



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

Section des Unités de recherche

Evaluation report

Federation :

Institut Medicament-Toxicologie-Chimie

Environnement (IMTCE)

University Paris 5



May 2009



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Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

May 2009



Evaluation report

The Federation :

Name of the research unit : Institut Medicament-Toxicologie-Chimie-Environnement (IMTCE)

Requested label : IFR

N° in case of renewal : 71

Head of the research unit : Mr Frédéric DARDEL

University or school :

University Paris Descartes

Other institutions and research organization:

CNRS

INSERM

IRD

ENSCP

Date of the visit

March 31, 2009



Members of the visiting committee

Chairman of the committee :

Mr Guerrino MENEGUZZI (Université de Nice)

Other committee members :

Mr Jean-Marie RUYSSCHAERT (Université Libre de Bruxelles)

Mr Timothy EBBELS (Imperial College London)

Mr Joachim DREVS (Université de Freiburg)

Mr Frédéric BRAU (Université de Nice-Sophia Antipolis)

Mrs Anne GILLET (Université de la Méditerranée, Aix-Marseille 2)

Observers

AERES scientific representative

Mr Jacques BARATTI

University or school representative

Mr Bruno VARET

Research organization representatives

Mr Thierry MEINNEL, CNRS

Mrs Catherine LABBE-JULLIE, INSERM

Mr Alain FUCHS, ENSCP

Mr Jacques CHARMES, IRD

Mr Robert GARDETTE, Ministère de l'Enseignement Supérieur et de la Recherche



Evaluation report

1 • Short presentation of the federation

– Number of members in the federation :

303 researchers :

- 193 researchers with teaching duties;
- 110 full time researchers;

And :

- 48 engineers;
- 64 technicians;
- 29 administrative assistants;
- 26 PhD students.

– Constituent groups

- U685 INSERM Plasticité phénotypique de la cellule tumorale : signalisations, mécanismes et implications thérapeutiques. Director: M. LANOTTE
- U745 INSERM Génétique et biothérapies des maladies dégénératives et prolifératives du système nerveux. Director : P. AUBOURG
- U747 INSERM Pharmacologie, Toxicologie et Signalisation Cellulaire. Director : R. BAROUKI
- U765 INSERM (+ ex EA2510/IFR71) Thrombose : épidémiologie, physiopathologie thérapeutiques innovantes Director : J. EMMERICH
- U767 INSERM Grossesse normale et pathologique : développement, fonction du placenta et de l'utérus. Director : D. EVAIN-BRION
- U775 INSERM Bases moléculaires de la réponse aux xénobiotiques. Director : P. LAURENT-PUIG
- UMR8015 CNRS Cristallographie et RMN biologiques. Director : F. DARDEL
- UMR 8601CNRS Chimie et biochimie pharmacologiques et toxicologiques. Director : I ARTAUD
- UMR8638 CNRS Synthèse et structure de molécules d'intérêt pharmacologique. Director : J.ARDISSON
- FRE CNRS Chimie et toxicologie analytique et cellulaire. Director :O. LAPREVOTE
- U640/UMR8151 Pharmacologie chimique et génétique. Director : D. SCHERMAN
- U705/UMR7157 (+ex EA 3621/IFR71) Neuropsychopharmacologie des addictions : vulnérabilité et variabilité expérimentales et cliniques. Director : JM SCHERRMANN
- UR 10 IRD (+ ex EA 209/IFR71) Santé de la mère et de l'enfant en milieu tropical. Director : P.DELORON
- EA2498 + EA 3617 Stress cellulaire: physiopathologie, stratégies nutritionnelles et thérapeutiques innovantes. Director : L. CYNOBER
- EA 4064 Epidémiologie et environnement: impact des pollutions. Director : I. MOMAS
- EA 4065 Ecosystème intestinal, probiotiques, antibiotiques. Directecto : MJ. BUTEL
- EA 4066 Physicochimie industrielle du médicament. Director : P. ESPEAU
- EA (pending evaluation) Thérapeutique : efficacité et sécurité sanitaire. Director : GH. TROUVIN



2 • Preparation and execution of the visit

The visit of the IFR was held on March 31, 2009, between 9:30 am and 5:30 pm. The committee members and the AERES scientific delegate first met behind closed doors. Then, the new candidate director briefly highlighted the major achievements of the previous contract and gave a short outlook over the project for the future IFR. After this general overview, the scientific coordinators presented the main research lines of the three departments composing the future IFR/Institute. In the afternoon, the committee first met the representatives of the University and the research Organizations; then, the heads of the platforms presented the technical facilities of the IFR. After a short visit of the main platforms (Animal rooms, Imaging, Structural Biology) of the former IFR 71 at the Faculty of Pharmacy, the rest of the afternoon was devoted to a series of meetings with the candidate director, the unit directors and the staff of the technical platforms. The committee then proceeded to the deliberations in private. At the end of the visit, the committee thanked the candidate Director and his assistant for the organization of the day.

3 • Overall appreciation of the activity of the research unit, of its links with local, national and international partners

The application is aimed at creating a new Federative Institute gathering together 18 research laboratories of the Paris Descartes University working at the interface between chemistry and biology. According to the policy of the University, which has undertaken a general restructuring of its biomedical research activities, the ultimate goal of the present application is the creation of an IFR fostering the rapid emergence of a strong thematic University Institute (IMTCE). The IMTCE will be active in the fields of medical drugs, toxicology, chemistry and environment.

The new thematic IFR will comprise 14 laboratories (35 teams in total), which presently form the IFR 71 at the Faculty of Pharmacy, and four laboratories (17 teams for a total of 187 persons) of another IFR -the IFR95- which are located on a distinct campus (the "Saints-Pères" Faculty of Medicine) which is within 30-min walking distance. The technical platforms will essentially be localized within the Faculty of Pharmacy, thus the four laboratories at the Faculty of Medicine will rely on the technical facilities (i.e. the imaging and the animal rooms) of the IFR95.

In the current four-year contract, the IFR71 included 16 laboratories working at the development of new concepts in anti-tumoral, vascular, biotherapy, anti-infectious, and addiction therapy. Two novel teams were created in the frame of the INSERM and CRNS programs for the promotion of young researchers (AVENIR and ATIPE, respectively), and 4 teams merged into a larger research laboratory. With the inclusion of the four groups of the Faculty of Medicine, the future configuration of the new IFR is expected to significantly enhance its scientific consistency.

From the information delivered by the written report and the oral presentations, the end results of the IFR 71 are rather positive. Indeed, despite a relatively modest financial contribution for the equipment of the technical facilities, the IFR managed to strengthen the mass spectrometry platform, the proteomics and RMN platforms, to install a Q-PCR service and keep functional the animal rooms. The access to the equipments and technical supports is free of charge for all the IFR member teams, while the external users are charged on the basis of real costs. For each facility the charter use and the details for the access and conditions of use are clear. However, the capacity of the IFR to obtain funding from external sources (i.e. other than from Inserm, CNRS and the University) appears to be rather limited. The technological evolutions (i.e. replacements of old equipments, notably the electron microscopes) may have suffered from the fact that the contribution of the laboratories (5% of their specific budget) is put back into the free access to the facilities by the internal customers. This gives the feeling that in some instances the equipment should be considered more as a mutualisation of means rather than self-running services. However, the IFR has clearly played a significant role in the maintenance of the technical facilities, which accounts for the relatively high score of publications (60



papers) common to at least two groups of the Institute. This scientific production is fairly good and underscores the performance of the ongoing IFR project.

The major future evolutions of the technical facilities include an extension of the animal rooms which will be implemented in the current year. The availability of a novel A2 area for transgenic mice and that of an experimentation room will satisfy the crucial basic needs of the research groups. This structure is under the responsibility of a Professor assisted by a university engineer, one technician and four assistants. This common service integrates the animal facilities system (ANIMA 5) of the Paris Descartes University and is currently used by 10 research groups. The temporary employment status (contracts of defined duration) of two of the technical assistants may represent a potential problem for the efficient management of the animals in the future.

The scientific animation is the most remarkable achievement of IFR71, which includes thematic meetings, IFR forums, a weekly IFR scientific get-together, seminars from internal, national and international scientists. A weekly issue of the "IFR71 newspaper" played, and still plays, a constructive role in strengthening the feeling that the groups belong to a community with similar scientific interests, which also favours the desire of further integration, as said several times to the visiting committee. A very well conceived internet site (in French) provides a clear overview of the IFR composition and activities.

The IFR is heavily involved in education and training. The number of students and PhDs integrated in the different groups is impressive. The teams participate in the training of students of the Doctoral School of "Medicament" and the Doctoral School of "Cellular Genetics, Immunology, Infectious diseases and Development" (G2ID).

Concerning the national and international visibility, the committee feels that the IFR takes advantage of the well established reputation of its teams rather than from its own technical facilities, which are often parts of technological platforms of the Descartes University.

Starting from these facts, it is now proposed that a bi-localized multi-disciplinary Institution, the IMTCE, stems out from the present IFR71 to materialize a new IFR-University Institute devoted to the study of the "Interactions between Man and molecules", which covers research aspects with major societal and industrial applications for human health. The development of the new institute will be implemented in connexion with the 'Medicen Cluster' of the region Ile de France, which is aimed at promoting Innovative Therapies and Advanced Technologies in Health Care. In a much longer-term perspective, a global structuring of the research in this field will include forces of the sister Paris Diderot University.

To implement such ambitious goals, the new Institute will rely on teams developing either good or very good scientific projects, and will comprise three Departments: Toxicology, Pharmacology-Biotherapy and Chemistry-Living Systems. Of these, and despite its multidisciplinary (which makes its scientific strength), the department of Toxicology already appears to be the most homogeneous and unifying axis, with strong basic and clinical research activities. The composing groups are well positioned in the international competition. The foreseen developments are expected to further reinforce the performances of the composing teams and the visibility of the structure as a reference centre at the national and international levels. It is however unclear whether its location at the Saints-Pères campus will hamper the establishment of tighter connections with the groups at the faculty of Pharmacy. Concerning the department of Pharmacology-Biotherapy, the committee had some difficulties to appreciate the extent of the internal synergies between the teams. Indeed, the teams interested in the biotherapy aspects share common facilities, technical procedures and the technical support of an engineer, which underscores the mutual interactions and the common scientific interests. However, the existing/possible interactions with the groups working on the axis "Drug and perinatality" were not evident: even the "added value" brought by the IFR and its facilities to INSERM U767 (and vice versa) was not clearly perceived. Much tighter collaborations and interaction between the groups of this axis must be favoured, which, in addition, would better highlight the strategic vision of the Institute in the research fields covered by these groups. The department of Chemistry-Living Systems, which is made of 14 university and CNRS teams, will be organized by federating groups with an individual good/very good visibility. However, apart from the involvement in education and scientific animation, the added value brought in the past by the IFR to this thematic remained unclear to the members of the visiting committee. Also, because of the number and variety of the scientific programs, that only in a few cases stand on clear synergistic collaborations between partner groups, this axis appeared to present some risk of dispersion of the forces in front of the ambitious developments that are proposed. However, the adhesion to the project clearly expressed by most of the group leaders should facilitate the implementation of the plans proposed by the future director.



To this respect, the cohesion of the departments and that of the whole IFR-MTCE Institute should benefit from the planned creation of a metabolome-adductome platform, that will be the counterpart of the existing proteome platform - which already integrates the 3P5 network of the proteomic and mass spectrometry platforms of the Descartes University- and the establishment of a screening platform for novel molecules with antitumor and anti-angiogenic biological activity. To facilitate the financial administration of the central technical facilities, the maintenance and renovation of the equipments, the future director of the IFR has also decided that the consolidated operating costs will be entirely passed onto the customers. The declared aims of the future IFR are the implementation of a strong policy in defining the strategic choices in the development of the platforms in terms of equipments and the dedicated staff.

The interview of the representatives of the Public Funding Agencies clearly disclosed the strong support of the different institutions to the emergence of the novel IFR-MTCE Institute, this in agreement with the decision of the Paris Descartes University to promote the federation of its leading laboratories in Institutes with a strong international visibility.

4 • Appreciation of resources and of the life of the federation

– Management :

The IFR will be headed by a Director assisted by a Deputy Director (localized at the Saint-Peres campus) a Coordinator, who at present coordinates the IFR71, and two representatives for each department. The Board of the directors include the heads of the 18 research units, the Deans of the Descartes and Diderot Universities, and the IMTCE coordinator. Decisions and strategic directions will be taken collegially. As perceived by the evaluation committee during an open discussion with the group leaders in the absence of the future Director, the project leader and the proposed executive organization of the IFR are collectively well accepted. All stressed the importance of the IFR for the cohesion of the teams, sharing of knowledge and resources, and the scientific animation. The evolution of the IFR towards a research institute was enthusiastically supported by a number of group leaders but some degrees of reticence was also apparent, which may reflect either a preference for a federative organization or a fear of changes. The committee noted that the technical staff directly administered by the IFR is at present rather reduced in size: an effort to redeploy jobs towards the common facilities should be privileged, notably to decrease the ratio of temporary employments in the animal facility to avoid loss of productivity and financial burden associated with turnover and training of new staff members.

– Budget and finances :

In the past, a large part of the budget was used to offer an open access to the facilities to the IFR teams. As a consequence pieces of the equipment (electron microscopes, laboratory furniture, etc) appear to be rather outdated. The committee positively appreciated the decision of the future direction to shift to a real cost policy for the access to the facilities, which is expected to improve the auto financing capacity of the IFR and the openness of the management. Considering the planned evolutions of the facilities (novel metabolome-adductome platform, new electron microscopes...) the financial breakdown presented in the written document seems to be based on a modest evaluation of the required means.

– Scientific animation and formation :

The Scientific animation and formation appear to be a significant achievement of the IFR. In addition to 30 external invited conferences per year, the IFR organizes internal seminars (25-36 /year), a weekly "IFR71 scientific meeting" focused on specific themes, and an "annual IFR day". The visibility of the IFR is promoted in the Inter-IFR scientific day of the University, and an annual meeting in association with the Descartes University and the Barcelona Science Park. The implication of the research teams of IFR71 in the Doctoral Schools "Medicament" and "Gc2ID" results in the training of numerous students at M1, M2 and thesis levels.



5 • Conclusions

— Strong points :

- The number and quality of the research groups, a large majority of which has an excellent reputation and international recognition;
- The foreseen management staff;
- The scientific project presented by the candidate director is ambitious and coherent. It aims at actively promoting strong interactions between the teams and at achieving the establishment of solid and performing scientific community;
- The platforms, which are very useful and well maintained - despite the outdated state of the building - and are animated by motivated staff. The committee remarked on the enthusiastic adhesion of the technical personnel to the proposed project;
- The excellent contribution to the formation of students and postdocs ;
- The active scientific animation ;
- The strong support of the University and of the Public Funding Agencies that have developed an ambitious global strategy in which the future IFR is fully integrated.

— Weak points :

- The general impression suffered from a bad preparation of the visit ;
- The written document was of poor quality, with sections in English and others in French. Collection of useful information on the actual situation and the future needs was difficult and in some instances even impossible;
- The discontinuity between the talks and discussions confused the committee on how the aims of the project were perceived by the participants ;
- The adhesion of a large part of the group leaders to the project seemed doubtful ;
- The technical platforms: The small size of the animal facilities and the old equipments of the imaging service may quickly hamper future scientific evolutions. For instance the animal facility offers no real technologically advanced service and relies too much on temporary workforce. Also, the scientific programs justify the creation of the metabolome platform, but information on the means available for the concretization of the project was not provided.

— Recommendations :

The visiting Committee felt that the novel IFR is an emerging structure which, at the moment of the valuation, suffered from some immaturity of the project. Clearly a number of teams appeared “not in the project” and are not yet prepared to evolve towards a federation into a Scientific Institute as quickly as the Descartes University is requesting. The visiting Committee also found rather difficult to decide whether the future direction of the IFR had a clear vision for the new IMTCE Institute and exactly what that vision entailed. Despite the evident weaknesses of the proposal, which also suffered from largely inadequate presentations exclusively focused on the scientific aspects without mentioning the local context and the positioning in the common perspective of a research centre, the committee considers that enough positive elements exist that could justify the renewal of this IFR, which would back its evolution towards the IMTCE Institute.

Le Président
Axel KAHN

Paris, le 21 juillet 2009

DRED 09/n° 267

Monsieur Pierre GLORIEUX
Directeur de la section des unités de l'AERES
20 rue Vivienne
75002 PARIS

Monsieur le Directeur,

Je vous remercie pour l'envoi du rapport du comité de visite concernant l'Institut Fédératif de Recherche « IFR 71 - Institut Médicament - Toxicologie - Chimie - Environnement (IMTCE) » rattaché à mon établissement.

Nous remercions le Comité de visite de l'AERES pour son rapport. De ce dernier il ressort que l'IMTCE est une opération importante mais dont tous les acteurs n'ont pas encore pris conscience.

Cette remarque est exacte et il reviendra aux responsables de l'IMTCE et à l'Université de transformer un projet scientifique et organisationnel majeur en réalité appropriée par tous les chercheurs concernés.

L'Université s'engage à contribuer autant qu'elle le pourra au succès de cette entreprise structurante, que ce soit en hâtant les rénovations de locaux qui s'imposent (et sont déjà programmés) ou en facilitant ses initiatives scientifiques.

Je vous prie de croire, Monsieur le Directeur, à l'expression de ma meilleure considération.

Le Président de l'Université



Axel Kahn

Paris, July 24th, 2009

We wish to thank members of scientific visit committee for their time and effort in evaluating our federative project. We are happy to see that the efforts made by the former IFR71 and the overall scientific quality have been positively evaluated.

The current IMTCE project is a major change in focus, which is in essence to transform platform-based, single site clusters into a strong, larger institute focussed on a major scientific theme, with a much weaker emphasis on technical facilities. This is a major endeavour which we believe is in line with the strong commitment of the University to foster coordinated research in the fields where it has clear strengths by creating university institutes. IMTCE is one of those, it is more scientifically ambitious than the previous IFR. Because of this change, it is a novel project, which has emerged recently as part of University-wide re-evaluation of its scientific policy in the frame of the new *LRU* bill which grants further independence to French universities. We are grateful to the committee for his positive opinion on the strategic importance of the proposed institute in the fields of Drugs, Toxicity, Chemistry and Environment.

This major reorganisation and change of focus is still in the making. As a consequence, not all aspects of our project are equally mature, something which was rightfully noted by the committee and of which we are fully aware. Of all three projected departments, indeed not all are equally well-integrated. Bridging this gap will clearly be our goal for the the next four years. The committee has expressed some doubts about the feasibility of some aspects of the project or about the commitment of some group leaders to this new focus. We believe that this opinion is mostly related to the conditions of the site visit. Indeed, we feel that the organisation by the AERES was not satisfactory and was different from that of other IFR visits. The practical conditions had important effects on the way our project was perceived by the experts.

Despite officially pressing AERES for a schedule in mid-February, at a time where many of the other IFRs in the University already had a date arranged, the final day for the site visit was fixed only in the second half of March, leaving only **six working days** to prepare the visit on March 31st. The final program was fixed only on the Saturday for the next Tuesday, leaving only **one working day** (the Monday) for adjustments. As a consequence of that, it turned out to be impossible to organise a prior meeting of the directors of the *unités* or *équipes* on such short notice for preparing the visit, «polishing» presentations, coordinating their content. Furthermore, during this incredibly short period of time, several of the directors were completely unavailable, either being abroad, sitting on committees, or having the AERES site visit for their own *unité*. An consequence of that is that the presentations were not all sufficiently prepared and coordinated, something which is more complex to organise for a large institute than for a standard *unité de recherche*. This gave that impression of «lack of cohesion» of some aspects of our project which we believe has prejudiced the committee members.

Since the evaluation of IFRs is a competitive call, it seems reasonable to expect similar conditions for all site visits, which was not the case here.

Despite our comments above, we will take into account the criticisms stated by the committee that can help us in implementing a strong and ambitious institute. The long term prospects of this project are extremely promising, which accounts for the positive conclusion of the committee's report. We are grateful for that conclusion.



Pr. Frédéric Dardel
Directeur de l'IMTCE