

Research evaluation

# EVALUATION REPORT OF THE UNIT

GRAP - Groupe de Recherche sur l'Alcool & les Pharmacodépendances

# UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université de Picardie Jules Verne

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

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

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## In the name of the expert committee :

Véronique Deroche-Gamonet, chairwoman 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:	Ms Véronique Deroche-Gamonet, Inserm, Bordeaux		
Experts:	Mr Pierre Bourdoncle, Inserm, Paris (supporting personnel) Ms Monique Majchrzak, université de Strasbourg (representative of CNU) Mr Philippe Marin, CNRS, Montpellier Ms Émilie Olie, CHU de Montpellier (representative of the CSS Inserm)		

## HCÉRES REPRESENTATIVE

Mr Bruno Guiard

#### REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Mr Étienne Hirsch, Inserm Mr Denis Postel, université de Picardie Jules Verne



# CHARACTERISATION OF THE UNIT

- Name : Groupe de Recherche sur l'Alcool & les Pharmacodépendances
- Acronym: GRAP
- Label and number: UMR 1247
- Composition of the executive team: Mr Mickael Naassila (director) and Mr Eric Nguyen-Khac (deputy director).

#### SCIENTIFIC PANELS OF THE UNIT

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

#### THEMES OF THE UNIT

GRAP (for Groupe de Recherche sur l'Alcool et les pharmacodépendances) is the only French team exclusively dedicated to multidisciplinary research on alcohol-related diseases. GRAP is a single-team unit. Over 2018-2023, research at GRAP was dedicated to the study of behavioral and liver impacts of alcoholism and alcohol consumption.

GRAP was notably interested in the deleterious effects of a specific form of consumption, called binge drinking. At the behavioral level, GRAP focuses on the mechanisms of addiction, the associated cognitive dysfunctions and psychiatric diseases. At the liver level, GRAP research focuses on the biological mechanisms of alcohol acute hepatitis and alcoholic hepatocellular carcinoma. Bringing together fundamental researchers in neuroscience, clinical researchers and hospital practitioners in psychiatry, neuropsychology or hepatology, GRAP sets the conditions for a holistic and translational approach of research on alcoholism and the consequences of alcohol consumption. As an illustration of holistic research, they recently evidenced that alcohol use disorder patients with cirrhosis present more severe cognitive impairments than those without cirrhosis, questioning the link between liver and brain dysfunction.

GRAP has two major goals. One is to produce knowledge to be used for personalized care and precision treatment for alcohol use-related psychiatric (including addiction) and liver pathologies. The other goal is for the produced knowledge to benefit society rapidly through, for example, the development of prevention actions or tools, the training of healthcare professionals, and the promotion of changes in clinical practice.

Over the last six years, research at GRAP has been organized around four main research objectives:

- understanding the individual/environmental factors and disease modifiers underlying problematic alcohol consumptions and alcohol-related liver diseases.

- understanding the pathophysiological mechanisms of problematic alcohol consumption (binge drinking) and alcohol addiction, and associated psychiatric diseases (notably schizophrenia) and liver pathologies (acute hepatitis and hepatocarcinoma).

- studying the individual factors underlying phenotypic pleiotropy and moderating treatment response.

- testing new pharmacotherapies in a translational manner combining several animal models of excessive alcohol intake and clinical trials, based on the results of their fundamental research.

Research involves studies using rodent models and/or human subjects belonging to cohorts or not. In rodents, a multi-level approach is applied ranging from cognition to system and molecular levels. In humans as well, a multi-level approach can be applied combining neuropsychology, neuroimaging, genetics..., depending on the question of interest.

#### HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

GRAP was created as a Junior Research Group in 2004 and was renewed as the ERI 24 (joint unit between the Regional Council and Inserm) in 2007 and 2012. GRAP obtained the Inserm unit label (Inserm UMR1247) starting January 1, 2018. This contract 2018-2023 is the first contract of the GRAP as an Inserm labelled unit.

The DU of the GRAP is professor at the university of Picardie. He is the official director of the GRAP since 2012. His expertise is on fundamental preclinical research on the psychobiology of alcohol addiction. He his assisted since 2016 by a deputy director, who is PU-PH and head of the hepatology and gastroenterology Department at the university hospital of Amiens.



GRAP moved to a new building in 2015; the CURS (Centre Universitaire de Recherche en Santé). The CURS is located on the university hospital (CHU) site, facilitating the interactions between basic scientists and clinical researchers or hospital practitioners working in hepatology, oncology or psychiatry. Two associate researchers, expert in neuropsychology, are located at the University of Reims – Champagne Ardennes and in The College of New Jersey (Ening, USA). Two psychiatrists joined the team in 2023 and exert at the CHI Clermont de l'Oise.

#### RESEARCH ENVIRONMENT OF THE UNIT

At the local and regional level, the GRAP is involved in university and health-related coordination and research bodies. The deputy director is the head of the CRBSP (Biomedical Research & Public Health Committee) and a member of the Board of Directors of the University. An IR is an elected member of the administrative council of the Pharmacy School of the UPJV. An IR is member of the doctoral school. Several members of the team are members of the Faculty Management Council (Medicine and Pharmacy) and are members of the Regional ethics committee on animal experimentation. The GRAP is member of the FHU A2M2P.

The unit is represented within the GHT Addictions (Territorial Hospital Grouping), where it interacts with all representatives of services and stakeholders in the field of addictions in Picardy. Within this GHT, the unit has contributed to the establishment of level 3 addictology (Research-Education-Care).

In terms of education, eight members of the unit have teaching duties and some have responsibilities in initial or continuing training. The DU is educational coordinator for the 'Diplôme Universitaire d'Addictologie' of the UPJV. A professor is educational coordinator for the Master2 'Developmental, Cognitive, and Addiction Neurosciences'.

The GRAP is a key player in local, regional, national, and international research on alcohol use disorders, encompassing fundamental research, clinical research, prevention, and healthcare improvement. The DU is coordinator of the national alcohol research network REUNIRA and creator of the AlcoolConsoScience resource website to train healthcare professionals on the impact of alcohol consumption on health. A professor is in the board of the Fetal Alcohol Syndrome network. An IR is team leader within the NACRe network (Nutrition, Physical Activity, and Cancer Research Network brings together public research teams and experts involved in the 'nutrition and cancer' field). The deputy director is leader of a cohort of 5 000 patients with Hepatocellular Carcinoma (cohort CHIEF).

The DU is president of the French Society of Alcoholology (SFA) and of the European Society for biomedical research on Alcoholism (ESBRA), vice-president of the International Society for biomedical research on Alcoholism (ISBRA). He is co-leader of the GDR 3557 Psychiatry-Addictions.

The team has organized key international events such as the 17th ESBRA congress in Lille (350 participants) and three Sino-French Oncology Congresses in China.

At the national institutional level, the DU is a member of the Study Section 4 (Neuroscience) of Inserm. A professor is member of the 69e section of the CNU.

The unit has worked to promote collaborations between Inserm and the NIAAA (National Institute on Alcohol Abuse and Alcoholism), which is the US national institute of the NIH (National Institutes of Health) dedicated to research on alcohol use disorders. This resulted in the participation of the NIAAA's director to the first national translational research day on addictions on June 3, 2024 organized by the unit, and the DU taking part with the NIAAA's director to a French-American roundtable in Washington for the 60 years anniversary of Inserm in November 2024.



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

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maîtres de conférences et assimilés	5
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	8
Sous-total personnels permanents en activité	16
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	3
Post-doctorants	2
Doctorants	6
Sous-total personnels non permanents en activité	13
Total personnels	29

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	С	PAR
Université de Picardie Jules Verne	6	0	6
Autres	2	0	2
Total personnels	8	0	8

# **GLOBAL ASSESSMENT**

Strengths:

Area 1: GRAP is the only French team exclusively dedicated to research on alcoholism, and uniquely combining research on the psychiatric and hepatic consequences of alcohol misuse.

From basic research using cellular and animal models to clinical trials, GRAP works along two main axes, i.e. the neurobiology of alcohol addiction and the pathophysiology of two major alcohol-related liver diseases. The GRAP has a great, and a rather unique potential for investigating the hepatic/brain cross-talk in alcohol-related hepatic and psychiatric diseases.

GRAP has two major relevant goals. One is to produce basic knowledge to be used for personalized care and precision treatment for alcohol use-related psychiatric (including addiction) and liver pathologies. The other goal is for the produced knowledge to benefit society rapidly through, for example, the development of prevention actions or tools, the training of healthcare professionals, and the promotion of changes in clinical practice.

The GRAP is a small unit composed of permanent scientists and hospital practitioners with a well-balanced expertise in preclinical and clinical studies particularly adapted to the unit's project. The GRAP's financial resources have allowed the recruitment of non-permanent staff (PhD students, postdocs and engineers), equipment renewal and the acquisition of novel equipment.

Area 2: GRAP's scientific reputation is excellent. The unit is leader at the national research area and is part of the European research area, with fruitful collaborations with major European research groups (e.g. CIMH, Germany; Univ Camerino, Italy). As signs of national, European and international recognition in the alcohol field, the DU is president of the French Society of Alcoholology (SFA), European Society for Biomedical Research on Alcoholism (ESBRA), and vice-president of the International Society for Biomedical Research on Alcoholism (ISBRA).



Regarding attractiveness over the last contract, the team has recruited a MCU, attracted two psychiatrists and obtained two new university positions (MCU and Junior Professor Chair). Thanks to its high funding capacity (>650 k€/per year), the GRAP benefits from top-notch equipment and technologies, that are all relevant to the unit's research project and contribute to its attractiveness.

Area 3: Regarding scientific production, the team has followed an upward trajectory in both research axes, with publications in more generalist journals that have greater visibility (Neurosci Biobehav Rev, 2019; Science advances, 2021; Cell Mol Life Sci, 2022). Moreover, this trajectory seems secure with publications in even more impactful journals in 2024 (Brain, Gut microbes).

Area 4: The unit connection to society is impressive. The unit maintains extensive connections with the society at both local and national levels. These interactions are reflected in its participation in public scientific outreach events, prevention campaigns, collaborations with patient associations, and initiatives to promote research to a broader audience.

#### Weaknesses and risks:

The committee has no concerns about the few minor weaknesses noted below, which the unit has the means to address, considering the upward trajectory it has taken over the past contract and some already engaged actions.

Area 1: All researchers are teacher-researchers. Therefore, the team suffers from a lack of full-time permanent researchers, even if two tenured research engineers fulfill all requirements of full-time researchers. The unit would benefit at applying to tenured researcher positions at the different *ad hoc* Inserm scientific committees.

Area 2: The funding of GRAP mostly depends on regional (University, regional council) and national foundation (INCA, IRESP) calls. The unit now has the publication track record and collaborative network to apply as a PI for competitive national (ANR) and international grants.

The committee has however a concern about the communication between the members of the two research axis. The scientific relevance of testing collaborative hepatic/brain hypotheses is growing. The preclinical and clinical expertise present is exceptional and complementary for tackling the associated challenges. There is a risk that this unique strength of the unit and valuable opportunity may be lost or underexploited if a joint research strategy and human resources plan between the two axes are not implemented by consensus.



# **DETAILED EVALUATION OF THE UNIT**

# A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Regarding 'Scientific quality and output', research groups studying alcohol bingeing and addiction were advised to aim for at least one high-impact journal publication per year by focusing on key research questions, utilizing advanced technologies, and gathering multidisciplinary data. The committee recognized that implementing this process will take time. The unit has considered this recommendation as evidenced by a review in the prestigious Neurosci Biobehav Rev. in 2019, and an original publication in Science Advances in 2021. Although not to be considered for this contract but supporting the ascending trajectory, a publication by the 'addiction' group has been accepted by the high profile journal BRAIN in April 2024.

Regarding academic reputation and appeal, the committee advised working on enhancing academic recognition. During this contract, the unit has established new collaborations with the most renowned European teams working on alcohol and alcoholism (CIMH, Germany; Univ Camerino, Italy), associated with a grant (ERANET 2018 – PSI-ALC) and results published in shared (Science Advances 2021) or independent (Brain, 2024) publications, and with generating new grant applications (pending results; PRCI-ANR-DFG 2024). Regarding the USA, work is currently in progress with the DU promoting the development of a research program between Inserm and the NIAAA (National Institute on Alcohol Abuse and Alcoholism), with the objective of securing funding for collaborations between GRAP and alcohol addiction laboratories in the USA.

Regarding unit organisation and life, the committee advised to run the lab meetings in English and to organize annual retreats. Regarding the first point, progress have been made in this matter. Regarding the second point, this has not been implemented yet. To the suggestion made to the team leader to increase balance between research activities and health policy/prevention-related activities, he has applied for a professor position at the IUF (French Institute for Advanced Studies), which would relieved him from 2/3 of his teaching duties if accepted.

Regarding the strategy and the five-year plan, the recommendation to focus on a limited number of hypotheses and explore them from different and complementary perspectives has been taken into account. This is notably reflected in the focus on studying new treatments for AUD, from neurobiological mechanisms to therapeutic effects, within a translational and precision medicine framework. Complementary perspectives have been provided through new French and European collaborations. The advice to implement state-of-the-art technologies has been followed with the addition of calcium imaging techniques, optogenetics, and chemogenetics, complementing existing challenging methods such as in vivo fast-scan cyclic voltammetry and patch clamp.

It was also recommended to refine the translational studies by establishing connections between basic research and clinical work within the unit. In terms of translational research on AUD and psychiatry, studies on AUD and schizophrenia (Gierski et al; Addict Behav, 2022), as well as AUD and anxiety (Persyn et al., Alcohol Clin Exp Res. 2018), have been published, involving both clinicians and basic researchers from the team. Given the context and available resources, translational research on biological markers and the treatment of AUD has logically been conducted through external collaborations, resulting in two papers, including one published in Science Advances. Additionally, results from a holistic approach have been published, establishing relationships between cirrhosis and alcohol-related cognitive impairments (Angerville et al., Alcohol Alcohol. 2024), involving clinicians from the team.

# **B - EVALUATION AREAS**

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

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

The GRAP is the only research unit in France exclusively focused on alcohol consumption, which makes the unit highly visible in France and abroad. It is a single-themed unit dedicated to the neurobiological mechanisms of excessive alcohol consumption, the development of alcohol use disorder (AUD), and their consequences on hepatic physiology, that it investigates by combining preclinical and clinical studies. Over the evaluated period, the team was particularly focused on the vulnerability to develop binge drinking behaviour and alcohol-related liver diseases, including alcoholic hepatocellular carcinoma. This project addressed a major public health challenge related to increased binge drinking among the young population. Its strength relies on its translational and holistic nature. Overall, over the evaluated period, the scientific objectives of GRAP were well defined, well focused and can be considered as **excellent to outstanding**.



#### Assessment on the unit's resources

The GRAP is a small unit exclusively composed of permanent scientists with teaching duties (lecturers and professors) and hospital practitioners, with a well-balanced expertise in preclinical and clinical studies particularly adapted to the unit's project. However, it suffers from a lack of full-time permanent researchers, in spite of the presence of two full-time research engineers serving as principal investigators. The GRAP receives substantial recurrent funding from its institutions (75 k€ yearly) with respect of its size. It has been very active and successful in fundraising (>650 k€/per year), allowing the recruitment of non-permanent staff (PhD students, postdocs and engineers), equipment renewal and the acquisition of novel equipment. This also allows the GRAP to be fully autonomous for most of its research. Overall, the unit's resources are **very good to excellent**.

#### Assessment on the functioning of the unit

The expertise is well balanced between basic researchers and clinical scientists, favouring the development of translational research. The transdisciplinary feature of the unit (psychiatric and hepatic levels) offers unique opportunities for a holistic research. However, suboptimal communication between these two major axes could endanger this key strength of the unit. Scientific animation appears to be quite limited, with no seminar program with external speakers, and only monthly lab meetings. However, regarding this last point, the small size of the GRAP certainly facilitates one-to-one daily communication. Training opportunities are offered to all staff, and students are encouraged to participate in national and international conferences. The policy of the unit is to pool funds within the unit as far as possible and to mutualize common reagents and equipment, favouring the emergence of as-yet-unfunded projects, testing novel hypotheses and realisation of pilot studies. Overall, the functioning of the unit is **very good**.

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

#### Strengths and possibilities linked to the context

The GRAP is the only unit in France working on the causes and consequence of excessive consumption of alcohol that it investigates through a translational approach combining preclinical and clinical studies and transdisciplinary approach (hepatic and psychiatric impacts). Its major strength relies on its unique capacity to conduct studies devoted to brain mechanisms of alcohol addiction and to alcohol-related liver diseases. This allowed the GRAP to acquire a leading position on these topics at the national and international levels.

The main discoveries of the GRAP in the field include, among others, *i*) the characterization of the cerebral and cognitive impacts of binge drinking, including white matter damage, impairments in memory, recognition, and emotion processing, *ii*) the demonstration of the moderating role of a genetic polymorphism in the BDNF gene in the relationship between the intensity of binge drinking and impulsivity and negative emotions, *iii*) the demonstration of the effectiveness of psilocybin in reducing relapse in alcohol consumption after abstinence in "alcohol-dependent" rats, through the restoration of the altered mGlu2 receptor expression in the nucleus accumbens, in frame of an international consortium gathering several labs in Europe, Australia, and the US, *iv*) the establishment of a new statistical model for binge drinking pattern classification in college-student populations and *v*) the identification of mechanisms underlying tumor aggressiveness in a model of "ultra-chronic" exposure of liver cells to alcohol.

The GRAP is the first lab that developed an animal model of binge drinking behavior in the rat that enabled the unit to propose a mathematical and statistical model of binge drinking behavior.

The GRAP implemented and is leading the CHIEF cohort of nearly 5000 patients with alcohol-related hepatocellular carcinoma (HCC), allowing them to access to a population of patients with HCC of alcoholic origin for clinical studies.



#### Weaknesses and risks linked to the context

There is no major weakness or risk identified in the GRAP scientific strategy, which relies on the complementary expertise of its staff in preclinical models and clinical studies, well-established international collaborations and strong interactions with the University Hospital as well as regional (FHU A2M2P), national (GDR Psychiatry/addiction, National Alcohol Network REUNIRA, NACRe, etc.) and international (European and International Societies for Biomedical Research on Alcoholism) networks.

However, the absence of full-time tenured researchers in the unit could hinder or slow down the development of ambitious projects and the mastering of key technologies by the laboratory. For instance, the development of electrophysiological studies associated with optogenetics is uncertain following the departure of the researcher in charge of these studies recruited thanks to the Chair of Excellence funded by the Picardie Region. In this regard, the recent allocation of a Junior Professorship position to the GRAP is certainly an important asset in the scientific strategy of the unit.

Although they are organized to engage in research activities (HDR in progress), the psychiatrists on the team hold exclusive clinical positions at a psychiatric hospital (CHS), which poses a risk. It is therefore critical to continue strengthening ties with the new teams at the university hospital (CHU) and to define clear scientific objectives for the psychiatry research line.

The scientific relevance of testing collaborative hepatic-brain hypotheses is growing. The preclinical and clinical expertise present is exceptional and complementary for tackling the associated challenges. There is a risk that this opportunity will be missed if a joint research strategy between the brain and hepatic research axes is not discussed and implemented by consensus.

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

#### Strengths and possibilities linked to the context

The GRAP benefits from substantial financial support from its institutions (~ 75 k€ yearly) that is mostly used for common reagents, equipment renewal and novel technology. In addition, The GRAP has been very successful in securing fundings, mostly from national and regional agencies (IReSP, INCA, Hauts de France Region, ACESF, Association GRAMM), with a total annual income >650 k€. The majority of these grants (18/21) are coordinated by the GRAP members. This demonstrates the support and credit of the unit among the French scientific community.

This substantial financial support enabled the GRAP to acquire novel equipment over the reporting period, including a fluorescence imaging-optogenetic system for the patch-clamp set-up, a β-scintillation counter, 12 operant cages, mazes for rats and mice, a video tracking system, an *in vivo* calcium imaging setup (INSCOPIX system) and a mobile rodent anesthesia system. Together with previously available equipment, this allows the unit to benefit from state-of-the-art technological resources adapted to its projects, not only within the unit, but also within the platforms hosted in the CURS building (MRI imaging, cellular imaging and animal facility platforms).

Regarding human resources, the GRAP has recently integrated two psychiatrists of the CHI Clermont de l'Oise with respective expertise in treatment-resistant schizophrenia, and psychosocial rehabilitation. Both will bring their expertise as clinicians to several research axes of the unit (e.g. risk and vulnerability factors, comorbidity with schizophrenia etc.) and participate in the inclusion of specific patients in clinical research protocols.

#### Weaknesses and risks linked to the context

Although the GRAP is successful in fundraising, the number of ANR and international grants obtained by the unit remains quite limited.

As previously mentioned, the human resources in terms of tenured scientists, is currently limited in the GRAP, which may preclude the development of novel research axes and ambitious projects on the long term.

The integration of new psychiatrists into the team is an opportunity; however, as a recent development, it should be a point of attention for the team to ensure mutual benefit.



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

#### Strengths and possibilities linked to the context

The unit is strongly committed to providing all its staff training opportunities, including qualifications, continuous education, and participation in conferences. Students and post-docs are encouraged to participate in training schools and to participate in national and international conferences, where many of them received poster and/or presentation prizes (9 congress prizes from 2019 to 2023).

They are also encouraged to acquire an experience in teaching. The majority of GRAP past members have secured permanent positions or continue in postdoctoral positions, underlying the quality of the training to research at the GRAP.

The GRAP has implemented a health and safety orientation booklet for newcomers, designed to introduce the structure, contacts for occupational health, first aid responders, etc. This booklet also outlines the laboratory's principles and best practices, and explains the role of the Health and Safety Register.

Regarding sustainable development, the unit donated an operant behavior equipment (value at 140 k€) to the Sciences Faculty of the Ibn Tofail University in Kenitra in Morocco, to enable a laboratory to be equipped and facilitate future collaboration, rather than disposing of an equipment in perfect working condition.

Regarding protection of scientific data and computer systems, the unit members have access to secured storage spaces for several years at UPJV, and updates or renews software and computers as much as possible. The unit also complies with data protection rules (GDPR) with requests made to the CNIL, CMR product storage and handling, with the Nuclear Safety Agency for radioactivity manipulation, and with the policy of Inserm in terms of prevention of psychosocial risks. Notably, the GRAP has a point of contact for gender-based and sexual violence.

#### Weaknesses and risks linked to the context

The human and scientific cohesion between the unit's two major research axes (cerebral mechanisms underlying alcohol addiction and alcohol-related liver diseases), which form the foundation of its unique positioning both in France and abroad, as well as its visibility, needs to be actively strengthened.

Lab meetings are only organized monthly, which provides students and postdocs limited opportunities to present their work and discuss their data with permanent scientists in a formal manner.

The gender parity is not yet achieved (especially among tenured researchers: 6 males and 3 females) and needs to be improved.

Regarding the issue of gender-based and sexual violence, it is important to continue the pedagogical efforts within the team and with the ongoing engagement of the DU.

The GRAP has not yet implemented an electronic notebook, which is essential to ensure data traceability and scientific integrity.

Communication within the unit should be improved. Information about training sessions offered by the supervising authorities, as well as key deadlines for filling annual evaluation documents or applications to internal courses for career progression, is not consistently shared with all BIATS staff. Additionally, the mandatory annual interviews for all BIATS are not conducted every year.



#### Assessment on the attractiveness of the unit

The GRAP attractiveness is **excellent**, as shown by i) the frequent invitations of GRAP scientists to give conferences at national or international congresses or institutions (26 over the reporting period), ii) their high fundraising capacity (> 650 k€ collected yearly, mostly from national agencies) that allows the recruitment of non-permanent staff and the renewal of the unit's equipment, iii) their participation in various scientific boards (Inserm neurosciences panel, CNU, national Academy of Pharmacy) and meeting organization (European congress of the ESBRA society, national alcohology meeting, Sino-French oncology congresses), iv) their responsibilities in national and international learned societies (SFA, ESBRA, ISBRA), and networks (REUNIRA, GDR Addiction, NACRe), v) their affiliation with a European multicenter 'preclinical trials' platform (Germany, Italy, and France), vi) the regular opening of positions to attract young scientists in the GRAP (chair of excellence, junior professor chair, assistant professor), that also demonstrates a strong support from the UPJV. GRAP researchers and students also received 12 awards over the reporting period.

- 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 success of the GRAP in fundraising allowed the unit to hire seven postdocs, fifteen graduate and PhD students (5 of them coming from a different university) and two assistant-engineers and technicians (all funded by the unit) over the reporting period. The GRAP also hosted two PhD students from Italy and Spain for their 6-month mobility training course, and three students for their final pharmacy thesis (ERASMUS Program), and recruited a young scientist on a permanent position (Lecturer position at UPJV in 2022). The GRAP hosted two visiting scientists (one professor from New Jersey University who visited the GRAP once a year during the reporting period and one professor from the University of Reims Champagne-Ardennes).

The UPJV strongly encourages the expansion of the GRAP through the regular opening of positions in the unit. These include a Junior Professor chair position (tenure track position) that should lead to the recruitment of a new PI on a permanent position as a university professor, and a new lecturer position.

GRAP researchers are regularly invited (more than 25 invitations over the reporting period) to give conferences at national and international congresses and institutions (congresses of the European Society for Biomedical research on Alcoholism and the International Society for Biomedical research on Alcoholism, Congrès français de psychiatrie, Société Française d'alcoologie meeting, congress of the European Association for the Study of the Liver...etc.).

They are also very active in meeting organization. They organized the 17th congress of the European Society for Biomedical Research on Alcoholism in Lille in 2019 (more than 350 participants), the first Fall e-School of Alcohol Addiction Research in 2021 and the first national alcohology meeting in 2018 in Paris with the support of Inserm (>150 participants). They coordinate the national alcohol research network REUNIRA and created the AlcoolConsoScience resource website to train healthcare professionals on the impact of alcohol consumption on health. They contribute to the NACRe network on cancer and organized three Sino-French congresses in this context.

They regularly review grants from various French (ANR, IReSP-INCA) and foreign (FNRS in Belgium, DFG in Germany and FNS in Switzerland, Austrian Research Agency) agencies and are part of various scientific boards (Inserm neurosciences panel, CNU, national Academy of Pharmacy) and of editorial boards of specialized journals (Journal of Dual Diagnosis, the Alcohol & Alcoholism Journal).



Several GRAP researchers obtained prizes, including prestigious ones such as the "Prix lutte contre l'alcoolisme" from the National Academy of Medicine in 2019, and the prize MILDeCA-OFDT" from Inserm in 2018. Notably, several prizes rewarded early career scientists (best oral communication prize at ESBRA meeting (2), thesis prize from UPJV), underscoring the quality of the formation through research and mentoring at the GRAP.

Despite the lack of local research dynamics in neuroscience, GRAP has established collaborations with two other laboratories at the CURS and the CHU (LNFP: Laboratory of functional neurosciences and pathologies and CHIMERE: Surgery, Imaging, and Tissue Regeneration of the Cephalic Extremity - Morphological and Functional Characterization). Of note, UPJV is in the process of launching a call for proposals for collaborative projects by for teams on site, to energize local collaborations.

Thanks to its high funding capacity, the GRAP benefits from top-notch equipment and technologies, such as a fast-scan cyclic voltammetry set-up, three electrophysiology set-ups including one patch-clamp set-up equipped with optogenetics, an *in vivo* calcium imaging set-up, operant drug-self-administration battery (24 cages), and cages equipped with automatic sippers and touchscreens that are all relevant to the unit's research project and contribute to its attractiveness. In the CURS building, the GRAP benefits from shared technological facilities, including a cellular imaging and protein analysis platform, an MRI platform for small animals, an animal care facility platform where the GRAP has its own rooms. The GRAP has also access to local mass spectrometry, electronic microscopy, imaging and flow cytometry facilities at UPJV.

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

The GRAP still suffers from the absence of permanent researchers. During the reporting period, a regional excellence chair focused on the development of electrophysiological studies was opened in the GRAP but the recruited scientist did not meet his research objectives and his contract was not renewed by the unit. This strongly limits the opportunity to develop novel research axes. The report mentions the potential recruitment of new group leaders and the growth of the unit, but there is no clear strategy to achieve that goal.

Despite its efforts, the team has not been successful in sustainably motivating CURS teams to contribute to scientific animation at the CURS level, which could serve as a lever to promote collaborations and energize the neuroscience community.

There is no seminar program with external speakers.

The GRAP has limited access to patients with AUD at CHU-AP, even though this did not significantly impact its research, as access to human samples and datasets is ensured through well-established collaborations with other hospitals. The situation should progressively improve thanks to the recruitment of two hospital practitioners specialized in psychiatry and addictions medicine at the CHU.

The funding of the GRAP mostly depends on regional and national (INCA, IRESP) calls and the unit only obtained one international grant (ANR-Eranet).

The capacity of the GRAP to attract students and early career researchers from abroad is limited.

#### EVALUATION AREA 3: SCIENTIFIC PRODUCTION

#### Assessment on the scientific production of the unit

The scientific production was **excellent** with 165 publications (125 original research including around 40% as PI, and 40 reviews) mainly in international peer-reviewed journals, around 200 oral and poster presentations in national and international meetings, ten PhD thesis defended, and seven book chapters. Thanks to their extensive preclinical and clinical collaborative research network, some laboratory members have contributed to many journal articles publications as collaborators (around 47% of the total), most of them dealing with issues related to alcohol consumption in humans.

- 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 unit has made major contributions in the fields of binge drinking, alcohol addiction, and alcohol-related hepatocarcinoma over the reporting period. For example, its preclinical models of binge drinking and relapse after abstinence in alcohol-dependent subjects are well established, enabling the unit to investigate the underlying neurobiological mechanisms, identify biomarkers of susceptibility, and test therapeutic innovative tools. During the reporting period, the unit has been very productive on these preclinical approaches and published about 18 original research articles, and 1 review in the high-profile Neuroscience & Biobehavioral Review. A major advance in this work has been the identification of potential biomarkers of alcohol withdrawal-associated brain suffering in AUD patients and in the preclinical model.

Original research publications with members of the unit as first (or co-first) and/or last or corresponding author have been published mainly in international peer-reviewed journals. Most of these journals were specialized (e.g. Alcohol & Alcoholism, Addiction Biology, Addictive behaviors) or more generalist recognized journals (e.g. Psychopharmacology, Frontiers in Pharmacology, Frontiers in Psychology...) of low- to medium-profile, but recent original studies have been published in more generalist high-profile journals (e.g. Gut microbes, Cellular and Molecular Life Science; Science Advances). Clinical work in gastroenterology, which accounts for a significant proportion of the total unit's output, has been published in recognized journals in the field, such as Lancet Gastroenterol Hepatol.

The number of citations for articles produced during the reference period has significantly increased compared to the previous contract period and is now between 2,000 and 3,000 citations.

The unit has developed fruitful collaborations with national and international preclinical and clinical researchers, leading to significant publications.

Ten students defended their PhD thesis, which is a significant number considering the team size and number of HDRs.

In total, the unit produced 165 journal articles publications over the reporting period. Excluding PhD, and postdoc and including associate professors (2) in the unit research workforce (2 PU-PH, 2 PU, 1 MCU-PH, 3 MCU, and 2 full-time engineers), this leads to around 2.2 journal articles publications/year/researcher. If only journal articles publications with a GRAP leadership role (87) are considered, this leads to around 1.2 journal articles publications/year/researcher which remains an excellent publication rate for a unit where most of the researchers also have teaching and/or clinical duties. Even if the PhD students contribute to only 12% of the total number of journal articles published during the reporting period, they contributed significantly to GRAP's output as co-authors and, with one exception, as first authors, accounting for around 40% of journal articles publications. PhD students also make a significant contribution to GRAP's output through oral communications, and poster presentation at national and international congress/journeys.

Regarding scientific integrity and ethic, the unit's policy is to present and discuss all projects including experimental design and scientific results in lab meetings. The unit has also incorporated the recommendations from the ARRIVE Guidelines into the design of their scientific production. Unit members are well-informed of the new recommendations for animal experimentation, as some permanent researchers are members of the "Comité Régional d'Ethique en Expérimentation Animale", leader of the Structure du "Bien-Être Animal", and training supervisor for Master students. For studies on hepatocarcinoma, the unit has also recently developed a cellular model of alcohol exposure and is also engaged in the development of organoids. The unit is committed to Open Science: about 40% of the publications with members of the unit as first (or co-first) and/or last or corresponding author were published in Open access journals.

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

Few works have been published in international journal with high profile. Participation in international general meetings appear limited. It is advisable to avoid rather than limit publication in certain journals whose publication processes are criticized, such as Frontiers, which is often considered a predatory journal.

The scientific production of the unit's members with teaching activity (lecturer and PU) is uneven.



The unit's commitment to Open Science seems still limited. Beyond publications in open access journal, the unit should provide greater transparency regarding raw data and experimental methods to improve reproducibility and to strengthen confidence in the published results. As stated by the unit, the implementation of an electronic laboratory book could facilitate regular monitoring and control of experimental works by Pls.

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

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

The inclusion of the unit's research in society is **excellent to outstanding**. The unit maintains extensive connections with society and the scientific community. These interactions are reflected in its participation in public scientific outreach events, prevention campaigns, collaborations with patient associations, and initiatives to promote research to a broader audience. By taking part in national and local public outreach initiatives, the unit effectively shares its research findings with non-academic audiences, contributing to societal debates on health and addiction. Disseminating research results constitutes an essential part of the unit's activities, representing about 10% of its overall efforts.

- 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 is well-established within the institutional landscape (such as "Santé publique France", OFDT), which facilitates its participation in public health initiatives and prevention campaigns. Participation in national campaigns such as "Dry January" demonstrate the unit's strong presence in public health initiatives, further connecting their research to societal needs. The unit contributed to the latest Inserm collective expertise on alcohol consumption-related harm.

The unit is part and/or coordinates networks like the REUNIRA or NACRe networks, which involve patient associations, and actively contributes to various scientific committees and working groups, demonstrating its commitment to advancing addiction and cancer research.

The unit collaborates with pharmaceutical companies (4P-Pharma for the development of a medication in the field of addictions, Bioprojet Biotech company on the development of an inverse agonist of histamine H3 Receptors).

The unit has created multiple resources aimed at both the general public and specific stakeholders. These products range from articles and book chapters in French, to educational websites, and tools to contributions in national awareness campaigns. The creation of the "AlcoolConsoScience" website and the development of self-assessment tools are crucial products that directly benefit the general public and healthcare professionals by providing reliable information and resources to manage alcohol consumption. The unit also offers an online self-assessment tool recommended by the Addiction Prevention Network.

The unit offers a wide range of training opportunities, from master's courses to autumn schools, and participates in educational programs.

The unit is deeply involved in public dissemination, frequently contributing to societal debates around alcohol and addiction. This occurs through various channels, including media appearances, educational programs, and participation in public events. For example, the unit is involved in national initiatives such as the Brain Week and the Science Fair, as well as local events like "Les Mardis de la Santé" in Amiens. The unit regularly engages with media outlets to raise awareness about alcohol risks, leveraging their research to inform and educate the public. These events enhance its visibility and social impact by sharing knowledge on alcohol and addiction with a broad audience.



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

While the unit has developed valuable tools like the online self-assessment for alcohol consumption, the absence of patents or clear valorization strategies might limit the potential for these tools to have a broader impact. The long-term sustainability could be improved by formalizing procedures for updating, disseminating, and analyzing the impact of these resources, such as the activity of the "AlcoolConsoScience" website.



# **ANALYSIS OF THE UNIT'S TRAJECTORY**

#### ACHIEVEMENTS:

This single-team unit has a unique feature in France: it studies both alcohol addiction and alcohol-related liver diseases, utilizing preclinical approaches on rodent models as well as clinical research in patient populations and healthy subjects, leading patient cohorts and conducting clinical trials.

The general aim is to develop translational research to better understand the role of vulnerability factors in alcohol addiction and associated damages, and to develop new treatments.

The unit's research lines of the previous plan were (i) the study of factors involved in binge drinking behavior, (ii) the study of psychiatric comorbidities of alcohol use disorder (AUD), (iii) the search for new treatments, and (iv) the study of the pathophysiology of alcohol-related liver diseases.

(i) Research on the factors involved in binge drinking has produced a significant amount of results with 20 publications (10 clinical and 10 preclinical). Importantly, the unit has built a cohort of young binge drinkers (n=100) with behavioral data, EEG, fMRI, and genetic data, which is unique in France. Regarding human studies, complementary approaches have been used to classify binge drinking behavior, to characterize it at the psychological level, to identify genetic moderators and neurobiological markers. Advanced relevant methods have been used from psychometric tests and statistical methods (unsupervised machine learning techniques, dominance analysis) to neuroimaging (fMRI) and genetics (Tagman allelic discrimination assay), legaling to an integrated conceptualization of binge drinking. Also, GRAP's research included development of tools for prevention (e.g. MyDefi smartphone application), their evaluation through collaborative research (SmartBinge study, multicenter national randomized controlled trial), their adoption by healthcare personnel for prevention (interview of 101 pharmacists in Hauts-de-France, Hien et al., 2022). Regarding animal studies, the unit has developed a voluntary consumption-based binge drinking model in rats, which has been implemented in other labs, including in the USA. This model has been used to evaluate cognitive and neurobiological alterations resulting from binge drinking history. This model has also been used to evaluate alcohol use disorders pharmacotherapies including baclofen on alcohol self-administration and neurobiological consequences of binge drinking. Sex differences have been considered, notably regarding the effect of binge drinking on hippocampal- and striatal-dependent functions, as well as baclofen effect.

(ii) Regarding psychiatric comorbidities of AUD, the departure in 2021 of the two addiction psychiatrists has limited the study of psychiatric comorbidities of alcohol use disorder (AUD). An interesting attempt toward a holistic approach has been produced with the study of Alcohol-related cognitive impairments in patients with and without cirrhosis (Angerville et al., 2024).

(iii) Regarding the search for new treatments, over the last years, a focus has been made on the evaluation of treatment for alcohol addiction, and in particular the use of psychedelics. This has led to a publication in Scientific Advances in 2021 and the collection of results for a publication in BRAIN in May 2024. Based on their preclinical research based on several complementary animal models, they have evidenced several targets, tested several molecules and hypothesis, some of them being already translated in humans and published (sugar as a powerful substitute during alcohol withdrawal in a subpopulation in AUD inpatients and in post-dependent rats; Alaux-Cantin et al., Addict Biol, 2021; Alarcon et al. Addict Biol, 2021). Regarding molecules tested in rats (HDAC inhibitors, N-acetylcysteine (NAC), DRD3 inhibitors, H3 inhibitors, R- and S-baclofen, psilocybin, LSD, R- and S-ketamine), NAC has been submitted for a PHRC (Hospital Clinical Research Program) application, the H3 inhibitor has been tested in patients (NCT03424824), and two clinical trials on psilocybin and LSD are currently awaiting ethical approval.

(iv) Regarding research on the pathophysiology of alcohol-related liver diseases, the team focuses on severe alcoholic hepatitis and hepatocarcinoma from cellular models and studies in humans, to clinical trials.

Studies on non-alcohol related hepatocarcinoma also bring critical knowledge: comparing patients with alcohol-related hepatocellular carcinoma (HCC) or non-alcoholic etiology, the team confirmed that treatment response depends on the cancer's etiology.

A major objective of the group is precision medicine, through the identification of markers of treatment resistance or response, and the improvement of treatments by studying the underlying mechanisms of efficacy or resistance. In this context, the team has established an original cellular model of ultra-chronic exposure (several months) to alcohol in liver cells at various stages of hepatocarcinoma. Basic research is devoted to understand the molecular mechanisms, an important aspect of the basic research is the identification of mechanisms supporting resistance to treatment (Fouquet et al., 2022) or the identification of new treatments. This preclinical research led to a publication as last author in a generalist renowned journal in 2022 (Marié et al., Cell Mol Life Sci) where the team identified the mechanisms underlying tumor aggressiveness together with the effects of alcohol withdrawal.



Regarding severe alcohol hepatitis, research is devoted to gaining knowledge on the mechanisms by which the reference treatment improves or not the poor prognosis of this disease. This notably led to a publication as last author in 2024 in a highly renowned journal (Gut microbes). In parallel, the team has co-signed in high impact specialist or generalist medical journals (Lancet Gastroenterol Hepatol. 2022, JAMA 2023) the results of two clinical trials evaluating additives or alternatives (early liver transplantation) to medical treatment in non-responding patients, as well as the results of a multicenter clinical study evaluating the influence of low alcohol consumption on the outcomes of alcohol-related compensated cirrhosis (J. Hepatol., 2023).

The CHIEF cohort of 5000 patients with hepatocarcinoma established by the team during this contract, together with the contribution to clinical trials published in prestigious journals, is supporting the French position of the team in clinical research on alcohol and non-alcohol related liver diseases. The basic research line is undoubtedly following an ascending dynamic with the last publications with high and increasing visibility as last authors.

**DIFFICULTIES:** The departure in 2021 of the two addiction psychiatrists has limited the study of psychiatric comorbidities of alcohol use disorder (AUD).

**REORIENTATION / STRATEGY:** Two hospital practitioners in psychiatry joined the team in June 2023. Their hospital practice is focused on psychosocial rehabilitation. For the next plan, their research activity is proposed to be focused on evaluating personalized therapeutic strategies for psychiatric disorders based on endogenous and environmental risk factors of vulnerability, the known impact of addictive behaviors on psychiatric disorders and cognition, the known pharmacological impact of psychotropic treatments on addictions and psychiatric disorders.

# INVOLVEMENT OF THE UNIT IN THE FIELDS OF ITS VARIOUS INTERVENTIONS AT THE NATIONAL AND INTERNATIONAL LEVELS

The GRAP is a key player in local, regional, national, and international research on alcohol use disorders, encompassing fundamental research, clinical research, prevention, and healthcare improvement.

The DU is coordinator of the national alcohol research network REUNIRA and creator of the AlcoolConsoScience resource website to train healthcare professionals on the impact of alcohol consumption on health. A professor is in the board of the Fetal Alcohol Syndrome network. An IR is team leader within the NACRe network (Nutrition, Physical Activity, and Cancer Research Network brings together public research teams and experts involved in the 'nutrition and cancer' field). The deputy director is leader of a cohort of 5000 patients with Hepatocellular Carcinoma (cohort CHIEF).

The DU is president of the French Society of Alcoholology (SFA) and of the European Society for biomedical research on Alcoholism (ESBRA), vice-president of the International Society for biomedical research on Alcoholism (ISBRA). He is co-leader of the GDR 3557 Psychiatry-Addictions.

The team has organized key international events such as the 17th ESBRA congress in Lille (350 participants) and three Sino-French Oncology Congresses in China.

At the national institutional level, the DU is a member of the Study Section 4 (Neuroscience) of Inserm. A professor is member of the 69e section of the CNU.

The unit has worked to promote collaborations between Inserm and the NIAAA (National Institute on Alcohol Abuse and Alcoholism), the US national institute of the NIH (National Institutes of Health) dedicated to research on alcohol use disorders. This resulted in the participation of the NIAAA's director to the first national translational research day on addictions on June 3, 2024 organized by the unit and the DU taking part with the NIAAA's director to a Franco-American roundtable in Washington for the 60 years anniversary of Inserm in November 2024.

Regarding training, almost all GRAP members are teachers and have responsibilities in training programs at UPJV. They have also produced e-learning modules. Regarding dissemination, the unit's work is remarkable with contribution to numerous of actions toward the lay public and the youth in particular. They have developed a smartphone app (MyDefi) which is used for both prevention, research, and sensitization to binge drinking of healthcare professionals.

#### THE UNIT SCIENTIFIC PROJECTION

In the next plan, the unit wants to more exclusively focus on alcohol addiction, the most severe form of AUD and alcohol-related liver diseases. They will continue working on binge drinking as a risk factor in the development of addiction and liver damages. They plan to continue using a multimodal approach. They will follow their cohorts, further develop the MyDéfi smartphone application, and continue their interventional efforts.



**From a prevention perspective**, they plan to develop actions within the university environment and work on initiatives during the Dry January campaign to promote the use of the MyDéfi coaching application. Studies on the effectiveness of smartphone applications in reducing alcohol consumption among young people are burgeoning. The GRAP current work is truly innovative in this context because their protocol includes a "placebo" application as well as measurement of the ethanol exposure marker.

#### THE POSSIBILITIES OFFERED BY THE UNIT'S ENVIRONMENT AND THE RISKS LINKED TO THE ENVIRONMENT

There is no real risk linked to the environment, which is supportive in terms of allocated positions, allocated fundings, and funding opportunities. Rather the committee feels that there are missed opportunities for improved organization. Even if the CURS is 'only' a building, integrating researchers into its management is important to its technical development and innovation capacity. Also, PhD students and post-docs should be motivated and given responsibility for organizing social events in the building. This would help foster collaboration and exchange.

Regarding science within the unit, the committee estimates that there is a risk of scission between the addiction/neuroscience axis and the liver axis. This would be detrimental to the identity of the unit and a big loss for research, patients, and Inserm. As stated by Dr Anne-Lise Pitel, renowned world expert in the Korsakoff syndrome (Cyceron, Caen), 'Despite numerous studies focusing on the effects of alcohol on the brain or liver, few studies have simultaneously examined liver function and brain damage in alcohol use disorder, and even fewer investigated the relationship between them'. Her team published a translational study in 2021 linking liver cytokines to brain damages, and concluded that their 'findings encourage considering new therapeutic strategies aiming at treating peripheral organs to limit alcohol-related brain damage.' These observations, together with the complementary expertise of the two lines of research of the GRAP unit, open very interesting perspectives for integrated research work between the two axis and for integrated therapeutic strategies.



# **RECOMMENDATIONS TO THE UNIT**

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

The committee recommends the GRAP to enhance the scientific and human cohesion between its two major research axes (cerebral mechanisms underlying alcohol addiction and alcohol-related liver diseases) which are the foundation of its original positioning in France and abroad and its visibility. In this regard, the GRAP should ensure that all strategic decisions are taken in a collegial manner and as far as possible on a consensual basis between the PIs of the two axes, notably considering that for the new contract, both the DU and co-DU will belong to the first research axis. The unit should establish equitable conditions and implement concrete actions that allow staff to develop a sense of fairness, of belonging to the same entity, and of commitment to the same scientific and medical challenges.

The committee recommends the unit to work on correcting the imbalance between the two axes in terms of human resources. The liver axis should play an active role in its development. It should focus on identifying a candidate to present for the Inserm recruitment competitions for tenured researcher positions. Various Inserm scientific committees could be relevant: CSS3, CSS2, CSS7 or even CSS6, depending on the candidate's profile.

The committee recommends that the GRAP organizes annual retreats and social events that bring together all team members to help foster scientific discussions, and a sense of belonging to a common entity.

The unit must continue encouraging researchers to defend their HDR and supporting them in preparing for their defense.

The GRAP must pursue its discussions with the university to become more involved in the governance of the CURS and in the operation and equipment policy of the platforms hosted at the CURS. Regarding scientific animation and interactions within the CURS, the committee recommends that early carrier scientists of the GRAP joint their forces with colleagues from other CURS units to re-establish regular seminars and organize joint social events, in order to foster scientific exchanges and collaborations.

The committee recommends the GRAP director and PIs to systematically run the annual interviews of BIATS staff (including those hired on fixed term contracts) and to schedule them earlier in the year, to allow for a better preparation of evaluations and/or applications to obtain promotions.

Finally, it recommends the GRAP to implement as soon as possible an electronic notebook which has become an indispensable tool for project follow-up and data traceability.

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

The committee recommends the GRAP to diversify its fundings and to increase the number of applications in response to ANR and international calls, taking advantage of its multidisciplinary approach, its recent successes and its numerous national and international collaborations.

In the same line, the GRAP should consider applying to Doctoral networks and Marie Skłodowska-Curie postdoctoral fellowships, in order to attract high-potential research fellows from abroad who will be potential candidates to University or Inserm tenure positions.

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

The team should continue on its positive current path by publishing articles with greater visibility, targeting more general scientific journals. Leveraging their strong translational approach, which is a key asset of the team, they can highlight their interdisciplinary work (brain-liver) and integration of clinical and preclinical studies. Additionally, they can further strengthen their scientific collaborations with international teams, capitalizing on the extensive scientific network in which they are already well established and recognized.

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

It is important for the team to continue their collaborations with industrial partners for their research results to further benefit to society. They should also consider the economic valorization of the tools they are developing, such as applications and assessment tools. Strategically promoting these innovations, could strengthen the team's presence in both the scientific and industrial sectors, while contributing to the broader dissemination of their work.



# CONDUCT OF THE INTERVIEWS

#### Date

**Start:** 01 octobre 2024 à 09h00

**End:** 01 octobre 2024 à 16h00

#### Interview conducted: online

#### INTERVIEW SCHEDULE

- 8:30-8:45 Huis Clos du comité en présence de CS Hcéres
- 8:45-9h00 Présentation du processus d'évaluation par le conseiller Hcéres et du comité d'experts
- 9:00-11h00 Présentation de l'Unité et de ses thématiques de recherche (réunions publiques)

9h00-10h00 : Présentation de l'unité avec les principales réalisations et le projet/la trajectoire par le directeur de l'unité GRAP, le Dr M. Naassila (30 min de présentation + 30 min de discussion)

10h00-10h30 : Présentation de la thématique «Troubles liés à la consommation d'alcool et maladies du foie » par I. Marcq (15 min de présentation + 15 min de discussion)

10h30-11h00 : Présentation de la thématique « Neurobiologie et traitement des troubles liés à la consommation d'alcool : modèles animaux et recherche translationnelle » par J. Jeanblanc (15 min de présentation + 15 min de discussion)

- 11:00-11:30 <u>Pause</u>
- 11:30-12h30 Discussions à huis clos entre le comité et 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-docs
  - 12:10-12:30 Discussion avec les scientifiques (sans le DU)
- 12:30-13:30 Pause déjeuner
- 13:30-14:00 Huis Clos du comité pour préparer les échanges/questions avec DU et tutelles
- 14:00-14:30 Discussion avec le DU
- 14:30-15:00 pause
- 15:00-15:30 Discussion avec les représentants des organismes de gestion/tutelles
- 15:30-16:30 Huis Clos du comité en présence de CS Hcéres en vue de la préparation du rapport
- 16:30 Fin de la visite



# GENERAL OBSERVATIONS OF THE SUPERVISORS



Amiens, le 10 Décembre 2024

Monsieur le Président

HCERES 2 Rue Albert Einstein 75013 PARIS

Direction de la Recherche 1, Chemin du Thil 80025 AMIENS Cedex 1 ☎ 03-22-82-74-55 *e-mail : drv@u-picardie.fr* 

Objet : Réponse officielle évaluation GRAP

<u>Vos Réf</u>: DER-PUR260025006 - GRAP- Groupe de Recherche sur l'Alcool & les Pharmacodépendances

Monsieur le Président,

Je tiens tout d'abord au nom de l'Université de Picardie Jules Verne et en particulier au nom du Directeur et des membres de l'unité de recherche Groupe de Recherche sur l'Alcool & les Pharmacodépendances – GRAP UMR INSERM 1247 à vous remercier pour la qualité du rapport d'évaluation ainsi que pour les échanges constructifs que nous avons pu avoir avec le comité lors de la visite du 1 octobre 2024.

En réponse aux points d'amélioration soulignés par le comité, le Directeur et les membres de l'unité ne souhaitent pas apporter d'informations complémentaires.

La gouvernance de l'UPJV tient à souligner qu'elle appuiera les recommandations formulées dans le rapport par les membres du comité concernant le maintien des actions préventives afin de limiter les violences sexistes et sexuelles. Également, la dynamique scientifique sous forme d'échanges entre les chercheurs des unités du CURS est encouragée. Toutefois le CURS étant un bâtiment hébergeant une partie des unités de recherche en santé, la notion de gouvernance qui lui est associée dans le rapport n'a pas lieu d'être.

Je vous prie d'agréer, Monsieur le Président, l'expression de mes sincères salutations.

Le Président de l'Université de Picardie Jules Verne Jules Mohammed BENLAHSEN The Hcéres' evaluation reports are available online: www.hceres.fr

Evaluation of Universities and Schools Evaluation of research units Evaluation of the academic formations Evaluation of the national research organisms Evaluation and International accreditation



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