 13: 45-14:30**      **Debriefing committee** *(closed door meeting)*
- 14:30-15:00**      **Meeting with the Director and the co-director of the unit** *(closed door meeting)*
- 15:15-18:30**      **Redaction of the final report** *(closed door meeting)*
- 18:30**              **End of the visit**

## GENERAL OBSERVATIONS OF THE SUPERVISORS



**Hcéres**  
**Département d'évaluation de la recherche**

Tours, le 6 juin 2023

**Objet : DER-PUR230023302 - MAVIVH - Morphogénèse et antigénicité du vih et des virus des hépatites.**

Au nom de l'unité de recherche MAVIVH, j'adresse mes sincères remerciements aux membres du comité de visite HCERES pour leur rapport et leurs recommandations.

L'unité de recherche MAVIVH n'a pas d'observations de portée générale à transmettre.

Je vous prie d'agréer l'expression de mes salutations distinguées.

Le Président de l'université de Tours

A.   
Arnaud GIACOMETTI

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