

## EVALUATION REPORT OF THE UNIT

LPPD - Physiopathologie et pharmacologie  
clinique de la douleur

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

Université de Versailles Saint-Quentin-en-Yvelines  
- UVSQ

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

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### **EVALUATION CAMPAIGN 2024-2025** GROUP E

Report published on March, 05 2025

High Council for evaluation of research and higher education



In the name of the expert committee :

Philippe Marin, chairman of the committee

For the Hcéres :

Stéphane Le Bouler, acting president

In accordance with articles R. 114-15 and R. 114-10 of the Research Code, the evaluation reports drawn up by the expert committees are signed by the chairmen of these committees and countersigned by the president 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:**

Mr Philippe Marin, CNRS, Montpellier

**Experts:**

Ms Sophie Crespín, Université de Lille

Mr Sylvain Rheims, Université Claude Bernard Lyon 1

Mr Éric Toussiot, Université de Franche-Comté (representative of CNU)

## HCÉRES REPRESENTATIVE

Mr Bruno Guiard

## REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Mr Philippe Arhets, Délégation Régionale, Inserm

Ms Coraline Besson, UFR santé, UVSQ

Mr Étienne Hirsch, Inserm

Ms Isabelle Homont, UVSQ

Ms Bérangère Szostak, UVSQ

## CHARACTERISATION OF THE UNIT

- Name: Physiopathologie et pharmacologie clinique de la douleur
- Acronym: LPPD
- Label and number: UMR 987
- Composition of the executive team: Mr Didier Bouhassira & Ms Nadine Attal

## SCIENTIFIC PANELS OF THE UNIT

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

## THEMES OF THE UNIT

The Laboratory of the Pathophysiology and Clinical Pharmacology of Pain (Laboratoire Physiopathologie et Pharmacologie clinique de la Douleur, LPPD) is a single-team and single-theme unit dedicated to clinical research on different types of acute or chronic pain syndromes. Within this general framework, the unit focuses on three main axes: *i)* the identification of predictive factors for chronic pain and the response to therapy; *ii)* the investigation of common mechanisms for different chronic pain conditions, including neuropathic pain, post-operative pain, nociplastic pain, such as irritable bowel syndrome and fibromyalgia, and inflammatory pains due to rheumatic diseases and *iii)* the development of innovative treatments for chronic pain. These issues are addressed by a multidisciplinary group of investigators including neurologists, anesthesiologists, rheumatologists and gastroenterologists, with recognized expertise in both clinical research and basic science. They are using a multimodal strategy, combining functional investigations of somatosensory systems with psychophysical and electrophysiological approaches, and specific questionnaires based on patient reported outcome measures (PROMS).

## HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

LPPD was created in the late 1990s by a small group of scientists, expert in clinical and fundamental research on pain. LPPD was further recognized as a mixed research team ('EMI' E-332) by Inserm and Versailles-Saint-Quentin University (UVSQ) in 2002. It was then renewed in 2006 as a mixed research unit (U792), and following Aères assessments in 2009, 2015 and 2018, consolidated as an UMR (U987) recognised by Inserm and University of Versailles-Saint-Quentin en Yvelines (UVSQ). Following the recent University reorganisation and the integration of UVSQ in Paris Saclay-University, LPPD is now affiliated to Paris-Saclay University.

Since 2001, LPPD has been headquartered at Ambroise Paré Hospital within the Pain Center, recognised as a center of excellence in the hospital, where it benefits from dedicated hospital facilities spanning approximately 120 m<sup>2</sup> for investigations in patients (or healthy volunteers) out of the total 350 m<sup>2</sup>. However, several members of the unit are dispersed in other hospitals of Paris area, which might be detrimental to the daily management of the unit and project follow-up as well as the cohesion of the group.

## RESEARCH ENVIRONMENT OF THE UNIT

The localisation of LPPD within the Pain Center at Ambroise Paré Hospital is a great asset for the recruitment of patients, with 6,000 consultations, representing 2,000 patients annually. The LPPD clinical research programs also benefit from an extensive network of collaborations at the local level (with the anaesthesia department of Ambroise Paré and Raymond Poincaré hospitals) which will probably continue to expand with the project of reorganisation of both hospitals and their merging on the same site. This will lead to the creation of one of the leader international hospitals in the management of disability (Nouveau Garches Ambroise Paré - NGAP - hospital), where pain medicine should represent a major cross-disciplinary aspect. In addition to local collaborations, the LPPD has established multidisciplinary collaborations with clinicians in the Paris region, including rheumatologists at Cochin and St Antoine hospitals, gastroenterologists at Avicenne hospital, ophthalmologists at Quinze-Vingt and Cochin hospitals, and Neurologists at "Amyloid Neuropathies Reference Center" at Kremlin-Bicêtre hospital.

At the international level, the LPPD has been involved in several European consortia, namely DOLORISK (HORIZON 2020), IMI PAIN CARE (IMI'S 2 call), PainOut (FP7)), aimed at assessing the prevalence of acute and chronic post-operative pain, and at identifying clinical, biological, genetic and/or psychological risk factors for chronic pain. Over the last five years, the LPPD has developed a large technological platform, that allows the generation of laser evoked potentials, conditioned pain modulation, cortical excitability modulation (with Transcranial Magnetic Stimulation), nociceptive flexion reflex (Rfll), quantitative sensory testing (QST), measurement of electrochemical skin conductance (Sudoscán) and skin punch biopsy. The LPPD technical plateau hosts a unique « thermal grill » machine, conceived with the help of French technicians and used for patients, two repetitive TMS

(rTMS) instruments, including conventional rTMS (figure-of-eight-coil, MacVenture) and a new "deep" rTMS machine using an H coil (Brainsway), a double face coil to ensure true double blinding, a neuro-navigation system (Syneika) and a robot (Axilum Robotics).

## UNIT WORKFORCE: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	5
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	7
<b>Sous-total personnels permanents en activité</b>	<b>14</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	6
<b>Sous-total personnels non permanents en activité</b>	<b>8</b>
<b>Total personnels</b>	<b>22</b>

## DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: in physical persons at 31/12/2023. Non-tutorship employers are grouped under the heading "others".

Nom de l'employeur	EC	C	PAR
Inserm	0	1	5
UVSQ	3	0	0
Autres	3	0	2
<b>Total personnels</b>	<b>6</b>	<b>1</b>	<b>7</b>

## GLOBAL ASSESSMENT

The LPPD is a single-team research unit that brings together a dynamic, multidisciplinary group of clinician-scientists focused on clinical pain research. They are using an original reverse translational, patient-centered, strategy to improve neuropathic pain diagnosis in multiple clinical contexts and better predict response to therapies in order to implement personalised medicine. This is a highly coherent project that addresses important societal needs. Over the past years, including the reporting period, LPPD has successfully tackled these timely questions and has become one of the most attractive and reputed laboratories in the field of clinical pain research in France and Europe. Their scientific appeal is demonstrated by i) the worldwide use of their validated pain questionnaires (translated in more than 90 different languages), namely "DN4", which estimates the probability of neuropathic pain, and "NPSI" that assesses the presence and monitoring the evolution of neuropathic pain symptoms and treatment efficacy. These questionnaires are officially recommended by the European Medicine Agency as the gold standard for clinical trials, ii) their participation in four European consortia (Dolorisk - HORIZON 2020 -, IMI Pain care - IMI -, and Doctoral Networks - Marie Skłodowska-Curie actions - HapPy and Fresco4pain), iii) their contribution to the international classification of pain 11th Edition (ICD-11), iv) their editorial responsibilities (Editor in chief of the European Journal of Pain, Section Editor of the European Journal of Anaesthesia) and v) their invitation to give more than 100 conferences at international meetings, including plenary lectures (e.g. Ed Charlton plenary at London, International Congress on Neuropathic Pain, Richard Hugues lecture at the Kings College meeting on pain, Rynd award lecture at the congress of the Irish Society of anesthesiology). Among the major scientific achievements of LPPD over the reporting period, one can quote i) the validation of OASIS, a new specific questionnaire assessing multiple

dimensions of pain in osteoarthritis (OA) and the efficacy of new therapeutic strategies, *ii*) the demonstration of long-term efficacy and safety of repeated sessions of rTMS of the primary motor cortex in fibromyalgia, one of the most difficult to treat pain conditions, in frame of a national clinical hospital research program (PHRC). This project has resulted in rapid clinical applications and *iii*) the demonstration of the clinical benefit of botulinum toxin A (injected subcutaneously) for the treatment of peripheral neuropathic pain and the elaboration of a predictive algorithm to detect responders to the treatment, which is now used in routine in multiple pain centers in France and is part of national and international recommendations for neuropathic pain.

LPPD also stands out by its excellent scientific production, with more than 200 publications in peer-reviewed journals during the reporting period, including original and review articles in broad readership medical journals, such as *Brain*, *Lancet*, *Neuron*, *Nat Rev Rheumatol*, *JAMA* and *E Clinical Medicine*, and recognized journals specialized in the field of pain research, such as *Pain*, *Eur J Pain* and *J Pain*. Some of these articles (mostly review articles) are already highly cited, with 12 of them being cited more than 50 times (including 3 cited more than 200 times). LPPD is well-funded, with more than 3M€ income during the reporting period, including 2 PHRC, one ANR grant and 4 European grants (*vide supra*). However, given the scientific appeal of LPPD, and the scale and impact of its research, the overall funding raised by the unit (especially PHRC fundings) might be increased and most of the grants, especially the most competitive ones, are led by the current and/or future director of LPPD.

LPPD is also well managed and generally complies with the rules and directives of its supervisory bodies in terms of human resource and data management. The dispersal of LPPD scientists over several sites is offset by the organization of fortnightly staff hybrid meetings to discuss the scientific progress as well as any organizational aspects of their different projects. However, the communication within the unit, especially toward technical staff, is not always optimal and actions to promote cohesion and the feeling of belonging to LPPD should be reinforced. In line with the high societal impact of LPPD research program, they are strongly involved in knowledge diffusion to the lay public through numerous interventions in TV shows, radio broadcasts and the written press. They are also strongly committed in teaching and training, with their participation in more than 100 teaching courses in France and Europe. Finally, LPPD scientists are consultants for numerous pharmaceutical companies, including big pharmas and biotech companies, but the funding of LPPD from the private sector might be increased given their longstanding relationship with pharmaceutical industry.

In conclusion, LPPD is an **excellent to outstanding** research unit, which should capitalize on its original positioning, exceptional visibility and recent successes to define a strategy for the generational renewal of its scientific staff in order to ensure its long-term future beyond the next mandate.

## DETAILED EVALUATION OF THE UNIT

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

*The previous committee recommended that LPPD hires more young researchers (including foreign students) working full time on their research project.*

The number of PhD students trained at LPPD has increased over the past 5 years (9 PhD trained, 5 of them have defended their PhD). LPPD also trained a Vietnamese PhD student, financed by the prestigious Eiffel scholarship program of excellence, and a Cuban PhD student who is recipient of a Cifre fellowship ("Convention industrielle de formation par la recherche"). LPPD is also involved in two European doctoral networks (Marie Skłodowska-Curie actions) that allowed them to hire an Italian PhD Student who will join LPPD after being trained got one year in the Heidelberg Pain Consortium and Kiel University and to benefit from two other Marie Skłodowska-Curie fellowships in 2025.

*It recommended that LPPD also attracts researchers who can bring expertise complementary to the strong clinical expertise of the unit, such as expertise on psychophysical methods, data modelling and statistics, to further increase the quality and innovation of the unit's research.*

In spite of its original positioning and strong visibility in France and abroad LPPD did not succeed in attracting any new permanent researchers. This is probably due to its clinical research-centered topics, its small size and the dispersion of its manpower in several sites.

*It recommended that LPPD implements a clear vision to ensure the legacy of the unit through the identification of a new effective leadership at the end of the mandate.*

The current associate director of LPPD, who already assists the director in topics related to clinical research and research meetings, is proposed as the future director of the unit. This will certainly guarantee the continuity of research in the unit and its international visibility among clinicians (she has authored major international guidelines during the previous term), but not beyond. In the absence of recruitment of a younger researcher capable of ensuring the leadership within the unit, its long-term future remains uncertain.

Overall, LPPD partially addressed the recommendations of the previous committee.

## B - EVALUATION AREAS

Guidelines for all areas of evaluation (1, 2, 3 and 4): 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

LPPD is a single-themed unit exclusively devoted to clinical pain research based on studies in patients with various types of acute or chronic pain. This is a highly coherent research program that addresses a major public health challenge, since chronic pain is the first cause for visits to a general practitioner and a prevalent global medical condition, affecting one out of five adults. LPPD was the first unit in France exclusively focused on patient-centered pain research, which makes it highly visible in France and abroad. Overall, the scientific objectives of LPPD are well-defined, well-focused and clinically-relevant. They can be considered as **excellent to outstanding**.

#### Assessment on the unit's resources

LPPD is a multidisciplinary team of researchers, teachers-researchers and hospital physicians (neurologists, anesthesiologists, rheumatologists, gastroenterologists) with expertise in both clinical research and basic science on topics related to the pathophysiology and pharmacology of nociceptive systems highly relevant for the objectives of the unit. However, LPPD only includes one full-time researcher and the majority of its permanent scientists have important teaching (lecturers, professors) and clinical (hospital practitioners) duties. Regarding financial resources, LPPD receives substantial recurrent fundings from its institutions (65 k€ yearly) with respect of its size, but they are insufficient to cover the costs of their clinical research projects. Accordingly, LPPD has been very active and successful in fundraising (>3 M€ raised over the reporting period), including national (PHRC, ANR etc.) and European (Horizon 2020, IMIPain Care, PainOut, FP7) grants. Overall, the unit's resources are **excellent**.

#### Assessment on the functioning of the unit

LPPD is a small unit with a strong thematic coherence that gathers specialists in clinical pain dispersed in several hospitals of Paris area, which is detrimental to the interactions between the personnels of the unit and supervision of students. To overcome this difficulty, fortnightly meetings bringing together all the staff to discuss the scientific, organisational, financial and logistical aspects of the different projects, are held at Ambroise Paré hospital. However, the diffusion of information within the unit and the actions to favour staff cohesion are not optimal. The unit's functioning generally complies with the rules and directives defined by its supervising bodies on human resources management, safety and environment, but the unit's governance and decision-making procedures lack transparency. All scientific members of the unit, including non-permanent staff and students, are encouraged to participate in international congresses and the quality of training provided at LPPD has been outlined by students. Overall, the functioning of the unit is **very good to excellent**.

*1 / The unit has set itself relevant scientific objectives.*

#### Strengths and possibilities linked to the context

LPPD was the first unit in France performing clinical research on pain with a leading position. Capitalising on its original positioning, longstanding expertise in the field and the societal and economic impact of its research, the unit has acquired a high visibility at the national and international levels.



The relevance of LPPD objectives entirely oriented towards clinical applications and the success of its strategy are highlighted by the worldwide use of their questionnaires, DN4 and NPSI, translated in over around 90 languages each. They are also used in multiple medical schools in France and Europe, and recognised as the gold standard to phenotype neuropathic pain in large scale European consortia. Collectively, they allowed i) a better recognition of neuropathic pain around the world in multiple clinical contexts, ii) accurate prediction of response to therapy, iii) prediction of the development of chronic postsurgical pain and iv) implementation of multiple epidemiological studies in countries where such studies were lacking.

The relevance of LPPD objectives is also illustrated by the development of non-invasive brain neuromodulation using repetitive sessions of rTMS for the treatment of refractory chronic pain and the demonstration of the benefit of botulinum toxin A (injected subcutaneously) for the treatment of peripheral neuropathic pain. Finally, LPPD has largely contributed to the international classification of pain 11th Edition (ICD-11) that will facilitate hospital coding of pain and epidemiological studies.

## Weaknesses and risks linked to the context

Even though the research strategy of LPPD is clearly oriented towards clinical applications, it might give greater consideration to the mechanistic aspects of pain through, for example, collaborations with laboratories carrying out preclinical studies. The success of LPPD strategy strongly relies on the internationally recognised expertise of its current and future directors, and is more uncertain on the long-term in absence of recruitment of younger permanent scientists capable of taking over the leadership in the field.

*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

Regarding human resources, LPPD gathers a multidisciplinary team of permanent scientists and University hospital physicians (neurologists, anaesthesiologists, rheumatologists, gastroenterologists) with a recognised expertise in both clinical research and basic science as well as in the pathophysiology or pharmacology of nociceptive systems. This expertise is highly relevant to the LPPD scientific policy. LPPD has also recruited more early career scientists (9 PhD students and 3 postdoctoral fellows) over the past five years than in the previous mandate, including foreign students (3 recruited over the reporting period, and 2 to be hired thanks to funding from a European doctoral network). Regarding financial resources, LPPD has been very active and successful in fund raising in response to national and international calls, with more than 3 M€ income over the past 5 years. These include two Hospital Programs for Clinical Research (PHRC), one industrial grant, one ANR grant, several grants from charities or patient associations (Ligue contre le Cancer, Fibromyalgie SOS) and 4 European grants (Horizon 2020, IMIPain Care, and 2 doctoral networks). LPPD also benefits from technological resources allowing for generation of laser evoked potentials, conditioned pain modulation, cortical excitability modulation (rTMS, developed in collaboration with French and foreign small companies which provided their device), nociceptive flexion reflex (Rfll), quantitative sensory testing (QST), measurement of electrochemical skin conductance (Sudocan) and skin punch biopsy and also hosts an in-house developed "thermal grill" machine.

## Weaknesses and risks linked to the context

There are no research facilities such as functional neuroimaging (MRI) or other large research platforms at Ambroise Paré Hospital due to the small size of this hospital. Nevertheless, this lack of local technological resources encouraged LPPD to develop a large network of collaborations with other hospitals of the Paris area. With the planned retirement of the current LPPD director, there will be no full-time permanent researcher at LPPD during the next mandate. The LPPD scientific strategy mostly relies on the well-recognised expertise of its current and future directors. In spite of the multidisciplinary expertise of its hospital physicians, and the presence of younger talented University hospital researchers/teacher-researchers at LPPD, the identification of scientist(s) capable of taking over the leadership on the long-term remains to be done.



- 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 LPPD follows the general principles defined by both Inserm and the hospital, regarding safety and health issues at the workplace even though the unit does not use any wet lab, thus limiting risks inherent to chemical and biological sample manipulation. They follow "local regulation issues" including specific measures to be taken for health and safety issues related to research activities in general. Fortnightly hybrid meetings where the staff can discuss about scientific, organisational, financial and logistics aspects of their projects are organised at Ambroise Paré Hospital. Although LPPD does not have a written sustainable development charter, they consider sustainable development when defining research projects and experiments. For instance, all clinical studies prioritise patients living in the Paris area, to limit transportations and reduce environmental footprints. All LPPD staff, including students, postdocs and technical staff are encouraged to present their data at scientific meetings. However, only scientists who have presentations (posters, workshops, plenaries) participate in international congresses outside Europe and prioritise the train over the plane whenever possible for French and European congresses.

#### Weaknesses and risks linked to the context

The LPPD governance, especially the decision-making process concerning any strategic issues, such as scientific orientations, recruitments, collaborations, grant applications, etc., are a bit vague. Although lab meetings gathering all the staff as well as more informal meetings are regularly organised to discuss about scientific issues and the progress of the projects, the diffusion of information within the unit is not optimal. For instance, technical staff lack information regarding career progression, formation available, bonus attribution, etc. Measures to promote staff cohesion of the staff and a sense of belonging to the LPPD are currently limited.

### EVALUATION AREA 2: ATTRACTIVENESS

#### Assessment on the attractiveness of the unit

The attractiveness of the unit is **excellent to outstanding**. The current and future directors of the unit have an outstanding international recognition. The unit had several successes in European and national competitive grants. However, the ongoing projects are mostly coordinated by the current and future directors and involvement of more junior investigators at a coordinator level would be important to reinforce the future projects of the unit. The direct integration of the unit within the pain department of the Ambroise Paré hospital ensuring easy access to large cohorts of patients is a strong asset contributing to the unit's attractiveness.

- 1/ *The unit has an attractive scientific reputation and is part of the European research area.*
- 2/ *The unit is attractive because for the quality of its staff support policy.*
- 3/ *The unit is attractive through its success in competitive calls for projects.*
- 4/ *The unit is attractive for the quality of its major equipment and technical skills.*

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

The national and international reputation of the team is demonstrated by the involvement of both the current and the future director in several national or international guidelines on pain management/research, or their involvement, sometimes as work package leaders, in large European projects (IMI-PainCare and Horizon 2020 DOLORisk). Over the past years, and following the recommendations of the previous Hcéres evaluation, the unit has hosted several foreign PhD students, which should be considered as a marker of the quality of the PhD student supervision beyond the scientific recognition of the team. In addition, the unit has been able to recruit two permanent Inserm technicians over the past years, which is a key aspect for the organisation of the staff

and reflects the commitment of the unit to ensure the continuity of the research projects. In addition to the two major European projects cited above, the unit had successes in various national competitive calls, including PHRC or Foundations. The team is localised within the Pain Center of the Ambroise Paré Hospital offering it a direct access to patients and strong interactions between clinical research and medical management, which is the key asset of the unit. Accordingly, its expertise in designing and conducting clinical studies in pain research is excellent and highly recognised. This interaction with the clinical department at Ambroise Paré Hospital as well as the other collaborations with APHP Departments ensure easy access to the equipment. The unit staff has excellent expertise for the technics used in routine in past and ongoing projects (quantitative sensory testing, rTMS, electrophysiology, skin punch biopsy).

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

The unit has been the partner of a single ANR project over the past period. Most of the projects, especially the most competitive ones, are leaded by the current and/or the future unit director. Currently, the visibility and success in competitive calls of more junior permanent staff is lower, including at the national level. The 2019 Hcéres report had suggested to try to enlarge the skills and/or staff of the team with the objective of reinforcing its strengths in patient-centered pain research, such as expertise in data modelling and statistics in one hand or neurophysiological and/or neuroimaging expertise to reinforce the development of multimodal projects on the other hand. However, these evolutions have remained modest.

## EVALUATION AREA 3: SCIENTIFIC PRODUCTION

### Assessment on the scientific production of the unit

The scientific production of the unit is **excellent**, as indicated by the number of publications and citation records. The visibility of the works by the unit is national and international. Over the last five years, the unit has published 220 articles including 46% original research articles in good-quality specialist journals in the field of pain research, such as *Pain*, *Eur J Pain*, *J Pain*. Certain clinical studies have been published in journals having a broader readership, such as *Brain*, *Eur J Anaesthesiol*, *Br J Anaesthesiol*, *Lancet Neurol*, *Nat Rev Rheumatol*, *JAMA*, *E Clinical Medicine*. The unit has also published an important number of review articles (narrative reviews and systematic review/metaanalysis/recommendations, representing each 15% and 15% of the scientific production, respectively). 48% of the papers were authored as first/last or corresponding author and 16% were authored/coauthored by the PhD students of the unit (35 peer reviewed papers were authored by young researchers).

- 1/ *The scientific production of the unit meets quality criteria.*
- 2/ *The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.*
- 3/ *The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.*

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

The scientific production of the team is substantial and of great quality as indicated by the number of papers in good-quality specialist journals or journals of medicine with broader readership. It was well balanced between senior and junior members. Some LPPD articles published over the reporting period are already well cited, with at least 5 papers cited more than 100 times and 7 papers cited between 50 and 100 times. The scientists of the unit, especially its current and future directors, are active members of the boards of different scientific societies, including the International Association for the Study of Pain (IASP), the European Pain Federation (EFIC), the Neuropathic Pain Special Interest Group (NeuPSIG), and the European Academy of Neurology (EAN). They were head or members of the Scientific Program of national or international congresses: IASP, Efic, NeuPSIG, Eular, Euroanesthesia. They are members of the editorial board of several journals in the field of pain research, including the *European Journal of Pain*, *Br Journal of Anesthesia and Pain Reports*.

The team is involved in 4 major European consortia: Dolorisk (HORIZON 2020), IMI Pain care (IMI), HapPy Fresco4pain (International Doctoral Network, Marie Skłodowska-Curie actions) and 5 Eranet-Neuron Projects.

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

We identified no specific weakness in LPPD production. One limit cited by the unit is the time before starting a clinical study (delay for finding grants and time to submit to regulatory authorisation).

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

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

LPPD scientists are very active in knowledge diffusion and training activities at national, European and International levels, with the participation in more than 100 teaching courses dedicated to selected European researchers or French physicians. They are also extremely active in knowledge diffusion toward the lay public, with numerous interventions in various audiovisual media and the written press, edition of books for the general public and participation in debates with the general public. They have also developed strong interactions with patient associations as well as consulting activities with various pharmaceutical companies or start-ups, but the funding of LPPD from the private sector remains limited and the unit did not fill any patent over the reporting period. Overall, the inclusion of LPPD's research in society is **excellent to outstanding**.

- 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 LPPD is strongly involved in training activities at national, European and International levels. LPPD staff participated in more than 100 teaching courses over the past 5 years. They were involved in the European School of the European Pain Federation (EFIC Pain School) which provides high-level international education to selected European doctors or researchers. The unit's director is involved in the prestigious Neuroscience School of Advanced Studies (<https://www.neurosas.org/home2>) and has created the first French Society of Pain School in 2019, which proposes high-level teaching courses to selected physicians from France. They edited the book entitled "What do I do now: neuropathic pain" (Oxford University Press, 2023), the official book of the "Collège des enseignants en médecine de la douleur" for medical students on pain and palliative care ("Douleurs, soins palliatifs, accompagnement ") and coordinated books on chronic pain and cognitive behaviour therapy for pain (Dunod, 2018; in press, 2021). They also edited books for the general public ("La douleur je m'en sors", In Press Editions, 2018; "L'anti-douleur", Cherche Midi 2018; and "Intestin Irritable: les raisons de la colère", Larousse). All LPPD senior scientists are consultants for pharmaceutical companies (Pfizer, Lilly, Merz, Grunenthal, Sanofi-Aventis, Novartis, Medtronic, TEVA, Johnson and Johnson, Air Liquide, Biogen,...) or startups (Theranexus, Paris; Pharmaleads for drugs acting on endopeptidases, Paris; Tafalgie for TAFA4 compound, Marseille; Homebiosciences, from the private fund Sofinova, Montpellier; Biodol therapeutics for FLT3 compound, Montpellier). They have participated in a variety of TV shows (France 2, TF1, France 5, M6, BFM...), radio broadcasts (France Inter, France Culture, RTL, RFI, RCJ) and contributed to several articles in general public journals (Le Figaro, Le Monde, La Recherche, Le Nouvel Obs., Santé Magazine, Elle, Femme Actuelle, Paris Match, Pleine Vie, Bien être et Santé, Avantages, Ça m'intéresse, Sciences et vie) or in more specialized press (Le Quotidien du Médecin, Impact Médecin). They have long standing interactions with French patients' organisations (Apaiser (Syringomyélie), Neurofibromatosis patient association, Fibromyalgie France, Fibromyalgie SOS, Association Française pour Vaincre la Douleur (AFVD), Association Française des Polyarthritiques et des rhumatismes inflammatoires chroniques, etc.) and animated or contributed to debates with the general public at the Académie de Médecine, Académie des Sciences, Institut Imagine, or with patient associations.

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

LPPD fundings from the private sector are somewhat limited (only one contract with Grunenthal/CapsaNep providing 200 k€ funding over the reporting period) with respect of the numerous consulting activities of LPPD scientists and their regular interactions with various pharmaceutical companies and start-ups. The unit did not fil any patent over the reporting period.

## ANALYSIS OF THE UNIT'S TRAJECTORY

The "Pathophysiology and Clinical Pharmacology of Pain" unit is very active and dynamic in clinical pain research with a national and international visibility at a high level. The research program is highly consistent and centered on the identification of mechanisms and risk factors for chronic pain development and innovating treatment strategies. Innovative non-pharmacological treatments such as brain neurostimulation (rTMS) and identification of predictive factors of response to rTMS are among the objectives of the unit in line with previous results in the field. The projects aimed at developing innovative non-pharmacological approaches for chronic pain and elucidating mechanisms for chronic pain well underline the coherence of the research and organisation strategy. The unit involvement in European consortia and collaborative projects will ensure multidisciplinary approach a good progression of the research.

The unit has very solid background in studies using quantitative sensory testing, rTMS, electrophysiology. While remaining focused on core areas of expertise of the unit in terms of scientific questions, enlarging the skills and methods of future projects might be fruitful. Example to be discussed might be functional imaging in addition to electrophysiology for studies investigating mechanisms of pain or skills in biostatistics and modeling to propose additional approaches in studies investigating risk factors of pain, especially when considering large and multimodal datasets.

The unit identified a new director for the next 5-year period. She is PU-PH and professor of therapeutics and pain medicine. She has been working in the unit for a long time and will give new opportunities for the unit. However, the identification of a new leadership at the end of this next 5-year period will be a challenge. In addition, after the retirement of the current director, who is Inserm research director, all permanent researchers will be hospital-University practitioners and hospital practitioners. Although the presence of several Inserm technicians and engineers is a strong asset to conduct the projects and maintain the expertise, the absence of the full-time researcher might represent a threat for the unit, including to ensure appropriate supervision of future PhD students and/or post-docs.

## RECOMMENDATIONS TO THE UNIT

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

The committee recommends that LPPD anticipates the retirement of its future director at the end of the forthcoming mandate and defines a strategy ensuring the unit's long-term future in a collective process associating all its permanent staff. This will probably involve a generational renewal of the unit's permanent scientific staff, and the enlargement of its scientific orientations and technical skills to attract young researchers and strengthen the unit over the coming years. The recent development of epidemiological studies is an important step in this direction. The unit might also consider developing neurophysiological and pathophysiological studies to attract a full-time permanent researcher with new skills while keeping the core expertise of the unit.

The committee recommends that LPPD organises periodically formal meetings (with minutes) gathering at least all permanent staff to discuss about any strategic issues, such as future recruitments, collaborations, grant applications etc.

It also recommends that the current and future directors improve communication within the unit, especially communication toward technical staff about career progression, formation and bonus attribution. It recommends that the criteria for the latter are clearly explained to the staff.

Finally, the committee recommends that the unit sets up actions (e.g. convivial events) to increase the cohesion within the unit and the feeling of belonging to LPPD.

### *Recommendations regarding the Evaluation Area 2: Attractiveness*

The committee recommends that the unit capitalises on the strong support of its supervising bodies (Inserm and UVSQ) to ask for a tenure-tracks position (Chaire de Professeur Junior - CPJ) and attract a talented young scientist capable of participating in the management of the unit or taking over its direction after the retirement of the next director.

Another crucial step in the unit's long-term development will be the renewal of its technical staff at the end of the next mandate. In this respect, the committee recommends that LPPD also asks UVSQ for a technical staff position, which would give the University the opportunity to demonstrate its support to LPPD on this occasion.

### *Recommendations regarding Evaluation Area 3: Scientific Production*

The committee recommends that the unit maintains its high-level scientific article production and that junior scientists progressively increase their leadership in publications.

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

The committee recommends that LPPD better exploits its multiple interactions with the economic world (e.g. consulting activities to the benefit of big pharmas, biotechs and start-ups), to increase its fundings from the private sector.

## CONDUCT OF THE INTERVIEWS

### Date

**Start:** 14 janvier 2025 à 08h30

**End:** 14 janvier 2025 à 17h

**Interview conducted: online**

### INTERVIEW SCHEDULE

8:30-8:45	Huis Clos du comité en présence de CS Hcéres
8:45-9:00	Présentation du processus d'évaluation par le conseiller Hcéres et du comité d'experts
9:00-11:00	Présentation de l'unité et de ses thématiques de recherche (réunions publiques)
09:00-09:30	Présentation de l'unité avec ses principales réalisations par le Dr Didier Bouhassira, DRE (15 min de présentation + 15 min de discussion)
09:30-10:00	Présentation des projets principaux et de l'organigramme futur de l'Unité par le Pr Nadine Attal (15 min de présentation + 15 min de discussion)
10:00-11:00	Illustration d'études et projets de recherche réalisés au sein de l'Unité par les doctorants, post-doctorants, jeunes chercheurs.
•10:00-10:40	Etudes pharmaco-épidémiologiques. Consommation d'opiacés en France par le Dr Anne Priscille Trouvin, MCU-PH (PhD en 2023 dans l'Unité) (10 min de présentation + 10 min de discussion)
	Consommation d'opiacés en Afrique par le Dr Yacine Hadjat, doctorant (10 min de présentation + 10 min de discussion)
•10:40-11:00	Mécanismes physiopathologiques et biomarqueurs de douleur chronique FibroNep par le Dr Hailinh Nguyen, doctorante (10 min de présentation + 10 min de discussion)
<b>11:00-11:30</b>	<b>Pause</b>
11:30-12:30	Discussions à huis clos avec les différentes catégories de personnels
•11:30-11:50	Discussion avec ingénieurs, techniciens, personnels administratifs
•11:50-12:10	Discussion avec les étudiants en thèse et les post-doctorants
•12:10-12:30	Discussion avec les scientifiques (sans le chef d'équipe)
<b>12:30-13:30</b>	<b>Déjeuner</b>
13:30-14:00	Réunions à huis-clos du jury pour préparer les échanges/questions avec DU et tutelles
14:00-14:30	Discussion avec les DU
<b>14:30-15:00</b>	<b>Pause</b>
15:00-15:30	Discussion avec les représentants des organismes de gestion/tutelles
15:30-16:30	Réunion privée du comité de visite en vue de la préparation du rapport (huis-clos)
<b>16:30</b>	<b>Fin de la visite</b>

### PARTICULAR POINT TO BE MENTIONED

The Committee acknowledges the strong support given to LPPD by its supervising bodies (Inserm and UVSQ), and recommends that this will be concretised by favoring the mobility of a permanent researcher at LPPD, and/or by opening a tenure-track position in the unit. The committee also recommends that the University confirms its support by allocating a R position to LPPD in anticipation of the planned retirement of the unit's ITA staff (currently all from Inserm) at the end of the next term.



## GENERAL OBSERVATIONS OF THE SUPERVISORS

Le Président de l'Université de  
Versailles Saint-Quentin-en-Yvelines

A

Monsieur Stéphane Le Boulter,  
Président  
Haut Conseil de l'évaluation de la  
recherche et de l'enseignement  
supérieur  
2 rue Albert Einstein - 75013 PARIS

A Versailles,  
Le lundi 17/02/2025

Ref. DER-PUR260024913 - LPPD - Physiopathologie et pharmacologie clinique de la douleur

**Objet :** Evaluation des unités de recherche – Volet Observation de portée générale

Monsieur le Président,

Nous avons pris connaissance avec le plus grand intérêt du rapport de l'HCERES concernant la demande de renouvellement de l'Unité de Recherche (UMR 987), dénommée « Physiopathologie et pharmacologie clinique de la douleur (LPPD) », portée par M. Didier Bouhassira Directeur et Mme Nadine Attal, Directrice Adjointe.

Nous remercions l'HCERES et le comité pour l'efficacité et la qualité de leur travail d'analyse et pour leurs recommandations constructives que le directeur d'unité et son équipe ne manqueront pas de mettre en œuvre avec le soutien de l'Université et de l'INSERM pour la période quinquennale 2026-2030.

La direction du Laboratoire ainsi que ses membres remercient également le comité pour leur excellente évaluation ainsi que pour les conseils apportés afin d'encourager le développement de l'unité et les recommandations pour pérenniser son rayonnement.

Nous vous adressons ci-joint les observations et commentaires du porteur de ce projet formulés au regard du rapport de l'HCERES.

Nous vous prions de croire, Monsieur le Président, à l'expression de nos cordiales salutations.

  
Professeur Loïc Josseran  
Président de l'UVSQ

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[www.hceres.fr](http://www.hceres.fr)

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