Research evaluation

EVALUATION REPORT OF THE UNIT

OPTeN – Optimisation thérapeutique en neuropsychopharmacologie

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université Paris Cité,
Institut national de la santé et de la recherche médicale – Inserm

EVALUATION CAMPAIGN 2023-2024
GROUP D

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High Council for evaluation of research and hgher education

In the name of the expert committee[1] :

Valérie Sautou, Chairwoman of the committee

For the Hcéres[2] :

Stéphane Le Bouler, acting president

Pursuant to Articles R. 114-15 and R. 114-10 of the French Research Code, evaluation reports drawn up by expert committees are signed by the chairmen of these committees and countersigned by the Chairman of Hcéres.

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

Chairperson:	Ms Valérie Sautou, Université Clermont-Auvergne, Clermont-Ferrand
Experts:	Ms Mélina Fatseas, Université de Bordeaux, Bordeaux Mr Philippe Garrigue, Aix-Marseille université - AMU (representative of Inserm CSS7), Marseille Ms Catherine Le Moine, Université de Bordeaux, Bordeaux Ms Suzanne Lesage, Institut national de la santé et de la recherche médicale - Inserm, Paris Ms Frédérique Liegeois, University College London, Royaume-Uni Ms Cécile Vindis, Institut national de la santé et de la recherche médicale - Inserm, Toulouse

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Ms Marie Josephe Leroy Zamya, ITMO Technologie pour la Santé, Inserm
Mr Richard Ladine, délégation régionale Inserm

CHARACTERISATION OF THE UNIT

- Name: Therapeutic Optimization in Neuropsychopharmacology
- Acronym: OPTeN
- Label and number: UMR_S1144
- Composition of the executive team: Prof. J-L Laplanche, PharmD, PhD

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement
SVE5 Neurosciences et troubles du système nerveux

THEMES OF THE UNIT

The 'Therapeutic Optimisation in Neuropsychopharmacology' (OPTeN) unit (UMR-S1144 Inserm/Université Paris Cité) is composed of three teams and accounts for 95 persons (31/12/2022), including 52 permanent staff (31 researchers and 21 engineers and technicians). A fourth Team will join the OPTeN unit during the next contract. The unit's research main topic is to optimise the therapeutic management (psychotropic drugs) of patients with psychiatric or neurological diseases by predicting their therapeutic response and/or preventing adverse effects and toxicity, using translational research strategy. At the interface between basic research, animal modelling and clinico-genetic research, the OPTeN unit has focused on two transversal common research themes regarding (1) Lithium therapy and (2) understanding the variability in the response to psychostimulants.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The current OPTeN research unit was created as a follow-up of a previous unit (Inserm U26, 1995–2004), called 'Neurokenetics Toxicology' dedicated to clinical toxicology projects. With the integration of permanent researchers working on drug addiction and extension of the former research unit, the new unit was reorganised under INSERM and Université Paris Descartes supervision (UMR_INSERM U705, CNRS 8206, Paris Descartes and Paris Diderot universities, 2004–2014). Since 2014, with the arrival of psychiatrists treating bipolar disorders and permanent researchers and neurologists specialised in neurodegenerative disorders, the INSERM UMR_S 1144 was created under the supervision of INSERM and Paris Descartes & Paris Diderot universities now merged into Université Paris Cité and renewed in 2019 as 'Therapeutic Optimisation in Neuropsychopharmacology' unit.
The unit is located at the Faculty of Pharmacy of Paris (Université Paris Cité) with a 700 m²-surface area for experimental research (molecular, cellular and animal studies). Additional offices and meeting rooms in accordance with clinical activities are also available in various AP-HP university hospitals (Lariboisière, Ferdinand Widal, Saint-Louis, Cochin, Necker, Beaujon) belonging to Université Paris Cité.

RESEARCH ENVIRONMENT OF THE UNIT

The OPTeN unit is well integrated in its academic, hospital and educational ecosystem. It is one of the 9 research units located at the Faculty of Pharmacy during its last contract, some of them; particularly CitCom and UTCBS have developed various collaborations with the three OPTeN teams. This allowed to share common and complementary expertise of chemists, biochemists on drug targets and galenists. The unit has its own on-site platforms with shared equipment, such as animal facility with its platforms of rodent behaviour, cell culture rooms (L1 and L2), cell imaging lab, mass spectrometry platform, radiopharmacological lab, qPCR facility…. Thanks to tight collaborations, the unit also uses outside platforms, such as the platform Claude Kellershon on Saint-Louis Hospital site, or BIOMAPS at the Service Hospitalier Frédéric Joliot (SHFJ) and CEA sites for TEP studies, as well as high throughput sequencing and data analysis at Cochin institute, Imagine, ENS or Paris Brain Institute (ICM).
The OPTeN unit is also a member of the Graduate School 'Drug Development' which aims at training researchers and healthcare professionals in the field of discovery and development. It is also affiliated to the doctoral school 'Médicament, Toxicologie, Chimie, Imageries', and leads two master 2 programs ('Preclinical and Clinical Pharmacology' and 'Modelling in Pharmacokinetics'). The unit also has access to patient cohorts through different networks as well as biological resources. In addition, the OPTeN unit was involved in the creation of AP-HP's Federation of Toxicology (FeTox) regrouping 6 departments at Lariboisière-Fernand Widal Hospital.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	14
Maîtres de conférences et assimilés	16
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnel d'appui à la recherche	21
Sous-total personnels permanents en activité	**52**
Enseignants-chercheurs et chercheurs non permanents et assimilés	6
Personnel d'appui non permanents	2
Post-doctorants	2
Doctorants	33
Sous-total personnels non permanents en activité	**43**
Personnel total	**95**

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

Nom de l'employeur	EC	C	PAR
UNIVERSITÉ PARIS-CITÉ	19	0	12
Inserm	0	0	1
AUTRES	11	1	7
Total personnels	**30**	**1**	**20**

GLOBAL ASSESSMENT

The Unit is recognised for its excellent level of expertise in neuropsychopharmacology through its research work aimed at improving the therapeutic management of patients on psychotropic drugs by predicting the therapeutic response and/or preventing the risk of serious side effects. Examples include the implementation of analytical techniques (HS-HRM and Simoa) to identify biomarkers and understand the mechanisms of toxicity of psychotropic drugs, the identification of epigenetic biomarkers in the response to lithium, the study of the links between microbiota and drug addiction, the development of PET imaging to assess the transporters of the blood-brain barrier, and the development of pharmacological models to modulate this barrier in pathological states; among others. The scientific stakes are important on the health and societal level and the unit fits perfectly into this dynamic of personalised medicine. The unit develops a translational research strategy combining fundamental, preclinical and clinical research within each team and their framework of collaborations. The scientific objectives of the Unit are ambitious but realistic with regard to the excellent expertise on the disciplinary field of the researchers as well as the unit organisation and the exceptional local environment. The scientific production is excellent and the unit is also excellent in raising funds from research funding agencies as well as industrial companies. However European or even international funding remains low compared to national funding. They could be significantly improved in view of the visibility of the unit at the international level. The unit has also promoted its research work by obtaining patents and by increasing its partnership with private companies. Its direct connection with society is excellent to outstanding given the interest of their research directly to patients and the presence of unit members in various media or national medical instances. The unit displays strong national and international visibility, its attractiveness being materialised by an increase in the number of researchers and doctoral students in recent years. The supervision capacity has been notably reinforced by the increase of researchers holding an HDR. The unit has been proactive in its attractiveness policy by attracting new permanent researchers and facilitating the arrival of foreign students. However, the recruitment of post-doctoral fellows still needs to be improved, as well as that of full-time permanent researchers in order to maintain the high level of scientific performance of the unit. The arrival of team 4 is an undeniable opportunity for the unit with the arrival of permanent researchers likely to bring increased attractiveness and visibility internationally.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

In the previous report, recommendations have been made 1) to increase publications in top-ranked international journals and socio-economic interactions; 2) to attract foreign PhD students and postdoctoral fellows, with more supervisors with HDR diploma (French habilitation to direct research), 3) to obtain additional support in order to recruit additional full-time researchers, and 4) to limit the number of research axes and deepen some in order to increase chances to publish in outstanding journals.
As recommended, 1) the Unit has globally increased the number (about 800 during the last contract) and the level of publication both in clinical and preclinical research: increase of publications in the very good journals from 69% in 2017 to 82% in 2022. This has also allowed to develop their socio-economic impact by obtaining an increasing number of financial resources (5 European fundings including an H2020 R-LINK project, 6 ANR including two as coordinators, such as ANR 2021 Crack-Target, IRESP 2021 ADELY), eight patent applications and one declaration of invention, allowing increasing partnership with private companies (10 partnerships and 2 CIFRE PhD and interactions with several SMEs such as Acobiom, Alcym and Monsenso).
2) Nine members obtained their HDR during the period, and the unit hosted several foreign students (8 from Norway, Italy, The Netherlands, India…) but only five French post-docs.
3) If the Unit has attracted new permanent researchers, one critical point remains the lack of full-time permanent researchers (only one CNRS research director during the last contract) in the three teams. However, during the next contract, the Unit will host a new team with four INSERM permanent researchers which is a strong opportunity to develop preclinical research and new team interactions with potential new recruitment.
4) In terms of scientific strategy and in order to limit dispersion in too many projects, the Unit has focused its activities toward two main axes, 1) lithium therapy in mood disorders and 2) variability in the response to psychoactive drugs and vulnerability to addiction. However, due to the COVID pandemics, some members of the unit (mainly Team 2) were at the front line of this topic to perform several single- or multi-centre studies that had a high impact in the medical scientific community (NEJM, Lancet, JAMA, Intensive Care Med, J Infect, …).
Globally the Unit has organised more frequent seminars and steering committees of team leaders to better organise scientific strategy toward promising projects with a very good publication output.
Overall, the Unit has succeeded in improving both the quantity and the quality of the scientific production and socio-economic impact, together with better attractiveness, research supervision and capacity to obtain external research grants. However, the Unit still needs to recruit full-time researchers to develop preclinical research.

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 main research topic of the OPTeN unit is to improve pharmacological treatments of patients with psychiatric and neurodegenerative disorders by developing new tools to identify biomarkers predicting treatment failure or relapse (Team 1), to understand the mechanisms of psychotropic drug toxicity (Team 2) and to predict interindividual variability in drug exposure (Team 3). The scientific objectives from basic science to clinical research (and back) are excellent and ambitious, but realistic regarding the real expertise of the unit staff even if full-time researchers are lacking (1 permanent researcher, 31 researchers with teaching duties, 21 permanent technical assistants), its own excellent funding resources (~5M€ from European, national and private sources, 85% as leader), and its excellent work environment at the Faculty of Pharmacy in which collaboration with several other units provides expertise in chemical synthesis or screening of pharmacophore, galenic or analytical chemistry. In addition, the OPTeN unit is affiliated to the Université Paris Cité (UPC) and, through its linked hospitals, has thus access to patient collecting and care services ((Lariboisière, Ferdinand Widal, Saint-Louis, Cochin, Necker and Beaujon hospitals), and indirectly to patient associations as well; these are major assets for achieving these objectives. The unit has access to on-site platforms with shared equipment for rodent behaviour, cell culture, cell imaging, mass spectrometry, radiopharmacology and qPCR. In addition, OPTeN benefits from outside local platforms for TEP studies or high throughput sequencing and data analysis. All these elements made this unit a reference unit during the COVID pandemics in France.

Assessment on the unit's resources

The OPTeN unit displays all the necessary human and financial resources to conduct its own research. The unit increased the number of permanent staff members from 40 (at 30/06/2017) to 52 (31/12/2022), including 31 tenure researchers, professors and university hospital professors but only one full-time CNRS Researcher and 21 permanent administrative and technical staff. During the last contract, 28 researchers were holding an HDR, showing the capacity of the unit to train a large number of PhD students. A total of 33 PhD students (versus 13 at 30/06/2017) were trained during the evaluated contract period with seventeen theses defended. Only five post-doctoral fellows were hired during this period. In terms of financial resources, the unit has increased an overall budget by 2.5 compared to the previous contract period from 2017 to 2022 for an amount of ~5M€ through various sources of external funding: five European grants, one as coordinator (Horizon 2020 RLiNK); six supported by ANR (2 as coordinators); five IDEX from UPC; and thirteen contracts with industrial/pharmaceutical companies (such as Servier, UCB and SANOFI). Overall the resources are then excellent for the proposed project.

Assessment on the functioning of the unit

The OPTeN unit has an outstanding functioning regarding the human resources management, safety and ethical protocols, environment and data protection. In accordance with the principles of human resource management, the principal investigators of the OPTeN unit have a clear and open policy to value the skills of their team members with respect to gender equity. Training plans are regularly proposed for all staff members. The unit has budgetary policy by dedicating an annual endowment of 200 k€ for common expenses, renewal of equipment, and open calls for internal emerging projects. All people working on animals underwent a mandatory and traceable training program. An officer in charge of preventive measures was elected to prevent risks and handles accidents and to ensure quality control such as welcome procedures for newly hired staff members, procedures for archiving laboratory notebooks, follow-up of laboratory material and standard procedures. Also, a radio-competent supervisor was elected for use, storage and waste of radioactive compounds. The unit is aware of the working conditions, health and security of its staff. The unit has set up a psychosocial risk monitoring committee to prevent from harassment and working outside dedicated works. As a result, no safety or psychological issue involving OPTeN members has been reported during the evaluated contract. The direction committee of the unit and monthly meetings are set up to discuss the organisational, financial, scientific aspects of the unit whereas the Board of the Unit with voluntary members representative of each college per team meets each semester to discuss the organisation chart and functioning of the unit. Of note, there is no lab council of elected members. The unit applies the recommendations of environmental risk prevention by reducing waste and energy consumption. It complies with the protection of scientific assets and computer systems through its supervising administration of INSERM and University.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The unit's overall strategy is to develop innovative technologies and methods to improve the diagnosis, stratification, and treatments of individuals with neurodegenerative and substance disorders. The unit is particularly focusing on predicting interindividual variability in treatment response and on limiting adverse effects. This is a highly relevant strategy, given the recent international trends to develop personalised medicine. The unit examines these scientific questions across various conditions (neurodegenerative, psychiatric, and substance abuse disorders) and across scales, including basic science, animal models and clinic-genetic research with patients. The strategy is ambitious at the society level as these conditions cause an increasing economic cost and burden to health systems worldwide. The unit has established links with patient support groups as well as clinical settings to accelerate the translational perspectives. The unit's strategy sits well with its two supervising bodies, namely Université Paris-Cité and INSERM.
The unit uses a cross-disciplinary approach (e.g. pharmacokinetics) and also develops novel tools (e.g. PET, animal models). There is an outstanding record of innovation across the unit, all teams having developed novel approaches in their field: Team 1 has implemented the Simoa technology and developed the first French MS-HRM assay, both for biomarker identification and to better understand the mechanisms of psychotropic drug toxicity; Team 2 has set up targeted and untargeted metabolomics analyses using chromatography in addition to high-resolution tandem mass spectrometry, an EEG approach of drug-induced encephalopathy and has

validated a murine model and the new concept of connecting microbiota and drug addiction (invention patented); to understand variability in drug exposure, Team 3 has developed physiologically based pharmacokinetics models, PET radiolabeled probes of BBB transporters and the first pharmacophore model; all this work has allowed to file the patent of a possible pharmacological target for modulating the BBB in disease state. To achieve their initiatives, the unit teams have developed scientific collaborations with European groups (e.g. E. Derks, the Netherlands; Vrije University of Brussels).

Weaknesses and risks linked to the context

Despite the efforts made by the unit's Director to focus on two transversal common research themes which are the Lithium therapy and the variability in the response to Psychostimulants, the committee finds a somewhat underlying scattering of some subprojects i.e. during the COVID pandemics, as shown by publications on COVID-19 (10 from Team 1, 80 from teams 2 and 5 from Team 3).

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

One major strength of the OPTeN unit is its outstanding local environment (university and hospital) with varied expertise on fundamental, notably drugs and pharmaceutical sciences, and clinical research through the access of large clinical databases and biobanks (CRBs Cochin, PRB Créteil and Lariboisière). The unit is a multidisciplinary large unit of 95 staff members, including 52 permanent and 43 under contract, dedicated to basic and human sciences. Of these, there were 33 PhD students and five post-doctoral fellows trained during the evaluated period, including three at the end of their contract for the next term. The unit includes 21 engineers/technical staff for 31 tenure clinicians, researchers, professors and associate professors, which was an exceptional ratio to support research activities. The unit has secured funding to expand with a fourth team comprising four new permanent team members to be created in the next contract. It has demonstrated a high capacity to raise funding (total ~*5M* € during the evaluated period, 85% of the contracts as main leader). The external budget of the unit from academic institutions was 1069 k€ in 2022, more than double the amount in 2017. Funding from national calls has increased significantly during the contract (70 k€ in 2017, 161 k€ in 2019 and 727 k€ in 2022), including 6 grants from research ANR projects, including two as leaders (CrackTarget and Alconet). International funding has also increased (93 k€ in 2017 to 186 k€ in 2022, with a total of 715 k€), including a H2020 contract as leader and an ERA-NET project as partner. Funding from industrial collaborations has fluctuated, totalling 1,195 k€ during the evaluated contract from Sanofi, Servier, UCB, MeRLib, Phinc and Vect-Horus. Overall, these data indicate an excellent upward trajectory, with a notable Horizon 2020 grant (Team 1). Each team retains the full control of its own external resources as the unit does not retain a percentage. The yearly endowment from supervising bodies (approximately 200 k€) is spent on common expenses, equipment upgrades, and about 100 k€ is dedicated to an open call aimed to foster inter-team collaboration and innovative ideas. All funding is managed by a lab administrator. The unit benefits from outstanding shared facilities within the Faculty of Pharmacy, including a cell culture laboratory, luminescence and Fluorescence Optical Animal Imagery (UMS25, LIOPA), a mass spectrometry platform and qPCR facility. Outside the Faculty, the unit has access to a PET platform, high-throughput sequencing, bioinformatics and data analysis platforms.

Weaknesses and risks linked to the context

The main weakness in terms of the human resources is the low number of full-time researchers (n=1) versus part-time researchers, such as professors/associate professors/hospital practitioners (n=30); this has not been compensated by post-doctoral positions (n=5) during the evaluated term. However, this weakness will be compensated in the future contract by the inclusion of a fourth team bringing up to 4 new permanent researchers (3 DR INSERM and 1 CR INSERM). Only one international and two national grants as coordinators were obtained for the whole unit during the past term.

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 OPTeN unit complies with the regulation on human resources management with respect to gender equity. In terms of daily life, lab organisation, scientific and financial aspects, the unit has striven to set up monthly or every semester, meetings through the COPIL-U and the Board of the Unit. The Director and the steering committee of the unit made sure that the scientific objectives of each of the three teams are compatible with the premises and equipment. Continued professional training requests by INSERM and University are submitted by a dedicated staff member and evaluated by the unit Director. In terms of Health and safety, the animal

behaviour facility and labs (the radioactivity lab, the L1 and an L2 cell culture labs, and the molecular biology lab) have restricted access. Individuals external to OPTeN can only use lab facilities when accompanied by an authorised staff member and under the Director's approval. A logbook system is in place for monitoring of drug storage and delivery, with management restricted to one dedicated staff member ('drug manager'). The unit is authorised to store and handle ^{14}C and ^{3}H radiolabeled molecules. The unit also elected a 'prevention officer' who assists the unit director with health and safety, risk prevention and accident handling. This officer is also responsible for the DUER document ('document unique d'évaluation des risques professionnels'), updated annually with preventative measures. This officer is also in charge of training for new staff and students, including online training, notebook keeping. Regarding psychosocial risks, a recent survey indicated low or managed risks (92% positive staff responses). The committee also welcomed the initiative to set up a committee dedicated to psychosocial risks. Animal experimentation is managed via a monitored mandatory training system. At the unit level, efforts are made to reduce the carbon footprint by encouraging train travel rather than plane for national events. There is advice to switch off all unused electrical equipment overnight. The unit uses a regulated process for the disposal of chemical and biohazardous waste.
Overall, the committee estimates that the unit's health and safety procedures are appropriate and that there is strong evidence of commitment in reducing psychosocial risks. Regarding sustainability, both INSERM and University guidelines are followed. As a whole, during the specific meetings with all categories of staff, the committee noticed an excellent working atmosphere transpiring from all staff members.

Weaknesses and risks linked to the context

Although the OPTeN unit is mainly located in the Faculty of Pharmacy, additional platforms and premises related to clinical activities are available in different sites of AP-HP hospitals. This geographical scatter may limit a strong interaction and cohesion of the unit, and may alter the supervision of their respective students. There is no formal process to support the career development of junior researchers (PhD students and postdocs), providing for example grant writing guidance or feedback on fellowship applications (e.g. via internal review panels or mentorship scheme). The male/female ratio at senior level is 4:1, with no standalone female team leader. There is no forum where representatives of each staff category can raise issues or suggest changes. During meetings with each category of staff, some members deplored the lack of official laboratory council of elected representatives from the different staff categories.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The OPTeN unit shows outstanding national and excellent international visibility in the field of clinical toxicology and therapeutics, brain barriers and drug transport. Its attractiveness is supported by the constant increase in staff members (61 to 95 between 2027 and 2022), including PhD students (13 vs 33 during the 2 last contracts), and its capacity to raise funds, including at the international level compared to the previous contract (e.g. one European Horizon 2020 grant as coordinator). Its visibility in the private and academic sectors is also outstanding as illustrated by its role during the COVID19 pandemics, its twelve collaborative contracts with pharmaceutical companies (with 4 international partnerships), its 186 invitations to international congresses and participation to the organisation of twelve international congresses or meetings (i.e. every year FHU for both NOR-SUD symposium or French Norway meeting; a symposium of the international collaboration on ADHD and Substance Abuse in 2022), a huge number of the editorial responsibilities and scientific expertise (i.e. European Society of Clinical Microbiology and Infectious Disease, International Group for The Study of Lithium Treated Patients, The International Association of Forensic Toxicologists…), and the winning of various scientific prizes and awards (i.e. Foundation Chatrier prize, Joël Ménard Fondation Alzheimer prize, Prix FACE Fondation Fondamental, Marcel Dassault Prize of Fondation Fondamental).

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

Members of the OPTen unit were regularly invited to give lectures at international and national congresses and meetings in their field of expertise (186 during the previous contract period, i.e. the International Conference on CerebroVascular Biology meeting, Gordon Research Conference). Three PIs of Team 1 have been involved in the organisation of symposia (the International Collaboration on ADHD and Substance Abuse network meeting in 2022, the FHU NOR-SUD network research in substance use disorders symposium, French-Norway meeting of the INTPART International Partnerships for Excellent Education, Research and Innovation); two PIs of team 3 as members of the scientific board of French Society on Brain Barriers annually organise a multinational meeting bringing together English, Belgian and French teams. As members of the scientific committees of national and international societies (i.e. EAPCCT, sTC, MenaTOX, SRLF…), some PIs were involved in the organisation of scientific events and congress programs. The unit members take part in research steering or scientific expertise bodies at European (H2020 proposals, European Society of Clinical Microbiology and Infectious Disease, International Group for The Study of Lithium Treated Patients, Middle East & North Africa Clinical Toxicology Association, the International Association of Forensic Toxicologist) and national level (as support to research policy and administration, i.e. the CNUs, the GRCI idF, the scientific council of the faculty of health, INSERM CSS4 or CSS6/CSS7, and as clinical and pharmaceutical support: the National Academy of Pharmacy, the College of the French Anti-Doping Agency, the GDR 'Appicom', ANSM/INSERM 'Previtox' network and various patient associations – France Alzheimer, Fondation Vaincre Alzheimer, European Dementia with Lewy Bodies consortium, the Lewy body patient association – A2MCL-…).
The reputation of the unit is also emphasised by the nomination in key roles of one member of the unit as the chair of two APHP regulation committees (COMED and COMEDIMS), and at the policy level, one member of Team 1 was appointed as ministerial delegate for mental health and psychiatry at the Ministry of Health in 2019. During the contract period, several PIs obtained academic recognition for the quality of their pedagogic and scientific implication (i.e. PEDR, RIPEC C3). They also hold key positions in editorial boards of internationally recognised journals in the field (e.g. Frontiers in CNS Drug Delivery, Clinical Toxicology, Journal of Affective Disorders, Journal of personalised medicine…). The Unit also provides a strong contribution to the training of future scientists via its teaching involvement (M2 in and masterclass). In addition, the unit members won various scientific prizes and awards (i.e. Foundation Chatrier prize, Joël Ménard Fondation Alzheimer prize, Prix FACE Fondation Fondamental, Marcel Dassault Prize of Fondation Fondamental, Louis Roche Award of the Clinical toxicologist, the Chancellerie des Universités de Paris en Pharmacie Prize…) and several PhD students also received best presentation/poster awards in different meetings (i.e. ISBD, SEISC, GPCO…). A total of 33 PhD students were enrolled during the last contract. The obtaining of 28 HDR diploma (9 newly obtained during the last term) has reinforced the ability of the unit to recruit and attract students. Among these 33 PhD students, seventeen have defended their thesis with published articles relative to their PhD. PhD students and post-doctoral fellows enjoy an environment and good working conditions. They have access to state-of-the-art facilities and skill training. They have the opportunity to develop their teaching skills via 'Moniteur (Mentor)' roles, and to interact with R&D small companies. PhD students and post-docs have the opportunity to present their work through an active local seminar program and through the Faculty of Pharmacy campus. The unit welcomed four invited international professors during the evaluated period.
The unit members have also active partners in international projects (Team 2: EuroDEN; Team 1: European – Dementia with Lewy Bodies (E-DLB) Consortium). The committee welcomed the inter-team collaborations (36 inter-team publications). The OPTeN unit is attractive: a position of CNRS Research Director and in 2023, four full-time tenure INSERM researchers have joined the unit. The unit has demonstrated a large success in competitive calls at the national level (two ANRs as coordinators, four as partners) and at local/regional level, five IDEX from UPC. At the international level, they led one European initiative (H2020 project 'RLiNK', Team 1) and obtained 4 further grants as partners (CURE2DIPG, ERASMUS+ 2019 and 2022, European Joint Program Rare diseases) totalling an amount of 3,782 k€ during the evaluated period. In addition, the clinicians of the unit won several national and international calls for clinical proposals, such as PHRC or IRESP, or research funding from private Foundations or from patient associations. The committee noted the considerable increase in obtaining international funding (93 k€ in 2017 vs 186 k€ in 2022) and in national funding (70 k€ in 2017 vs 729 k€). Industry collaborations are also excellent with twelve research contracts with pharmaceutical and biotechnology companies (10 by Team 3, e.g. Servier, Sanofi, UCB, PHINC and MeRLiB). PhD grants were provided mainly by the doctoral school (n=8) and private contracts (n=9), or international programs (n=3); the remaining students received other various grants (n=14). The valorisation through patent is also outstanding with ten filled during the period. The creation of the AP-HP Federation of toxicology (FeTox, Team 2) and FHU NOR-SUD research network (Team 1, 210 k€ of raised funds) during the past contract demonstrated the outstanding attractiveness of the unit. These networks could provide an excellent opportunity to attract major funding in the future. The OPTeN unit has an excellent research environment with its own or shared platforms for 1) fundamental research (animal facility with its platforms of rodent behaviour, cell culture (L1 and L2), cell imaging lab, mass spectrometry platform, radiopharmacological lab, qPCR facility, bioinformatics…); 2) clinical, preclinical and pharmaceutical tools (analytical toxicology, evaluation of drug entry in the brain by radiolabeled in situ perfusion, evaluation of animal toxicity…). The unit members are highly involved in the scientific and managerial coordination of platforms and facilities, as 1) head of the whole platform, UMS25 and animal facilities, 2) head of PICMO (cellular

and molecular imaging), 3) head of the rodent behaviour facility, 4) head of the radiopharmacy platform, 5) head of the quanterix platform for very sensitive protein quantification and 6) qPCR platform. Three staff members take part in the ethics committee, CEAA 34. A team member has obtained funding to renew equipment such as confocal microscope (200 k€) or a transmission electron microscope (680 k€). In addition to supervision duties, the unit members have developed innovative tools, i.e. PET imaging probes for studying transporters at the BBB, validated in rodents and non-human primates; an innovative combination of enzymatic and magnetic-activated cell sorting to investigate cells composing the neurovascular unit; new data analysis methods in omics. Overall, the unit therefore holds high quality equipment and skills for both fundamental and preclinical research that is highly competitive at the national/international level.

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

The committee did not identify major weaknesses in each specific field since the unit is visible in multiple ways but the committee noted that>50% of participation to meetings and congresses were in France. The unit is aware of some weaknesses mainly to develop the international visibility with students and early career researchers from abroad. In particular, the attractiveness of the unit to postdoctoral positions (only 5 post-docs from France reported during the last term) is insufficient for a unit of this size and reputation. The capacity to obtain European and national funding was insufficient, particularly as coordinators (one out of 5 international grants and two out of 6 ANRs as coordinators during the last evaluated period). The committee noted an imbalance between teams in obtaining international grants. No team obtained the highly competitive ERC grant, for example.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The overall scientific production could be considered as excellent in numbers>800 publications), leadership (40% of the publications as first or last authorship) and quality (66% of the publications in major and renowned journals of large readership) but largely due to the clinical aspects of the research. However the scientific production is unbalanced between the three teams of the unit (371, 353 and 176 publications for teams 1 to 3 respectively), partially explained by the team size.

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

During the evaluation period, the unit has published 838 original papers and 62 reviews with 636 in the scope of the unit. Nearly 66% of the unit scientific productions were published in high-profile journals (including generalist journals such as NEJM, Lancet Respir Med, JAMA), thus attesting of the strong quality and high standard of the unit scientific production. A tutorial to conduct GWAS studies is in the Top 1% most cited publications of the academic field of Psychiatry/Psychology. Two transversal themes defined within the unit have led to the production of 68 publications on lithium and 33 publications on psychostimulants. Inter-team interactions led to 39 co-authored articles. According to the size of the unit and the number of permanent researchers, the scientific production is excellent with an average of 120 publications/year, 10,350 citations were reached during the 2017–2022 period mainly in clinical journals. The scientific production proportionate to the research potential of the unit is excellent but unbalanced among the three teams (Team 1:371, Team 2:353; Team 3:176) due to the difference in the number of permanent members (Team 1:21, Team 2:17, Team 3:13). The unit put in place policies for open-access publications and since 2023 the unit has a HAL identifier (OPTeN: 1004834). The unit made efforts to comply with the need to respect fundamental principles of research integrity (new entrant has to read validate and sign the 'research integrity agreement'), specific meetings (3/year) are organised to inform all new students on best practices to statistical analysis, members of the unit are encouraged to contact the Inserm Office for research integrity. The unit's policy on respect for human and animal life complies with the applicable guidelines: Research Ethics Boards, CNIL and animal ethical authorisations.

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

The number of publications in generalist journals and on the fundamental aspects (cellular and molecular mechanisms, cellular or mouse models) of the physio- and pathological processes studied in the unit remain limited.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The contribution of the unit to society could be considered as excellent to outstanding. This is particularly illustrated by the development of diagnostic tools with clinical applications (10 patents related to biomarker clinical applications, 5 submitted and 5 delivered), multiple interventions in the media (for example 20 interviews per year), yearly interactions/interventions dedicated to lay people or patient associations, and interactions with industrial partners (n=12 such as with Servier or Sanofi; 2 led to CIFRE contracts). Some PIs are clinicians and involved in patient care and also implicated in national instances such as the Comité du Médicament. These contributions are, however, unbalanced between the three teams of the unit.

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 unit has developed several partnerships with actors from the non-academic world: national public health (Santé Public France), pharmaceutical and medical device (Ansm), and vigilance agencies (Anses, and toxicovigilance, pharmacovigilance, and addicto-vigilance). Regarding interactions with the industry, there are two CIFRE thesis grants and ten partnerships with big pharma or biotech companies such as Servier, Sanofi and UCB. The unit has also developed interactions with several SMEs involved in the European H2020 RLiNK (Acobiom, Alcym and Monsenso). During the COVID-19 pandemic, outside the main research topics of the unit, several researchers have set up partnerships with industrial and pharmaceutical companies to find timely solutions for patient management improvement (facilitated oxygen delivery systems, specific interfaces and masks, pronation) and caregivers' security (shields and protective glasses). The Unit has developed several products for the cultural, economic, and social world. A member of the unit is in charge of the French Roadmap for mental health and psychiatry. During the contract, research projects on biomarkers led to the development of patented tests for clinical applications (e.g. 'Method for predicting the response to a bipolar disorder treatment', 'Biomarkers combination of cognitive deficits in alcohol use disorders'). The Unit regularly shares its knowledge with the general public and takes part in debates in society. OPTeN members regularly interact with patients and caregiver associations with bipolar disorder (ARGOS2001), Lewy body disease (A2MCL), SUD (ASUD), psychiatric disorders (Psychodon, UNAFAM), Alzheimer's disease (France Alzheimer). Several team members are involved in the public education and information. They are regularly solicited in Medias (TV, radio, newspapers, internet) in relation to their expertise in pharmacology, in therapeutic strategies in drug dependence, neurodegenerative disorders or mood disorder (average of 20/year interviews to general public media such as 'Le monde', 'Libération', France TV, TF1. The front page of the Unit is updated on a regular basis with the news and events of the team (Prizes, organisation of congresses, main scientific advances and members of the unit relay the main publications on their Twitter or LinkedIn accounts). The publications are updated automatically. During the contract several publications of the team have been highlighted by the Fondation Fondamental, in 2021 members of the Unit participated in two sections of the digital book of the Fondation Fondamental for the general public. Finally, one of the OPTeN PI was nominated as the Director of AP-HP's COMDIMS ('Commission du médicament et des dispositifs médicaux stériles') and COMED (Comité du Médicament). Another PI is a ministerial delegate for mental health and psychiatry at the ministry of solidarity and health.

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

The contribution of research activities to society is unbalanced between the three teams.

ANALYSIS OF THE UNIT'S TRAJECTORY

Initially the unit was focused on neurokenetics toxicology. Since the '90s, the unit has grown and has been enriched with the arrival of many researchers, psychiatrists and neurologists. Their expertise on drug addictions, bipolar disorders and neurodegenerative diseases has led to a better understanding of the variability of vulnerability to drug addiction, and the variability of therapeutic response to psychotropic drugs in psychiatric and neurological disorders. The scientific objectives of the unit have expanded as new researchers arrived while maintaining a common main research topic that is to optimise the therapeutic management of patients with psychiatric or neurological diseases on psychotropic drugs by predicting their therapeutic response and/or preventing adverse effects and toxicity. The unit has been able to federate around two thematics (lithium therapy and understanding the variability in the response to psychostimulants) in order to promote collaborations between researchers from the three teams, to focus the available resources around these promising areas and prevent researchers from dispersing in this very broad field of neuropsychopharmacology.
One of the major assets of the unit is the diversity of the profiles of the researchers and their complementarity, which leads to real translational research. There are very few units at the international level focusing on the response to pharmacological treatments
Co-direction of teams combining an experimental scientist and a physician is very interesting and consistent with this complementarity of fundamental, preclinical and clinical research. The number of permanent researchers has increased and enriched the unit, but special attention must be paid to the insufficient presence of full-time researchers.
Globally, the trajectory of the unit was found feasible given the financial and human resources secured for the future mandate: one new team arriving with 30 new unit members (1 DR Inserm, 2 CR Inserm, 6 PUPH, 2 MCUPH, 3 MCF, 7 ITAS and 9 PH, and with five ANR obtained on its projects. This new team arrival for the future contract, and, inconsequence, the reorganisation of the unit, promise to be a real asset on the scientific level but also in terms of human resources with the arrival of permanent full-time researchers. This will also increase the topics to neurovascular and neuroinflammation, critical subjects in pharmacovigilance.

RECOMMENDATIONS TO THE UNIT

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

The committee strongly recommends that the unit improve its strategy to obtain more external grants (only one international and two national grants as coordinators for the whole unit during the past term) and to extend its visibility with more collaborations inside international networks.
The unit's Director should reinstate the laboratory council with the attendance of elected representatives from the different staff categories. It would also be beneficial to hold their monthly meetings in a hybrid format, with a mix of in-person and remote attendance for the clinicians outside the faculty. This would increase interactions, and give junior staff opportunities (i) to present in-person post COVID and (ii) to network across teams.
Social events, such as outside days and journal clubs (e.g. coffee mornings, lunchtime), would also enhance interactions between individuals who are on different sites. Occasional meetings could be held in English to prepare junior staff for international careers and conference presentations. The management must ensure that cohesion is maintained and/or reinforced within the unit because of the dispersion of the premises over several sites. The experts of the committee did not identify major weaknesses and risks regarding the equipment and then encourage the unit to pursue its efforts in developing new tools and in maintaining high quality equipment in their platforms and training of technical staff in charge of managing the equipment and supporting the users of the platforms.

Recommendations regarding the Evaluation Area 2: Attractiveness

The unit would benefit from a strategy aimed at still increasing the proportion of permanent researchers. The recruitment of foreign PhD students or foreign postdoctoral fellows should be increased, and participation in international teaching exchange networks could be improved, particularly by increasing the unit's participation to international congresses on their two main research collaborative themes. In addition, the committee recommends the unit's Director or PIs to apply for competitive European grants for the recruitment of talented early-career researchers (i.e. Marie-Sklodowska-Curie Actions). In addition, the committee encourages the unit to pursue its efforts for the licensing of its patents and to take all opportunities to participate in the creation of start-ups to exploit their findings. The arrival of team 4 should represent an undeniable advantage on a scientific level. The arrival of full-time researchers in team 4 should make it possible to gain in attractiveness and visibility at international level. A point of vigilance must, however, be given to the fact that this integration radiates throughout the unit with inter-team scientific projects. Following the arrival of team 4, it will also be necessary to pay attention to ensuring that everyone finds their place, that the reorganisation of the premises is beneficial to the members of the different teams and makes it possible to resolve the problems of dispersion on different sites.

Recommendations regarding Evaluation Area 3: Scientific Production

During the visit (oral presentations and discussion with the unit director), the committee acknowledged the translational approaches of the unit and its efforts to focus on two main transversal common research themes (Lithium therapy and the variability in the response to Psychostimulants), leading to the production of 68 publications on Lithium and 33 publications on Psychostimulants and 39 co-authored articles through inter-team interactions. However, the committee thinks that the unit should ensure that its affiliation is correctly referenced within all publications to ensure its visibility, particularly by clinicians. The imbalance in terms of production among some PIs may be prevented in the future by co-directions of students, for example.

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

The committee recommends that the unit facilitate the inclusion of junior staff in public engagement activities, especially given that their research theme of addiction has broad society appeal and impacts young people. 'Fete de la science'/' Semaine du Cerveau » events, school workshops, YouTube video research abstracts, social media posts, and blogs are examples of activities that would upskill junior researchers and increase the visibility of the unit's work.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Biomarkers of Therapeutic response and relapse in neuropsychiatric disorders

Name of the supervisor: Mr. Frank BELLIVIER/Ms Cynthia MARIE-CLAIRE

THEMES OF THE TEAM

The research themes developed by the team are related to the identification of molecular, clinical and neuroimaging biomarkers of relapse vulnerability and treatment response in patients with mood disorders, addictions and neurodegenerative diseases. This team combines clinical and fundamental expertise and is organised in three research groups: mood disorders, substance-use disorders, and neurocognitive disorders. The main scientific orientation is to optimise therapeutics of psychiatric and neurological diseases in the clinical settings through the development of new innovative tools to better predict therapeutic response or improve the pathology monitoring, in a perspective of personalised medicine.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations were to get more publications in top-ranked generalist journals and to develop socio-economic interactions (contact with the industry), to improve efforts to attract foreign PhD students and post-doctoral fellows, to push more teachers researchers to be officially involved in the supervision of PhD students and post-doctoral fellows, particularly in getting the HDR diploma.
The proportion of publications related to clinical research significantly increased in the 25% of top-ranked journals from 69% in 2017 to 82% in 2022 (Psychopharmacology, Neurology, Translational Psychiatry). A tutorial to conduct GWAS studies is in the Top 1% most cited publications of the academic field of Psychiatry/Psychology. The quantity and the quality of the scientific production led to improve the socio-economic interactions (2 patents 'New biomarkers of alcohol use disorders' and 'Method for predicting the response to a bipolar disorder treatment') and promoted collaborations with several SMEs especially in the context of the H2020 R-LINK project (Alcym, Acobiom). A significant number of financial resources have been obtained with a notable Horizon 2020 grant (H2020 R-LINK project; ANR 2021 Crack-Target; IRESP ADELY). As recommended, four teachers researchers defended their HDR, with thereby increased ability to supervise students. The team hosted several foreign students (3 from Norway, 1 from India, 3 from Italy, 1 from The Netherlands, India…) and three post-docs (1 for 12 months only).
It was also asked to pay particular attention to the coherence of the projects within the team and improve scientific animation. As recommended, efforts have been made to maintain scientific coherence within the team. To limit dispersion, research area has been focused on variability in treatment response, vulnerability to addictions and collaborative research has been reinforced by developing intergroup projects (neurocognitive deficits/SUD/MD). Finally, efforts have been made to increase inter-team collaborations (20 collaborative papers) and improve scientific animation through the invitation of external guests.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	6
Maîtres de conférences et assimilés	6
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	8
Sous-total personnels permanents en activité	**21**
Enseignants-chercheurs et chercheurs non permanents et assimilés	3
Personnels d'appui non permanents	2
Post-doctorants	2
Doctorants	11
Sous-total personnels non permanents en activité	**18**
Total personnels	**39**

EVALUATION

Overall assessment of the team

The overall assessment of the team is outstanding as the team succeeded in improving significantly the scientific production (41% of the unit production, 47% of them as leading authors) and has increased financial resources through national (3 ANR, 2 as coordinator) and international (one Horizon 2020 as coordinator) grants (>5M€ during the evaluated period). Research is based on cohorts that constitute a large clinical database and provide important phenotypic information based on biological and clinical markers, critical for more accurate phenotyping of mood and addictive disorders. It is a major issue to model clinical heterogeneity, comorbidity and treatment response in psychiatric disorders. In this framework, the team has shown its ability to coordinate and unify several partnerships, at a local, national and European level.

Strengths and possibilities linked to the context

The team has an outstanding and impressive scientific production (4.6 articles per year per PI). During the evaluation period, the team has published 371 papers, 26 being review articles and 150 with first and/or last authorship by team members. Over 80% of publications are in the 25% of top-ranked peer-reviewed international journals and the team benefits from a high citation index (2802 citations in 2022). Among their main results can be cited as the identification of an epigenetic signature in response to lithium treatment (Marie-Claire et al., Sci Rep 2020), the identification of plasmatic biomarkers of alcohol weaning (patent) and the identification of a marker of synaptic suffering from Alzheimer's disease (Vrillon et al., Alzh Res Ther 2022). Several excellent funded collaborations at the national (coordination of 2 ANR, partner in 1, 4 IRESP grants, 1 FHU), European and international levels (coordination of 2 international grants, leader of 1 H2020) have been developed. It should also be noted that, over the past contract, the team was involved in the creation and the coordination of the first national federative research network dedicated to SUD (substance use disorders), including the major clinical and fundamental research teams of the Ile-de-France Region (210 k€ of raised funds). This initiative reflects the unit's leadership in the field of SUD research as well as the potential to bring together local care and research partners. The affiliation to several university hospitals and care services also constitutes an excellent environment to reinforce the interactions between basic science and clinical research with the development of cohorts and the access to a large clinical database and biobanks. The team also welcomed new lecturers and clinicians (3 new professors or Assistant Professors) during the contract, as well as several international visiting fellows. The team leader is globally recognised for his work at the national and international level (e.g. 38 invitations to international congresses and 23 to national congresses). Indeed many members are 1) members of international and European societies in the field of psychiatric disorders and neuropharmacology (e.g. European College on Neuropsychopharmacology, European Psychiatric Association, International Society of Bipolar Disorders, International Society of Mood Disorders, International Group of Lithium Treated Patients); 2) associated editors or board members in journals in the field of psychiatric and substance use disorders; and 3) recognised experts for national authorities (MILDECA, French Brain Council). Team members have developed strong interactions with patients and caregivers' associations (board members, conferences, patients' association partners of several research projects) and private companies in the European H2020 RLINK (Acobiom, Alcym). Furthermore, during the contract, members of the team were very much involved in the administration of research at the national (CNU, scientific council of the faculty, INSERM) and European level (European Commission) but also the Ministry of Health. As the ministerial delegate for mental health and psychiatry at the 'Ministry of Solidarity and Health', one PI of the team has organised the first national consultation of professionals in mental health and public whose results were presented at the 'Mental health conference' in September 2021. Several team members are also involved in the dissemination of scientific information and therapeutic strategies for a general audience based on general public media (an average of 20 interviews to general public media such as 'Le monde', Libération, France TV per year).

Weaknesses and risks linked to the context

While the scientific production of the team is outstanding, the main weakness is the lack of full – time permanent researchers (only 1 full time CNRS researcher) which may impact student supervision, as the team is mainly constituted from teacher researchers with hospital responsibilities and activities. Despite the attractiveness of the team, only two post-doctoral fellows have been hired during the last contract. The lack of space may limit the recruitment of new researchers, PhD students and post-doctoral fellows. Scientific coherence could be improved given the large scope of the themes from psychiatric to neurodegenerative disorders (Lewy Body/Alzheimer disease, a topic still very exploratory). Finally, the team has no publication in top-ranked generalist journals and the interaction with industrial companies remains still limited (2 patents submitted, in collaboration with 2 SMEs in the context of the H2020 project).

Analysis of the team's trajectory

During the next contract Team 1 will pursue the main research themes focused on the identification of biomarkers to predict the disease course (relapse risk and poor treatment response) in the perspective of more predictive and personalised medicine. The team will consolidate this research 1) in the field of SUD through new collaborations with other FHU to constitute a large and shared biobank; 2) in the field of MD by extending the study on the methylomic signature of lithium response to other mood stabilisers. Translational approach will also be strengthened with the expertise of two new members as well as new collaborations with teams working on animal models. The goal will be to integrate the identified biomarkers into physio-pathological models of neurocognitive disorders. The team will also develop preclinical approaches in the field of SUD with collaborative research projects with team 2 to test new hypotheses including those targeting the microbiota as a vulnerability factor to cocaine use disorder. Another major challenge is the development of new therapeutic approaches to move from predictive biomarkers of treatment response to innovative therapeutic trials in MD and SUD. Furthermore, the exploration of cognitive deficits in SUD and MD is a priority collaborative project from this five-year term for the three research groups.
The team's trajectory is excellent as the translational approach will be reinforced through collaboration with team 2 and new collaborations with teams working with animal models. Furthermore, efforts are made to translate results of previous works into the development of new therapeutic approaches to prevent relapse in MD and SUD. Attention should be paid regarding the scientific coherence of the team, particularly the scientific/experimental models linking neurodegenerative disease and mood/addictive disorders.

RECOMMENDATIONS TO THE TEAM

The team's trajectory is excellent. Caution should be made for the supervision of research students and post-doctoral follows given the lack of full-time researchers in the team. Furthermore, given the health and societal costs of psychiatric, neurodegenerative and substance use disorders and the major issue to optimise treatment management, industrial partnerships should be reinforced to promote the development of new innovative therapeutic tools. Scientific coherence should be further reinforced concerning the themes developed in the team concomitantly with the development of experimental and preclinical approaches. The extension of the themes to neurodegenerative forms (Lewy body diseases) needs to be consolidated before investing too much.

Team 2: Mechanisms of toxicity and therapeutic optimisation of psychotropic drugs

Name of the supervisor: Mr. Bruno MEGARBANE/Ms Nadia BENTURQUIA

THEMES OF THE TEAM

The research themes developed by the team are all related to a better understanding of the mechanisms of toxicity of several psychotropic drugs (baclofen, opioids, psychostimulants, lithium…) in order to optimise their therapeutic use with a translational research approach from the bedside to bench and back. Researchers from this team conduct multidisciplinary preclinical research in animal models and clinical research in order to understand and solve questions regarding toxicity and adverse effects of psychotropic drugs, together with their potential addictive effects.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In the previous report, recommendations have been made 1) to increase the level of publications and of external funding, 2) to attract more foreign PhD students and postdoctoral fellows, with more supervisor with HDR, 3) to recruit full-time researchers, and 4) to prioritise their objectives in order to be competitive and improve the scientific outputs.
The number of papers related to clinical research significantly increased in top-ranked generalist journals (Lancet, JAMA, NEJM), even if this is mainly due to clinical activities during the COVID pandemics (123 articles out of 353 not directly related to the research axes of the team). It should be noted that the recommendation to improve the level of publications, especially for preclinical studies have been followed with four very good papers as senior authors in British Jour. Anaesthesia, Transl. Psychiatry, Jour. Psychopharmacology and Psychopharmacology. Collaborative papers with other OPTEN teams have also significantly increased reflecting the dynamics of the unit.
The team managed to obtain several external and competitive grants (IRESP-INCA, ANR, IDEX, PHRC).
Despite the COVID pandemic which drastically reduced international exchanges for post-docs, the team managed to attract two foreign PhD students through new collaborations.
As recommended, three teacher researchers defended their HDR.
Additionally, the team has increased its socio-economic impact with the registration of a patent for probiotics for treatment of cocaine addiction.
Overall, the team succeeded at improving both the quantity and the quality of the scientific production and socio-economic impact, together with better attractiveness, research supervision and capacity to obtain external research grants. However, the team still need to recruit full-time researchers to develop preclinical research.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	5
Maîtres de conférences et assimilés	6
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	**16**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	12
Sous-total personnels non permanents en activité	**13**
Total personnels	**29**

EVALUATION

Overall assessment of the team

Overall, this is an excellent team that has been successful in increasing its scientific production (353 articles, 5 articles per PI per year), including for preclinical research, and to secure funding (>1M€) at European (EuroDen) and national (ANR, PHRC...) levels. Its interaction with society was outstanding, particularly during the COVID19 pandemic as a recognition of their expertise in the field but also through their involvement in national regulation committees. The team still need to recruit a full-time permanent researcher(s) in order to sustain preclinical projects to fully develop the translational potential output of its research.

Strengths and possibilities linked to the context

The team has an excellent scientific reputation and is nationally and internationally recognised in the fields of clinical toxicology, pharmacology and therapeutics with collaborative studies in Rome, Basel, Brussels and the USA, for example. It has particularly reported the first neurotoxic effects of various drugs (Hanak et al, Bipol Dis 2017; Chartier et al, Tox Sci 2019, Lagard et al, Clin Tox 2018, Vidovar et al, Br J Anesth 2021), reported and adapted a novel opioid (Lagard et al, Pain 2017; Heresmans et al., J Control Release 2022), and also proposed a biostatistics model of the cocaine-induced conditioned place preference in male rats (Atehortua et al, J Psychopharmacol 2022). Many members are 1) board members of the main national and European societies in the field of clinical toxicology and therapeutics (e.g. EAPCCT, SCMC); 2) associated editors or board members in top-ranked journals in critical care medicine, toxicology and pharmacology; and 3) recognised experts for various national authorities in the field of pharmaco-toxicology (ANSM, ANSES, Santé Publique France). Some members are regularly invited to give conferences at international meetings (127 invited conference during the previous contract). The team also welcomed two new members during the contract (1 MCUPH and 1 PH), as well as several international visiting fellows (from Australia, the USA and Belgium). Success in obtaining external funding is excellent: seventeen contracts were led by the team (PHRC, IRESP, PHC, IDEX) and five were obtained as partner (ANR, IDEX …) and the team is a partner in various international projects (e.g. EuroDEN supported by the EMCDDA, PHC-CEDRE). Over the past contract, the production of the team was particularly abundant (with around five articles per year and per PI including medical and preclinical research). Overall, the publications were very good to excellent in different fields, including toxicology, pharmacology, and neuroscience (50% of the publications in 25% of top-ranked peer-reviewed international journals including Lancet, JAMA, NEJM). The production for preclinical studies has been improved with several papers as senior authors in British J. Anaesthesia, Transl. Psychiatry, J. Psychopharmacology and Psychopharmacology. These recent advances in the genetic and environmental risk factors of drug use disorders in appropriate animal models has supported valorisation including an international patent on probiotics for treatment of cocaine addiction. Collaborative papers between teams (n=22) have also significantly increased reflecting the internal dynamic of the unit. Apart from the main research axes of the team, its scientist production has been significantly increased during the COVID epidemic, with 123 papers out of 353, in the fields of clinical medicine, immunology and microbiology (with high citations) as the results of the recognised expertise of this team in these fields. One main achievement of the past contract is the creation of the AP-HP's Federation of Toxicology, which regroups several hospital departments to develop research from the bench to the bedside to optimise therapeutic options in clinical toxicology. Of note is that one team member is now the director of the APHP committee COMEDIMS, which drives drug policy. As a whole, team members have strong interactions with non-academic public health organisms and pharmaceutical companies, so that they are key players in public policy of risk reduction and optimising drug prescription. In parallel many members of the team have a very strong contribution to public dissemination, and this has been particularly the case during the COVID epidemic during which they participated in many debates and interviews, notably in the media (TV, radio, newspapers, web) or in think tanks among others.

Weaknesses and risks linked to the context

If the team has an excellent overall scientific production, there is however strong heterogeneities between team members, including for preclinical papers. The team still lack a full-time permanent researcher(s) to further develop preclinical research and animal models. The lack of space may limit the recruitment of new researchers, PhD students and post-doctoral fellows. Despite their strong commitment to pharmaco-toxicology and addiction, interactions with private companies are still limited. Conference invitations are also mainly limited to two team members both for international and national congresses.

Analysis of the team's trajectory

The team trajectory will mainly follow the research themes developed during the previous contract with the aim to conduct multidisciplinary approaches from basic research in animal models to human therapeutics. Their

preclinical research is devoted to solve questions arising from the clinic about toxicity, adverse effects and vulnerability to addiction of psychotropic drugs.
Their research activity (thanks to the expertise and responsibilities of several team members) is based on strong interactions with poison control centres allowing access to advanced databases and toxicovigilance networks.
Three main themes will be developed:

1- In addition to their classical pharmacokinetic/pharmacodynamic (PK/PD) approaches to study the mechanisms of drug-related neuro-respiratory effects and organ toxicity, tolerance and drug-drug interactions; the team will develop new tools (metabolomic, micro sampling and biological matrices) to investigate the benefit/risk ratio of new opioids and pharmaceutic delivery systems (e.g. hydrogels), and develop therapeutic optimisation (antidotes and drug elimination techniques).
2- The second theme relies on the characterisation of the peripheral and central signatures predicting addiction vulnerability and/or relapse to psychostimulant use. Based on their recent work, the next research direction will be to investigate the role of microbiota environment and gender in response variability to drug use with the aim to model these responses, identify biomarkers and ultimately find translational outputs. This will be developed through collaborations initiated during the past contract with several research units (INSERM U1139, UR 7537 BioSTM, INSERM U996 in Paris-Saclay, and DMU BioGem) and in interaction with team 1.
3- A new project to investigate the benefit/risk profiles of new anticoagulants and antiplatelet drugs will be developed in strong interaction with the newly integrated team 4. The idea here is to develop specific tools for the prevention of ischemic strokes in relation to individual variability (clinical, genetic, therapeutic effects) with a strong translational potential.

The team's trajectory is wide and may appear somewhat too ambitious. However, team members have multiple and complementary skills going from pharmaco/toxicology, cellular biology, genetics, behaviour, and new expertise will be acquired through a new organisation inside the unit and collaborations (EEG biomarkers, microfluidic, high resolution mass spectrometry, …). Their joint efforts from the bench to the bedside (and back) will certainly solve some critical issues regarding the toxicity and adverse effects of many drugs in order to optimise their therapeutic use.

RECOMMENDATIONS TO THE TEAM

Overall, the team's work is very good to excellent. However, a new research theme will also be developed (with the arrival of team 4) which may disperse the workforces. The team still need to recruit and/or attract full-time researchers to be able to successfully pursue its various and ambitious projects. Participation to more generalist scientific meetings (Société des neurosciences, FENS, SFN, EBPS) should be improved and help attract more researchers. Given the high involvement of the team members in teaching and in hospital and managerial activities, special attention should be paid to the organisation and life of the team to be able to correctly manage both research projects and student/postdoc supervision. The lack of permanent technical support may weaken the workforce, especially for preclinical research, and the team should pay special attention to focus on specific research themes. This is critical in order to improve both their scientific output toward top-ranked journals and their funding capacities, especially in the field of neuroscience, and to better develop the translational potential of their research.

Team 3: Blood-Brain Barrier: Pathophysiology and Therapy

Name of the supervisor: Mr. Xavier DECLEVES

THEMES OF THE TEAM

The Team 3 conducts basic research with translational perspectives into the role of the blood-brain barrier (BBB) and its implication in drug neurokinetics under (patho)physiological situations: 1) molecular and functional characterisation of drug influx and efflux transporters at the BBB; 2) modulation of the neurovascular unit (NVU) under physiological and pathological situations; and 3) other tissue barriers and variability in pharmacokinetics/pharmacodynamics (PK/PD) of CNS drugs.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous recommendations included: 1) the need to increase publications in top-ranked generalist journals and needs to develop interactions with cultural, social and health environment; 2) the need to have more teachers researchers officially involved in the supervision of PhD students and postdoctoral fellows (HDR diploma), 3) the requirement to recruit full-time researchers, possibly by selecting post-doctoral fellows with top-level CVs, and to prioritise the objectives due to the small number of full-time researchers, and 4) the need to gain in visibility by increasing its external public funding.
Regarding the scientific production and activities, the team published twelve articles as PI in top-ranked specialised journals in 'Pharmacy and Pharmacology', 'Nuclear Medicine' and 'Brain Barriers' categories, and one original article of collaborative research in a generalist journal (eLife). An effort still has to be made on the side of the interaction with society.
In regard with the small number of full-time researchers, the team better prioritised its scientific objectives around three themes, avoiding dispersion in too many projects and dropping two projects from the previous contract (Aβ amyloid peptide transport at the BBB and LCMSMS-based optimisation of BBB transporters quantification).
To increase their impact for translational studies and maintain their capacity to supervise PhD students and postdocs after the departure in 2020 of two teachers researchers, the team recruited a PU-PH (neurosurgeon) and one of their early-career researchers (MCU-PH radiopharmacists) obtained his HDR during the contract. Three postdocs were recruited during the contract but none of them applied for a full-time researcher position. The team was granted with several significant academic calls: two ANR, one ANSES, one IDEX as PI, and two PhD contracts from the MESRI, perfectly answering to the recommendations of the previous report.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maîtres de conférences et assimilés	4
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	7
Sous-total personnels permanents en activité	**14**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	10
Sous-total personnels non permanents en activité	**12**
Total personnels	**26**

EVALUATION

Overall assessment of the team

Overall, this is an excellent team with an increasing scientific production (3–6 articles per year per PI), patent submission (n=6) and grants [~1M€) at the national level (from academics and industries such as Servier). The team uses innovative methods in imaging and is recognised as one of few labs able to conduct this kind of research. The team still needs a full-time permanent researcher(s) in order to sustain projects and fully develop the translational potential output of its research, and more grants at the international level.

Strengths and possibilities linked to the context

Main contributions of the team during the last contract period included the characterisation of transporters in the BBB (Pharmacol Res 2021, Mol Pharm 2018, Pharmaceutics 2021 and 2022, Front Cell Dev Biol 2020, Mol Pharm 2019), the validation of TEP imaging tracers to analyse these transports (JCBFM 2017, Cells 2020, Molecules 2018) and the characterisation of vascular cells (Sci Rep 2018, Cell Disc 2017). The team is nationally and internationally recognised in the fields of BBB/CNS pharmacokinetics, pharmacology and drug delivery, as many members are board members of national societies in these fields (International Brain Barrier Society, Société d'Etude des interfaces sang-cerveau), associated editors, guest editors or board members of top-ranked journals in pharmacology (Fluids and Barriers of the CNS, Frontiers in CNS Drug Delivery) and recognised experts for various national authorities in the field of pharmaco-toxicology (ANSM/Inserm). The fruitful and historical collaborations with the BIOMAPS unit (CEA Orsay) and with the Unité Claude Kellershohn (UCK, Hôpital Saint-Louis) is one of the major strengths of this team for innovative radiotracers synthesis and in vivo molecular imaging, together with the on-site radiopharmacology lab. Three PIs contributed to oral communications in international meetings (20), notably in the USA, Australia, Italia, China, and Russia. The team also benefited from experiences in laboratories abroad (Germany, Sweden, Australia). Many members of the team were awarded in national (Groupe de Pharmacologie Clinique Oncologique, Société Française de Pharmacie Oncologique, Société d'études des interfaces Sang Cerveau, Ecole doctorale Médicament, Toxicologie, Chimie, Imageries) and international manifestations (International Congress of Psychology, Neuroreceptor Mapping Congress). The team attractiveness is excellent: the team has gained international visibility in the field of Brain Barriers and Drug Transport and attracted foreign researchers (3 invited professors from the USA and Australia), recruited eleven PhD (2 CIFRE, 2 MESRI, 1 China Scholarship Council, 6 private contracts), three postdocs (1 ANR contract, 2 contracts with the pharmaceutical industry), and three new teacher researchers (1 neurosurgeon, 2 assistant professors). Scientific production is outstanding (154 original scientific articles and 18 reviews), with high dynamics of publication especially of <40y.o. researchers (3–6 articles per year per PI). Over 50% of articles produced by the team as first/last/corresponding author positions were in Q1 peer-reviewed international journals, an elevated rate of articles with first/last author positions (42%) were in the 25% top-ranked journals of their discipline, and the team benefited from a high citation index (350 citations/year). It is noteworthy that the team published articles in an excellent variety of top-ranked generalist journals (1 in Cell Discovery, 1 in Nature Medicine) and top-ranked specialised journals of their discipline (3 in J Cereb Blood Flow Metab, 4 in J Nucl Med, 1 in Eur J Nucl Med Mol Im, 1 in J Control Release). Contribution of research activities to the society is excellent: the team registered 6 patents and exhibited very strong scientific interactions with pharmaceutical industries and biotechs (10 R&D contracts with Servier, Sanofi and UCB among others, 2 CIFRE grants), favouring the employability of their PhD students in private companies. The team effectively shared its knowledge with the general public (2 TV interviews, interaction with high school students and with industry-research students from the Faculty of Pharmacy: ab. 100 students each year).

Weaknesses and risks linked to the context

The team, being mainly consisted of teacher researchers with hospital responsibilities, lacks at least a full-time permanent researcher, and exhibits a disparity of scientific production between team members. Some publications lacked the OPTEN affiliation for their authors. Except an M2 and doctoral grant from the China scholarship council, the team had no other academic grants as PI and the reported conference presentations were mainly limited to 4 team members both for international and national congresses. The interaction with the general public could be more developed (i.e. Fête de la science, Forums des métiers, Forums des masters, associations de patients). Finally, it is noteworthy that the team was mainly auto-financed thanks to its contracts with the industry; still, no patent licensing was obtained during this contract.

Analysis of the team's trajectory

Team 3 will pursue the actual basic research themes focusing on drugs/proton antiporter, and will newly investigate the role of PPARdelta at the neurovascular unit, drug transporters in microglia, and the modulation of endoglin for drug delivery through BBB. The team will consolidate and acquire new skills and knowledge in connection with recently welcomed or upcoming team members' expertise (PK/PD and PBPK modelling,

exchanges BBB/CSF, cellular and molecular interactions at the BBB). One of the main challenges is the output consisting in developing new strategies to deliver therapeutics within the brain and modelling drug distribution in patients' CSF. These developments will be based on two pharmacological strategies, using either new medical devices or surgical procedures, with strong connection to clinics and benefiting from accessibility to human samples. Inter-team projects with Team 2 and Team 4 interestingly supports these goals. It is noteworthy that the team intends to set up a new platform dedicated to the evaluation and data analysis of therapeutics brain kinetics. The team's trajectory is excellent as it will contribute to answering medical/pharmacological needs and should develop the team scientific production in innovative domains, with controlled risk linked to innovative projects and an excellent international positioning with rare contestants.

RECOMMENDATIONS TO THE TEAM

The repartition of human resources between each project of the team's trajectory will have to be carefully set up given the actual lack of permanent researchers, and the intent of launching these new research themes. The positioning of Team 3/OPTEN as endorsed research unit of the radiopharmacy (UCK) platform as well as the collaboration with the BIOMAPS unit (Orsay) should be even more highlighted given the importance in terms of publication quantity and quality. Securing the management of in vitro/in vivo models and innovative techniques (molecular imaging, kinetics modelling) in terms of human resources, continuous training, and financing, will constitute a challenge to ensure projects continuity. The team leaders (and more globally, the unit leaders) should remind the researchers of the Publication Chart to ensure the OPTEN affiliation on all the papers linked with the research unit activities, and encourage junior and senior scientists to apply for national and international grants as coordinators (this recommendation could also be achieved with an industrial partner, given the strong bonds with pharmaceutical industries). Scientific animations and weekly lab/team meetings, including all the staff (PIs, students, ITA), should be regularly scheduled, preferentially face-to-face or hybrids in order to have all team members attending.

Team 4: Diagnostic and Therapeutic innovation for cerebrovascular and thrombotic diseases

Name of the supervisor: Benoit Ho-Tin-Noé/Mikael Mazighi

THEMES OF THE TEAM

The new Team 4 will conduct basic research with translational perspectives for the diagnostic and therapeutic innovation of cerebrovascular and thrombotic diseases. The five main topics are: 1) evaluation of new thrombolytic strategies at the acute phase of ischemic stroke; 2) investigation of mechanisms contributing to neuro- and trombo-inflammation in cerebral injury; 3) exploration of new platelet activation pathways; 4) development and evaluation of anticoagulant antidotes and 5) evaluation of potential markers of neuro- and tromb-inflammation for stroke occurrence, severity, response to treatment, or long-term outcome.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Not applicable

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

Not applicable

EVALUATION

Overall assessment of the team

Not applicable

Strengths and possibilities linked to the context

Not applicable

Weaknesses and risks linked to the context

Not applicable

Analysis of the team's trajectory

The new Team 4 for the next unit contract includes INSERM/CNRS researchers (n=4), PU-PH/MCU-PH (n=10), professors and assistant professors (n=4) in Pharmacy and Pharmacology as well as supporting staff (n=5) originating from INSERM units: U1148, U1140 and U1144. Their scientific strategies include five main topics based on shared interest and complementary expertise with the current three teams of OPTEN: 1) evaluation of new thrombolytic strategies at the acute phase of ischemic stroke; 2) investigation of mechanisms contributing to neuro- and trombo-inflammation in cerebral injury; 3) exploration of new platelet activation pathways; 4) development and evaluation of anticoagulant antidotes and 5) evaluation of potential markers of neuro- and trombo-inflammation for stroke occurrence, severity, response to treatment, or long-term outcomes.
The team's trajectory is excellent/outstanding and the leaders have an international track record in the field. The project is very ambitious and addresses a major clinical issue in view of the urgent need for personalised care during stroke. Among the different axes, valuable inter-team collaborations are planned to be set up with the unit's other teams (i.e. biomarkers of coagulation alterations and endothelial cell dysfunction in brain ischemic diseases with team 2). All subprojects are financed up to 2027, including with competitive national calls (4 ANR, RHU BOOSTER).
The integration of the new Team 4 will considerably broaden the unit's scope of expertise, thanks to their research activities and skills focused on the conception and evaluation of new therapeutic strategies for the management of stroke patient (i.e. by targeting actors of the thrombo-inflammation cascade). On the other side, the new team 4 will benefit from the unit's expertise on biomarkers for the prediction and prevention of cognitive decline in patients with cerebrovascular diseases to identify new therapeutic targets that will be tested in future clinical trials. In conclusion, this is a very good operation for the unit, particularly with the welcoming of 4 full permanent researchers, a critical lack in OPTEN.

RECOMMENDATIONS TO THE TEAM

The team's 4 trajectory is excellent/outstanding in terms of the project's strategies, financial resources and track record. The project is wide and ambitious, we recommend to the team's leaders to be careful not to disperse too much of the workforces as integration into a new environment can take time, and not necessarily in terms of time devoted to research.

CONDUCT OF THE INTERVIEWS

Date

Start: 05 septembre 2023 à 8 h 30

End : 05 septembre 2023 à 17 h 30

Interview conducted: online

INTERVIEW SCHEDULE

Research Lab Interview program
Optimisation Thérapeutique en Neuropsychopharmacologie (OPTEN)
Date of the interview: September 5th 2023 (online)
Present Lab director: Jean-Louis Laplanche

HCÉRES Scientific advisor: Mr. Giovanni Stevanin
Research committee:
Ms. Mélina Fatseas, Expert
Mr. Philippe Garrigue, CSS7 representative
Ms. Catherine Le Moine, Expert
Ms. Suzanne Lesage, PAR representative
Ms Frédérique Liegeois, Expert panel HCÉRES
Ms Valérie Sautou (President), CNU representative
Ms. Cécile Vindis, Expert

Observer : Mme Marie-Josèphe Leroy Zamia, ITMO, Inserm

September 5th

8:30-9:30 Private meeting of the visiting committee with the HCÉRES advisor

9:30-9:45 Presentation of the evaluation process to the unit by the HCÉRES advisor

9:45-10:30 Presentation of the unit scientific outputs and strategy by the present/future lab directors (25′ presentation + 20'discussion)

10:30-11:00 Coffee break

11:00-12:30 Presentation of the scientific programs and research results by group leaders (15′ presentation + 14'discussion)

Team 1: Biomarqueurs de réponse thérapeutique et de rechute dans les maladies neuropsychiatriques (Frank Bellivier/Cynthia Marie-Claire)

Team 2: Mécanismes de toxicité et optimisation thérapeutique des psychotropes (Bruno Mégarbane/Nadia Benturquia)

Team 3: Barrière hémato-encéphalique : Physiopathologie et Thérapie (Xavier Declèves ; for the future: Xavier Declèves/Salvatore Cisternino)

12:30-13:40 Lunch and private debriefing of the committee and HCÉRES advisor

1:40 p.m.-2 p.m. Presentation of a new team: Innovation diagnostique et thérapeutique en pathologies cérébrovasculaires et thrombotiques (Benoit Ho-Tin-Noé/ Mikael Mazighi) (10′ presentation + 10'discussion)

From 2 p.m. Meetings with the various categories of personal

2 p.m.-2:30 p.m. Discussion with PhD students and post-docs (private meeting)
2:30 p.m.-3 p.m. Discussion with engineers, technicians and administrative personnel (in French, private)
3 p.m.-3:30 p.m. Discussion with scientists (without team leaders, private meeting)
3:30 p.m.-4 p.m. Discussion with the representative of the managing bodies (private meeting)
4 p.m.-4:30 p.m. Discussion with the director and future directors with team leaders (closed-door)

4:30 p.m.-5:30 p.m. Private meeting of the visiting committee

5:30 p.m. End of the interviews

GENERAL OBSERVATIONS OF THE SUPERVISORS

Université Paris Cité

Le Président

Paris, le 13 février 2024

HCERES
2 rue Albert Einstein
75013 Paris

Objet : Rapport d'évaluation de l'unité **DER-PUR250024191 – OPTeN – Optimisation thérapeutique en neuropsychopharmacologie**

Madame, Monsieur,

L'Université Paris Cité (UPCité) a pris connaissance du rapport d'évaluation de l'Unité de Recherche **OPTeN – Optimisation thérapeutique en neuropsychopharmacologie.**

Ce rapport a été lu avec attention par la direction de l'unité, de la part de laquelle vous trouverez ci-joint un courrier listant quelques erreurs factuelles à corriger, le vice-doyen Recherche et le doyen de la Faculté de Santé d'UPCité, qui rapportent des erreurs factuelles page 3 (section REPRÉSENTANT(S) DES ÉTABLISSEMENTS ET ORGANISMES TUTELLES DE L'UNITÉ DE RECHERCHE) du rapport provisoire (cf tableau joint aux erreurs factuelles listées par la direction de l'unité), par la vice-présidente recherche d'UPCité et par moi-même.

Le doyen de la Faculté de Santé et moi même souhaitons préciser que l'unité OPTeN est une unité reconnue dans le domaine de la neuropsychopharmacologie, réalisant une recherche fondamentale, pré clinique et translationnelle en lien avec l'APHP. Cette unité fait partie intégrante du paysage d'UPCité puisqu'il s'agissait d'une unité mixte Diderot/Descartes avant même la fusion des deux universités. Elle se restructure et se renforce pour le prochain quinquennat, et un groupe est venu la rejoindre dès 2023 afin de constituer une quatrième équipe dans la future unité. Cette restructuration s'est faite en totale harmonie avec les tutelles (Inserm et UPCité).

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

Édouard Kaminski

Présidence

Référence
Pr/DGDRIVE/2023

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