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PERITOX - Périnatalité, risques toxiques et physiques environnementaux

Rapport Hcéres

► **To cite this version:**

Rapport d'évaluation d'une entité de recherche. PERITOX - Périnatalité, risques toxiques et physiques environnementaux. 2011, Université de Picardie Jules Verne - UPJV. hceres-02030377

HAL Id: hceres-02030377

<https://hal-hceres.archives-ouvertes.fr/hceres-02030377v1>

Submitted on 20 Feb 2019

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agence d'évaluation de la recherche
et de l'enseignement supérieur

Section des Unités de recherche

AERES report on the research unit

PériTox : Perinatalité and toxic risk

From the

University of Picardie

INERIS

February 2011



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Le Président de l'AERES

Didier Houssin

Section des unités
de recherche

Le Directeur

Pierre Glorieux

February 2011



Research Unit

Name of the research unit: PeriTox : Perinatality and Toxic Risk

Requested label : UMR INERIS

N° in the case of renewal : EA4285, UMI 01

Name of the director : Mrs Véronique BACH

Members of the review committee

Committee chairman :

Mr Robert BAROUKI, Université Paris Descartes, Paris

Other committee members :

Mr Denis SARIGIANNIS, Aristotle University of Thessaloniki, Thessaloniki, Greece

Mr Pierre-Louis TOUTAIN, Ecole Nationale Vétérinaire de Toulouse, Toulouse

One member of the review committee could not be present (CNU)

Observers

AERES scientific advisor :

Mrs Hélène GRANDJEAN

University, School and Research Organization representatives :

Mr Said KAMEL, University of Picardie

Mr Pierre TOULHOAT, INERIS

Mr George FAURÉ, University of Picardie

Mr Etienne DUVAL, University Hospital of Amiens

Mr Philippe MERVIEL, University Hospital of Amiens

Mr Emeric FREJAFON, INERIS

Mr Mhand HIFI, University of Picardie



Report

1 • Introduction

- Date and execution of the visit

The visit took place on February 2nd, 2011. It started by a short meeting of the committee. This was followed by a general presentation by the Unit head describing the history of this new unit and the general strategy (30 mn). Then, four themes were concisely presented and discussed for approximately 30 mn each. Presentations per se lasted for half of the time and the other half was left for discussion. The committee met with local and national representatives (University, medical faculty, clinical department, INERIS, etc.) and with the research scientists, technicians/engineers and students/post docs. An internal meeting of the committee members took place to discuss the evaluation report and included a short discussion with the unit director.

- History and geographical localization of the research unit, and brief presentation of its field and scientific activities

The PeriTox unit was created in 2008. It resulted from the gathering of a research team in the University which has traditionally focused on environmental regulation of general physiological parameters of the newborn, and of an Ineris team involved in toxicology (mostly electromagnetic waves, nanomaterials and pesticides). Staff members from clinical departments also joined the unit. Thus, in 2008, there was a major increase in the number of unit members. The unit staff kept increasing up to 52 in the present project. In its present outline, the unit has a strong expertise in studying the effect of perinatal exposure to diverse stressors on a variety of physiological parameters.

- Management team

The unit is headed by a Director from the University, a deputy director from Ineris and a deputy director from UPJV. The major themes of the unit are led by young scientists. The leadership of the unit has an important role in keeping close links between the different institutions supporting the unit.

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	8 (3,8 ETP)	12 (5,5 ETP)
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	6 (2 ETP)	8 (2,6 ETP)
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	9 (PH...) (2,1 ETP)	11 (2,6 ETP)
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	11 (6,1 ETP)	10 (5,1 ETP)
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	
N6: Number of Ph.D. students (Form 2.7 of the application file)	12 (30/6/11) +4 (9/11)	
N7: Number of staff members with a HDR or a similar grade	6	8 (ratio 0.36) 100% supervise thesis



2 • Overall appreciation on the research unit

- Summary

This is a single team unit with a variety of projects dealing with environmental effects on fetal and newborn development, with particular emphasis on global physiological energy balance, sleep, intestinal system, pulmonary and reproductive systems. The unit includes personnel from different origins : INERIS, University and Medical School at Amiens. The personnel number is quite large (52), however the average percent research activity of this personnel within the unit is around 33%.

The unit has developed technological platforms for the assessment of global physiological parameters (thermoregulation, sleep, ...) that are unique. More generally, the unit profile is unique in France in the sense of bringing together academic and research centre staff around a topic (perinatal toxicity) with very relevant implications for later life human health effects. In this way, the unit benefits from existing infrastructure both at the University and INERIS, as well as from actual clinical data from the Medical School of Amiens. In addition, it is vertically integrated coupling laboratory and pilot scale (mock-ups) installations, clinical observations and mathematical modeling in the attempt to track the continuum from in utero and post-natal exposure to clinical health effects during infancy as well as later life.

Although all projects have some connection with the general goals of the unit, there seems to be a need to pursue and possibly amplify the management policy for more focus.

The multiple origins of the scientists within the unit is certainly an asset for complementary expertise, but there are issues to be addressed related to geographical dispersion.

- Strengths and opportunities

- This unit is unique in France. It gathers several types of expertise in the field of perinatal pathology and toxicity. Projects dealing with general physiological homeostasis are original. The interaction between the INERIS, university and faculty of medicine appears to be fruitful despite the geographical separation;
- The unit gathers projects in human, in animal and model systems and in mathematical modelling. This should help in the interaction between experimental and clinical studies and indeed, this is the case for some of the projects;
- The unit has been able to develop novel experimental systems to detect general physiological parameters. The interaction with a small company in the field will help to develop these methods and is a good opportunity for valorisation;
- The unit has been able to establish several international connections (Australia) and to enter in national networks;
- It was also very successful in obtaining numerous grants.

- Weaknesses and threats

- During the last few years, the unit has grown and has added novel projects which have not all been fruitful. There is a risk of going into multiple directions and away from the most original aspects of the unit expertise. The unit has been able to obtain grants for its projects, but it should be careful to keep focused. While this is a threat, the committee is confident that the unit management is aware of this question and is determined to address it;
- While the general publication record is good in the investigated field (specialized journals), it is not outstanding. It could certainly be improved for some publications because of the unique expertise they have and the interaction with the clinical departments. The current rate of publications per scientist is ca. 2 per year over the multi-annual program 2006-2010. The policy leading to the increase in the quality of the publication (increase in the average IF) which has been successful during the last period should be pursued for the next period;
- The unit can still improve its international recognition;



- Multiplicity of locations : The distance separating the Ineris location and that of the University is a threat. While the committee believes that this has been addressed, the interaction can be enhanced by making use of modern telecommunication tools, creating thus virtual labs and joined-up teams;
- Absence of full time scientists may be a threat.

- **Recommendations**

- Keep the growth of the unit under control and do not agree to add new divergent projects even if they are supported by a grant.
- The rather relative low number of peer-reviewed publications is possibly related to the launching of too many new projects simultaneously. Even though this strategy helps fuel the growth of the research team by bringing in new funds, it poses the risk of steering the team towards a reduced focus. The Direction Team should make sure that the unit remains focused and that not too many disparate projects are launched at the same time. This « deepening » strategy will have certainly beneficial effects on the publication record of PERITOX. In addition, setting concrete individual targets on the annual publication record of the key unit scientists would definitely help in this direction.
- Hire or attract full time scientists. This is clearly not an easy task, but the originality of the team main projects can certainly be attractive.
- Improve international connections by engaging proactively in some of the following activities
 - International student and academic/research staff exchange within the European Union but also outside of the European borders (e.g. with US, Japanese and Chinese institutions);
 - Proactively engage in international research projects benefitting from the possibilities offered by the EU RTD framework programs (the 7th one is running throughout the next planning period) instead of focusing primarily on national funding;
 - Be more proactive in attracting international students by promoting advanced research training programs in languages such as English.
- Keep the close interaction between the clinical departments and the science departments;
- Improve the interaction with INERIS by increasing the research time of the INERIS scientists. Continue institutional incentives in INERIS to push the INERIS staff affiliated to PERITOX towards more peer-reviewed journal publications.

- **Production results**

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	20
A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research	9
A3: Ratio of members who are active in research among staff members $[(A1 + A2)/(N1 + N2)]$	100%
A4: Number of HDR granted during the past 4 years	3
A5: Number of PhD granted during the past 4 years	13 Mean duration : 40.8 month 0% abandon



3 • Specific comments

- **Appreciation on the results**

This unit has a unique expertise in the global physiological analysis of newborns, in particular thermal regulation, energy exchange, monitoring of sleep and respiration. They have made significant contributions on the perinatal regulation of these physiological parameters notably by environmental conditions including heat, humidity as well as chemicals. More recently they have studied the effect of electromagnetic waves and generated unpublished interesting data. The committee found that the mainstream studies carried by the unit are original and interesting, some of the minor studies were found to be less relevant.

During the last four years the unit published 88 original papers. This figure may not seem impressive considering the number of people in the unit, however it should be stressed that only part of the activity of the unit members is devoted to research as all of them have either teaching, hospital or routine toxicology duties. Most of their publications are in good specialized journals. During the last 4 years, their average IF was around 3,5 whereas the average IF was only of 2,7 during the previous term. They have therefore been able to improve the quality of the publications. Typically their work is published in J Pediatrics, J sleep research, AJP and sometimes in higher impact journals such Pediatrics, Gut, AJRCCM. Thus, considering their specific field of expertise (and the relatively low IF in this particular field) their scientific output can be considered as good to very good but not outstanding.

During the last 4 year period, 13 students obtained their PhD and several scientists their HDR (total number of HDR in 2010 = 8). Furthermore, the majority of the scientists in this unit have teaching duties. This is a very good educational activity.

The unit results from a unique partnership between the University, the medical campus and the INERIS. This partnership was established two years ago. Although no common publications have arisen from this partnership yet, both the data that were presented and the discussions with the different unit members and representatives of these institutions convinced the committee that the foundations of the partnership were now solid and continuously improving. There are additional national partnerships (the toxicology Antiope network for example) and there is a partnership with a private company for the modeling of newborn physiological homeostasis.

- **Appreciation on the impact, the attractiveness of the research unit and of the quality of its links with international, national and local partners**

When examining the history of the core group of this unit, it is clear that its attractiveness was considerable. Indeed, several university and clinical departments (for example pediatrics, obstetrics/gynecology) progressively established links with the unit in order to develop research capacities. Similarly, Ineris established an institutional link in order to strengthen its research in the perinatal toxicology field. Currently the unit has a well established expertise in perinatal toxicology as well as in electromagnetic wave effects and nanotoxicology.

This expertise of the unit translates into a remarkable ability to generate funds and to collaborate with French laboratories. The unit budget is high considering its size. In addition the unit was able to establish links internationally, for example with a laboratory in Melbourne Australia as well as with other labs. Although perinatal toxicity is a quite appealing topic nowadays, there were no European programs involving this unit during the last period.

Several foreign students (3) are carrying their thesis work within the unit but there are no foreign post docs.

Some of the unit members have been invited in international conferences. This is clearly limited to the historical focus of the unit in perinatal physiology. Other minor themes are less recognized internationally.

The unit has made a significant effort to valorize its findings although no patents have been recently filed. Valorization was in modeling premature newborns and intestinal physiology as well as in some alternative methods to animal testing. There is also a close collaboration with a private company (Médipréma).



- **Appreciation on the management and life of the research unit**

Although the management issue is seemingly simpler for a single team unit, the committee feels that this particular unit has benefited from the qualities and leadership of its director. Indeed, interaction with different supporting institutions and integrating different groups with specific aims and methods has been a challenge and will continue to be so for the following years. The management has been able to identify coherent aims and to establish a hierarchy in the research interests. It is encouraged to keep and amplify this policy. Furthermore, the unit includes a few young scientists with potential leadership qualities. In addition, the management was successful in making this unit a critical player in the Picardie region because of its role in fostering interactions between Ineris, the University and the medical campus. The PhD students and Post-docs were unanimously grateful for the unit governance and felt that they were very well looked after.

- **Appreciation on the scientific strategy and the project**

The general focus of the project is perinatal toxicity. As such this is a very important issue in modern toxicology since it is now believed that alteration of fetal or neonatal programming is an important mechanism accounting for later life pathologies.

It is difficult to give a uniform assessment of the project as a whole. Some of the projects are extremely original. This is the case of the environmental regulation of physiological parameters such as energy exchange, respiration and sleep. The effect of chemicals or of electromagnetic waves on these parameters is particularly novel and in some respect unique. Some of the clinical projects are also original, for example detection of fetal exposure to chemicals by the analysis of meconium. Other projects targeting reproduction are certainly timely but they have to face much stiffer competition internationally and they are less original. Clearly there are fields in which the unit can have a leading position whereas in other fields, it can have a contribution within a large network.

Another positive point is the combination of basic aspects with clinical aspects and more applied research. This is possible because of the structure of the unit. However, the fact that the unit has multiple local interactions, which is certainly an asset, can prove to be a threat if the unit gets involved in too many subprojects. The management appears to be aware of this issue. The impressive ability of the unit to obtain funding is certainly a strong point. A wise policy would be to apply for large funding for a limited number of projects.

To sum up, the committee members encourage the management to establish a clear hierarchy in the unit projects and to support long term projects in which the unit has leadership

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
PÉRINATALITÉ ET RISQUES TOXIQUES : PÉRITOX	A	A	A+	A	A

C1 Qualité scientifique et production

C2 Rayonnement et attractivité, intégration dans l'environnement

C3 Gouvernance et vie du laboratoire

C4 Stratégie et projet scientifique



Statistiques de notes globales par domaines scientifiques (État au 06/05/2011)

Sciences du Vivant et Environnement

Note globale	SVE1_LS1_LS2	SVE1_LS3	SVE1_LS4	SVE1_LS5	SVE1_LS6	SVE1_LS7	SVE2_LS3 *	SVE2_LS8 *	SVE2_LS9 *	Total
A+	7	3	1	4	7	6		2		30
A	27	1	13	20	21	26	2	12	23	145
B	6	1	6	2	8	23	3	3	6	58
C	1					4				5
Non noté	1									1
Total	42	5	20	26	36	59	5	17	29	239
A+	16,7%	60,0%	5,0%	15,4%	19,4%	10,2%		11,8%		12,6%
A	64,3%	20,0%	65,0%	76,9%	58,3%	44,1%	40,0%	70,6%	79,3%	60,7%
B	14,3%	20,0%	30,0%	7,7%	22,2%	39,0%	60,0%	17,6%	20,7%	24,3%
C	2,4%					6,8%				2,1%
Non noté	2,4%									0,4%
Total	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

* les résultats SVE2 ne sont pas définitifs au 06/05/2011.

Intitulés des domaines scientifiques

Sciences du Vivant et Environnement

- SVE1 Biologie, santé
 - SVE1_LS1 Biologie moléculaire, Biologie structurale, Biochimie
 - SVE1_LS2 Génétique, Génomique, Bioinformatique, Biologie des systèmes
 - SVE1_LS3 Biologie cellulaire, Biologie du développement animal
 - SVE1_LS4 Physiologie, Physiopathologie, Endocrinologie
 - SVE1_LS5 Neurosciences
 - SVE1_LS6 Immunologie, Infectiologie
 - SVE1_LS7 Recherche clinique, Santé publique
- SVE2 Ecologie, environnement
 - SVE2_LS8 Evolution, Ecologie, Biologie de l'environnement
 - SVE2_LS9 Sciences et technologies du vivant, Biotechnologie
 - SVE2_LS3 Biologie cellulaire, Biologie du développement végétal

Amiens, le 14 avril 2011

**Direction de la Recherche,
de la Valorisation et de l'Innovation**
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Monsieur le Président

AERES
20 rue Vivienne
75002 PARIS

2011.04.055. GF/SD

Objet : réponse officielle évaluation PERITOX

Référence AERES : S2UR120001852 - PERINATALITE, RISQUES TOXIQUES ET PHYSIQUES ENVIRONNEMENTAUX : PERITOX - 0801344B

Monsieur le Président,

Nous tenons tout d'abord, au nom de l'INERIS et de l'Université de Picardie Jules Verne et en particulier au nom du directeur et des membres de l'Unité de Recherche « Périnatalité, Risques Toxiques » (PériTox) 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 2 février dernier.

A la suite de la transmission du rapport d'évaluation, le Directeur, les membres de l'unité et nous-mêmes tenons à apporter les précisions suivantes.

La dispersion géographique est inhérente à l'origine institutionnelle des différents membres de l'Unité. Elle ne constitue par un handicap à l'heure actuelle. En effet, l'ensemble des projets menés en partenariat Amiens – INERIS témoigne que les interactions entre les deux sites se font de façon régulière, lors de réunions périodiques et par des échanges de doctorants et d'enseignants-chercheurs. Ces échanges constituent d'ailleurs un facteur moteur de synergie en vue de nouveaux projets de recherche.

La mutualisation des moyens techniques et des plateformes favorise ces échanges. Cette mutualisation va être encore accentuée par l'ouverture courant 2011 de la plateforme ANIMEX (« Plateforme d'ANIMAlerie pour Expérimenter sur l'organisme entier ») sur le site de l'INERIS. Des espaces numériques partagés communs, créés sur le site intranet de l'Unité ont également été mis en place.

A noter qu'en 2014, l'ensemble des locaux universitaires amiénois de PériTox et les différents services hospitaliers impliqués dans le laboratoire ou en étroite collaboration sera regroupé sur un site unique dans le cadre du monosite hospitalier - recherche.

Nous sommes d'accord avec le constat du comité de visite de la nécessité d'arriver à encore davantage de recentrage thématique. De nombreux efforts par tous les enseignants-chercheurs et chercheurs de PériTox ont été faits en ce sens dans le CQ passé, avec succès, et seront poursuivis dans le cadre du prochain contrat.

Par ailleurs, depuis sa création en 2008, l'attractivité de PériTox s'est traduite par la candidature de plusieurs enseignants-chercheurs afin d'y être intégrés. L'acceptation de leur intégration le cas échéant a été faite, lors d'un conseil de laboratoire élargi aux enseignants-chercheurs validé par le comité stratégique de l'Unité. Elle s'est faite sur la base d'un projet d'intégration à moyen terme et non dans une optique de croissance de l'Unité en vue d'atteindre une masse critique. Ces intégrations ont été réalisées parce qu'elles permettaient d'augmenter les compétences de l'unité de façon complémentaire sur les thématiques spécifiques du laboratoire.

Il convient actuellement de conforter l'Unité selon ce schéma. Le Contrat à venir aura pour objectif de recentrer les recherches de ces nouveaux entrants sur les thématiques du laboratoire. Il ne s'agit aucunement de créer de thématiques nouvelles mais bien d'enrichir les études des impacts sanitaires des expositions toxiques depuis le développement embryonnaire précoce - étape que nous pouvons aborder à présent par l'arrivée de biologistes de la reproduction dans l'Unité - jusqu'aux effets sanitaires potentiels observés sur les fonctions physiologiques vitales de l'enfant, et ce grâce à des approches transversales et complémentaires.

La politique menée depuis quelques années dans l'Unité a permis, comme cela a été souligné dans le rapport, d'augmenter l'IF moyen des publications. Elle va être poursuivie et accentuée au cours du prochain CQ. Le bilan 2006-2010 présente 2 publications ACL / an / scientifique. Parallèlement, une politique est actuellement menée en ce sens par l'INERIS auprès de ses chercheurs. Le bénéfice de ces incitations sera cependant à pondérer par le relatif faible temps recherche des enseignants-chercheurs et personnels hospitaliers et INERIS (en moyenne de 33%) liés à leurs fortes implications au niveau des enseignements, activités cliniques ou d'expertise. Notre souhait serait de rendre l'Unité plus attractive vis-à-vis des chercheurs temps plein.

Pour des raisons de calendrier lié à la création de PériTox en 2008 et au recentrage des thématiques de recherche qui en a découlé, de nombreux projets de recherche ont été lancés en quelques années. Certains de ces projets sont dans leurs dernières étapes. Les 1^{ères} publications issues de ces projets sont acceptées et nous attendons pour les semaines et mois à venir une augmentation notable du nombre de publications liées l'ensemble de ces projets, et notamment des publications communes entre l'UPJV et les chercheurs de l'INERIS.

L'Unité comporte actuellement de nombreux doctorants d'origine étrangère (5/16) ainsi qu'un ATER (précédemment post-doc dans l'unité). L'attractivité internationale (1 professeur invité australien, 1 chercheur invité hongrois présent dans l'unité pour 3 ans) sera développée notamment dans une politique de montage de projets de thèses en cotutelle (actuellement un projet est élaboré avec le Liban) et des projets en collaboration avec des partenaires internationaux.

Malgré la difficulté liée à l'absence de chercheurs temps plein dans l'Unité, nous avons pour objectif d'intégrer des projets européens mais également de renouveler les demandes pour ceux déposés précédemment.

Nous vous prions d'agréer, Monsieur le Président, l'expression de nos sincères salutations.

Le Président de l'Université de Picardie
Jules Verne

Le Directeur Général de l'INERIS


Georges FAURÉ





Vincent LAFLECHE