CESP - Centre de recherche en épidémiologie et santé des populations

Rapport Hcéres

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

Section des Unités de recherche

Evaluation report

Research unit :

Centre for Research in Epidemiology and Population Health (CREPH)

University Paris 11

January 2009

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

Section des Unités de recherche

Evaluation report

Research unit :

Centre for Research in Epidemiology and Population Health (CREPH)

University Paris 11

Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

mars 2009

Evaluation report

The research unit :

Name of the research unit : Centre for research in Epidemiology and Population Health (CREPH) / Centre de Recherche en Epidémiologie et Santé des Populations (CESP)

Requested label : UMR_S INSERM

N° in case of renewal :

Head of the research unit : M. Denis HEMON

University or school :

Université Paris 11

Université Saint Quentin en Yvelines (UVSQ)

Other institutions and research organization:

INSERM

INED

Dates of the visit :

22, 23 Janvier 2009

Members of the visiting committee

Chairman of the committee :

Mr Roger SALAMON, Université Bordeaux 2 (and also chairman of sub-committee A)

Mrs Claire JULIAN-REYNIER, Institut Paoli-Calmettes de Marseille (chairwoman of sub-committee B)

Other committee members :

Mr Fabrice CARRAT (Université Paris 5)

Mrs Sarah DARBY (University of Oxford, UK)

Mr Paul FRANKS (Umeå University Hospital, Sweden)

Mr Roger INGHAM (University of Southampton, UK)

Mrs Diana KUH (Medical Research Council, UK)

Mr Franco MERLETTI (University of Turino, Italy)

Mr Geert MOLENBERGHS (Hasselt University, Belgium)

Mr Merete OSLER (Glostrup University Hospital, Denmark)

Mr Frits ROSENDAAL (Leiden University Medical Center, The Netherlands)

Mr Jordi SUNYER (Institut Municipal d'Investigation Medicale, Spain)

Mrs Alicja WOLK (Karolinska Institut, Sweden)

Mr Giorgios GROPETIS (Université Paris 6)

CNU, CoCNRS, CSS INSERM, représentant INRA, INRIA, IRD...) representatives :

Mr Pascal AUQUIER, Marseille, CNU representative

Mrs Catherine DENEUX, INSERM CSS representative

Composition of the 2 sub-committees

Committee A	Committee B
Team 4 : Epidemiology of HIV and sexually-transmitted diseases *Chairman* : R. Salamon *Other committee members* : P. Auquier, F. Carrat, G. Gropetis, R. Ingham G. Molenberghs, J. Sunyer.	**Team 8 : Cardiovascular disease and hormones** *Chairwoman*: C. Julian-Reynier *Other committee members* : S.C. Darby, C. Deneux-Tharaux, P.W. Franks, D. Kuh, F. Merletti, M. Osler, F. Rosendaal, A. Wolk.
Team 2 : Epidemiology of reproduction and child development *Chairman*: R. Salamon *Other committee members* : P. Auquier, F. Carrat, C. Deneux-Tharaux, R. Ingham, G. Molenberghs, J. Sunyer.	**Team 10 : Epidemiology of diabetes, obesity and renal disease: lifelong approach, early nutritional determinants** *Chairwoman*: C. Julian-Reynier *Other committee members* : S.C. Darby, P.W. Franks, G. Gropetis, D. Kuh, F. Merletti, M. Osler, F. Rosendaal, A. Wolk.
Team 5 : Respiratory and environmental epidemiology *Chairman*: R. Salamon *Other committee members* : P. Auquier, F.Carrat, G. Gropetis, R. Ingham F. Merletti, M. Osler, J. Sunyer.	**Team 12 : Lipid nutrients, metabolism and cancer risk** *Chairwoman*: C. Julian-Reynier *Other committee members* : S.C. Darby, C. Deneux-Tharaux, P.W. Franks, D. Kuh, G. Molenberghs, F. Rosendaal, A. Wolk.
Team 11 : Epidemiology of social and occupational determinants of health *Chairman*: R. Salamon *Other committee members* : P. Auquier, F.Carrat, G. Gropetis, R. Ingham F. Merletti, M. Osler, J. Sunyer.	**Team 9 : Nutrition, hormones and women's health** *Chairwoman*: C. Julian-Reynier *Other committee members* : S.C. Darby, C. Deneux-Tharaux, P.W. Franks, D. Kuh, G. Molenberghs, F. Rosendaal, A. Wolk.
Team 1 : Biostatistics *Chairman*: R. Salamon *Other committee members* : F. Carrat, G. Gropetis, R. Ingham, G. Molenberghs, M. Osler, F. Rosendaal, A. Wolk	**Team 3 : Cancer epidemiology: radiocarcinogenesis and iatrogenic effects of treatments** *Chairwoman*: C. Julian-Reynier *Other committee members* : P. Auquier, S.C. Darby, C. Deneux-Tharaux, P.W. Franks, D. Kuh, F. Merletti, J. Sunyer
Team 7 : Gender, sexual and reproductive health *Chairman*: R. Salamon *Other committee members* : F. Carrat, R. Ingham, G. Molenberghs, M. Osler, F. Rosendaal, A. Wolk	**Team 6 : Environmental epidemiology of cancers** *Chairwoman*: C. Julian-Reynier *Other committee members* : P. Auquier, S.C. Darby, C. Deneux-Tharaux, G. Gropetis, F. Merletti, P.W. Franks, D. Kuh, J. Sunyer,

Observers

AERES scientific representative :

M. Alexis ELBAZ

University or school representative:

M. Gerard CAUDAL, Université de Versailles-Saint Quentin en Yvelines

M. Marc LOMBES, Université Paris 11

M. Jacques BITTOUN, Université Paris 11

Research organization representative :

Ms. Marie-Josèphe LEROY-ZAMIA, Inserm representative

Evaluation report

1 • Short presentation of the research unit

The "Centre for Research in Epidemiology and population Health" (Centre de recherche en épidémiologie et santé des populations, CESP) is a scientific project based on three principal axes:

- Etiologic and clinical epidemiology of chronic diseases
- Fertility/perinatal and child health
- Health Determinants and joint effects

Twelve teams are involved in this 2010-2013 project: 1) Biostatistics 2) Epidemiology of reproduction and child development 3) Cancer epidemiology : radiocarcinogenesis and iatrogenic effects of treatments 4) Epidemiology of HIV and sexually-transmitted diseases 5) Respiratory and environmental epidemiology 6) Environmental epidemiology of cancers 7) Gender, sexual and reproductive health 8) Cardiovascular disease and hormones 9) Nutrition,hormones and women's health 10) Epidemiology of diabetes, obesity and renal disease : lifelong approach,early nutritional determinants 11) Epidemiology and socialand occupational determinants of health 12) Lipid nutrients, metabolism and cancer risk.

The CESP is organized through 6 transversal scientific axes : Child and adolescent health ; environmental health; cancer epidemiology ; health practices ; social determinants of health ; public health and multidisciplinary ; approach to HIV infection/AIDS and 2 transversal departments: information technology platform and administration and support service.

The center will include a total of 258 members:

- 45 full time researchers
- 21 researchers with teaching duties
- 3 researchers with hospital activities
- 43 PhD students and 22 Post-doctoral fellows
- 2 invited scientists
- 57 engineeers, 43 technicians, 20 administrative assistants, 2 supporting personnel (other category)

In addition,

- 44 researchers and researchers with teaching duties have a HDR
- 66 out of 66 full-time researchers and researchers with teaching duties, are "publishing"
- 54 students were granted a PhD degree during the past four years

The teams of the CESP have published 1536 papers in the past four years.

The total surface dedicated to CESP research is 4353m2 composed by

- Paul Brousse Hospital (2721 m2 for teams 1,5,6,8,10,11)
- Bicetre hospital (1076 m2 for teams 2,4,7)
- Gustave Roussy Institute (556 m2 for teams 3,9,12)

The links of the CESP and the universities are very important; in the field of Public Health, there are 500 registered students and 120 in research field, and the members of CESP play a major role in this activity.

2 • Preparation and execution of the visit

The assessment of the CESP was carried out during 2 complete days. Because of the international composition of the visiting committee, everything was organised in English (written documents, oral presentations and oral exchanges). All the documents had been made available on the website of the centre before the evaluation; copies of the slides were available on site as well as copies of the complete reports. We highlight here the excellent quality of all the written documents submiitted. A CD-Rom containing the report of the centre was sent to all the members of the visiting committee. All the oral presentations were very good and respected the time-constraints.

On the morning of the first day (9 am:1pm), the applicant director presented the project for half an hour and 2 simultaneous scientific sessions occurred afterwards (with the visiting-committee split in two). This allowed the presentations of 4 teams of the project (Teams 4, 2, 8, 10). Each team presented their project and past activity during 45-60 minutes and left half an hour for the questions of the committee. The review committee had a short closed meeting of 15 minutes after each complete presentation of the teams. This allowed discussion of the most relevant positive and negative issues assessed.

In the afternoon (2pm-5:45pm) the committee auditioned three of the institutions involved (the 2 university presidents, and the INSERM representative) during half an hour and 4 of the other teams (Teams 5, 11, 12, 9) with the same process as in the morning session. The day (5:45pm:8:00pm) ended with a closed meeting of the AERES committee to complete the assessment grids of the eight teams auditioned during the day.

On the second day, the morning (9:00am-12:15pm) was spent on the assessment of the last 4 teams (teams 1, 7, 3 and 6) with the same format as the day before (2 simultaneous sessions). In the afternoon (1:20pm-5:45pm), we first met during 40 minutes (in three simultaneous subgroups) the doctoral and postdoctoral personnel, the researchers and the technicians. This was followed by a short presentation by the applicant-director to introduce transversal/thematic reflexions across the different teams and by a session of questions-answers with the visiting committee (closed meeting with the applicant-director and the Secretary General of the Centre). This exchange ended at 3:30 pm and was followed by a closed meeting of the AERES group to complete the grids of the last 4 teams auditioned during the day and by a summary discussion on the assessment of the centre.

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

The network of researchers involved in this research project comes from one of the most famous schools in Epidemiology in France. The links of this research group with the teaching of epidemiology at the University Paris 11, is not only in a particularly relevant position for both the development of teaching and research in epidemiology in Paris, but also for the whole country. Many researchers are involved in teaching activities in Epidemiology, both at the masters and doctoral levels (The CESP-CREPH director has been the head of the doctoral school in Public Health until now).

The research activity covers most of the key contemporaneous and relevant Public Health issues in France. The research questioning focuses on descriptive and etiological epidemiology, and is approached both from the disease and exposure “entrance”:

“Disease entrance”: Cancer (Teams 3, 6, 9, 12), Cardiovascular Diseases (Team 8), Respiratory Diseases (Team 5), Diabetes, Obesity (Team 10), HIV and Sexually Transmitted Infections (Team 4), Diseases Child development (Team 2), Reproduction, sexual and reproductive health (Team 2, 7)

“Exposure entrance”: Environment (team 5, 6) including radiations (Team 3), Hormones (Teams 8, 9), Nutrition (Teams 9, 10), Occupational, social and personal characteristics (Team 7, 11)

Two teams differ in their focus: one is on methodology (Biostatistics, Team 1) and the other on biological aspects in cancer (Team 12).

The scientific production of the whole group (1500 publications in the last four years) and the panel of well-known and competent researchers involved in this project, gives this centre a unique expertise in the field of Public Health both on methodological and application grounds.

Links with local partners:

Strong structural links with the universities were highligthed during the visit by their delegates: University Paris 11, University Paris 5, Paris 12 and Versailles Saint-Quentin-en-Yvelines,

Good collaborations with the 3 University hospitals (Bicêtre, Paul Brousse, Gustave Roussy Centre). However these collaborations could be improved further in the future development of the centre.

Good exchanges with the National Health insurance organisation (CNAMTS).

The different teams of the centre have already some "inter-teams" collaborations. They are likely to increase in the years to come thanks to the different researchers involved belonging also to national research institutes and networks (INSERM, INED, University) but also to the transversal research axes developed in the future research project.

Links with national partners:

For the research projects, several data bases are based on national collaborations for their recruitment (children tumour registry, national E3N cohort, EDEN cohort, Gazel cohort….).

Links with international partners:

Each team has its own network for international collaborations (European projects or other international projects). Two international INSERM laboratories include two teams of the centre (Team 5 - Barcelone, Grenoble; Team 9 - Mexico)

4 • Specific appreciation team by team and/or project by project

Team 1 : Biostatistics :

Overall, the visiting committee assessed the past activity and the research project of this team as VERY GOOD.

This team is divided in two groups:

- An excellent group in the field of pharmacoepidemiology (one of the best in France), where relevant problems are attacked, from both a methodological as well as from a substantive point of view.
- A strong biostatistical/methodological group with very good previous work but a level of sub-optimal functioning.

The somewhat sub-optimal functioning of the team also shows in the research output. While there are publications in both the statistical and the substantive literature, there are problems with both quantity and quality. For example, while there are several papers in Statistics in Medicine, papers in such journals as Journal of the American Statistical Association, Journal of the Royal Statistical Society, Biometrika, Biometrics, Biostatistics, etc. are largely missing or at least very infrequent.

The need of a team such as team 1 for a project like the one evaluated here is beyond question; however, every effort will need to be made to shift to a higher gear.

Nom de l'équipe : **Biostatistics**

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
B	B	B	B	A

Team 2 : Epidemiology Of Reproduction And Child Development :

Overall, the visiting committee assessed the past activity and the research project of this team as VERY GOOD.

Presentation and strengths :

This team has two distinct research axes. The first group develops epidemiological research on fertility and infertility treatments with a well–recognised national expertise in this field, and an important past scientific production on methods for measuring fertility and of the role of environmental exposures on fertility.

The second and recent axis focuses on paediatric diseases, and research activity so far has been mostly based on a cohort of children with multiple sclerosis – created and maintained by a young researcher specialized in paediatric neurology, who recently joined the team - leading to an abundant and high-level scientific production.

Weaknesses and recommendations :

An important issue with this team is that the two sets of projects that the group develops do not clearly fit well together, either in terms of topic or of method. In particular, although the paediatric research axis is presented as "epidemiology of child development", the past activity and the projects would be better characterized as clinical epidemiology in the field of paediatrics. Because of this heterogeneity in the research activity, it was somewhat difficult to arrive at a common assessment of the entire team. Strategies for long term viability may include re-considering the definition of research topics around a clear scientific axis.

The level of international collaborations, and of involvement in international networks, should be increased in order to improve the visibility of the group and to enrich research questions and available data. Given the strong potential clinical utility of the research projects on infertility, interactions with clinicians and/or professional organisations in the field of reproductive medicine, regarding the definition of research questions or the transfer of research results, could be more fully developed.

Despite the team leader's strong involvement in teaching at pre-doctoral and doctoral level, the past and current number of doctoral students trained in the team is rather low when compared to the number of entitled researchers.

Nom de l'équipe : **Epidemiology Of Reproduction And Child Development**

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
B	A	B	A	B

Team 3 : Cancer Epidemiology: Radiocarcinogenesis And Iatrogenic Effects Of Treatments :

Overall, the visiting committee assessed the past activity and the research project of this team as GOOD.

The research topic of this group is original and highly relevant in clinical oncology. The researchers have strong and historical collaborations with a very famous local cancer centre. Cancer is now more frequently considered as a chronic disease involving long term follow-up. Taking into account the deleterious aspects of previous cancer treatment, radiotherapy in particular, is therefore a key issue in medical practice. This means a high potential for application of research results to clinical practice.

The profile of publications is heterogeneous according to the researchers. It is very good for the team leader (high IF journals in clinical oncology (JCO, Lancet, Oncology) best journal in epidemiology (AJE), and specialised journals in radiotherapy). The valorisation of the research could be improved by participating more frequently in international conferences. Partner in one European Project (CEE-Euratom-GEN-RAD-RISK), and coordinator of several others with no particular financing from international institutions. 3 PhD students are presently being supervised by the team leader.

This small team (3 FTE INSERM researchers) has been focussing on a specialised but important research topic. At the moment the team appears intellectually somewhat isolated and its long term viability seems uncertain. Participation in the proposed Centre for Research in Epidemiology and Population Health (CESP) should enable greater interaction with colleagues working in related areas which should be beneficial. Indeed, there may be a case for merging this group into one of the other, stronger, groups.

The dosimetry work is clearly innovative but this is not yet adequately reflected in peer-reviewed publications. Priority should be given to achieving this. It is also important for those involved in the dosimetry work to maintain and build on links with other academic medical physicists.

The observational epidemiological studies are of interest. However, they are mainly concerned with comparing disease rates in patients who have been given different treatments that have not been allocated at random. Under these circumstances, great care is needed before it can be concluded that any differences in disease or mortality rates are causally related to the treatments rather than simply reflections of the fact that different treatments are given to different types of patients. Greater attention to justifying the causal interpretation of such differences is necessary. In addition, the possibilities of carrying out long term follow-up of patients in clinical trials should be explored.

Nom de l'équipe : **Cancer Epidemiology: Radiocarcinogenesis And Iatrogenic Effects Of Treatments**

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
B	A	B	B	B

Team 4: Epidemiology Of HIV And Sexually Transmitted Diseases :

Overall, the visiting committee assessed the past activity and the research project of this team as GOOD.

The Team 4 is involved in clinical and quantitative epidemiology of HIV infection. The Team has conducted nationwide prospective cohorts, mostly supported by ANRS (the French national Agency on AIDS and hepatitis). The Team has provided original results in the field of mother-to-child transmission or long term prognosis of HIV infected persons with known date of infection, and was the first to describe HIV controllers. These studies have led to numerous publications in high ranking journals specialised in the field of HIV or infectious diseases (AIDS, J of AIDS, HIV Medicine, J Infect Dis).

The current project is centred on 4 topics 1) optimal timing for prevention of mother-to-child transmission of HIV and long term effect in children of maternal exposure to ART 2) outcome of HIV infection including prognosis studies and study on living conditions of subjects with HIV 3) pathophysiologic studies in HIV disease progression focusing on HIV controllers and genetic association studies in this setting, and 4) assessment of the dynamics of HIV epidemic in France. The part of these topics focusing on tolerance to prenatal or exposure during childhood to HAART is highly innovative and relevant.

The Team will use original data and cohorts, some of which (e.g. HIV controllers) are unique in Europe. The Team participates to European studies focusing on long term prognosis of HIV infected adults or children. The Team's leader is vice-chairperson of an international project coordinated by the MRC.

Weaknesses and recommendations: This is a small team (1.6 fte senior researchers with permanent faculty position), with a large number of non permanent staff devoted to monitoring of cohorts and data management. The Team has only two PhD students and one post-doctoral position. Analysis of therapeutic observational data is a challenging issue. To that respect, the scientific project lacks statistical experts but the team could strongly benefit from methodological inputs from other teams of the centre. Mother-to-child transmission of HIV is a major concern in low-income countries and the team has too few collaborations and projects in this area. Research on sexually transmitted diseases other than HIV is poorly addressed.

Nom de l'équipe : **Epidemiology Of HIV And Sexually Transmitted Diseases**

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
B	B	A	B	B

Team 5 : Respiratory And Environmental Epidemiology :

Overall, the visiting committee assessed the past activity and the research project of this team as EXCELLENT.

This is a small, focused and structured group, with a strong leader in an international arena, with a long and successful track record of respiratory epidemiology that fits coherently with the well planned project for the new period (on respiratory effects of cleaning products, nursing, air pollution, dietary products and genes). The group research lies in either international collaborative projects or the French EGEA case-control that they lead. EGEA incorporates clinical, environmental, molecular and genetic epidemiology, collaborating with other INSERM units. The group is evolving successfully with young researchers.

Weaknesses: The group has limited teaching activity and a short record of PhD students; it is too small to face the high specialized technical challenges in the statistical analysis (spatial statistics, genetic analysis) that probably would require external technical support, and does not take advantage of the life-course studies carried out at INSERM.

Recommendations: The group needs to plan the new incorporation of new researcher, a senior with a long career, to fit successfully in their well structured project; the panel advise to incorporate psychosocial determinants; even though their record of publications is in the upper decile, they should plan how to capitalize in a more efficient way their production; a final recommendation refers to increase the number of PhD incorporations.

Nom de l'équipe : **Respiratory And Environmental Epidemiology**

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	A+	A+	A	A+

Team 6 : Environmental Epidemiology Of Cancers :

Overall, the visiting committee assessed the past activity and the research project of this team as EXCELLENT.

The Team (5,6 FTE researchers) has three distinct research axes: the first axis addresses the risk factors for cancer in adults with a strong focus on occupational risk factors; a second axis addresses childhood cancer and is largely based on the National Registry of Childhood Malignant Blood Diseases; a third line of research is in biostatistics. Important studies were also conducted on the effect of heat waves in France.

Large databases have been compiled over the last years associating high quality environmental and DNA data.

The team has a long-standing tradition of research in occupational epidemiology with an interdisciplinary team of industrial hygienists, chemists and occupational physicians, and is recognized at international level for its work on both development and use of job exposure matrices and expert assessment in occupational health.

The team has developed recently an interest in genetics and epigenetics of cancer and articles have been published on the topic exploiting French data or larger data sets of consortia of childhood cancer, lung cancer and head and neck cancers, where the data of the team represent a large and important contribution to international consortia.

The team is strongly involved both in research training with a large number of successful master, medical doctoral, doctoral theses (10 theses during the last 5 years), dissertations and in teaching in French Schools of Public Health. It presently has 9 PhD students for 4 HDR.

The scientific productivity of the team is very good, considering that the activity of exposure assessment on such large databases is extremely burdensome and time-consuming both in the task of developing job exposure matrices and in case by case expert assessment. An impressive number of national contracts has been collected by the group during the last years.

The team is well integrated in research programmes with other teams, and team 11 in particular. Nevertheless, enhancing links between teams (especially with team 1 and teams where there is expertise in genetic epidemiology and environmental exposure assessment) seems essential for further development and better exploitation of large-scale epidemiological databases of the team and of the Centre.

The objective of developing research on gene-environment interactions and in epigenetics will need a clear decision as to either decide to develop in house large economic and human resources or extend cooperation with units and laboratories with strong expertise outside of the Centre.

A final recommendation is to develop and promote new or more efficient methods regarding the assessment of environmental exposure (geo-coded database, pertinent biomarkers etc…). At the moment, exploitation of large-scale epidemiological databases is being done at the occupational level, but much more could be done at the level of environmental exposures. The many links the team already has with centres of excellence such as CREAL in Barcelona or IRAS in Utrecht provides good opportunities to develop new collaborations on the topic.

Nom de l'équipe : **Environmental Epidemiology Of Cancers**

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	A+	A	A+	A

Team 7 : Gender, Sexual and Reproductive Health :

Overall, the visiting committee assessed the past activity and the research project of this team as EXCELLENT.

It is a large team (7.8 FTE researchers). This team's work covers sexual and reproductive health and concerns a variety of aspects: sexual behaviour, abortion, contraception, sexual dysfunction, sexual violence, sexually transmitted infections and others.

Relative weaknesses mentioned: (1) a relatively low number of completed PhDs in the past four years, but this is presently evolving favourably with 5 doctoral students, (2) overlapping interests (although the reasons for this are not clear), and (3) possibly a relative lack of high level statistical contribution.

The publication record is relatively weak in terms of the leading journals in the field although they have a very impressive book and monograph publication record.

The review group was extremely impressed with this team's past work and future plans. Despite varied disciplinary and epistemological backgrounds there is a synergy and consistent thread that runs through their work. They are well integrated internationally both in richer and poorer countries.

Nom de l'équipe : **Gender, Sexual and Reproductive Health**

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A+	A	A+

Team 8 : Cardiovascular disease and hormones :

Overall, the visiting committee assessed the past activity and the research project of this team as VERY GOOD.

This is a strong and productive group that is clearly content-driven, and performs important epidemiology of hormone-related cardiovascular disease with a focus on public health and clinical utility.

The team has executed several well-designed studies that have led to publications in high-impact journals. The group collaborates with several of the leading research groups in the field, in Europe and the USA.

The team has major expertise in observational studies. They have identified small and large randomised trials as a necessary next step in their line of research. While the committee agrees this type of research is needed, it was not convinced that this team has considered in detail all requirements for such a major change in type of studies, which are extremely labour-intensive and require different methodological expertise than is currently present.

The team is small (1 FTE INSERM researcher, 1 University Professor in Rennes), and given the age distribution within the team should consider strategies for long-term viability.

Nom de l'équipe : **Cardiovascular disease and hormones**

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A+	A	B	B

Team 9: Nutrition, Hormones and Women's Health :

Overall, the visiting committee assessed the past activity and the research project of this team as EXCELLENT.

Team 9 is a large group (but only 2 FTE INSERM tenure position, 2 part-time physicians) with responsibility for a high quality prospective cohort with repeated measurements of many lifestyle factors among 100,000 women and a high response rate after many rounds of data collection. Data from the cohort is used by many other teams at the Centre. There are very good management and maintenance skills in the group guaranteeing high quality of data. The internationally unique high quality of data is well reflected in a long list of publications in high impact journals. The Team 9 has an intensive international collaboration within Europe (EPIC, IARC in Lyon), but even with Mexico (newly established). The strong skills within EPIC consortium are reflected in many publications based on this collaborative project. The French part of the EPIC with 100,000 women (of 500,000 women and men totally), i.e. 20% of the entire EPIC, has enough statistical power for breast cancer analyses (about 5000 cases) to enable many of their own analyses before contributing with the data to the consortium.

The weakness is that there are only 2 senior researchers responsible for both the data collection and management of this very large and rather complex database with repeated longitudinal data, as well as for supervision of many PhD and MSc students. The full scientific potential of the E3N cohort could be better used/utilized by extending the group with additional senior researchers with permanent positions. A close collaboration with Team 1 – biostatistics - is encouraged to improve/develop statistical analyses.

In summary, Team 9 needs strengthening with more senior researchers to publish more papers based on only French data (first, before contributing with data to the EPIC analyses). This will highlight French epidemiology on a very competitive international arena.

Nom de l'équipe : **Nutrition, Hormones and Women's Health**

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A+	A	A	A

Team 10 : Epidemiology of diabetes, obesity and renal disease: lifelong approach, early nutritional determinants :

Overall, the visiting committee assessed the past activity and the research project of this team as VERY GOOD.

This research group, with a relatively large research team of 5.2 FTE researchers, has a very good international profile and has produced a large volume of research publications in recent years covering several research themes. The senior scientists are highly internationally ranked in their field and one has a very prominent position within international advisory groups for diabetes recommendations.

Of all teams evaluated in the Centre this one has the most expertise in genetic epidemiology. However, this is almost completely isolated to one junior level researcher. This researcher performs cutting edge studies in DNA methylation and would benefit from a wider base in genetic epidemiology in the Centre. It is hoped that more young researchers are attracted to the team, possibly from their pool of seven PhD students. The team has just one postdoctoral fellow. Therefore, additional training and/skilled personnel are required. The group has established and nurtured several well conducted cohort studies which have been used in several very high profile genetics and to a lesser extent non-genetic studies. The contribution to the genetics studies has been largely contribution of data and some data analysis (i.e. they did not lead these projects). Although some of the research plans are cutting edge, particularly those which relate to genetics and epigenetics, the group will require additional intellectual support to carry out this work (either through collaboration or by appointing new personnel).

The written report did not do justice to the team's research. The report did not lay out the conceptual framework or place the team's past or future research in the context of the scientific field (it was surprising, for example, that there were no references). The presentation filled some of these gaps by providing a conceptual framework although this was not entirely convincing, and the connections between the various research projects were not clearly elucidated and perhaps do not all fit so readily within the life course theme.

The team are responsible for several cohort resources, and these appeared to be well maintained with good response rates. The team's interpretation of a life course approach was somewhat limited, and involved undertaking studies at different stages of the life course. While these studies would appear to be of high quality, this design cannot investigate the long-term effects of risks in earlier life on later life outcomes, nor the potential interactions between earlier and later life risks, which are key components of such an approach. The team was aware that the interpretation of any comparison of their findings across the life course would be potentially confounded by cohort effects. There seemed to be little integration of social and biological risk factors (another key component of a life course approach) and research on the social aspects appeared to be undertaken by a different team. To maximise the scientific and life course potential of these studies, I would recommend that more collaborative links be set up with other European cohorts, such as ALSPAC (based at Bristol University) or the Southampton Women's Survey (based at the MRC Unit at the University of Southampton).

Although this group has more expertise in statistical genetics than the other groups, there does not appear to be any sharing of this expertise. Thus, enhancing links between teams seems essential if the unit is to benefit from joining together under the same banner.

Nom de l'équipe : **Epidemiology of diabetes, obesity and renal disease: lifelong approach, early nutritional determinants**

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A	A+	A

Team 11 : Epidemiology and social and occupational determinants of health :

Overall, the visiting committee assessed the past activity and the research project of this team as EXCELLENT.

Strong points :

The team includes a number of innovative projects within the field of social and occupational epidemiology. Relevant sub issues include programmes on social inequalities, in ageing, muscoskeletal and mental disorders.

The team is highly productive and has a high scientific standard; this is also reflected in a ERC young researcher award.

The team also hosts a number of relevant cohorts and related biobanks.

The team played a significant role in the development of Occupational Epidemiology in France and is still one of the few French teams in the field, with an important recognition at the international level.

The team is involved in many international collaborations.

Weak points and suggestions :

The team research activities are heterogeneous. It is not clear which of the different sub issues has priority in the team and some innovative projects of the document were not part of the presentation. This might indicate that they could lack sufficient attention and resources.

Many resources are used for the establishment and hosting the cohorts which could be better integrated in projects of other teams in the centre. Furthermore, such large and important cohorts should be better exploited with respect to a wider range of exposures (e.g. focusing also on environmental exposure).

It is not clear at what level research for the development of new methods of studying and measuring social inequalities in health is present in the team. This field of research should be strengthened.

Nom de l'équipe : **Epidemiology and social and occupational determinants of health**

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	A	A	A	A+

Team 12: Lipid nutrients, metabolism and cancer risk :

Overall, the visiting committee assessed the past activity and the research project of this team as insufficient.

Team 12 has a molecular epidemiology approach to study the etiology of breast cancer (and other cancers in the future). The research is focused on the role of specific fatty acids as well as related genes/enzymes involved in fat metabolism which may be of importance in the development of breast cancer. Team 12 uses biologic material (blood for analyses of biomarkers) from the E3N cohort under management of Team 9.

The strength of Team 12 is the availability of a lipidomic platform for analyses of fatty acid composition as well as carotenoids and other fat-soluble components in biologic material.

The weakness of Team 12 is its very small size, with only 1.1+1 senior persons involved. They use data from Team 9. They propose an interesting very broad interdisciplinary biological approach; however, such very broad competence seems to be not available in this small team, thus they have to rely very extensively on collaboration with other experts (eg. within epigenetics).

It should be mentioned that the presentation of the T.12 was made by the researcher involved only 10% in the T.12 work, not by the team leader (the leader was sick). Maybe therefore the committee has not got the most appropriate presentation of their ongoing work and future plans. In some proposed future projects there may be problems of statistical power (eg. colon cancer); candidate genes approach and choice of genes were not well motivated. There was not a convincing explanation as to why these few researchers should be constituted as a separate group. The group produced some good papers, but the authorship was rather in the middle of all co-authors, thus not indicating a leading role in these studies.

Nom de l'équipe : **Lipid nutrients, metabolism and cancer risk**

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
C	C	C	C	C

5 • Appreciation of resources and of the life of the research unit

The annual resources of the CESP total 6900 KEuros divided into: 1000 KEuros as recurrent funding and 5900 KEuros from project grants.

Human resources have been merged to cope with the management of a research centre with 250 persons. A huge number of national and international contracts have been collected during the previous years by all the research teams (more than 40 different contracts to be managed at the same time with many different institutions). To be effective, this means that it is essential to have a very specialised administrative team of people well trained and well informed.

The localisation of the different teams on 3 different sites is a difficult issue to consider in terms of the effective allocation of resources.

The optimal use of resources has to be analysed and discussed specifically (and in depth) outside the scientific assessment by competent administrative managers used to structures of this size.

Life within the centre (appreciated through 3 sub-groups meetings):

Among the researchers with permanent positions, 3/4 are affiliated to INSERM and 1/4 have faculty positions. Researchers feel free to choose their area and topic of research. Four to five (out of 20) of them would like to create their own teams in the next 5 to 10 years.

Researchers are involved in teaching duties to very different degrees depending mainly on their willingness to teach – they feel free to accept or refuse teaching. However, teaching load is not equally distributed among teams.

Rules for authorship are those commonly shared across research units in France and favour publication of PhD students as first author, and supervisors in last position.

In all teams, regular scientific and bibliographic meetings are organized, and one team (11) has organized regular journal clubs.

The main difficulties encountered by researchers concern technical and administrative support. They claim not to have enough permanent positions, and have difficulties to keep non permanent technical staff for administrative reasons. Researchers encounter huge difficulties to invite foreign students, post-doctoral fellowships or visiting researchers.

The students who discussed with the committee were fluent in English. Four post-doctoral students coming from abroad gave a very positive outlook of their visit to the research teams. PhD students all need to publish to pass their thesis (3 articles accepted and one submitted necessary for submitting a thesis in Paris 11). PhD students consider the grouping of the 12 teams is a very good initiative for internal exchanges but also to make the centre and "French" epidemiology more visible internationally. PhD students are encouraged to attend international meetings every year and to present their results in oral presentations. They are also encouraged to arrange post-doctoral stays abroad. Seminars in English are planned for the future.

The only wish expressed by the students for improvement (except the wish to have more permanent positions offered) was to have more information on possible occupations after their thesis.

The CESP research centre brings together technical staff from 7 INSERM - University mixed structures, in twelve teams and two cross-cutting services. Of a total of 252 officials, 103 people are engineers, technicians and administrative staff, with only 40 permanent agents and 63 under contract or from other institutions. The management was presented in the introduction and provides effective representation in decision-making: several types of committees and groups or levels of management.

Three AERES visiting committee members met in the framework of the visit, about twenty representatives of ITA for about 45 min. They found that there are many hopes, but also many concerns. Indeed staff in spots often similar within each structure must find their place in the new organisation, while for some spots, agents fear a lack of human resources, such as for the General Secretariat. The interaction between groups and themes for a transitional period will, without any doubt, clarify the individual tasks. In any case there is a strong need for establishing solid democratic procedures in the areas of communication, decision making, training, career promotion, distribution of bonuses, the positions and career management for agents under contract. The Rules of Procedure, in preparation-negotiation, must be the guarantee of effective daily functioning.

6 • Recommendations and advice

- Strong points :

The scientific visibity of the scientific director is excellent and his ability to organise the overall scientific and administrative management of the structure is a guarantee of the success of this creation.

The creation of this centre by the grouping of previously and well-known INSERM teams will increase the international visibility of epidemiology in France.

The increase in the number of PhD students and post-doctoral fellows will allow the organisation of more relevant initiatives in their direction. The dynamics of the overall group will clearly be improved (international exchanges and seminars in English for example).

The overall atmosphere of the centre appears to be very good and the meeting with doctoral/postdoctoral students convinced the subgroup of the committee who audited them that the dynamics of the overall research centre were excellent.

The large range of public health fields covered by the centre gives a unique network of researchers for this scientific expertise.

Very large and relevant cohorts centralised by the grouping of the research teams in the centre (E3N, Gazel, EDEN, …) and also a well designed national cancer registry.

- Weak points :

Having a common and same location for the centre would be better to be able to organise scientific exchanges between people. Presently there are at least 3 locations for these 12 teams (Paul Brousse Hospital, Kremlin Bicêtre and Institut Gustave Roussy).

There is a need to be more attractive for international doctoral/postdoctoral students and for the processes to be simplified.

Measurement of environmental exposure could be improved in some of the projects studied.

Expertise in genetic epidemiology is not covered "in house" which can be deleterious for keeping the lead on these research themes when the biological material is issued from the cohorts.

- Recommendations :

The administrative workload of the management of 250 people has clearly to be considered with caution and needs to be supported both by the university and the INSERM institution. The need for permanent or contractual positions for high level administrative staff is highlighted. A possibility to complement the regular budget would be to systematically take overheads from the contracts. This could allow the centre to have a grant officer, for example. This is an important issue for such a volume of contracts to be managed.

Many resource-consuming data bases are implemented in all the 12 teams. However, some choices will have to be made when implementing new cohorts, for example, with the necessity for the teams to share their experience.

The issue of "in house" genetic epidemiology has been debated. It would be a big improvement for future years to attract researchers involved in that field to give to the centre the possibility to have cutting-edge projects on these issues which are very relevant to the work of many of the teams.

The issue of improving, in the centre, the expertise on environmental measurement was also discussed. Several teams need this competence. The committee suggests being pro-active on this question to maintain a high level research in that field.

Transversal research axes were presented in the written documents; they were discussed in depth during the visit with the CESP director. These axes should be helpful in structuring the future developments of the research teams, in particular for those which are smaller in size or for those appearing to be more fragile (for whatever reason).

Such a centre would need to have a specific organisation for diffusion of professional information for technical staff and also for the doctoral and post/doctoral fellows.

Note de l'unité	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	A	A+	A+	A+

UNIVERSITÉ
PARIS-SUD 11

Le Président de l'Université Paris-Sud 11

à

Monsieur Pierre GLORIEUX
Directeur de la section des unités de recherche
AERES
20, rue Vivienne
75002 Paris

Orsay, le 17 avril 2009.

N/Réf. : 135/09/GCo/LM/LS

Objet : Rapport d'évaluation d'unité de recherche
N° S2100012406

Monsieur le Directeur,

Vous m'avez transmis le seize mars dernier, le rapport d'évaluation de l'unité de recherche « Centre de Recherche en Epidémiologie et Santé des Populations » - CRESP, et je vous en remercie.

L'université prend bonne note de l'appréciation et des suggestions faites par le Comité.

Les points à améliorer seront discutés avec le directeur d'unité dans un esprit constructif pour l'avenir de la recherche à l'université.

Vous trouverez en annexe les éléments de réponse de monsieur Denis HÉMON, Directeur de l'unité de recherche.

Je vous prie d'agréer, Monsieur le Directeur, l'expression de ma sincère considération.

Guy COURRAZE
Président

UNIVERSITE PARIS-SUD 11 - Présidence - 91405 ORSAY CEDEX

P.J. : Commentaires de Mr HÉMON

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Centre for Research in Epidemiology and Population Health
Centre de Recherche en Epidémiologie et Santé des Populations (CESP)

Answers to the AeRES evaluation report (April 3rd 2009)

CENTRE FOR RESEARCH IN EPIDEMIOLOGY AND POPULATION HEALTH (CESP)
Project leader: Denis HÉMON, Research Director, DRE - Inserm
Permanent position researchers: 69 (47.2 FTE); of whom 43 Research Management Accredited (HDR), 45 full time researchers, 21 academics and 3 hospital researchers.
Engineer and technicians: 103 (64.4 FTE); of whom 40 permanent EPST or academic positions.
PhD students: 50, Post-doc fellows: 30

Complementary information and comments relating to § 6"Recommendations and advice"

6 • Recommendations and advice

- Strong points:

"The scientific visibility of the scientific director is excellent and his ability to organise the overall scientific and administrative management of the structure is a guarantee of the success of this creation.

The creation of this centre by the grouping of previously and well-known INSERM teams will increase the international visibility of epidemiology in France.

The increase in the number of PhD students and post-doctoral fellows will allow the organisation of more relevant initiatives in their direction. The dynamics of the overall group will clearly be improved (international exchanges and seminars in English for example).

The overall atmosphere of the centre appears to be very good and the meeting with doctoral/postdoctoral students convinced the subgroup of the committee who audited them that the dynamics of the overall research centre were excellent.

The large range of public health fields covered by the centre gives a unique network of researchers for this scientific expertise.

Very large and relevant cohorts centralised by the grouping of the research teams in the Centre (E3N, Gazel, EDEN, …) and also a well designed national cancer registry."

- "Weak points" and "Recommendation"

(1) Geographical location of the Centre

"Having a common and same location for the centre would be better to be able to organise scientific exchanges between people. Presently there are at least 3 locations for these 12 teams (Paul Brousse Hospital, Kremlin Bicêtre and Institut Gustave Roussy)."

The *Santé Publique Paris Sud* campus is made of 3 compact components, located at the 3 sites of *Faculté de Médecine Paris Sud* - Hôpital Paul Brousse (2700m2, Teams 1, 5, 6, 8, 10, 11), Institut Gustave Roussy (600 m2, Teams 3 and 9) and CHU Bicêtre (1100 m2, Teams 2, 4, 7). These three are located within 2 kms of each other and have collaborated closely for a long time:

- scientifically, particularly in the context of the *IFR69 Santé Publique Paris Sud,* from 1997 till the end of 2009, that involved sharing of administrative and computer facilities, collaboration on large-scale multi-team research projects and scientific exchange,

- academically, joint organisation and teaching of high level university courses and training sessions in Public Health (Masters, Doctoral School, Summer and Winter courses) which are followed by about 600 students every year.

Considering Hôpital Paul Brousse, Institut Gustave Roussy and CHU Bicêtre clinical, scientific and academic specificities the location of a team at one site or another allows closer interaction with many on-site departments: the clinical services, research lab or university training facilities at the specific site.

Further, the 2700 m2 Inserm - Public Health building at Paul Brousse will benefit by the end of 2010 of the availability of a further 600 m2 to welcome new scientific teams to the Centre.

(2) Improving the attraction of students and scientists from other countries

"There is a need to be more attractive for international doctoral/postdoctoral students and for the processes to be simplified".

The ability of the CESP and its Teams to attract PhD students, post-doctoral fellows and scientists is clearly of strategic importance.

Currently, the CESP Teams welcome 5 foreign scientists but also 30 post-doc fellows and 50 PhD students. Three of the PhD/post-doctoral fellows are from other countries. Although significant, these numbers could and should be increased.

In order to attract foreign students and colleagues the Centre can and does take advantage of the strong international visibility of its scientific programs and Teams. However, it also faces difficulties at several levels that have been well identified:

- the relative lack of high-level administrative and logistic support for researchers in order to allow them to welcome their foreign students and/or colleagues efficiently,

- the still too limited use of English in local scientific exchanges with our foreign students and/or colleagues (while the *ability* to use English language is widespread among the Centre's members),

At CESP we intend to develop a very active strategy in order to increase the number of its foreign scientific guests:

- encouraging the Teams to propose scientifically attractive PhD and Post-doc programs,

- developing and updating the English version of the Centre's web site in tandem with an English version of the website of the Paris South Doctoral School in Public Health,

- promoting much larger use of the English language in the scientific exchanges that take place within the Teams and the transversal scientific axes,

- hiring high level administrative support in order to help our researchers attract and welcome scientists from abroad, prepare grant applications, follow-up these applications, help with the logistic and administrative aspects of the arrival for international colleagues, help in the setting up of bilateral exchange programs between the Centre and foreign homologous excellence sites in Public Health.

(3) Measuring environmental exposures

"Measurement of environmental exposure could be improved in some of the projects studied" ... "The issue of improving, in the centre, the expertise on environmental measurement was also discussed. Several teams need this competence. The committee suggests being pro-active on this question to maintain a high level research in that field.

Research on environment and health is central to the research of Teams 5 and 6, and also present in the programs developed by Teams 3, 9, 10 and 11.

This is a key issue for CESP; to promote exchange on the measurement of environmental exposures is one of the objectives of transversal axis #2: Environment and Health. It will benefit from the skills present within the CESP and the various partnerships established by the teams in order to allow: construction of specialized questionnaires, ad hoc evaluation procedures, sophisticated exposure measurements technologies; and use of biological markers, geographical information systems, and modelling sources of exposures and diffusion of pollutants, etc.

(4) Improving the scientific potential of the CESP research Teams in Genetic epidemiology

"Expertise in genetic epidemiology is not covered "in house" which can be deleterious for keeping the lead on these research themes when the biological material is issued from the cohorts. ...The issue of "in house" genetic epidemiology has been debated. It would be a big improvement for future years to attract researchers involved in that field to give to the centre the possibility to have cutting-edge projects on these issues which are very relevant to the work of many of the teams."

There is "in-house" expertise in genetic epidemiology as more that half of the CESP Teams undertake research on genetic risk factors. Within the Centre, there is a high statistical level, especially in genetic epidemiology, a specialty, which is taught in our Master and Doctoral School of Public Health.

The teams involved have also developed collaborations with external teams, in France and abroad, to complement expertise in the technological, biological and methodological aspects of their projects.

The Centre ranks it as a priority to promote exchange on research on genetic components of complex mutifactorial diseases and how they combine their "effects" with environmental, behavioural and psychosocial factors. This issue is central to 3 of the transversal axes: 1. Life course approach to epidemiology - Child and adolescent health ; 2. Environment and Health ; 3. Cancer epidemiology. Thus, further improving in-house expertise in this domain by attracting new researchers and/or Teams is also a priority of the CESP.

(5) Administrative resources of the CESP

"The administrative workload of the management of 250 people has clearly to be considered with caution and needs to be supported both by the university and the INSERM institution. The need for permanent or contractual positions for high-level administrative staff is highlighted. A possibility to complement the regular budget would be to systematically take overheads from the contracts. This could allow the centre to have a grant officer, for example. This is an important issue for such a volume of contracts to be managed."

As underlined by the AERES evaluation group, one of the key objectives of the Centre is to equip itself with the best administrative resources. The CESP Teams are preparing the necessary collaborations and synergies between their administrative staff, in relation with the administrative team of IFR69. They plan to pool a part of their financial resources to create 1 or 2 additional high-level administrative positions within the CESP.

(6) Developing an optimal strategy for the setting up of observational data-bases

"Many resource-consuming data bases are implemented in all the 12 teams. However, some choices will have to be made when implementing new cohorts, for example, with the necessity for the teams to share their experience."

The CESP Teams are principal investigators of studies involving broad-spectrum (GAZEL, E3N, CONSTANCE, EDEN ...) or specialized (follow-up of children born to HIV-positive mothers and HIV-infected adults, survivors of a cancer in childhood…) cohorts, large-scale case-control studies and registry data.

As noticed by the AeRES evaluation group, the CESP transversal axes have been set up to promote exchange and to help pool skills and resources. Furthermore, a number of collaboration between the teams in CESP do already exist.

TEAM 1. BIOSTATISTICS
Project leader: Pascale TUBERT-BITTER, Research Director, DR2 - Inserm
Permanent position researchers: 4 (3.5 FTE); of whom 3 Research Management Accredited (HDR), 3 full time researchers and 1 academic researcher
Engineer and technicians: 3 (1.0 ft); of whom 3 permanent positions.
Doctoral students: 4

We thank the visiting committee for their overall appreciation and their comments. We would like to stress a few points.

Functioning of the team: The division in two research axes reflects our specialization and does not imply the lack of scientific exchange within the team. For example, some members of the team belong to both "groups". The successful development of the pharmacoepidemiology field within the team reflects the quality of its functioning.

Publications: Our scientific production includes 93 publications in peer-reviewed journals between 2003 and 2008 (85 for 4.7 full time researcher equivalent on average over that period and excluding the production of the member who has just joined the project). Among them, 82% (76) as first, second, second-last, or last authors and 32% (30) in statistical journals. According to the first quartile of impact factors within categories (JCR 2007), 43% belong to the top 25% of Public Health pooled with Medicine, Research, 73% in the top 25% of Probability and Statistics (including 2 papers in Bioinformatics ranked first, 10 papers in Statistics in Medicine as acknowledged by the report), and 48% in the top 25% for the other categories.

We fully agree with the committee on further improving the profile of our statistical publications. In order to publish in high quality statistical journals (which do not rank necessarily in the top impact factors of the JCR category "Probability and statistics"), it is necessary to devote more time in developing and submitting research on more general and somewhat fundamental statistical issues. The scientific strategy to achieve this objective is a subtle question as we are a group of moderate size. We are thus involved in a more proactive and focused publication approach, based on our strengths:

(i) by advancing collaborations with statisticians from mathematics departments at universities: already strengthening the existing collaboration with members of the MAP5 laboratory, creating links with the mathematical statistics department of the Besançon University which is in progress and developing our top international collaborations that are notably all of this nature;

(ii) by enhancing this publication strategy that already showed some success in particular with our PhD students: for instance with articles in Biometrics (just accepted for publication) or in Biostatistics. We are a team strongly involved in teaching and research training. All members of the teach, and the team leader share the responsibility of the Biostatistics Masters degree at Paris 11 – Paris 5 Universities; there are currently 5 PhD students under supervision in Team 1;

(iii) by increasing interactions with other teams of the CESP while keeping our core focus (these interactions are explicitly recommended by the committee in the evaluation reports of some teams): we are currently developing collaborations within the Centre, through co-supervision of students (e.g. with teams 2, 5, but not limited to those in the future), and as our colleagues we see these interactions as a positive outcome.

Overall, we feel encouraged to continue directing our efforts towards a more ambitious publication record, while keeping the leadership of the majority of our production and sustaining the quality of our research output in the substantive literature.

TEAM 2. EPIDEMIOLOGY OF REPRODUCTION AND CHILD DEVELOPMENT

Project leader: Jean BOUYER, Research Director, DR2 - Inserm

Permanent-position researchers: 9 (4 FTE), of whom: 6 HDR, 5 full time researchers, 3 academic researchers, 1 hospital practitioner

Engineers and technicians: 6 (4.8 FTE), of whom 3 permanent positions,

Doctoral students: 2 Post-doc fellows: 1

Publications in international peer reviewed journals: 130 articles between January 2003 and September 2008 for 4,4 FTE researchers (i.e. 5.1 articles per researcher-year). Among them 58% as 1st or last authors, and 27% in the Top 10 (and 40% in the Top 20) of published papers in the disciplines of the team.

The "Epidemiology of reproduction and child development" team focuses principally on epidemiology, but is enriched by input from other disciplines, especially paediatrics, obstetrics and demography. This pluridisciplinarity is one of the strengths of the team. It enables us to develop an original global approach to research questions, that is, to consider subjects' entire pathway. For instance, we are examining the course of sub-fertile couples through their treatment period and onward to several years after its end, including the consequences of treatment on women and children. More globally, there are questions on the consequences for children's health of the conditions of their conception and gestation. These issues require links between reproductive and paediatric epidemiology, a specific focus of our team.

In paediatrics, a significant part of our research goes beyond the physical or biological health of children and is focused on the psychomotor development and social and the familial environment (particularly in ELFE study). Consequently, the title of the team includes "child development". However, we acknowledge "child health and development" would be more precise.

Another characteristic of the team is the profound evolution of its research themes, especially in paediatrics thanks to the arrival of two paediatrician-researchers who are developing research in clinical paediatrics (in neurology and infectious diseases). This development will continue with collaborations with the maternity ward of Bicêtre University centre, due to open in 2009. These projects, focused on long term outcomes of both mother and child with a “non confirmed” antenatal abnormality diagnosis, will enable us to reinforce our links with clinicians as well as allow interactions between the reproductive and paediatrics research axes of the team.

We have strong links with paediatric and perinatal clinicians, as well as clinicians in reproductive medicine. For instance, the DAIFI study involves 10 IVF centres. The study design, the results and the publications are discussed with these clinicians.

We agree on the importance of training doctoral students. Indeed, the team has welcomed 6 doctoral students since 2003 (for only 2,3 FTE entitled (HDR) researchers).

The team has several international collaborations in neurological paediatrics, fertility epidemiology, and child development as mentioned in our written assessment and project files. However, we agree that we could further increase our international collaborations.

TEAM 3. EPIDEMIOLOGY OF CANCER: RADIOCARCINOGENESIS AND IATROGENIC EFFECTS OF TREATMENTS

Project leader: Florent de VATHAIRE, Research Director (DR2), Inserm

Permanent-position researchers: 4 (3.4 FTE), of whom 1 HDR, 3 full-time researchers, 1 academic researcher

Engineers and technicians: 7 (6.7 FTE), of whom 2 permanent positions,

Doctoral students: 3 ; Post-doc: 1

Regarding publications, team members part of the project (including researchers with permanent positions (1DR2, 2CR1, 2PU and 1 post doc researcher) published in the 2003-2008 period 103 papers with 43, i.e. 34% in a leading position, and 40 of those in the top decile of JCR, ie 38%.

Excluding publications of team members done outside the team (before joining, post doc, etc...), figures were 83, 38/83 i.e. 46% in leading positions and 29/83 i.e. 35% in the top decile, with a majority of publications in the best journals of Epidemiology and Oncology, which cover most of our research activities.

Publications: The visiting committee noted our high level of publications but also noted the "heterogeneous" profile of publications. We would like to assure the committee that this will improve by the end of 2009 due to the following.

• We will reach the end of a very long period of updating (3 cohorts) or constitution (2 cohorts, 1 large scale multi-centre case-control study) of our data bases.

• The lack of publications on our dosimetric works is due to efforts devoted to the development of parts of a dosimetric software in collaboration with a private company in order to obtain intellectual property rights. This has now been achieved (Patent on Human Phantoms and Global Beam Model: (APP) DDN.FR.001.220011.000.S.P.2008.000.31230). This was a high-risk strategy but it is our feeling that is has been successful. The downside has been that we haven't been able to publish in this domain for a few years. However, this has now changed as we have begun to publish on our dosimetric approach: 2 articles are in press in the International Journal of Radiation Oncology, Biology & Physics and in Physical in Medecine an Biology.

• Finally, the publication situation will improve after the reintegration of one of the 3 researchers after a prolonged maternity leave.

Long-term viability: The visiting committee was concerned about our "long term viability" and wondered if we should consider "merging" with "one of the other stronger groups". This is not a solution as most of the patients in our cohorts are from IGR and our dosimetric work cannot be done outside of a strong Physics department. We would prefer to resolve our problems of size, by improving our implantation in IGR. In the next 4 years our strategy will be to increase our links with IGR, both in dosimetry and in epidemiology. In dosimetry by the formalisation of a common structure with the Physics department. In epidemiology, by strengthening a strategy, initiated in 2008, of increasing the number of medical onco-paediatricians in our team. Indeed, one such full time person joined us in March 2008, and 2 further part-time in 2009.

Isolation: There was some concern that we were "intellectually somewhat isolated". This is clearly not the case as we are currently involved as members in 2 Europeans projects funded by EURATOM : GENE-RAD-RISK (genes and radiation in the risk of second breast cancer), CHILD-MED-RAD (Cancer following scanner in childhood), and in 3 international projects MOBIKIDS (Brain tumour following mobile phone use in childhood), PIRATES (thyroid cancer following radiation), and THYGENE (genetic of thyroid cancer). During the reported period, we were also partner of another EURATOM funded project, CHLD-THYR (thyroid cancer following 131I exposure due nuclear fallout). In addition, we have just finished updating a multi-centre cohort of 14 000 patients from 3 European countries who received iodine for a thyroid cancer, which was constituted during a EURATOM concerted action coordinated by the team leader. All but one (a cohort of women who survived from a breast cancer) of our cohorts / case-controls studies includes several other centres in France and contributes to international pools. As an example, the cohort of childhood cancer survivors that we still follow has been initiated 20 years ago in a "Europe Against Cancer" integrated project coordinated by the team leader. In dosimetry, we have a collaboration (INCA grant coordinated by Ibrahima Diallo) with the Physics departments of IGR and of Institut Curie, and several private companies. Furthermore, we have just submitted a project in collaboration with France-Telecom to the ANR and are members of an industrial project (INSPIRA) submitted to the OSEO. Finally, we are also currently working on the setting up of a European project.

Causal Interpretation: The AERES Committee was concerned by the fact that we do not work on randomised trials, and had to be cautious about "causal interpretation". We agree entirely and the high level journals (JCO, Lancet, AJE) in which we publish also have this concern. Some further clarifications on this point which is indeed of importance for any pharmaco-epidemiological investigation of the iatrogenic risks associated with drug use:

1) As patients with more aggressive tumours also received more aggressive treatments more frequently, both for radiotherapy and for chemotherapy, the specificity of our team is precisely to collect all the information needed to control in detail all aspects of the treatments. As an example, our childhood cancer survivors study is the only one in which each dose, starting and end time, the method of administration of each drug received of each cure of each child has been collected, and the radiation dose received by most of the healthy tissues estimated.

2) As patients with more aggressive tumours are more likely to be carriers of a genetic predisposition to a second cancer, independently or not of the treatment they received, one of our priorities now is to examine gene – radiation interactions by participating as a member of the project board in the Gene-Rad-Risk project and by undertaking a large size case – control study.

3) Our main objective is to provide information needed to anticipate the effects of new radiotherapy techniques, such as IMRT or tomotherapy and therefore to study not only the effect of a given treatment versus another (two modalities of radiotherapy, for example) but also to investigate specific questions such as the effect of dose-fractionation or irradiated volume, which cannot be investigated in randomised clinical trials because of the small number of such trials dealing with these specific problems.

4) Lastly, the average follow-up of our cohorts is 10 years or longer compared to cohorts based on a pool of randomised clinical trials, and this aspect is essential when examining the long term effects of cancer treatments.

TEAM 4. EPIDEMIOLOGY OF HIV AND SEXUALLY-TRANSMITTED INFECTIONS

Project leader: Laurence MEYER, University lecturer, Hospital practitioner (MCU-PH), HDR

Permanent-position researchers: 5 (3.3 FTE), of whom 3 HDR, 4 academic researchers, 1 hospital practitioner

Engineers and technicians: 17 (17.0 FTE), of whom 7 permanent positions,

Doctoral students: 3 ; Post-Doc: 1

Corrections of mistakes:

- 3 PhD Students instead of 2
- Title of the team is 'Epidemiology of HIV and Sexually Transmitted Infections' (not Diseases)

Structure of the team: Team 4 is a focused group comprising 4 senior researchers with permanent faculty positions, leading to an administrative count of 1.6 FTE senior researchers. An important category of personnel is however missing from this count. In effect, our team also has 1 full-time epidemiologist Medical Doctor (AP-HP), and a further 4 full-time Inserm "engineers" with one devoting 30% of his time to researcher activities, as is evident from our publications. The team also benefits from a close collaboration with clinicians and biologists who are not based within our team, and thus not counted in the FTE calculation, but provide excellent feedback on the numerous studies that we carry out requiring clinical expertise.

Productivity: The team has produced since 2003 a total of 114 papers, in high ranking journals as underlined by the visiting committee. In 35% of these papers, the team is 1st or last author, and in 24 % 2nd or second last author. Overall 26% of the papers are in the top 10 % cited articles (source: Bibliometry Department, Inserm, 2008). Two of the engineers have developed a computer program for cohorts referenced at INSERM Department of Technology Valorisation and Transfer, number DVTT 02358.

Our activities: The team concentrates most of its activity in France, but is also part of large collaborations in Europe and at the international level. Indeed, the team leader is vice-chairperson of a European collaboration, and the team is involved in collaboration with one of the best teams in the world developing innovative methods for analyzing therapeutic observational data, the Harvard School of Public Health. The team also comprises several researchers and engineers with high-level statistical kills.

Our research on tolerance to prenatal or childhood exposure to HAART was seen as highly innovative and relevant by the AERES visiting committee, as is the research program on HIV controllers where we are the leaders in Europe; the first patients were described by the team in 2005. The increase in incidence of sexually transmitted infections in France concerns both epidemiological surveillance, under the responsibility of *Institut de Veille Sanitaire*, and research, which is our speciality in both HIV-infected subjects and in the general population using large population-based studies such as CSF (*"Comportements Sexuels en France"*) and KABP studies.

Finally, we have also recently implemented several projects in low-income countries such as Cameroon, Thailand and Ivory Coast, not only on mother-to-child transmission but also on prognosis of HIV-infected subjects.

Future of the team: The team currently hosts 3 PhD students and one post-doctoral researcher, in charge of an innovative cohort of young adults infected at birth. This post-doc is going to apply for a permanent position at Inserm.

TEAM 5. RESPIRATORY AND ENVIRONMENTAL EPIDEMIOLOGY

Project leader: Francine KAUFFMANN, Research Director, DR1 - Inserm

Permanent-position researchers: 5 (3.4 FTE), of whom 3 HDR, 3 full time researchers, 2 academic researchers

Engineers and technicians: 3 (1.5 FTE), of whom 3 with permanent positions,

Doctoral students: 1 ; Post-doc researchers: 1

Team 5 is grateful to the visiting committee for their recognition of its past activity and the appreciation of its project.

Regarding publications, team members part of the project (including researchers with permanent positions (1DR1, 2CR1, 1PU, 1PU-PH) and 1 post doc researcher) published in the 2003-2008 period 222 papers with 166, *i.e.* 75% in a leading position (51 of those in the top decile of JCR, *ie* 31%). Excluding publications of team members done outside the team (before joining, post doc, etc...), figures were 50, 41/50 *i.e 82%* in leading positions and 21/41 *i.e. 51%* in the top decile, with a majority of publications in the best respiratory and allergology journals, corresponding to our focused activities.

Three PhDs have been defended in the last four years, another is due to start soon. In the context of the European Associated laboratory set up with CREAL in Barcelona, that is developing very successfully, we plan to increase the number of PhD students through co-supervised theses.

Besides the current participation of a Professor of Biostatistics in the team, several young researchers have a good background in statistics, allowing them to determine the appropriate methods for the questions under study. They also have the competence to assess their needs for more complex issues and establish appropriate collaborations within or outside the CESP.

The team has an international reputation in genetics in respiratory diseases, attested by publications in the field in leading positions (Plos One and Am J Respir Crit Care Med in 2008 and 2009), invited conferences, requests of post doctoral stays, etc. Furthermore, the team has a long standing and very close collaboration of mutual benefit with Inserm U 946, a group renowned world-wide of very high methodological level, which has led to numerous publications in genetic, respiratory and general journals.

Besides the work in progress on asthma severity and control with the senior researcher who recently joined the team, specific new projects are planned in the context of understanding asthma heterogeneity, such as the epidemiological study of allergic and non allergic rhinitis, an aspect in which he is a worldwide specialist.
Besides work in progress on aspects dependent on socio-cultural determinants such as education, studies on the healthy worker effect and determinants of perceived health, the team plans to take advantage of specialized teams within the CESP centre to incorporate psychosocial determinants of respiratory health.

TEAM 6. ENVIRONMENTAL EPIDEMIOLOGY OF CANCER

Project leader: Jacqueline CLAVEL, Research Director (DR2), Inserm

Permanent-position researchers: 7 (5.8 FTE), of whom 4 HDR, 5 full-time researchers, 2 hospital practioner

Engineers and technicians: 8 (7.4 FTE) of whom 4 with permanent positions,

Doctoral students: 7

Team 6 published 105 papers in a steady rhythm during the period 2003-2008 (less than 5.2 full-time equivalents on average over that period), 64% of which were signed as 1st, last, 2nd, last or second-last authors (increasing to 79% in 2007, 88% in 2008). The Impact factors of the journals we publish in are in the best 10% of their JCR category for 19% or our papers, and in the best 20% for 39% of them (stable over the period), which is high in our research field. Meanwhile, team 6 produced large sets of data (interviews + biobanks) on breast cancer (1200 ca/1200 co), lymphoma (800 ca/800 co), lung cancer (3000 ca/3000 co), thyroid cancer (1000 ca/1000 co), childhood cancer (1500 ca/1700 co) and set up the national survey on childhood cancers and environment (geocoded addresses for 12000 ca/18000 co).

The AERES report acknowledged our longstanding experience in occupational epidemiology, but the absence of reference to our current works on the general environment may be misleading: we fully agree with the recommendation of the AERES experts to develop research in the general environment and we therefore feel it is important to underline that the members of Team 6 have been developing this field actively for many years in unit 754. Our commitment in this field has already produced papers, published in high-ranking journals, particularly on environmental exposures to ionizing radiation, UV, petrol stations, pesticides and infectious agents.
Our on-going projects on this issue include large-scale studies based on geo-coded addresses and ad hoc geo-coded environmental databases (e.g. roads and traffic, high power lines, campaigns of radon measurements and geology, waste incinerators). We obtain quantitative estimates of intensities of exposures by modelling the exposures in collaborations with experts from specialized institutions and agencies (IRSN[1] for exposures to ionizing radiation due to radon and nuclear sites, ADEME[2] and AIRPARIF for air pollution due to traffic, RTE3 for electromagnetic fields due to high-power lines, InVS[4] for dioxins from waste incinerators).
Another innovative aspect of our research related to the general environment is the use of exposure biomarkers: serum levels of persistent organochlorine compounds are used in a large study on breast cancer, and lifetime exposure profiles are being derived from physiologically-based pharmacokinetic models.

Regarding research involving genetic factors, we agree that collaboration with teams having a strong expertise is essential. For candidate gene approaches, which we mostly favoured during the last decade, our works have been developed in collaboration with French teams specialized in pharmacology and toxicology (Inserm U775), in

[1] Institut de Radioprotection et de Sûreté Nucléaire
[2] Agence de l'Environnement et de la Maîtrise de l'Energie
[3] Réseau de Transport de l'Electricité
[4] Institut de Veille Sanitaire

genetic epidemiology (Inserm U535) and in genomic technologies (CNG), and with other teams from abroad (McGill, IARC, international consortiums on lung cancer). Besides the continuation of candidate gene approaches, we are currently involved in GWAS within international consortiums. We have ranked the development of this field as high priority for several year, and we have subsequently organized multidisciplinary seminars with research teams involved in cancer epidemiology, genetic epidemiology, statistics and biology to exchange in depth on various related topics such as genotyping strategies, biostatistical methods for genome-wide association studies, molecular biology of several pathways of interest. These seminars will now go on in the framework of the 'Cancer Epidemiology' transversal axis of the CESP.

Our team involves several researchers and engineers with high-level statistical skills. We considered it critical for both the environmental and genetic aspects of our works. We collaborate with Team 1 on methods for spatial epidemiology, a topic that was previously developed within Unit 754 (the third axis of unit 754 is transferred into Team 1).

The 2 last sentences on Team 6 may not refer to Team 6 (and this may be the case for the whole last paragraph). We actually develop strong collaborations with IARC and with centres of research in the US and in Canada.

TEAM 7. GENDER, SEXUAL AND REPRODUCTIVE HEALTH

Project leader: Nathalie BAJOS, Research Director, DR2 - Inserm

Permanent-position researchers: 9 (7.8 FTE) of whom 4 HDR, 7 full time researchers, 2 academic researchers

Engineers and technicians: 5 (4.3 FTE) of whom 3 with permanent positions,

Doctoral students: 5 ; Post-docs: 3

Number of PhDs defended: we have only indicated in our report the number of PhDs defended under the supervision of the researchers from INSERM entitled to direct PhD students (with an "HDR"). Three researchers (Nathalie Bajos et Alain Giami, et Virginie Ringa since 2008) meet this criteria. We also make sure young researchers take responsibilities in ongoing research projects, supervise students and rapidly obtain their HDR, which allows them to supervise PhD students.

The impression de overlapping expressed by the AERES experts may be explained by the multidisciplinary dimension of our work which allows the exploration of similar themes through the prism of different theoretical and methodological approaches. This is precisely the aim of a true multidisciplinary approach, which has been underlined by the AERES reviewers. Thus for example the key issue of the medicalisation of sexuality is explored from a socio-demographic point of view in the analysis of the social norms of sexuality, from an epidemiologic point of view in the analysis of medical prescriptions for contraception and from a psychosociological point of view in the qualitative study of health professions. The confrontation of these various points of view creates a unique opportunity to refine the interpretations of each discipline and to make new research questions emerge.

The AERES experts underline **a relative lack of statistical contribution** in our team. We acknowledge that we have little developed the statistical aspects of our work in our oral presentation, which focused on the outline of our research questions and the multidisplinary dimension of our work. However, we would like to point out that we do have statistical expertise in the team, as one of our senior researchers, Laurent Toulemon is a demographer and statistician, who specialises in the design and analysis of complex survey design and multivariate analysis. We would also like to emphasize the strong ongoing collaborations we have developed with biostatisticians of other teams in the Centre (teams 2 and 4 in particular), other research organisations in France (INED) and abroad (Princeton University, London School of Hygiene and Tropical Medicine). Their statistical expertise directly contributes to our work in designing complex survey protocols, discussing and implementing statistical methods for the analysis (random effects models, hierarchical models, multiple imputation techniques for missing data or factor analysis, used in social science but rarely applied in the field of Public Health).

As for publications, we appreciate the fact that the experts acknowledged the importance book publishing in our team. We publish in a variety of peer review journals in social science, Public Health, Medicine (especially in the field of Obstetrics & Gynecology) and Epidemiology. We publish both in French and International journals, and publish in level A journals in social science (*Actes de la Recherche, Sociétés Contemporaines,* Social Science and Medicine), in the best journals in the field of reproduction (Obstetric and Gynecology, Human Reproduction, Menopause), and in general medical journals where usually our research themes are little represented (The Lancet, American Journal of Public Health).

Between 2003-2008, the members of the team n° 7 have published :

- 87 original papers in peer reviewed journals, (including 22% in Top 10 and 36% in Top 20);
- 10 books as major authors and 41 book chapters;
- 21 other publications (including didactic and text books);
- have been invited to 41 national and international conferences.

TEAM 8. CARDIOVASCULAR DISEASES AND HORMONES

Project leader: Pierre-Yves SCARABIN, Research Director (DR1), Inserm

Permanent-position researchers: 3 (1.8 FTE) of whom 2 HDR, 1 full-time researcher, 2 academic researchers

Engineers and technicians: 3 (1.5 FTE) of whom 2 with permanent positions

Doctoral students: 2 ; Post-doc: 2

Factual correction: Team 8 includes 3 and not 2 permanent researchers. One MCU-PH (Hôpital Hôtel-Dieu and University Paris 5) has been omitted in the report from the AERES visiting committee.

We thank the visiting committee for their comments. We would like to address the following:

Regarding the type of investigation set up, we would like to make it clear that our project focuses on observational studies and not on clinical trials. The role of sex hormones in the development of cardiovascular diseases will be investigated in both case-control and cohort studies. For example, our program includes a hospital cohort study aimed to assess the impact of progestogen-only contraceptives on the risk of venous thromboembolism as well as collaborative works relating hormone therapy among postmenopausal women (E3N, Million Women Study in UK,..). We will also investigate the role of sex hormones in the development of arterial disease among men and women over 65 years in the 3 Cities (3C) cohort study and in the Women's Health Initiative program (in collaboration with Harvard University). In our project, a large trial has been identified as a necessary next step in the development of knowledge. Such a trial was only a research perspective and requires considerable resources which we do not have at our disposal.

Regarding the size and age distribution of the team, our group consists of 3 and not 2 permanent researchers. One MCU-PH (Hopital Hotel-Dieu and University Paris V) has been omitted in the report from the AERES visiting committee. The team also includes 2 young post-doc researchers and 2 new thesis students. One of the post-doc fellows has now become a highly productive researcher and has submitted her application for the Inserm competitive recruitment. We are hopeful that this researcher will be recruited in the near future and we think that this renewal of the team is an adequate strategy for the team viability.

During the last five years, the team has published 76 original articles indexed in Medline. Most of these papers (89%) were signed in a leading rank (first, second, next to last or last rank). The mean impact factor was close to 6. About 50% of these articles belong the top10 of the JCR impact factor and 85% are in the top 50.Some of our works have been published in leading medical journals such as The Lancet or the British Medical Journal as well as in high quality specialty journals. For example, two papers have been published in Circulation and eight have been published in the Journal of Thrombosis and Haemostasis.

TEAM 9. NUTRITION, HORMONES AND WOMEN'S HEALTH

Project leader: Françoise CLAVEL-CHAPELON, Research Director (DR2), Inserm

Permanent-position researchers: 3 (2.5 FTE) of whom 2 HDR, 2 full-time researchers and 1 academic

Engineers and technicians: 12 (12 FTE) of whom 1 with a permanent position

Doctoral students: 7; Post-docs: 6

We thank the visiting committee for their constructive comments, which are in agreement with our intention of fully exploiting our data-base, in order to continue to produce high impact epidemiological papers based specifically on French data.

Indeed, with one full-term researcher with a permanent position until 2005, then 2 full-time senior researchers since January 2005, team 9 published 174 scientific peer-reviewed papers in the 2003-2008 period, including 64 papers (37%) as 1st, 2nd, last or second last author; 64 papers (37%) were in the top 10% and 92 (53%) in the top 20% of the JCR categories corresponding to our activities (public health, oncology, medicine general and internal, nutrition and dietetics, respiratory systems, cardiac and CV systems, endocrinology and metabolism, multidisciplinary sciences, genetic and heredity, psychology, paediatrics, medicine research and experimental, obstetrics and gynaecology).

"The full scientific potential of the E3N cohort could be better utilized by extending the group with additional senior researchers with permanent positions"

Collection and setting up of a large cohort is a long-lasting procedure and perhaps not attractive to young or senior researchers, since no important publications could be produced during the period of data collection. However, our team is now in a position to present young researchers for Inserm recruitment (next year, A Fournier is a candidate for a CR2 position). Concerning senior researchers, our team has attracted MC Boutron-Ruault in 2005, and Prof Franck Carbonnel in 2009, thus enabling us to offer more doctoral and post-doctoral positions within our team. This shows that we are training potential future researchers who will later be candidates for institutional positions. In addition, Prof I. Romieu, with whom an International Associate Laboratory has been set up, is planning to join our team at the end of her 3-year IAL contract.

"A close collaboration with Team 1 – biostatistics - is encouraged to improve/develop statistical analyses."

We agree, and intend to expand existing collaborations. A tripartite collaboration (P Tubert Team 1, FCC Team 9, and A Fourier Bordeaux) has been set up in the field of pharmaco-epidemiology; it is currently assessing the quality of self-reports of drugs consumption and further collaborative projects are envisaged.

TEAM 10. EPIDEMIOLOGY OF DIABETES, OBESITY AND RENAL DISEASES: LIFELONG APPROACH, EARLY NUTRITIONAL DETERMINANTS

Project leader: Marie-Aline CHARLES, Research Director (DR2), Inserm

Permanent-position researchers: 6 (5.4 FTE) of whom 3 HDR, 5 full-time researchers, 1 academic researcher

Engineers and technicians: 5 (3.3 FTE) of whom 5 with a permanent position

Doctoral students: 1

A correction of fact: add "renal disease" onto the list of pathologies which are a part of the research axis of the CESP-CESP

Publications of Team 10 in international peer reviewed journals: 188 articles over the period September 2003-September 2008 for 6,2 effective full time researchers (a mean annually of 5,3 per effective full time researcher and 6,2 for the researchers (182 articles for the 5,2 effective full time researchers participating in the team projet); 107 articles (60 %) published as 1st, 2nd, second last or last author, 61 (31 %) in the top 10 % and 99 (55%) in the top 20 % of the JCR categories covering the work of the team (endocrinology metabolism, nutrition, urology nephrology, public health, genetic and heredity).

The comments of the expert committee concern two important domains for the orientation of future research in the team: genetic epidemiology and life course epidemiology.

Over the past decade, ***genetic research*** has evolved towards large-scale association studies along with the development of genotyping capacities. This research has been led by geneticists. Results have often been based on epidemiologic data sets such as those of team 10 and *this is not to be dismissed*. With the identification of frequent polymorphisms associated with chronic diseases, the participation of epidemiologists in genetic research will be increasingly needed in the future. Team 10 has anticipated this evolution and one young researcher has received training in genetic epidemiology. She will be leading cutting edge (as acknowledged by the visiting committee) projects in our domain, in collaboration with renowned specialized teams in genetics (Pr K Clément) and epigenetics (Pr Y Le Bouc) from outside the centre. New researchers in this field within the centre are also expected. Since the visit of the AERES committee, plans for a one-year post-doc of a researcher from China (ZHOU Quin, Fudan University in Shanghai) are underway in team 10.

Results from other countries have clearly shown the importance of considering the development of diseases such as obesity, diabetes, renal and cardiovascular disease ***over the life-course***. Team 10, which has a long experience in the epidemiology of these diseases in adults, has recognised this as an important issue, underdeveloped in France. Through its implication in the EDEN study, the team has decided to contribute to this field by *focussing mainly on understanding the early life aspects* which modulate the risk for these chronic diseases. Although we acknowledge that this is only the first part of the life-course, early life is specifically characterised by the rapid succession of several critical periods, from foetal life to 5 years. The understanding of the interactions of risk factors at these different periods and their relations with intermediate phenotypes in later

childhood and adolescence, is a key part of our approach. Team 10 also contributes to life course research on longer term data, for example, in collaboration with team 9, with a study of the relations between risk factors in childhood and in young adulthood with adult diabetes (article submitted to Diabetes). As pointed out by the visiting committee, Team 10 has also developed *skills in the analysis of cohort effects* (article under revision for Epidemiology). It is important to discuss the applicability of results based on adults, to younger generations.

It is difficult to build long-term expertise in all domains of epidemiologic research within a single team. This is one of the reasons for the creation of the CEPH. Beyond the CEPH, team 10 works in *collaboration with many teams from outside the centre, teams specialized in clinical, biological and social aspects* related with its research. For example, there are skilled researchers (MJ Saurel, M Kaminski) in social epidemiology involved in the EDEN project who ensured that key social factors have been recorded in the study. They will contribute as collaborators to the research of Team 10.

As suggested by the expert committee, the research of Team 10 on early life determinants will benefit from collaboration with renowned European teams in the field. While preparing the document for the AERES visit, team 10 was also preparing the *application for a EU collaborative project* on the "determining factors and critical periods in food habit formation and breaking in early childhood" as workpackage leader for the epidemiologic part of the project. Researchers from the ALSPAC study are involved in this workpackage.

Lastly, we certainly have some projects that do not fit the early life or life-course approach. They belong to the more classical approach of the epidemiology of adult disease, led by senior researchers (B Balkau, B Stengel) and concern the definition, prognosis, complications of diabetes and renal disease. However, both approaches contribute to our understanding of the pathophysiology of these diseases over the life-course.

TEAM 11. SOCIAL AND OCCUPATIONAL DETERMINANTS OF HEALTH

Project leader: France LERT, Research Director (DR2), Inserm

Permanent-position researchers: 11 (9.2 FTE) of whom 6 HDR, 8 full time researchers, 3 university researchers

Engineers and technicians: 27 (27.0 FTE) of whom 4 permanent positions

Doctoral students: 6 ; Post-docs: 1

The committee noted that team 11 is "highly productive and has a high scientific standard". In effect, this is reflected in 244 publications over the evaluation period of 2003-2008, with less than 8.4 full-time equivalent researchers over this period. We were first author for 57%, second author for 6%, second last for 10% and last for 10% of these publications. The median Impact Factor of **our** publications in JCR categories is as following: Public Health: 2.8; Infectious Diseases: 5.8; Social Sciences: 2.4; Medicine: 12.6; and Psychiatry: 3.1.

Our evaluation raised the following 3 "Weak points /Recommendation".

1. *Some innovative projects not presented – do they lack sufficient attention and resources?*

We thank the committee for highlighting the innovative character of our programme. In effect, the time allocated to each team in the Centre for the presentation did not allow us to present all our projects. We, as a team, decided to present only a selection of the projects with the team leader presenting everyone's work briefly in the introductory presentation. The selection of projects involved discussions within the group and the final choice was a consensual one, made by all researchers in the team.

2. *Resources used for the cohorts could be better integrated in projects of other teams in the centre, and better exploited with respect to a wider range of exposures (e.g. focusing also on environmental exposure).*

The main cohorts (GAZEL and CONSTANCES) were designed as open epidemiological cohorts. Within GAZEL, there are currently more than 40 nested research projects, from about 20 different teams in France and abroad; among them, teams 2, 4, 6, 7, 10 of the Centre are directly involved. The preparation of the protocol of CONSTANCES, which is still in its pilot phase, involved researchers from numerous groups, including several teams of the Centre.

In terms of the range of exposures we are interested in, we collect extensive data on the working environment, taking into account chemical, ergonomic and psychosocial factors, and we are geocoding all residency addresses from birth on for both cohorts in order to link the individual data with environmental exposures.

3. *Is the development of new methods of studying and measuring social inequalities in health present in the team?*

The core focus of team 11 is the social and occupational determinants of health; methodological competence in this field is evident in our publications on measures of socioeconomic position, on modelling strategies, on mechanisms, applications using multi-level analysis, assessment of both relative and absolute risk in order to understand social inequalities in health and trends in social inequalities. Thus, we feel that our work contributes to advancing current methodology in this field.

TEAM 12. LIPID NUTRIENTS, METABOLISM AND CANCER RISK

Project leader: Virginie JOULIN, Research Director (DR2), Inserm

Permanent-position researchers: 2 (1.4 FTE) of whom 2 HDR, 1 full-time researcher, 1 academic researcher

Doctoral students: 1 ; Researcher under contract: 1 (1 HDR)

In accordance with the AERES report, Team 12 will not maintain its request of being integrated in the Centre (CESP/CESP) as a separate group.

Indeed, the initial research projects proposed were relatively considerable compared to the present size of the group, and required extensive collaborations. Before proposing projects based on an interdisciplinary biological approach, the group should be extended with junior and senior scientists.

The strength of Team 12 is a focus on relationship between nutrition and cancer risk based on biomarkers of nutritional exposure (fatty acids, vitamins, carotenoids) that give considerable strength to epidemiological studies on diet and disease risks.

The availability of a Lipidomic platform, providing access to biomarkers of nutritional exposure, has already lead to collaborative studies with Team 9, and several collaborative epidemiological studies within the Centre (Team 9) and outside the Centre (IARC, WHO) are on-going.

In order to maintain this research activity in the Centre, an alternative to Team 12 would be to become integrated in a larger Team in the Centre. Extensive discussion is on going in order to find the most appropriate solution.