CESP - Centre de recherche en épidémiologie et santé des populations

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Research Center in Epidemiology and Population Health

CESP

Under the supervision of the following institutions and research bodies:

Université Paris-Sud

Institut National de la Santé et de la Recherche Médicale - INSERM

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

February 2014

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

Department for the evaluation of research units

On behalf of AERES, pursuant to the Decree of 3 november 2006[1]*,*

- Mr. Didier HOUSSIN, president
- Mr. Pierre GLAUDES, head of the evaluation of research units department

On behalf of the expert committee,

- Mr Thierry LANG, chair of the committee

[1] The AERES President "signs [...], the evaluation reports, [...] countersigned for each department by the director concerned" (Article 9, paragraph 3 of the Decree n ° 2006-1334 of 3 November 2006, as amended).

Evaluation report

This report is the result of the evaluation by the experts committee, the composition of which is specified below.

The assessment contained herein are the expression of independent and collegial deliberation of the committee.

Unit name:	Research Center in Epidemiology and Population Health
Unit acronym:	CESP
Label requested:	UMR_S
Present no.:	UMR_S 1018
Name of Director (2013-2014):	Mr Denis HÉMON
Name of Project Leader (2015-2019):	Mr Paolo BOFFETTA was supposed to be the leader, but he resigned less than a week before the visit Interim leaders: Mr Jean BOUYER, Mr Alexis ELBAZ, Ms Laurence MEYER

Expert committee members

Chair:	Mr Thierry LANG, Toulouse University – Inserm, Toulouse (representative of CNU)
Experts:	Ms Isabelle BALDI, ISPED, Bordeaux
	Ms Carol BRAYNE, Cambridge University, UK
	Mr Fabrice CARRAT, Pierre et Marie Curie University, Paris
	Mr Roch GIORGI, Université de la Méditerranée, Marseille
	Mr Jaume MARRUGAT, Hospital del Mar Medical Research Institute, Barcelona, Spain
	Mr Scott MONTGOMERY, Örebro University Hospital, University & Karolinska Institutet, Sweden
	Ms Carla MAKHLOUF OBERMEYER, American University of Beirut, Lebanon
	Mr Rachid SALMI, ISPED, Bordeaux (representative of INSERM)
	Mr Anthony SWERDLOW, Institute of Cancer Research, UK
	Mr Jerome WITWER, ISPED, Bordeaux
	Ms Shelia ZAHM, National Cancer Institute, USA

Scientific delegate representing the AERES:

Mr Emmanuel LAGARDE

Representative(s) of the unit's supervising institutions and bodies:

Mr Jacques BITTOUN, Université Paris-Sud

Mr Jean BOUYER, (representative of École doctorale ED 420)

Mr Thierry DAMERVAL, Inserm

Mr Jean-Luc VAYSSIÈRE, Université de Versailles Saint-Quentin-en-Yvelines

1 • Introduction

History and geographical location of the unit

The Research Center in Epidemiology and Population Health (CESP) is the continuation of a research center which was directed by Mr Denis HÉMON during the period 2010-2014. It was composed by 11 research teams located on three physical locations: 1/ Paul Brousse hospital, a Paris university hospital, in Villejuif; 2/ Bicêtre hospital, a Paris university hospital, in Bicêtre and 3/ Institut Gustave Roussy, a cancer hospital, in Villejuif.

Three teams that were part of the previous center will join other centers: past team 10 (MA Charles) and 6 (J Clavel) will join the Centre de Recherche Epidemiologie Biostatistique Sorbonne Paris Cité de l'Université Paris Descartes directed by P RAVAUD. Past team 1 (P TUBERT) and 5 (R NADIF) will join teams at the Université Versailles Saint-Quentin en Yvelines (UVSQ). A research platform: Population based cohorts, directed by M ZINS, will become a "Unité Mixte de Services" (UVSQ, Inserm, CNAMTS).

Management team

The time of the AERES visit is a very special one for the CESP. The director of the CESP had been planned to be Mr Paolo BOFFETTA, who decided to renounce the direction of the CESP less than one week before the AERES visit. The written description of the perspective and future plans of the CESP are thus those written and discussed with the personnel of the CESP under the supervision of Paolo BOFFETTA.

Very rapidly, the researchers from the center have decided to form an interim steering group composed of Mr Jean BOUYER, Mr Alexis ELBAZ and Ms Laurence MEYER. These three persons are in charge of the CESP until a new director is selected.

AERES nomenclature

SVE1_LS7

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	16	28
N2: Permanent researchers from Institutions and similar positions	26	33
N3: Other permanent staff (without research duties)	18	15
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	1	1
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	17	20
N6: Other contractual staff (without research duties)	68	75
TOTAL N1 to N6	**146**	**172**

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	50	
Theses defended	46	
Postdoctoral students having spent at least 12 months in the unit*	12	
Number of Research Supervisor Qualifications (HDR) taken	24	
Qualified research supervisors (with an HDR) or similar positions	35	27

2 • Assessment of the unit

The absence of the candidate director creates a special situation, in which the project of the CESP has been discussed by Mr Paolo BOFFETTA with the researchers, but is not going to be, obviously the project which will be endorsed by the future director. However, the three interim directors have stated not to have major divergences with the project of the center. The following evaluation is thus based on the written texts, the presentations, answers and explanations of the interim steering group. The evaluation and the recommendations might thus be used for the writing of the future plan of the CESP as organized by the future director.

The CESP gathers high quality teams and researchers, technicians and engineers. The scientific appeal and production is excellent as a whole. There is an outstanding investment in training in public health and training young researchers. The center is a most valuable center of expertise in many fields of knowledge necessary to base public health decision on scientific evidence. A huge collection of data has been collected and organised by the teams of the centers, ranging from cohorts, registries to more complex designs as well as linkages with administrative databases. The major challenge for the CESP is to specify how to translate into action and organisation the added value of being

a center, as opposed to the sum of research teams acting independently. Most of them seem to be able to run independently of the center. This is a main challenge, all the more necessary to address as the Doctoral School may evolve toward a School of Public Health. The CESP is one major pillar of this School and the scientific strategy should specify which concrete incentives and organisation should be used to achieve this goal.

Strengths and opportunities related to the context

- The center has acquired an international visibility in epidemiology and public health due to the excellence of most of its teams.

- The quality and scientific outputs of the center is excellent and outstanding for some of the teams.

- The center is rich in disciplines (teams as well as researchers) and interdisciplinarity has already been developed.

- A wide access to data has been created, thanks to numerous epidemiological tools developed by the teams.

- The center has strong national and international connections.

- The center benefits from a strong institutional support.

- The CESP offers an exceptional resource for translational research for evidence-based public health.

- The center is a center of excellence and of strong involvement in training for research and public health.

- An international advisory board regularly provides advice for the orientation of the CESP.

Weaknesses and threats related to the context

- The center looks at the moment much more like a sum of research teams which pursue their scientific objective and goals than like an integrated center.

- The difficulties in relation to the recruitment of the director of the center have underlined the necessity to ensure the scientific integrity of the center1.

- The difficulties related to the short term contracts imposed by the research institutions are a major threat.

Recommendations

- Develop the added value of the center, as compared to a sum of research teams.

- Develop the interdisciplinarity and exchanges between teams.

- Specify the incentives and organisation which will help the orientation toward clinical epidemiology and health services research announced in the perspectives.

- Develop perspectives and tools toward more shared resources and activities, including:

    - data collection and management;

    - organisation of the translation of the results of the research;

    - initiatives to recruit young researchers;

    - information systems (data base management, data management, bioinformatics, linkages with administrative data bases, networks…);

    - library, access to scientific information as well as translation of research to the public and public;

    - health authorities;

    - administrative and financial organisation;

    - skill transfer between teams (for example on competencies limited to one or few teams).

- Develop initiatives to ensure the scientific integrity of the center as a whole.

- Promote the principle of a declaration of potential conflicts of interest mandatory for researchers.

3 • Detailed assessments

Assessment of scientific quality and outputs

The unit is composed of 9 teams the scientific production of which is mostly excellent, sometimes outstanding.

Major achievements have been attained and published by the CESP in major scientific journals: among them, a decline in cognitive functions before the age of 60 has been documented ; an increase in CV risk in chronic kidney diseases; the induction of diabetes by irradiation; the risk-benefit balance of menopausal hormone therapy; an increased incidence of breast cancer in women working at night; the high contribution of men having sex with men to current HIV transmission; the pre-eminence of social norms over public health intervention; the possible role of pharmacist in the patient's care pathway and advances in meta-analysis.

The number of publications has doubled between 2008 and 2012, to a total of 1458 publications. Most of these papers are authored in leading position by members of the unit and the indicators show a high interest measured by impact factor of the journals (mean: 6.12) and a mean of citations per paper equal to 12.6, twice the international mean.

Large scale data collection includes large scale cohorts: E3N and E4N (nutrition and intra-generational); CKD-REIN (kidney diseases); FCCSS (survivors of cancer in childhood); HIV cohorts; ELFE (birth cohort); OBSEFF and FECOND (fertility). Large scale case-control studies include CECILE, ICARE, Epi Thyr. Among large scale complex design, CSF (sexuality) and Orange farm (Circumcision) are noteworthy.

The unit participates to and is often leader in international projects of research in various scientific fields developed in the CESP.

Assessment of the unit's academic reputation and appeal

The multidisciplinary expertise and scientific knowledge of the teams have as a consequence that the teams of the center have multiple leadership in international networks and projects and successful international collaborations which are going to be developed further. The number of foreign post-doctoral scientists researchers, the conferences, national and international, organised by the teams, the distinctions and awards to multiple researchers, as well as the grants they obtain and the journals to which they participate and edit, are convincing indicators of the excellence of the CESP in this respect. The unit's academic reputation is witnessed by the great number of PhDs which are defended or ongoing each year. However, as written in the report given to the committee, past academic reputation achievements are described in detail under each team, without any global evaluation of the center.

Assessment of the unit's interaction with the social, economic and cultural environment

The interaction with the environment of the teams of the center is very good. Almost all researchers from the center are asked, sometimes very frequently, to participate in various expertises, committees, giving advice for decision in public health.

Some results from the center have had consequences at a national (Haute Autorité de Santé, Direction générale de la Santé, Expertises collectives…) or international level (WHO).

However, the interaction of the center is more the sum of activities of each team in its own than the activity of the center by itself, that has not so far set up common resources and mutualized tools for knowledge communication.

Assessment of the unit's organisation and life

The CESP includes 79 researchers (Full time equivalent) among which 50 are permanent (63%). It includes 139 engineers and technicians among which 72 % are non-permanent. Fifty PhD candidates are currently working in the CESP.

The center gathers teams located on three sites which is an obstacle to the feeling of "centerness". The teams working nowadays in Bicêtre hospitals might in the near future move to the Paul Brousse center, which would reduce the number of sites.

The life of the unit is satisfactory as reflected by the fact that instances are running and that researchers, engineers, technicians, students or post-docs participate in the center council (conseil de laboratoire) and consider themselves as informed and able to participate in the decisions.

The ability to conduct a policy and a scientific coherent orientation at the center level is more questionable. Scientific seminars and meetings have been regularly organised. The coming project emphasize the needs for such exchanges. Two types of seminars are proposed : traditional seminars and cross-cutting programs. Organisation, goals and criteria for success of these programs are not clear. Whether this efforts are intended to be an incentive toward new research programs gathering researchers and engineers from different teams needs to be clarified.

The challenge is how to translate and manage a scientific policy at the center level.

When interviewed, the interim steering committee answered that they would let the competition between teams for their researchers candidates to apply freely to national research position to maximize the possibilities to recruit young researchers. However, other incentives should be found to follow-up a scientific policy and induce new lines and themes. For example, among the themes, practices in the health care system or inequalities in health are announced. How will they develop?

It is difficult to understand the heterogeneity of the organization of the disciplines within the center. For example, health economy is organized within a candidate team but is also present in some other teams, with researchers working independently, looking isolated from other disciplines. The same is true for statistics, where some teams have very strong competencies, while in other teams, some engineers may look isolated. Gathering these competencies in some way might increase the quality of their work.

The idea of a common data center has been considered for clinical trials, but does not seem to be considered for cohorts. At the moment, researchers seem to be hesitant or reluctant to this idea. A ISO certification is in progress in certains teams. This experience could be shared and diffused, if positive, to the center.

Common tools and services, such as information systems and tools, library, access to scientific information, documentation, have not been presented nor discussed as common tools of the unit.

Assessment of the unit's involvement in training through research

The unit involvement in training through research is outstanding, whether graduate programs, teaching or supervision of students is concerned. Members of CESP are head of a Master in Public Health, a doctoral school and Summer School in Epidemiology and Public Health. The master 1 in Public Health trains 350 students per year and the master 2 in Public Health trains 45 students per year; 50 % of them enter a doctoral school in Public Health.

60 PhDs have been defended in the doctoral school (led by Jean BOUYER) in 2009-2013. Among 35 research teams who offer practical training to students, 11 belonged to the CESP. Similarly 23 % of the 200 researchers authorized to supervise a PhD (HDR) work in the CESP. The high level of PhD teaching activity of the CESP is reflected by the fact that it welcomes 41 % of the PhD candidates.

The students who were met by the committee agreed they were in very good conditions for their PhD, from the point of view of the support from their supervisors, the doctoral school director or the scientific meetings, in general or dedicated to them.

This PhD program in Public Health intends to develop and leads the road toward a School of Public Health, within Paris-Saclay University, relying on the forces in the South Paris area. With this objective in mind, perspectives for the future development of the CESP should be clarified and invited to clarify a scientific strategy toward a wide range of disciplines and competency not present or still too modest within the CESP.

Assessment of the strategy and the five-year plan

The main research areas of the CESP include 1) etiology and clinical epidemiology of chronic diseases (cancer, respiratory, metabolic, cardiovascular, renal, and sexually transmitted diseases) 2) determinants of fertility, perinatal and child health 3) gender and sexual health 4) determinants of health 5) medical and health practices 6) social inequalities in health 7) methodology and biostatistics.

The exchanges of competencies between disciplines and between teams have been claimed by the teams as being necessary and of a great potential interest. Apart from the seminars, which are necessary, the project lacks a more visible organisation of the center which would structure and show this willingness. The perspectives look a little bit general. Concrete tools and ways of attaining the goals lack precision.

"Cross-cutting programs" have been proposed and announced. Their content should be more precise, as well as their goals and conditions and criteria of success. Do they intend to result in submission to grants in common by more than one team, or associate the researchers from different teams and same discipline to get grants to pursue a common research together?

The ways which are going to be used to transform a center which has inherited of a past into units gathered around a true school of public health is not clearly apparent from the document submitted to the visiting committee. This transformation might take time. However the long term perspective is lacking.

Most of the teams have invested a lot of efforts in organizing cohorts and will continue to do so. The committee emphasized that collecting data is a huge effort for researchers, which sometimes prevent them from producing results and publications a level that could be expected. Considering to what extent sharing common resources to manage these cohorts could free some time for the researchers to develop their own hypothesis might be useful.

How to avoid the duplication of efforts with regard to complex administrative, technical (tools) or scientific (competencies) issues?

According to researchers and technicians, the three sites hamper the communication between sites, as they make difficult an efficient information system between teams, which rely on different institutions with non easy possibility of connection.

The committee has not heard of any information system and resources in informatics for the center. It is not clear how this system is used for common purposes of the center.

Conclusion

The CESP gathers high quality teams and researchers, technicians and engineers. The scientific appeal and production is excellent as a whole. There is an outstanding investment in training in public health and training young researchers. The center is a most valuable center of expertise in many fields of knowledge necessary to base public health decision on scientific evidence. A huge collection of data has been collected and organised by the teams of the centers, ranging from cohorts, registries to more complex designs and connections with administrative data bases. The major challenge for the CESP is to specify how to translate into action and organisation the added value of being a center, as opposed to the sum of research teams acting independently and for most of them able to run independently of the center. This is a main challenge, all the more necessary to address that the Doctoral School may evolve toward a School of Public Health. The CESP is a major pillar of this School and the scientific strategy should precise which concrete incentives and organisation should be used to achieve this goal.

In the absence of a director, the committee is confident that teams will pursue their high quality research in the next coming five years within the teams. However, some questions and challenges should be addressed for the future mandate of the next director of the center.

The project of the CESP as presented in the written document and by the interim directors is very wide and covers almost every aspect of research in public health, as does the portfolio. Some perspectives (clinical epidemiology, health services research) need reinforcement. It would be most useful to specify which tools will be used to translate this perspective into coherence and how to enlarge the competencies of the center to new disciplines or fields.

Similarly, the center has to organise the translation of knowledge to the public and public health authorities at the center level.

In many teams with excellent production and high international appeal, the leaders have reached the seniority in research. One would like to know the strategy of the center to face this reality. Is the open competition between teams that will decide of the strategic orientations for the future or certain incentives have to found to orient the center toward a school in the future?

Strengths and opportunities related to the context

- The center has acquired an international visibility in epidemiology and public health due to the excellence of most of its teams.

- The quality and scientific outputs of the center is excellent and outstanding for some of the teams, reflecting the great quality of the teams and researchers gathered in the CESP.

- The center is rich of disciplines (teams as well as researchers) and interdisciplinarity has already been developed within and between a part of the teams of the centers.

- A wide access to data, due to numerous epidemiological tools developed by the teams of the centers. This includes cohorts, registries, platforms developed by the teams. This includes also access to administrative data with possible linkages and access to national and international data collections and cohorts.

- The center has strong national and international connections. It is often a leader in some international groups of research.

- The center benefits from a strong institutional support, from universities, Inserm as well as from university hospitals and cancer hospital. For example, Inserm invested 3 million euros for rehabilitation of the building.

- The CESP offers an exceptional resource for translational research. The expertise of its teams is most useful and used for public health issues. It is a strong element for evidence-based public health.

- The center is a center of excellence and of strong involvement in training for research and public health.

- A scientific committee regularly provides advice for the orientation of the CESP.

Weaknesses and threats related to the context

- The center looks at the moment much more like a sum of research teams which pursue their scientific objective and goals. Despite the organisation and willingness to develop interactions between the teams, the CESP lacks at the moment a true organization, sharing of resources, common goals which would give a structural and institutional visibility to the center.

- The difficulties in relation to the recruitment of the director of the center have underlined the necessity to confirm and ensure the scientific integrity of the center for the future. Working together with private sector is common and sometimes is a condition to get funding from the public institutions (e.g. the European Union). The question of the links of interest has been insufficiently addressed in this complex context. The organisation of a committee on professional ethics dedicated to take care of this aspect, as announced by the interim directorate is a first step to be encouraged.

- The difficulties related to the short term contracts imposed by the research institutions are a major threat, since it has for consequence a permanent renewal of the research personnel (researchers, engineers, technicians, administrative). This means a continuous effort to train personnel who will leave the unit and teams shortly after having acquired a good level of competency. In turn, this increases the difficulty to recruit new personnel.

Recommendations

- An orientation toward clinical epidemiology and health services research is apparent in the orientation of the center. The incentive and organisation which will help this axis to grow in competency is not clear and should be developed further.

- Develop the interdisciplinarity and exchanges between teams. For example, it might be possible to increase the number of PhD getting two supervisors from two different teams, in order to benefit from different experiences as well as stimulate exchanges between teams.

- Develop the added value of the center, as compared to a sum of research teams.

- On the road to transforming the Doctoral School in a school of public health and confirming the CESP as a center, this orientation might necessitate a reflexion and perspective toward more shared resources and activities. The road toward a development of the centerness is stated by each team. The question is how to organise it.

This shared vision should include :

- data collection and management ;

- organisation of the translation of the results of the research ;

- initiatives to recruit young researchers and track their future ;

- shared information systems (data base management, data management, bioinformatics, linkages with administrative databases, networks…) ;

- shared organisation of biobanks: organisational, confidentiality and ethical issues ;

- common library, access to scientific information as well as translation of research to the public and public health authorities ;

- administrative and financial common facilities ;

- Skill exchange between teams (diffusion of competencies from one team to another) ;

- Develop initiatives to ensure the scientific integrity of the center as a whole. The organisation of a committee on professional ethics dedicated to take care of this aspect, as announced by the interim directorate is a first step to be encouraged. This committee, in collaboration with institutions from Inserm, Universities, ITMO de santé publique, CNRS should take the initiative of building rules to make possible the combination of private fundings of research and scientific integrity, meaning that the results might be discussed from the only point of view of their scientific quality. The situation in 2014 at Inserm and University, is that the researchers do not declare their links of interest. They have to do it when acting as experts, members of scientific committees, but not as researchers. The declaration of links of interest should be mandatory for researchers, as soon as they are engaged in public research.

4 • Team-by-team analysis

Team 1 : Health Economics – Health Services Research

Name of team leader: Ms Nathalie PELLETIER-FLEURY

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	1	
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**6**	**5**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	4	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	5	5

Detailed assessments

Assessment of scientific quality and outputs

The total number of publications in peer reviewed journals is 26. Articles were published in international and national journals (5 in 2013, 10 in 2012, 4 in 2011, 0 in 2010, 2 in 2009, 3 in 2008) mostly BMC and PLoS One, with individual papers in specialty journals such as Medical Ethics, Sleep. Very few papers were published in high impact journals. One book chapter has been published.

Seven papers have been published in economic journals mainly in French, except one in Health Policy, one in Geneva Papers – Issue and Pratice.

The results are on a range of various topics, such as monetary incentives, new modes of cooperation between primary care professionals, patient's participation in medical decision or insurance access. Authors include the leaders, their students and external collaborations.

Assessment of the unit's academic reputation and appeal

The senior researchers have national roles such as presidency of scientific committee of journals and Public Health organisations. These academic memberships suggest reasonable visibility as respected national contributors in their fields of expertise.

Assessment of the unit's interaction with the social, economic and cultural environment

The implication of the team's members in public institutions of the health regulation system (Haute Autorité de Santé, Commission des Comptes de la Santé) underlines the involvement with local policy decisions. This latter is also underlined by the reports which support policy development.

The links of the team with general practitioners professional associations is also a valuable point for future research projects

Assessment of the unit's involvement in training through research

There is good evidence of contribution to training through modules in masters, masters, doctoral and postdoc training. Two PhDs have been defended and four are currently ongoing. This is admirable for such a small team.

Assessment of the strategy and the five-year plan

The plan concerns interesting and potentially important areas, some of them of international importance. The coherence of the project needs to be developed further as the program seems rather ambitious in terms of overarching aims, but based on smaller rather fragmented pieces of work which are only briefly described.

The orientation of the research is mostly based on the analysis that the French context is specific as far as organization of primary care is concerned. Little attention is paid to the fact that international comparisons, using the original aspects of the French system, may provide interesting results to more general questions about the delivery of primary care as an international theme of research.

Further outputs include national reports and contributions to local activities.

Due to the lack of a statistician, the work programme (econometric analysis models, exploratory statistical methods, decision analysis models) will be hard to follow through.

Interaction with other components of the center is unclear.

The strategy has been mainly developed by establishing a small group from the success of two leaders.

Conclusion

The scope of research, health services research, with a focus on primary care, is in an important area. This range of research areas is relevant to France.

The focus on primary care and collaboration with general practitioners is most interesting. However the analysis underlines the specificity of the French system and tends to make the research contextual, limiting the generalizability of the results. International comparisons are not considered by the team, which may prevent their possibilities to develop international collaborations and leadership.

The research project is promising in certain aspects, well positioned in the French academic environment, but appears fragmented and ambitious with regard to the team forces.

- **Strengths and opportunities:**

- the team is implied in an original research field, underdeveloped in the French context.

- the team is responsible for Health Economics courses at the Master of Public Health, Paris Sud.

- Creation of a master in Health service Research this year.

- **Weaknesses and threats:**

- the team is very small (three permanent researchers: two from Inserm, one from the university).

- a statistician is lacking for complex analysis.

- it is difficult to recruit in this field.

- the team lacks an international vision. It emphasize the specificity of the French system and tends to make the research contextual, limiting the generalizability of the results.

- **Recommendations:**

- Reinforce the coherence of the research project (strengthen the overarching vision).

- Develop international collaborations and leadership through works on international comparisons.

- Find linkages within the center and externally with national and international teams.

- Find mentorship in order to expand the national and international network and acquire international expertise and leadership.

Team 2 : Methodology and Clinical Epidemiology for Molecular Oncology

Name of team leader: Mr Stefan MICHIELS

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	3
N2: Permanent EPST or EPIC researchers and similar positions	8	8
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	3
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**13**	**14**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	4	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	2	4

• Detailed assessments

Assessment of scientific quality and outputs

The team is mainly involved in the design and statistical methods for experimental and observational studies, including studies with molecular markers, early phase clinical trials, meta-analyses, and health economics. The majority of the members of the team are affiliated to Gustave Roussy Institute, with very closed links with clinicians. The team members have published 333 articles in peer-reviewed international journal in 2008-sept 2013. Excluding editorials, about 75 (30 %) papers were signed in rank 1 (first or last author), with an average impact factor of 10 (whatever the research themes); when also including second or penultimate authorship this number increased to 130 (51 %). Among papers signed in rank 1, approximately, 41 have appeared in the top 10 % best specialty journals. Eight major publications fall into the top 0.1 % and 1 % category. On both papers in the main research themes and collaborative papers in various medical domains, the level of publication is excellent, with high level of publications at national and also international level. This scientific production should be also compared with the modest size of the team.

Compared to other themes the field of research in methodology, the level of publication in the economic evaluation theme is not high. Overall, however, members of the team published 39 methodology papers, 133 papers in clinical epidemiology in which the team has been leader, and 161 others papers in biomedical journals in which the team has been involved. Articles are published in journals of high level in methodology and in more general topics (N Eng J Med, Lancet Oncol). The scientific production shows also a high level of collaborations at national and also at international level.

The main results concern clinical designs and biomarker identification/validation, meta-analyses of treatments and biomarkers.

Assessment of the unit's academic reputation and appeal

Members of the team are involved in many national and international collaborative projects. Researchers have obtained grants from French national institutes (Inca, PHRC, STI), and also from international institutes (notably from FP7). Several team members have a national and international recognized expertise in the field of biomarkers and meta-analyses. The national recognition of the scientific expertise of some team members is also attested by their participation in committees of national agencies (AERES, ANR, Inca, PHRC). Some members are regularly invited to international meetings, and some exchanges at international level have been realized. One member has been an associate editor of Biometrics (2010-2012).

Assessment of the unit's interaction with the social, economic and cultural environment

The team has a strong interaction with clinicians of the Institut Gustave Roussy, but also with other institutes of the French Centres de Lutte Contre le Cancer. These interactions concern mainly economic evaluations, but there are also involvement in the design and analyses of many clinical trials and meta-analysis, as demonstrated by a large number of collaborative papers.

The team has also contracts with the pharmaceutical industry for the conduct of clinical trials of new drugs.

Some members of the team are members of working groups or committees indicating interactions in their main research fields. They also diffuse some of their results to non-researchers or to researchers, via websites.

Assessment of the unit's involvement in training through research

Some members of the team are involved in teaching and training through research in public health, biostatistics or health economics, and bioinformatics. In the 2008-2013 period, 22 Masters 2 students, and 8 PhD students have been supervised.

Main courses are delivered at Paris-Sud 11 University. One member is the co-leader of the M1 degree in Public Health. Another member is the co-director of the master in Bioinformatics and Biostatistics.

The team is also involved in numerous other courses, with no organizational duty.

Assessment of the strategy and the five-year plan

The five-year project is well justified, in line with their past work and the important challenges concerning the fields of biomarkers and targeted therapies in oncology. The project is well structured around 4 inter-related research themes. The two main ones concern “clinical trial methodology” and “meta-analysis of treatments and biomarkers”. Several original and useful methodological developments are planned in the field of phase 1 trials, clinical trials in rare diseases, clinical trials integrating molecular biomarkers, and meta-analysis of treatments and biomarkers. The third theme “economic evaluation of treatments and biomarkers” focuses on the economic impact of molecular medicine in oncology. It is well planned, mainly using standard and advanced methodologies rather than developing new methodology in order to answer to specific questions. The last theme “molecular cancer epidemiology” associates clinicians of Gustave Roussy Institute and researchers from another team of the unit in a trials programme around personalized medicine.

The project aims also to develop collaborations with other teams of the CESP, to foster the existing collaborations at national and international level.

Conclusion

- **Strengths and opportunities:**

Some members of the team have an excellent reputation in the field of the methodology in biostatistics and molecular epidemiology. The interaction with clinicians is strong allowing transfer of new methods and/or advanced methods to application. It also makes possible the development of innovative methods in molecular oncology. There is a great potential for relevant scientific interactions with some other teams of the CESP.

- **Weaknesses and threats:**

The team is mainly constituted of researchers from the Gustave Roussy institute, and hosts only 3 tenured researchers (from the University). While the number of HDRs will increase from 3 to 4, there is no possibility to advise PhD students in health economics.

- **Recommendations:**

Increase internal resources in biostatistics, methodological development, including in the field of economic evaluation.

As regard to economic evaluation, concentrate the researches in fields having methodological challenges.

Pursue and reinforce interaction with clinicians, and with some other teams of the CESP in order to contribute more in methodological new developments.

Team 3 : Radiation Epidemiology, clinical cancer epidemiology and survivorship

Name of team leader: Mr Florent DE VATHAIRE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2
N6: Other contractual staff (without research duties)	17	17
TOTAL N1 to N6	**23**	**23**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	5	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

This new team results from the merging of 3 teams: “radiation epidemiology”, “survivorship”, and “descriptive epidemiology”.

The team is involved in radiation epidemiology and iatrogenic effects of treatments, social and human sciences research, and descriptive epidemiology.

For the current (radiation epidemiology) team 3, 46 articles in peer-reviewed international journal in 2008-mid 2013. For 36 (78 %) papers team members were rank 1; 45 % published in the top 10 journals.

For the social and human science theme: 3 papers with impact factor, among a total of 11 (in various fields).

For the descriptive theme: 21 papers with impact factor, among 25. Signed in rank 1 or last: 5; 9 papers were published as member of a safety monitoring committee.

The Radiation Epidemiology part of the team has produced some important papers (Lancet Oncology, Brain, J Am Coll Cardiol, J Clin Oncol) and a considerable volume of other publications over the past 5 years, and has worked on an impressive range of adverse outcomes following cancer incidence and treatment. They have set up and followed up some cohorts of considerable size, although it is not clear how their value can be compared with cohorts established elsewhere. The other two parts of the team (Social Sciences and Descriptive Epidemiology) do not give clear evidence of high quality internationally competitive outputs.

Assessment of the unit's academic reputation and appeal

The 3 research themes are heterogeneous in term of scientific reputation.

The team has established national, and some international collaborative projects and is involved in several FP7 projects. It participates in different collaborative networks. This concerns mainly the radiation theme, in contrast with the two ther themes.

Team members are involved in many committees (INSERM, AERES, INVS, AFFSAPS).

The Radiation Epidemiology part of the team is prominent internationally in their areas of expertise. They also have collaborations with a large number of European teams and with various US national Cancer Institutes networks, although it is not explained what the outputs of the latter are. There have been a large number of invitations of team members to French conferences) and membership of French Boards (i.e. there is evidence of a national reputation), but few invitations abroad and modest evidence in that sense of an international reputation other than participation by the radiation part of the team in several European collaborations.

The descriptive epidemiology theme has mainly a national reputation and activity. The reputation of the Social Science theme is more modest.

Assessment of the unit's interaction with the social, economic and cultural environment

The team has established partnership in a project involving an industrial partner.

The team has an expertise recognized in the field of the risk attributable to some causes of cancer, with communications addressed to the population through the media.

Several interactions with the French social and cultural environment are described in the application but generally in terms too vague to be clear how substantive or important they are.

Assessment of the unit's organisation and life

The team appears to be the concatenation of three parts brought together for no obvious synergistic reason. The social sciences part of the team has worked on, and is proposing new studies relating to, cancer survivors, which has synergies with the radiation part of the team. Otherwise, there is little evidence of interaction between the parts

of the team or of any added value. The location of the team within the Gustave Roussy Institute appears as strength with good potential for interactions.

Assessment of the unit's involvement in training through research

The leader is head of the Masters professional degree in Health Law (University of Paris 8) and participates, in two Masters 2.

The team have contributed to substantial numbers of sessions of class teaching in Paris and have supervised substantial numbers of Masters and Doctoral students.

Assessment of the strategy and the five-year plan

The five-year plan aims at structuring the 3 teams around specific objectives. Some plans are in line with previous work, with the goal to improve international integration. The pursued objectives concern: “dosimetry and imaging”, “epidemiology of iatrogenic effects of radiation therapy and chemotherapy”, “survivorship-social impact of cancer and treatments on survivors’ life”, “epidemiology of low-doses of ionizing radiation”, “general cancer epidemiology”, “epidemiology of differentiated thyroid cancer”, and “breast implants”.

The ability for interdisciplinary work is not evident as described in the plan. No clearly defined strategy emerges from the document.

Future work on new dosimetry software and on statistical methodology is described. The proposals on substantive research are in several instances difficult to evaluate from the material provided, because the written application tended to sketch out areas of work rather than describe specific research proposals. There is often no indication of how the proposed work would (or would not) fill gaps in, or go beyond, the existing international research, or answer important currently unanswered research questions nor of the extent, completeness and quality of the data to be collected. An impressively large number of studies are alluded to, and an impressive wide range of outcomes will be investigated. The team has built up some important cohorts, and will pursue their follow-up. There was a lack of information, however, on their power and quality, and whether the proposed research will be cutting edge and likely to produce important findings

Conclusion

- **Strengths and opportunities:**

The team has developed cohorts which are original and are able to support research projects of interest in the future.

International recognition, involvement in European projects.

- **Weaknesses and threats:**

Few members have their HDR, therefore the number of PhD students is limited.

Lack of specific strategy to achieve the merging of the 3 teams.

Concurrence from research teams or institutions having official monopolistic position.

- **Recommendations:**

Clarify the strategy planned to integrate the new 2 themes (descriptive epidemiology and social sciences).

Clarify more precisely the projects involving social and human sciences research.

Consider carefully how to concentrate the radiation/aetiological epidemiology effort, and use of their strong existing cohorts, on questions where the team can produce results of international importance.

Team 4 :

Epidemiology and evaluation of prevention and therapeutic strategies: HIV, reproduction, pediatrics

Name of team leader: Ms Laurence MEYER, coleader : Mr Jean BOUYER

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	8	8
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	9	7
N4: Other professors (PREM, ECC, etc.)	1	1
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	7	6
N6: Other contractual staff (without research duties)	23	23
TOTAL N1 to N6	**50**	**47**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	13	
Theses defended	11	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken	9	
Qualified research supervisors (with an HDR) or similar positions	9	10

• Detailed assessments

Assessment of scientific quality and outputs

Team 4 has produced 436 papers (208 (48 %) signed as first or last authors, with 1 papers in top 1 % ISI Web of Knowledge). Leading papers with team leadership were published in PLoS Medicine, Human Reproduction, Fertil Steril, Lancet Infectious Diseases, Clinical Infectious Diseases, AIDS, J AIDS, and American Journal of Epidemiology.

During the last 5-years period, Team 4 has contributed to improved knowledge in epidemiology and management of infertility, quantifying the infertility rates in couples trying to be pregnant, the expected rate of medical visits for fecundity or the rate of spontaneous pregnancy in women after in vitro fertilization failure. They also developed new themes on management of pregnancy and child health strengthening collaborations. In the field of HIV and sexually transmitted infections, team 4 made an important public health contribution to estimate HIV incidence and transmission patterns in France and to quantify the reduction of HIV prevalence in the South-Africa associated with voluntary male circumcision. They also brought important results on « HIV controllers », and also regarding prevention of mother-to-child HIV transmission.

Epidemiologists from Team 4 have developed innovative statistical methods in their research areas. The team also leads several cohorts, particularly in the HIV field, and contribute to large European collaborations on this topic.

Assessment of the unit's academic reputation and appeal

The team maintains numerous national and international collaborations. In the last 5 years, 2 senior members were invited to give lectures in international conferences, and more in national meetings. Five members received European or national awards, one member received an award from the French national academy of sciences. The team co-chairs a FP7 European project on HIV and belongs to several international scientific committees, mostly in the field of HIV. Three post-doctoral students have been appointed to the team over the last 5 years. The team received several national grants.

Assessment of the unit's interaction with the social, economic and cultural environment

The team has conducted research that has had a major impact on policies and programs to prevent HIV through scaling up voluntary male circumcision, not only in South Africa but globally. The research conducted by the team has influenced guidelines on the Prevention of Mother-to Child Transmission (PMTCT). Their measure of incidence has been developed in collaboration with the World Health Organization epidemiology team. The team has significantly contributed to national guidelines regarding HIV care or ectopic pregnancy. Senior members of the team contribute to expertise in public health and epidemiology, leading the scientific council of Institut de veille Sanitaire (the French HPA/CDC) and participating to the scientific council for the French national committee of epidemiologic registries and the French ethics committee. They also contribute to national scientific councils in their respective field of expertise – ANRS, Sidaction. One member of the team belongs to the scientific council of the Paris Sud University. The team is inventor of two patents. Partnership with the pharmaceutical industry is organized through one European consortium or through ANRS in the HIV domain.

Assessment of the unit's involvement in training through research

The involvement of the team in training and teaching is huge: One of the team leaders leads the public health doctoral school from University Paris Sud / University Versailles Saint-Quentin-en-Yvelines / University Paris Est; the other team leader leads the Master 2 Research in Public Health and another researcher from the team leads the first year of the Master in Public Health. The team coordinates a summer school in epidemiology and public health.

In addition to these teaching responsibilities, the team has supervised 11 PhD students and 17 master students over the last 5 years. The follow-up of PhD trained in the group seems good as three have been appointed a permanent position as assistant professor or researcher.

Assessment of the strategy and the five-year plan

The project is innovative and addresses actual public health issues.

Projects related to the prevention of sexual HIV transmission in South Africa will pursue previous works from the team. They will benefit on sustained collaborations and will rely on new innovative studies. A sub-theme will explore the impact of new biomedical prevention strategies such as TASP or PREP on HIV incidence – benefiting from acquired experience in this field. This topic is highly original and relevant from the public health side.

Projects on HIV infection will continue to explore mechanisms involved in primary HIV infection and factors associated with sustained control of HIV infection based on original cohorts lead by the team on this topic. Two new sub-themes will be developed. The first will explore the role of inflammation in the control of HIV infection or the occurrence of metabolic disorders. The second will address accelerated ageing and long term clinical and social prognosis in patients with known date of HIV infection.

Projects on reproduction will continue to characterize the epidemiology of infertility and explore access to assisted reproductive technology. They will also describe the living conditions, health and development of children born after assisted reproductive technology. These new topics are original, address important public health issues. Regarding management of pregnancy, topics developed are clearly oriented towards the clinical side in obstetrics and gynecology with projects on management of gestational diabetes, pregnancy in obese women, mini invasive surgery and anxiety associated with prenatal diagnosis. These projects are feasible as they will rely on ongoing studies and involve clinicians from the team. A specific subtheme will address the issue of management of HIV pregnant women with projects on the HIV vertical transmission and its prevention based on existing cohort or planned randomized trials, and on long term impact of perinatal exposure to drugs or HIV maternal infection. This topic is highly relevant, original and will exploit the skills from various members of the team.

The fourth theme will extend previous clinical works on bronchiolitis in infant and will develop a new subtheme on paediatric inflammatory disease. Several clinical projects are ongoing to assess biological criteria for prognosis in bronchiolitis or to detect bacterial infection in infants, as well as to evaluate the effectiveness of treatments in bronchiolitis through large trials. Here again, the field is clearly clinical epidemiology with clinical leadership. The other sub theme will focus on etiology and pathogenesis of inflammatory diseases with three different projects based on registry and cohorts. However the consistency with other themes from the team is less obvious.

A fifth theme, new, will focus on long-term health and living condition of children with severe chronic diseases. The general aim will be to explore, in children with severe disease, the differential impacts on prognosis, quality of life or behaviours. Cohorts of young subjects with sickle-cell anaemia or haemophilia are planned.

Overall, parts of the strategy are clear and coherent with objectives. They rely on strong collaborations with experts in virology, physiology and clinicians actually involved in projects. The team leads several original studies and cohorts so that the five year plan seems feasible. Cohorts in the field of HIV (PRIMO, COPANA, collaboration COHERE, EPF) are well established original studies led by the team, with high international reputation. Also there is an obvious synergy between the projects in terms of designs and methods.

Conclusion

▪ **Strengths and opportunities:**

- Scientific coordination of original HIV cohorts, with sustained funding.

- Huge involvement in education and training in epidemiology.

- Opportunity to develop common research themes at the crossroads of HIV and pregnancy or paediatric areas.

▪ **Weaknesses and threats:**

- The number of full time equivalent senior researchers is relatively low. Administrative and management workloads and involvement in education activities limit time for research.

- Modest number of senior researchers which contrasts with a large number of objectives.

- The number of objectives is clearly too large.

- The large number of topics covered are not clearly linked and there is a risk of inconsistency among research objectives. This is in part as a result of joining of the two teams with very different research agendas, one on HIV the other on reproduction. It is unclear how this combination can add up to research strengths, and some thought has to be given to the coherence of the research agenda.

- Although clinically relevant, the added value of some clinical projects in the team (in obstetrics or on bronchiolitis) is questionable.

- The fifth theme (transition to adulthood in young subjects with severe chronic diseases) is not really convincing (if we exclude the part related to children with HIV) and a more efficient approach would be to develop a collaborative project on that topic on already existing cohorts (cystic fibrosis, etc...).

- **Recommendations:**

- Limit the number of objectives and increase consistency between the various subthemes.

- Improve attractiveness for post-docs and young scientists.

Team 5 : Epidemiology and Translationnal Research in Renal and Cardiovascular Disease

Name of team leader: Ms Bénédicte STENGEL, Deputy team leader : Mr Ziad A. MASSY

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		10
N2: Permanent EPST or EPIC researchers and similar positions		2
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		4
TOTAL N1 to N6		**16**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	6	
Theses defended	8	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	9	

• Detailed assessments

Assessment of scientific quality and outputs

Team 5's topic is Chronic Kidney Disease (CKD), which is a major public health issue that they address from very original perspectives. The investigators of this team devote 70 % of their efforts to research. They are leaders in setting major research tools, such as the REIN information system, they have obtained funding in the "Grand Emprunt" financial process for a cohort, and they are part of an important CKD consortium.

The major manuscript production is predominantly clinically oriented, although some important epidemiology papers are also present in the last 5-years scientific output. The 450 manuscripts published in good journals (almost 50% in the first decile of IF) show the scientific influence of this active team. This production corresponds to good individual publication records, but there are still relatively too few common publications and lead position signatures. The H factors of individual investigators is still relatively low, indicating an emerging recognition, except for one senior investigator, currently emeritus, and whose publication record indicates little copublication with the rest of the team.

The Team raised more than 6 M€ in competitive calls in the last 6 years, and 1,7 M€ in other type of contracts.

Assessment of the unit's academic reputation and appeal

Most team members participate in important expert boards, national and international working groups and networks, and give a large number of invited lectures. They have received several awards.

The three main PIs are leading important projects (the French REIN registry and CKD-REIN cohort networks, and the international SHARP and CKD prognosis Consortium collaborative international projects).

The fact that many manuscripts are co-authored by Team 5 PIs together with international researchers indicates the presence of the Team in international genetics, clinical trial and yet other research consortia.

Team 5 is oriented to biomarker research (biochemical and genetic) mainly on the CKD domain, but also in the diabetes field and in the assessment of clinical practice. This provides a wide setting that should allow the Team to covert the bench-to-beside as well as the bedside-to-bench together with bedside-to-public health approaches of biomedical research comfortably.

Assessment of the unit's interaction with the social, economic and cultural environment

Team 5 invests 10 % if its manpower to interaction with the environment. Some collaboration with other groups are observed in their activity (e.g., on the diabetes field), and collaboration with drug industry in several international clinical trials. Team 5 members also participated in population screening programs, and give support to patient associations and the World Kidney day. The leader has an interface contract with Agence de la Biomédecine and the links with this agency are strong and structured. There is also a strong interaction with the French health insurance system.

Assessment of the unit's involvement in training through research

Although direct research or pre-graduate teaching is not detailed, some team's members are teaching postdoctoral courses (Masters and courses in clinical practice).

Eight completed and 6 ongoing doctoral theses show the training capacity of Team 5.

Overall they declare that 10 % of their time / effort is related to teaching.

Assessment of the strategy and the five-year plan

The future plans, including relevant questions and an important focus on translational aspects, are well designed and exploit all potential strengths of the team. The proposal is ambitious but feasible. The probabilities of success are high.

Conclusion

- **Strengths and opportunities:**

Coherence of common grounds around patients at high risk of cardio-vascular diseases, and existing collaborations.

Complementarity multidisciplinary approach to cardiovascular and chronic kidney disease research, with genetics, physiopathology, clinics and epidemiology.

Familiarity with development and analysis of large cohorts; good ability to raise funds.

Proximity with decision makers (Agence de la biomédecine) with true translational aspects (from bench to public health), and involvement in international projects.

Possible recruitment of a professor of genetics.

- **Weaknesses and threats:**

Proximity of themes must be completed, especially with the cardiology and intensive care team of Ambroise Paré hospital.

This is a new team, including two groups of clinicians who were not part of the Center, with a relative unbalance with a stronger theme (CKD).

This is a relatively small team, especially to cover adequately two phases of translational research (bench to bedside, and bedside to public health); one of the productive senior researchers is emeritus.

There is no clear competency to carry in silico simulations for axis 3.

Group animation and motivation needs to be secured, especially given that the team is scattered on three locations.

- **Recommendations:**

Take advantage of the population and patient research capacity to go in deep in the biomarker research field to improve prediction of CKD patients more susceptible of developing CVD. In case of successful findings they could be straight-forwardly applied in clinical practice.

The CKD-diabetes link offers also good opportunities of biomarker research.

Developing the genetics potential of the group would probably be wise in view of the success in the area; more proximity with cardiology researchers might a plus.

Some researchers participated in EPIC IARC cohort. Maybe they could take advantage of the French part of this cohort to lead some research in their field.

Team 6 : Environemental Epidemiology of Cancer

Name of team leader: Mr Pascal GUÉNEL

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	3
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2
N6: Other contractual staff (without research duties)	4	4
TOTAL N1 to N6	**13**	**14**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	5	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	3	
Qualified research supervisors (with an HDR) or similar positions	4	4

• Detailed assessments

Assessment of scientific quality and outputs

Team 6 conducts research on environmental factors related to the development of cancer, particularly lung and hormonally-related cancers. The research program also includes investigation of genetic factors, gene-environment interactions, and the development of innovative statistical methods needed to examine combined effects of risk factors. Their scientific output includes important discoveries regarding female breast cancer and night work, menopausal hormone therapy, exposure to organic solvents and organochlorine chemicals; male breast cancer and exposure to organic solvents; lung cancer in relation to employment in construction crafts, exposure to mineral wools, cement dust, diesel, BMI, and, among women, hormonal factors; thyroid cancer and genetic susceptibility factors; tools for analyzing high dimensional genetic epidemiology data sets to uncover polygenic models of association; and statistical methods, including profile regression, to integrate different sources of information when analyzing epidemiology studies. A particularly notable finding from the group could help resolve whether a night work, which was classified by IARC as a 2A carcinogen in 2007, is in fact a carcinogen.

The group has been productive in terms of the number of scientific publications for the size of the group, authorship position, quality of journals, and subsequent citation of the articles. Between 2008 and mid-2013, the group published 122 articles, of which 42 % had team members as first or last author. The journals in which the publications appear include high-impact biomedical journals and high-impact, high-quality speciality journals for epidemiology, cancer, environmental/ occupational research, and statistical methods (Int J Cancer, Br J Cancer, PLoS Genetics, Envir Res, J Occup Environ Med). The 2013 report on night work and breast cancer is among the top 0.1% of the most cited articles in the ISI domain "Clinical Medicine". However, many of the last author, highly cited papers were authored by a scientist at MRC without other members of the CESP team. This researcher, although DR Inserm, is detached from Inserm and not formally part of the team, but an international collaboration. Thus these articles alone should not be included in the scientific production of this team.

In addition to scientific publications, successful data collection efforts are a major accomplishment, which will yield benefits as data and biospecimens are analyzed in the years ahead. They have also made progress in gaining experience with genetic epidemiology. With funding from INCa and the National League against Cancer, they constructed a candidate SNP genotyping chip for use in studies of hormone-related and other cancers.

Assessment of the unit's academic reputation and appeal

Several team scientists are internationally recognized experts in environmental cancer epidemiology. They lead projects and contribute data to the pooling efforts in international consortiums on Breast, thyroid, Lung Cancer; on hormonal and reproductive factors in female lung cancer. They are active collaborators in national and international research networks. The team leader is chairman of the Scientific Committee of the project "Cancer Incidence around Nuclear Sites in France" from the Institute for Health Surveillance (Institut de Veille Sanitaire). Another scientist is President of the Fondation de France scientific committee on "Cancers et troubles de la reproduction: rôle de l'environnement". Senior members of the team are members of committees or working groups on their topics of comptency. The team leader and another scientist have played leadership roles in several international scientific meetings. Evidence of the group's academic reputation and appeal comes also from the number of students and postdoctoral fellows who have been trained with the group. The group has been successful in obtaining research grants.

Assessment of the unit's interaction with the social, economic and cultural environment

Team members participate in working groups of experts convened by national agencies and advise on environmental or occupational health issues for public health decision makers, but there is room to expand their efforts to foster translation of their research results into prevention in occupational health and safety. The team's research findings have public health and clinical significance. For example, breast cancer risk and use of natural micronized progesterone or the team's findings for occupational exposures

Assessment of the unit's involvement in training through research

The team has been involved in training the next generation of researchers by hosting 10 doctoral and 11 masters students working on theses, as well as two medical residents in public health, during the evaluation period.

There is a good record of the doctoral students and many of the masters students having successfully published papers. In addition, one of the scientists teaches in the Master of Public Health program of Paris-Sud University, including courses on quantitative epidemiology and etiologic epidemiology, and manages the Epidemiology option of a Masters program.

Assessment of the strategy and the five-year plan

The team has done an excellent job of identifying critical elements that needed to be added to their program to enable them to be on the cutting edge of environmental epidemiologic research in the future: initiation of genetic related research and addition of team members with statistical expertise for methods development. They evaluate their findings and modify research plans to achieve their overall objective of identifying environmental causes of cancer. They also have identified potentially important "new" exposures that have not been adequately studied (e.g., ultrafine particles in relation to lung cancer) and made plans for investigation within existing studies. They have solid plans to assess etiologic heterogeneity, search for new susceptibility genes, describe the determinants of exposure, and evaluate the effect of environmental carcinogens on prognosis. Prostate cancer seems a curious and perhaps unlikely cancer for environmental research, but the team plans to pursue some innovative hypotheses on night work, sleep patterns, and chronotype. It is not clear if the team has adequate funding for such a large, new case-control study. In general, through their programs, collaborations, and involvement with national networks and international consortia, they are able to pursue good scientific courses for their research questions.

Conclusion

- **Strengths and opportunities:**

This team has highly qualified personnel that have successfully collected a large amount of epidemiologic data and biospecimens. They use excellent study designs, exposure assessment approaches (including critical time windows and physiologically-based pharmacokinetic modelling), and statistical methods. They have solid plans to assess etiologic heterogeneity, describe the determinants of exposure, and search for new susceptibility genes.

They participate in collaborations, networks, and international consortia. They could share the biostatistical methods developed for their work by their collaborator at MRC.

The team is comprised of recognized experts who are called upon by national agencies for their advice.

- **Weaknesses and threats:**

As recognized by the team, the case-control methodology has limitations in being able to address new hypothesis efficiently and in a timely manner. The unknown but probably large non response in the first phase of the random digit dialling process to select controls is a potential weakness to their work. They have compared the socioeconomic status of control participants to the general population, but no other methodologic work to evaluate possible selection bias was undergone. The case-control methodology also affects the confidence one can have in the value of some biomarkers for risk prediction. Will the group have the biospecimens needed to pursue important hypotheses in their field? The lead genetic researcher is a junior investigator. Their statistical collaborator, however, is senior and able to contribute to genetic projects, and the group participates in international consortium that include leading genetic researchers. Insufficient permanent positions hinder progress by the team. The lack of in-house expertise in retrospective occupational exposure assessment is a weakness. The team relies upon job-exposure matrices developed by a government agency (INVS) which has its own priorities and approaches and may not be as responsive as needed to the requirements of the team. The substantial cost of genetic approaches (e.g., exome sequencing or whole genome sequencing) that could enhance, for example, the study of familial thyroid cancer in New Caledonia could be a challenge for the team.

- **Recommendations**:

- The committee recommends more methodological work to assess the representativeness of the controls, taking into account the initial random-digit dialling phase and the interview phase of the selection process.

- The group could consider more biologically-intensive work site-based studies to further pursue and establish findings from their case-control studies.

- The team needs to increase expertise in genetics and genomics (either within the team or through strong collaborations across CESP), as well as think beyond genomics to what will be necessary to allow future expansion into other "omics", e.g., metabolomics, etc. Careful thought needs to be given to what biospecimens should be part of

future/ongoing studies to position the group for other technologies and how the case-control methodology affects their ability to move into other cutting edge areas of epidemiologic research.

- There is room to expand their efforts to foster translation of their research results into prevention in occupational health and safety.

- The team lacks in-house expertise in retrospective occupational exposure assessment and relies a government agency (INVS) to develop job-exposure matrices. We recommend that the team seek out experts in this area to either join the group or collaborate closely with them. Even adding a post-doc with training in retrospective occupational exposure assessment, such as those trained at Utrecht University, could have a positive impact on the work.

Team 7 : Gender, sexual and reproductive health

Name of team leader: Ms Nathalie BAJOS

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	6	6
N3: Other permanent staff (without research duties)	3	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)	3	3
TOTAL N1 to N6	**14**	**14**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	8	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	6	
Qualified research supervisors (with an HDR) or similar positions	2	

• Detailed assessments

Assessment of scientific quality and outputs

The team brings together a strong theoretical framework with focused research questions on topics relevant to health, dealing with the links between reproductive health, its context, and its health consequences. This includes changes in ideas and practices around sexuality, patterns of use of health services around contraception, user and provider perspectives on health services, perceptions of contraception and their behavioural consequences, and a life cycle approach to reproductive health from adolescence through menopause. Their framework also includes consideration of two important issues, medicalization and inequality, the latter including gender as one of the dimensions of inequality, along with socio-economic factors.

They consider sexual and reproductive health in context and have conducted comparative studies across countries. Though much of their work is carried out in France, they also have collaborations in the UK, Africa, Latin America, and the Middle East. This includes a study of changing conceptions of sexuality and gender in Brazil, a study of menopause in Tunisia, a study of contraception failure in West Africa.

They are a truly multi-disciplinary team, with demography, epidemiology, sociology, ethnography, psycho-social approaches, sexology, gender studies, and social studies of science. They focus on the links between ideas and behaviours, which are important in public health, and tend to be insufficiently addressed. They bring together good sociological and quantitative expertise, together with qualitative methods.

The team has been productive and some of their publications are in highly rated journals. They report 129 peer-reviewed papers, in addition to a book, and other publications. Their most prominent publications include:

Bajos' book on sexuality in France,

BMJ article on link between obesity and unplanned pregnancy and abortion,

Articles on biomedicalization of HIV prevention in Journal of Sex Research,

Contraceptive use in the US (Michigan) in Human Reproduction,

PrevMed article on inequalities in cervical cancer screening,

Emergency contraception in W Africa Social Science and Medicine.

Assessment of the unit's academic reputation and appeal

Their work is very well regarded in France and outside. They have conducted 2 major surveys, one on sexuality and HIV, another on sexual health, which are references for France. They contribute to surveys on sexual and reproductive health in the UK, and are asked to contribute at international conferences.

Assessment of the unit's interaction with the social, economic and cultural environment

The group has engaged with a number of stakeholders in the environment, including politicians/ ministries - the team leader is participating in the Haut Conseil à l'Egalité, which reports to the Prime Minister; the team has been asked by the Ministry of Social Affairs to evaluate the pill scare crisis of 2012. Members of the group have participated in interviews with the media and have contributed to public exhibits. They are invited to lecture, to organize events, they have external visitors, and they have collaborations outside of France. Some members of the group have adjunct appointments at universities outside France. They have been asked to provide expertise in public health at national and international level, including the World Health Organization, the World Association of Sexual Health, Unesco.

They have secured public funding (2.1 million) and private funding (65K) from national agencies and foundations.

Assessment of the unit's involvement in training through research

Team members contribute to teaching and supervising students (11 Doctoral, 10 Master) as well as post-docs (2).

The have links with Universities St Quentin Paris 1, Metz, Diderot, Paris 5 et 6.

They work in a strong multidisciplinary field that brings together demography, sociology, epidemiology, social studies of science etc., and hence likely contribute to a rich curriculum of teaching.

Assessment of the strategy and the five-year plan

The team has a detailed plan for continuing engagement in research and appear to have the resources and energy to achieve it. This agenda is held together by a very good energy in the team.

Most importantly, a strong theoretical framework is developed which puts together the different projects of the team. It is focused on the process of medicalization of sexuality which affects individuals accordingly to their social characteristics. This leads to analysis of social inequalities (lifetime accumulation, production and reproduction) as well as an, intersectionnality approach involving social class, sexual orientation and ethnicity issues.

Within this framework, the different axes proposed by the team do not lead to dispersion of thematics, but have a strong coherence within the team.

1. Sexuality and sexual health:

Sexuality and social contexts: military, migrants, MSM,

Life course approach to sexuality: norms /representation of children; urban poor; adolescents; aging,

Sexuality and chronic disease: HIV, pelvic floor.

2. Sexual and reproductive health care and access:

Medicalization of sexuality, representations and practices of contraception and abortion, cancer screening,

Patient-physician interactions.

3. The social production of scientific knowledge

Conclusion

- **Strengths and opportunities:**

Strong theoretical framework.

Real interdisciplinary team, with interaction between quantitative and qualitative methods.

Methodological concern and work on comparisons between sampling methodologies.

Exceptional involvement in dissemination activities toward the public and public actors.

Engagement of research in addressing social problems (contraception, abortion).

Strong international network and recognition.

High level of scientific production.

Attractiveness to young researchers.

- **Weaknesses and threats:**

The high level of demand for the team's expertise and their engagement in dissemination activities could compete with research production and activities.

- **Recommendations:**

Given the excellence of the team, the committee had no recommendation.

Team 8 : Epidemiology oh aeging and age-related diseaes

Name of team leader: Ms Archana SINGH-MANOUX, coleader : Mr Alexis ELBAZ

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions		4 + 1 emeritus
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		3
N6: Other contractual staff (without research duties)		3
TOTAL N1 to N6		**11**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		7
Theses defended		9
Postdoctoral students having spent at least 12 months in the unit		See above
Number of Research Supervisor Qualifications (HDR) taken		3
Qualified research supervisors (with an HDR) or similar positions		3

• Detailed assessments

Assessment of scientific quality and outputs

The scientific production of those forming this new team is outstanding.

Team members have produced 249 papers, 107 (43 %) signed as first or last authors. Of note 18 papers were published in high impact medical general journals (Br Med J, Eur Heart J, Ann Neurol). Other papers published in leading specialty journals in neurology and cardiovascular diseases and 27 papers in leading epidemiological journals. During the last 5-years period (2008-2013), team members have made important contributions on the roles of health behaviours, cardiovascular risk factors and biological markers (sex hormones) on cognitive and motor ageing and their contribution to dementia and mortality. They also led and contributed studies in the field of neurodegenerative diseases with important findings on the association between exposure to pesticides and Parkinson's disease. Finally, they highlighted the role of psychosocial factors or some biomarkers and sex hormones, including post-menopausal therapy, on the occurrence of cardiovascular diseases or dementia. Most results were based on two cohorts (Whitehall II and 3C) co-led by researchers from the team, and to a lesser degree from large population-based case-control study or through collaborations with other existing cohorts. Epidemiologists from this team have developed statistical expertise for the analysis of longitudinal data.

Assessment of the unit's academic reputation and appeal

There is a compelling list of engagement in a variety of wider academic activities for each of the three senior leads – providing scientific input into various programs, university bodies, institutes and policy arenas as well as EU work, public health contribution to EU meetings. Many national and European collaborations are listed as well as in the US. The investigators are involved in GBD and Geo-PD. ASM has been very active in organizing symposia and scientific meetings. All leads have given many lectures across Europe and US. Their achievements have been recognized with many honours and awards (Archana Singh-Manoux in particular). The team maintains numerous national and international collaborations. The team leader was awarded by ERC, and has been appointed to an honorary professor position at University College London. The team led a Work Package in a EU joint program. Two young researchers have been recruited (INSERM) in the team.

Assessment of the unit's interaction with the social, economic and cultural environment

The activity in this respect is overall excellent. The areas of research have led to them being involved in various activities at national level such as taking stock of social inequalities, pesticide exposures and being scientific representative on various national bodies including INSERM's expert collectives. The team leader was deputy director of the national body French Institute of Public Health which has been looking at research strategy including specific activities such as piloting cohorts based on medical administrative systems, promoting international collaboration and improving visibility of French research. Team leader's research to date has been very focused on Whitehall cohort but the proposed grouping will allow a broader program to emerge. Senior members of the team participated to INSERM's « expertises collectives » and were scientific delegate for AERES.

Assessment of the unit's involvement in training through research

There is good evidence of involvement in training focused on aging, neurology and epidemiology ranging from involvement in the doctoral program of Public Health (with four approved PhD supervisors within the University Paris Sud/University Paris Descartes and VSQ), involvement in masters teaching and supervising individual masters students in several programs including an online course. The team supervised 10 master students and 9 PhD students over the past 5 years, a further 6 PhDs are underway. The follow-up of PhDs trained in the group is not described.

Assessment of the strategy and the five-year plan

The project is very well written, original and consistent and there are really only small queries. It is structured into two themes exploring the entire ageing phenotype from the decline of cognitive and motor functions to the occurrence of age-related diseases (neurodegenerative and cardiovascular diseases). The addition of the new component is perhaps less integrated as yet. The work is focused on two cohorts lead by researchers from the team, and on a closed collaboration with the Constances and Gazel cohorts, and to a lesser degree, on other collaborations

(Institut de Veille Sanitaire), and obtained approval for access to the French health insurance database. There is an obvious synergy between the projects in terms of designs and methods.

The program is divided into 1. Determinants of cognitive and motor function with a focus on occupational, behavioral, psychosocial and biological factors using Whitehall and other cohorts. Comments here would be that Whitehall and the outputs that the team leader has from this work are really visible in the external world as University College London, not France so there is a visibility issue here. This work is highly dependent on the quality of analytical methods and there was little mention of the challenges of modelling multiple variable longitudinal data in a robust manner. The section outlining the potential use of Mendelian randomization similarly does not include the 'how' and the capacity element. The second theme is Epidemiology of age related disorders – neurodegenerative and CVD. These are highly specified projects and although only briefly described do look interesting, valuable and do-able. The challenge of the infrastructure to handle the databases is not covered but this is an issue for the whole of the research unit (including biological collections). The aspiration to examine time windows for risk prediction is very promising.

The case for particular expertise in the ageing phenotype is very well made for this strong group of researchers. This group has the potential for outstanding work.

Conclusion

Overall the strategy is clear and coherent with objectives and the five year plan seems feasible. It relies on two cohorts led by researchers from the team, and on a closed collaboration with the CONSTANCES and GAZEL cohorts, and to a lesser degree, on other collaborations. The team has developed collaboration with Institut de Veille Sanitaire, and obtained approval for access to the French health insurance database. There is an obvious synergy between the projects in terms of designs and methods.

The SWOT analysis made by the team does not ignore some challenging issues. They clearly indicate the need to develop collaborations with other teams from the center on aging.

- **Strengths and opportunities:**

- Scientific coordination of well characterised cohort studies.

- Consistency of the team with complementary expertise on the project themes.

- High scientific reputation and international visibility.

- Opportunity to develop collaboration with other team from the center, in order to increase statistical skills.

- **Weaknesses and threats:**

- The burden of administrative activities could undermine scientific activities.

- Difficulty to attract post-doctoral students from abroad.

- **Recommendations**:

- Develop new interactions with other teams from the center to mutualize statistical expertise on longitudinal data analysis, gene-environment interactions, ecologic methods, causal modelling…

- Improve international attractiveness for post-docs and young scientists.

Team 9 : Lifestyle, genetics and health: integrative trans-generational

Name of team leader: Ms Marie-Christine BOUTRON RUAULT

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)	21	21
TOTAL N1 to N6	**27**	**27**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	5	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	3	
Qualified research supervisors (with an HDR) or similar positions	3	

• Detailed assessments

Assessment of scientific quality and outputs

A total of 333 papers produced between 2008 and 2013 represents a large number for a group of this size although for the majority of these papers, members of this team were not first or last author. Thus they are effective collaborators with good scientific production, but may not be initiating a large proportion of their output. They have achieved publication in some higher range impact journals (N Engl J Med, Am J Clin Nutr, J Clin Oncol, Am J Hum Genet) as well as respectable number in journals with impact factors above six. This is consolidated by a number of papers in specific areas of their research, although so far there is nothing approaching a major step forward in these areas. This could be in part due to the range of research interests among the researchers, without a more specific focus as well as a more technical rather than substantive emphasis. Other scientific dissemination has been achieved through conference participation and presentation, including organisation of some events.

Assessment of the unit's academic reputation and appeal

The research covers several areas relevant to a large proportion of the population and represents both multidisciplinary and interdisciplinary approaches. The true integration of epidemiology and biological processes is becoming viewed as increasingly important and the group is actively involved in the process of integrating genetics and biomarkers with epidemiological materials and techniques: this is promising for the future, but this is an area that the team hopes to develop, but they have not yet fully capitalised on these techniques. Longitudinal cohort data are a potentially powerful research tool and this group have been involved in developing such cohorts, as well as utilising routinely collected material. They participate in major international collaborations.

Assessment of the unit's interaction with the social, economic and cultural environment

Some of the findings have been made more accessible to the general public though engagement with the mass media and though conferences and presentation organised by Inserm designed for the general public. Major French newspapers and television stations have covered some outputs. More work beyond mass media releases would be desirable. They have been involved in at least two public-private partnership enterprises. This included an organisation developing cancer risk prediction instruments but the quality of this interaction and the quality of the product are difficult to assess.

Assessment of the unit's involvement in training through research

A main training activity is for the six doctoral students who participate in research as the main vehicle for their doctoral development: this is not an excessively large number. Training is also provided at the postdoctoral level through participation in research. The team does not run a course of their own, but are involved in teaching on at least three courses and tutoring a respectable number of master students. There is also training for doctoral researchers attached to the group, as well as participation in training at a doctoral school.

Assessment of the strategy and the five-year plan

The strategy involves capitalising on the research material available to the group, as well as expanding resources by developing cohorts complimentary to this. There will also be interaction with other groups to allow for replication of results and joint analyses, and of course this will be important to maintain a similar volume of scientific productions. An issue with data collection is it can sometimes prevent staff from producing other scientific outputs, so it will be important to manage the balance between collection, planning and analysis for the staff involved. The planned programme is ambitious and in some areas would benefit from more specific development of hypotheses, so it will be important to maintain focus on feasibility and clear definition of objectives. Having said that, this group has great promise in terms of future production because of the resources they are developing and the techniques that are at their disposal. The increase in numbers of individuals with an HDR qualification will enhance the ability to supervise doctoral students.

Conclusion

This group is continuing to develop a multi- and inter-disciplinary approach to examining the aetiology of some chronic diseases that are of notable importance to public health. The group have a focus on scientific research with experts in several disciplines who are also engaged in collaboration with other groups. The group seems established but a feeling of sustainability may be an issue due to the lack of permanent positions. They have and are developing research resources that potentially could be able produce important results, so long as there is a careful focus on hypotheses and feasibility. In the past, collaboration has resulted in a good number of high quality publications. Continued collaboration in substantive areas will be important, but it would be desirable for the group to increase the development of their own areas. The group combines research with doctoral training and potentially large-scale data collection. Although there is a sense of continuity, this may be hampered by the low number of permanent or long-term positions.

- **Strengths and opportunities:**

The combination of expertise and data resources (of different types), as well as longitudinal cohort data, offer significant research opportunities in identification of life-course and intergeneration patterns of risk accumulation.

There is also an opportunity to better understand biological processes underlying the pathways though genetic, epigenetic and other mechanisms.

The interest in inter-generational influences, including through epigenetic mechanisms, continues to increase and the engagement in this area and collecting information (biological and epidemiological) promises potentially interesting results. Developing and maintaining cohorts tends to be a resource and time consuming activity that represents a very important investment for the future (at the possible cost of reducing scientific output during the time of development).

- **Weaknesses and threats:**

Continuity is potentially threatened by dependence on contract funding, as is the case for many research groups. Also, if funding for longitudinal cohorts is interrupted (and thus management and data collection), this can have adverse implications for their viability and utility.

There can be a tension between data collection and analysis as the former can interrupt the volume of possible output, therefore lowering scientific impact for a time, both for individuals and the group.

The specific hypotheses and mechanisms that are to be tested require development by the team and perhaps there could be a better balance for studies initiated by the group and those initiated by external collaborators for substantive issues.

- **Recommendations:**

Plans should be in place to ensure continuity, designed to cope with periods without a full complement of staff or resources, so that key opportunities (such as contact with cohort members) are not lost. The team could develop their own substantive research programme in conjunction with collaboration and focus on developing testable hypotheses, while assessing feasibility carefully throughout the programme.

5 • Conduct of the visit

Visit dates:

Start:	February 5th, 2014 at 8h30 am
End:	February 6th, 2014 at 7h20 pm

Visit site(s):	Hôpital Paul Brousse

Conduct or programme of visit:

Wednesday, February 5th, 2014

8h30-9h 50 :	Welcome the Site Visit Committee, AERES Advisor
9h50 :	Presentation of AERES evaluation and of Committee members by Mr Emmanuel LAGARDE
10h00 :	Presentation of the projet CESP
	Introduction : Mr Denis HÉMON
	Overview of Achievements: Ms Laurence MEYER on behalf of the Interim Management Committee
	Scientific project : Mr Alexis ELBAZ and Mr Jean BOUYER on behalf of the Interim Management Committee
10h30 :	Discussion
11h00 :	Scientific presentation + Discussion Team 1
12h00 :	Scientific presentation + Discussion Team 2
13h00 :	Lunch with representatives of institutions
14h00 :	Scientific presentation + Discussion Team 3
15h00 :	Scientific presentation + Discussion Team 4
16h00 :	Scientific presentation + Discussion Team 5
17h00 :	Meeting with researchers
17h15 :	Meeting with engineer and technicians
17h30 :	Meeting with doctoral students and post-doctoral fellows
17h45 :	Meeting with representatives of the doctoral school
18h00 :	Close-door debriefing meeting of the Committee
19h00 :	End of day 1

Thursday, February 6th, 2014

8h30 :	Welcome to the Committee
8h35 :	Scientific presentation + Discussion Team 6
9h35 :	Scientific presentation + Discussion Team 7
10h35 :	Break
10h50 :	Scientific presentation + Discussion Team 9
11h50 :	Scientific presentation + Discussion Team 10
12h50 :	Lunch break
14h20 :	Meeting with the Interim Management Committee (Mr Jean BOUYER, Mr Alexis ELBAZ, Ms Laurence MEYER)
14h50 :	Close-door meeting of the Site Visit Committee
17h20 :	End of the site visit

Specific points to be mentioned:

The following representatives of intitution attended the meeting :

Mr Joël ANKRI, Membre du Conseil scientifique de l'Université de Versailles Saint-Quentin-en-Yvelines, UFR des Sciences de la Santé "Simone Weil"

Mr Etienne AUGE, Vice-Président Recherche, Université Paris Sud

Mr Jacques BITTOUN, Président de l'Université Paris Sud

Mr Serge BOBIN, Doyen de la Faculté de Médecine de Paris Sud

Mr David BOUCARD, Direction de la Recherche Institut Gustave Roussy

Mr Thierry DAMERVAL, Directeur général délégué de l'Inserm

Mr Christian DELPORTE, Vice-Président du Conseil scientifique de l'Université de Versailles Saint-Quentin-en-Yvelines

Mr Marc HUMBERT, Vice-doyen Recherche, Faculté de Médecine de l'Université Paris Sud

Mr Jean-Paul MOATTI, Directeur de l'ITMO Santé Publique

Ms Laurence PARMANTIER, Déléguée Régionale Inserm Paris 11

Mr Jean-Luc VAYSSIÈRE, Président de l'Université de Versailles Saint-Quentin-en-Yvelines

Ms Christine WELTY-MOULIN, Directrice du Groupe Hospitalier Kremlin-Bicêtre/ Paul Brousse/ Béclère, Assistance-Publique/Hôpitaux de Paris

6 • Supervising bodies' general comments

UNIVERSITÉ DE VERSAILLES ST-QUENTIN-EN-YVELINES

Versailles, le mardi 29 avril 2014

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

à

Dossier suivi par :
Christian Delporte,
Vice-Président du conseil scientifique chargé de la recherche et du développement scientifique
Réf : JLV/CD/MC/DREDVal 14-165

Monsieur Didier Houssin
Président
Agence dévaluation de la Recherche et de l'enseignement supérieur
20 rue Vivienne - 75002 PARIS

Réf. : E2015-EV-0911101C-S2PUR150007980-004888-RT

Objet : Evaluation des unités de recherche : Volet Observations de portée générale

Monsieur le Président,

Nous avons pris connaissance avec le plus grand intérêt du rapport de l'AERES concernant la demande de renouvellement de l'Unité Mixte de Recherche, actuellement UMR_S 1018, dénommée «Research Center in Epidemiology and Population Health (CESP) ».

Nous remercions l'AERES et le comité pour l'efficacité et la qualité de leur travail d'analyse. L'UVSQ, en lien avec les autres tutelles, veillera à mettre en œuvre les recommandations constructives des experts pour la période 2015-2019 dans le contexte Paris-Saclay.

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

Jean-Luc Vayssière
Professeur des universités

UNIVERSITÉ DE VERSAILLES ST-QUENTIN-EN-YVELINES

UNIVERSITÉ PARIS SUD

Comprendre le monde, construire l'avenir®

Le Président de l'Université Paris-Sud

à

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

Orsay, le 29 avril 2014

N/Réf. : 114/14/JB/LM/AL

Objet : Rapport d'évaluation d'unité de recherche
N° S2PUR150007980

Monsieur le Directeur,

Vous m'avez transmis le 8 avril dernier, le rapport d'évaluation de l'unité de recherche « CENTRE DE RECHERCHE EN ÉPIDÉMIOLOGIE ET SANTÉ DES POPULATIONS » - CESP – N° S2PUR150007980, et je vous en remercie.

L'Université se réjouit de l'appréciation portée par le Comité sur cette unité et prend bonne note de ses suggestions. Lorsque le nouveau directeur de l'unité aura été nommé, l'Université suivra avec attention les efforts pour renforcer l'unité du Centre et la synergie entre les équipes.

Vous trouverez en annexe les éléments de réponse de Madame Laurence Meyer, Monsieur Jean BOUYER et Monsieur Alexis Elbaz, qui forment l'équipe de direction transitoire de l'unité.

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

UNIVERSITÉ PARIS SUD
PRÉSIDENCE
Bâtiment 300
91405 ORSAY cedex

Jacques BITTOUN
Président

Siège :
Université Paris-Sud
15 rue Georges Clemenceau
91405 Orsay cedex
www.u-psud.fr

Tél : 01 69 15 74 06 – Fax : 01 69 15 61 03 - e-mail : president@u-psud.fr

CESP | Centre de recherche en Épidémiologie et Santé des Populations
Inserm Chercheur en santé depuis 1964 Health research since 1964 — 50 ans
Université Paris Sud — Comprendre le monde, construire l'avenir
Université de Versailles St-Quentin-en-Yvelines

Inserm U1018, UPS UMRS 1018, UVSQ UMRS 1018

Villejuif, le 23 avril 2014

Monsieur Pierre Glaudes
Directeur de la section des unités de recherche de l'Aeres
20 rue Vivienne
75002 Paris

réf : E2015-EV-0911101C-S2PUR150007980-004888-RT

Monsieur le Directeur,

Vous trouverez ci-joint les commentaires de la direction du CESP (Centre de recherche en Epidémiologie et Santé des Population, UMR-S 1018) et des responsables de ses 9 équipes à la suite du rapport d'évaluation du comité d'experts de l'Aeres qui a visité l'unité les 5 et 6 février 2014.

Nous vous prions d'agréer, Monsieur le Directeur, l'expression de notre sincère considération.

Jean Bouyer

Pour la direction intérimaire du CESP (Jean Bouyer, Alexis Elbaz, Laurence Meyer)

Jean BOUYER
Direction.cesp@inserm.fr
Tél : +(33) 01 45.59.51.33

CESP Inserm U1018
16 avenue Paul Vaillant-Couturier
F-94807 Villejuif Cedex

Response to AERES report on CESP (Research Center in Epidemiology and Population Health)

Assessment of the unit

We thank the AERES committee for highlighting the strengths of the CESP, including:

- the scientific quality of its teams and researchers,
- interdisciplinary research,
- the strong involvement of CESP teams in national and international collaborations,
- the leading role played by CESP in training for research in public health.

We also thank the committee for raising the following issues, even though they concern the entire scientific community in France and not simply the CESP:

- the duration of fixed term contracts has been reduced to 3 years in France, making it increasing difficulty to undertake "sustainable research",
- the need to carefully consider the issue of potential conflicts of interest in public health research.

We are grateful for the recommendations made by the AERES committee, which we found to be very useful. They reflect the scientific and management policies currently being implemented at the CESP and those that we have planned for the future. The CESP was created relatively recently, in 2010. The first mandate (2010-2014) was devoted to the successful consolidation of teams, implying that research units which were previously independent came together to be part of the CESP. The forthcoming period will entail giving greater importance to collaborations between the CESP teams and strengthening the centre's identity. In order to do this, a number of steps have already been taken and others are being considered. Here we provide a brief clarification on these points.

- In order to provide core administrative services to all the teams in the entire centre a group of four persons (SAGe) work under the responsibility of the General-Secretary.
- The CESP has a data processing and information technology platform with extensive skills in management of servers, and databases in terms of issues like data confidentiality and security.
- At the present time 15-20% of the institutional funding is mutualized. We plan to increase it over the coming period in order to allow the implementation of strategic aims of the CESP. These will involve the promotion of new research projects that are common to more than one team, support for new emerging teams, and funding for visiting researchers where the focus is on cross-cutting aims or research involving several teams of the CESP.
- Two new teams have joined the CESP, one to enhance our competence in biostatistics, and the other to allow the emergence of health economics, an essential component of public health research, at the CESP.
- Two teams have merged in order to develop a joint research programme on the care of paediatric patients with chronic disease during the transition to adulthood.
- The cross-cutting programmes are intended to allow collaboration between the teams and this aspect will be supported by mutualized funds and researchers from different teams.
- We have already a monthly seminar in place, where one of the nine teams takes the responsibility of presenting research areas and preliminary work in order to generate collaborations with members from other teams.
- We beg to differ with the committee's view on candidacy for the national research positions. After much consultation amongst ourselves, we would like to continue our policy of not interfering with the decision of teams to present their young researchers as candidates for permanent positions. In fact; this is also the approach adopted by other research centres in France. Our objective is not to promote competition between teams, but a deliberate decision

not to select or screen candidates prior to the national selection process, which in France is undertaken by a specialized commission. This appears to be a good policy given the scarcity of permanent positions and the long period of preparation before researchers can successfully apply for these positions.

The committee noted the difficult transition period at the CESP, involving changes from the previous mandate to a ‘candidate director’ and then an interim management committee. We would like to highlight the strong cohesion between the CESP teams over this period which has allowed us identify key elements in the future development of the CESP. Briefly, these involve:

- Continuing to highlight the importance of scientific excellence.
- The CESP will be a key player in the future school of public health in the framework of the "Campus Sciences et Santé"
- We will implement a new management style involving
  - more collegial leadership, with Deputy Directors working alongside the future Director.
  - facilitating collaboration between teams by providing incentives to joint publications, projects (in response to call for funding), and co-supervision of PhDs.

Team 1: Health Economics – Health Services research

We are grateful to the AERES committee for highlighting the strengths of the team, particularly the fact that our research area is original and underdeveloped in the French context, that the links of the team with general medical practitioners is valuable, and that the involvement in training through research is admirable for such a small team.
The weaknesses and recommendations identified by the committee are very useful to the team and reflect our concerns for the future.

The team is very small (three permanent researchers: two from Inserm, one from the university)/ Reinforce the coherence of the research project (strengthen the overarching vision).

The team is new and small, this is true. The ambitious research project we propose, focused on primary care, is composed of separate research projects which are closely related to each other, some on the side of health care offer and others on the demand side. We hope to increase the size of the team through recruitment of researchers to strengthen coherence between research themes. In order to do this we have applied to the call 'BQR Emploi 2014' (University Paris Sud) in order to be able to recruit a lecturer in health economics, specialized in econometrics, who is currently finishing his PhD with us.

Develop international collaborations and leadership through works on international comparisons

We agree that the development of international collaborations allows international comparisons as we have done occasionally, working with Nivel Netherlands in 2008-2009. However, we also believe this will be possible using the links with international partners that we are in the process of creating on the following projects: 1/ the impact of economic incentives in primary care, with K. Janus (Columbia/Ulm Universities, US/ Allemagne) and, 2/ on the analysis of patients' preferences and participative medicine, with M. Ryan, HERU (Aberdeen University, UK, Health Economics unit where N. Krucien (one of our ex-PhD students) is doing his post-doc), and A. Gafni (Mc Master, Canada). The research questions, still underdeveloped in France, involve several teams of economists at the international level.

Find mentorship in order to expand the national and international network and acquire international expertise and leadership

We believe that international collaborations mentioned above, and the presence of K Janus in the International Scientific Advisory Board of the CESP will help us.

Find linkages within the center

Collaborations will naturally be developed with other teams in the center. Some have already started, for example with team 4 via the joint response to the PHRC 2014 call on the coordination of care between primary care and hospital services in the elderly. Others are under consideration, notably with an economist in team 2 for a PhD co-supervision in 2015, on the issue of methods to reveal 'willingness to pay' in cost-benefit analysis in the treatment of cancer. Significant interaction already exists, for many years, with members of team 4 via involvement in the Master of Public Health and the Doctoral School.

… the specificity of the French system and tends to make the research contextual, limiting the generalizability of the results

Our work, resulting from the nature of our health care system, is indeed specific to the French context. However, interest in the organization and financing of primary care is a global issue with features that are specific to each country. The analysis of different models plays a crucial part in taking the knowledge forward in the field. We contribute to this effort, 78% of our articles are published in English language journals.

A statistician is lacking for complex analysis

We work with a statistician specialized in econometrics; he will retire in early 2015. We are confident that by joining the CESP we will benefit from the statistical skills within the center. We also hope, with the support of the CESP, for the recruitment of a new statistician as soon as possible.

Team 2: Methodology and Clinical Epidemiology for Molecular Oncology

We are grateful to the AERES committee for appreciating the 5-year strategy for our proposed new research team at the CESP, evaluating both our publication record as our reputation in methodology and molecular epidemiology as being excellent, and providing recommendations for improvement. We would like to comment on some of the highlighted weaknesses and recommendations:

Number of tenured researchers

We would like to stress that the team is not constituted just of 3 tenured researchers. In fact, there are 11 tenured researchers in all: 3 of them have University positions, 3 are hospital practitioners, and 5 have tenured Gustave Roussy researcher positions in biostatistics or health economics.

Advise PhD students in health economics

Our short-term strategy to have PhD students in health economics is through co-supervisions. There is already an ongoing PhD, on developing methods for performing economic evaluations using individual patient data meta-analyses. As far as the long-term is concerned, the 2 health economics researchers in the team plan to obtain their HDR in 2015 and 2016-2017 respectively, increasing our ability to supervise PhD students in health economics..

Increase methodology in biostatistics, health economy and through CESP collaborations

The main objective of our proposed research team is precisely to further develop the methodology component of the different research axes. For illustration, we have recently replied to three calls for projects for post-doc positions in biostatistical methodology and are currently in the process of hiring a postdoc in health economics (grant already obtained). Finally, we are proactive in setting up collaborations with other CESP teams such as an individual risk prediction model for breast cancer risk based on integrating clinicopathological and genomic information with team 9.

Team 3: Radiation Epidemiology, clinical cancer epidemiology and survivorship

We thank the committee for their report and in the section below we provide a response to various issues raised by the committee.

Few members have their HDR, therefore the number of PhD students is limited.

As suggested by the AERES committee, this is a major limitation of our team. However, a physicist and 3 researchers plan to obtain their HDR accreditation in the next 4 years, and we hope that this will improve the situation.

Concurrence from research teams or institutions having official monopolistic position.

We are well aware of this issue. Our approach is to intensify collaborations with IRSN (Institut de Radioprotection et de Sureté Nucléaire), specifically on the following studies : cohort of workers from nuclear contracting companies, childhood CT-Scan cohort, and case-controls study on thyroid cancer in the East of France and Polynesia.

Clarify the strategy planned to integrate the new 2 themes (descriptive epidemiology and social sciences).

Clarify more precisely the projects involving social and human sciences research

Only one researcher, Catherine Hill, is dedicated to “Descriptive epidemiology” theme. Her focus is on the long term trends in cancer prevalence in France, the consumption of tobacco and alcohol, taxation of tobacco and alcohol, as well as cancer screening. She has an international recognition in these areas, which are of major public health importance. Her integration in our team will be through joint projects on nuclear workers, on cancer in French Polynesia (we have a long experience of collaboration with her in these areas, and have joint publications) as well as evaluation of breast and thyroid cancer screening in childhood cancer survivors, who are at a very high risk of developing these cancers.

The integration of the social sciences researchers is already underway and is focused on survivorship. These researchers are in charge of the sociological aspect of survivorship in 2 cohorts of major importance to us: the FCCSS and CANTO. On FCCSS, weekly working meetings have been held for more than one year, and several manuscripts are in progress. Their integration into our team is of major interest because:
1) in order to produce pertinent information, the study of the social outcomes of childhood cancer needs knowledge of medical issues in this very heterogeneous populations,
2) the knowledge of social issues is of an utmost importance for the investigation of the medical long term consequences of childhood cancer treatments. Collaborative research on the CANTO cohort will cover all aspects of the interaction between radiation exposure, long term iatrogenic events, and socio-professional future of women treated for breast cancer.
We believe that the integration of social scientists in our team is a great opportunity.

Consider carefully how to concentrate the radiation/aetiological epidemiology effort, and use of their strong existing cohorts, on questions where the team can produce results of international importance.

We fully agree with this recommendation, and have already begun to focus our efforts on questions and cohorts able to produce results of international importance. Indeed, the existing Euro2K cohort (4 500 children), which has already led to a large number of publications, is being extended to the larger "FCCSS" cohort including more than 20,000 survivors of pediatric cancer. FCCSS is a national cohort of 5-year survivors of childhood cancers will be constituted over the next 3 years as a result of enormous effort of our team. It will allow us to be competitive in term of size (and statistical power) compared to similar cohorts in the world. A large biobank is being set up in parallel for the entire cohort. This will allow us to put in place international collaborations in molecular epidemiology. To date, we already have an international position through this cohort, we are the coordinators of large international case control studies on leukemia, cardiac disease and cerebrovascular diseases after childhood cancer.
Similarly, we are moving our efforts from “Survsein” (breast cancer survivors) to the prospective large scale CANTO cohort (20.000 breast cancer women) where we are in the process of developing a unique centralized dosimetric data base, which will allow us to investigate the association between radiation dose to the heart and the risk of subsequent cardiac disease and its genetic modifiers, with a precision that has not previously been done.

Finally, the recent collaboration with Team 6 on the Epi-thyr network, which includes 5 thyroid cancer case-controls studies, will produce results of international importance.

Team 4: Epidemiology and evaluation of prevention and therapeutic strategies: HIV, reproduction, pediatrics

We thank the AERES committee for their evaluation of our project as being innovative and addressing real public health issues, highlighting our role in the scientific coordination of important HIV cohorts and studies, our major involvement in education/training in epidemiology, and recognizing that the new team is an opportunity to develop common research themes at the crossroads of HIV, pregnancy, and paediatrics.
Here is our response to some points raised by the committee.

Number of FTE senior researchers relatively low; the committee found that the number of objectives is too large. Recommendation to improve attractiveness for post-docs and young scientists

There are 10 senior researchers in the team, comprising 2 Inserm/Ined Directeurs de Recherche, and 2 permanent professors/associate professors in Public Health. The other researchers are part-time, being clinicians in hospital departments. This can be seen as a weakness, but is also strength given the team's ambition, including that of the CESP, to increase our profile in clinical epidemiology. This relatively large number of clinicians is a specificity of the team within CESP, and an added value. However, it may have contributed to the feeling that we have too many objectives. We also plan to welcome more post-docs, and are currently thinking of reallocation of internal funding to help resolve this issue.

The large number of topics covered are not clearly linked, in part as a result of joining of the two teams with very different agendas, one on HIV and one on reproduction. It is unclear how this combination can add up to research strengths, and some thought has to be given to the coherence of the research agenda.

The new team is the result of the merger of 2 previous CESP teams. We chose to combine our strengths in order to develop new projects in anticipation of the likely changes of our research agenda over the next 5 years. This relates to the evolution of the HIV paediatric aspect of the team towards greater involvement in non-HIV paediatric diseases or conditions, such as transition to adulthood (see point 3 below), or long-term health of children born with particular conditions, i.e. after exposure *in utero* to antiretrovirals and HIV, or as a result of assisted reproductive technology. There will be also an increasing involvement of some researchers of the team in clinical epidemiology and clinical trials in HIV and in paediatrics. Besides sharing these research areas, we also share method development, with interest and skills in clinical epidemiology. There exist several collaborations, which give us confidence in the future of the team.

The fifth theme (transition to adulthood in young subjects with severe chronic diseases) is not really convincing apart from the part related to children with HIV; a more efficient approach would be to develop a collaborative project on that topic on already existing cohorts (cystic fibrosis)

The study of transition to adulthood in young subjects with severe chronic diseases is clearly one of the common projects of the team, evident our project on HIV, severe pediatric chronic diseases, and comparisons with general population. Developing a collaborative project based on the existing cohort of cystic fibrosis patients is an excellent idea, but does not preclude from research on other diseases such as sickle cell disease, diabetes, and haemophilia.

Team 5: Epidemiology and Translationnal Research in Renal and Cardiovascular Disease

The report highlighted the team's strengths, including the very original perspectives for their research on chronic kidney disease, the complementary skills of team members in the field of cardiovascular and renal diseases with the intention to recruit a professor in genetics, the unique character of major research tools already developed, the ability of the team to conduct large cohort studies and to obtain funding for them, the proximity of team members to decision makers (Biomedicine Agency) and the involvement in major international consortia.

The overall positive evaluation of the team's scientific production included some comments and inaccuracies for which clarification is needed. Over one third (34%) of the 450 publications of the team is signed by a team member as first or last author, that is about 150 in total, indicating a substantial contribution of the team as lead authors, given its size and composition. The low number of common publications is directly related to the fact that this is a new team under construction, centred around a unifying project (CKD-REIN); and forthcoming publications will be in common. Inaccuracies relate to team member's H-indices. Four team members, and not one, have an H-index greater than 40, including the deputy director (H-index: 47), and these levels are generally rated as high.

Among the weaknesses identified by the committee, we are aware that creating a team *de novo* is a challenge especially given that it is scattered across three locations. However, the scientific coherence of the project and participants' shared interests are powerful drivers to motivate and bring people together. The use of video conference resources which is currently operational on the 3 sites will facilitate regular contact and working meetings between researchers beyond the face-to-face seminars and monthly team meetings.

Finally, concerning the team's competency to conduct *in silico* simulation studies, it is important to stress that these methods have been used for over 10 years by one of the team members at the Biomedicine Agency, and they have led to changes in graft allocation (see Ref 1 and 2). These simulations lead to public health interventions that may potentially put patients' lives at risk if there were errors in the behaviour of models, before implementation of interventions. The Biomedecine Agency simulation platform is at the heart of a research project (Optimatch) funded by the 2013 National PHRC. This project will serve to support the work of a PhD student supervised by C. Jacquelinet who plans to further develop these techniques as part of the present research team project.

1 - Rules for allocation of livers for transplantation. Jacquelinet C, Audry B, Pessione F, Antoine C, Loty B, Calmus Y. Presse Med. 2008 Dec;37(12):1782-6.
2 - Changing kidney allocation policy in France: the value of simulation. Jacquelinet C, Audry B, Golbreich C, Antoine C, Rebibou JM, Claquin J, Loty B. AMIA Annu Symp Proc. 2006:374

Team 6: Environmental Epidemiology of Cancer

We wish to thank the AERES committee for its constructive and overall positive assessment of the research undertaken in our team, our expertise, and the objectives of our research project. Most of the recommendations made by the committee fit our own view of the research needs in the future, and reassure us in relation to the strategic choices we have made.

We would like to take this opportunity to comment of some misunderstandings in the report.

- Our link with Professor S. Richardson (MRC, Cambridge) goes beyond a simple international collaboration. The development and use of innovative statistical methods, coordinated by SR, is fully constitutive of our research project and justifies her membership in the team. With this mode of organization, we have attracted funding for post-docs researchers, initiated a common research program and produced several research papers, published or submitted. Moreover, the participation of SR in our team should be seen as an asset to the CESP as a whole, as it will foster the collaborations between teams. Finally, SR's publications were included as part of the scientific production of our team as is the case for publications of members of any team, irrespective of where they were previously.

- The report points out the limitations of the case-control approach as a weakness of our project, with a particular focus on the supposedly low participation rate of controls during the first phase of recruitment by telephone, and recommends more methodological work to assess the representativeness of the control group. We are fully aware of the limits of the methodology, but would like to reiterate our conviction that the case-control approach is appropriate for testing most of our main research hypotheses (e.g. occupational exposures). Our method of recruitment for controls is based on quotas taking into account the low participation rates associated with certain social groups, and it has been validated repeatedly. This method is original and demonstrates our attention to selection biases in the collection of high quality data. We hope to look further into the selection procedures of population controls in collaboration with colleagues at the CESP who have expertise in population sampling techniques.

Among the recommendations made by the Committee:

- We anticipated developments "in genetics and genomics, as well as beyond" by collecting blood samples or tumor material in previous and on-going studies, and in some instances adipose tissue (storage of pollutants). Using these biological samples, we are able to consider medium-term developments in the fields of metabolomics or epigenomics.

- Our participation in expert committees (Expertise Collective at Inserm, Expert working group at ANSES, etc.) is an important part of our work. We hope to continue these activities..

- We recognize the importance of in-house expertise in the assessment of occupational exposures. In the past we hired Industrial Hygienists, but restricted resources no longer allow this option. We now mainly focused on collaborations with external teams with expertise in occupational exposure assessment, these include P. Guénel's collaboration with the Department of Occupational Health InVS for the elaboration of job-exposure matrices; development by I. Stücker of an algorithm for the assessment of exposure to asbestos in the ICARE study based on the description of work tasks in the questionnaire; collaboration with N. Bajos (team 7) as part of a PhD to examine gender differences in occupational exposure assessment.

Team 7: Gender, sexual and reproductive health

We would like to thank the AERES committee for the overall positive evaluation of our work.

We are indeed very pleased that the committee recognised our scientific perspective to address the links between theoretical issues and empirical data, which are important in public health and tend to be insufficiently addressed. The committee also stressed the interdisciplinarity of our work and the interaction between quantitative and qualitative methods.

We also appreciated that the committee underlined our strong international network and recognition.

We agree that the high level of demand for the team's expertise and our strong

Commitment to dissemination activities could compete with our scientific activities. Nevertheless, we are confident that some of our young researchers will have academic positions in the next few years and will take on and share these activities with the senior researchers.

Team 8: Epidemiology oh aeging and age-related diseases

We are a new team and we would like to thank the AERES committee for the overall positive evaluation. The committee recognised our publications in “high impact medical journals”, “high scientific reputation and international visibility”, statistical expertise in the “analysis of longitudinal data”, our five-year plan as being “very well written, original and consistent”, and the “obvious synergy between the projects in terms of designs and methods”. We also appreciate the assessment that “the particular expertise in the ageing phenotype is very well made for this strong group of researchers, the group has the potential for outstanding work.”

We would also like to provide a response to the queries from the committee.

Follow-up of the PhDs trained in the group: We supervised 9 PhD students in the past 5 years: four of them are in post-doctoral positions, five have permanent positions: one as an academic in Switzerland, one as a neurologist in a University memory research department in Paris, two as epidemiologists at Institut de Veille Sanitaire, and one in the pharmaceutical industry.

Visibility of the team leader: There was some concern that one of the team leaders (ASM) has more of an international than a national presence. We are surprised by this comment, the French members of the committee would have known that ASM has a prominent role in the French public health sphere (deputy director of French Public Health Institute, AERES delegate, member of many evaluation committees, numerous invited presentation, expertise activities, etc.).

Lack of detail on statistical methods to be used in the future: Lack of space did not allow us to provide details of our analytic strategy, highlight the challenges of longitudinal data, or describe Mendelian Randomization. Evidence of our competence lies in already published papers in all these domains as the committee also noted our future plans contain “highly specified projects and although briefly described do look interesting, valuable and do-able”.

Administrative burden of senior scientists: This is an important issue but we have been highly productive in the past few years and do not see why this should change in the future.

Interactions with other teams: We completely agree with the committee’s recommendation to increase our interactions with other teams in the centre. We are a new team and one of the reasons we want to be in the centre is to be able to collaborate with other teams both on substantive and methodological areas.

International attractiveness for post-docs: We, like everyone else in France, have trouble recruiting post-doctoral students from abroad due to the low and fairly tightly regulated pay structures. We are keen to find solutions and one of them, which we have used successfully with colleagues at University College London, is to employ post-docs in their country of origin using collaborative grants.

Team 9: Lifestyle, genetics and health: integrative trans-generational

We are thankful to the AERES Committee for their fruitful and positive comments regarding our team and interactions with CESP teams. The Committee has emphasized the fact that our group had great promise in terms of future production thanks to the resources we are developing and the techniques that are at our disposal.

We are also thankful to the Committee for emphasizing in the general part of their report the fact that we are in the process of getting an ISO certification, and for suggesting expanding this positive experience to all CESP teams. This was made possible through the Investment for the Future grant that we obtained for setting up our new cohort, which enabled us to recruit a stable project team (« CDI de mission ») for the 2011-2019 period.

Here are a few specific points that we wish to comment upon. Regarding our team's scientific production, we consider that the sentence « nothing approaching a major step forward in these areas » does not truly reflect reality. Our team is recognized as a leader in some specific fields such as menopausal hormone therapy in relation to cancer but also other major chronic conditions (e.g. diabetes, cardiovascular disease, digestive diseases etc…). We also have recognized expertise in nutritional epidemiology; even though this field rarely enables to produce papers in very high impact factor journals, papers are widely cited and represent important advances in the field. As an example, our recent work regarding vitamin D and breast cancer risk ranks among the top 1% of the most frequently cited papers in the relevant category according to Web of Science classification, and altogether we produced, with a leading position, 4 papers in the top 1% within the past 5 years. Other fields have indeed been more recently developed by our team but they already enabled us to produce high rank papers in the fields of inflammatory bowel diseases, diabetes or melanoma.

The development of these research areas must be put in perspective of the Committee's recommendations that CESP develops " a wide range of disciplines and competency not present or still too modest within CESP" with the objective of creating a School of Public Health within Paris-Saclay University. The wide range of competency and projects developed within our team, which have been rightly underlined by the Committee, is thus in true line of the Committee's recommendations. We are well aware, through our own experience with E3N, that setting up a new cohort in order to be able to achieve our research goals will hog part of our research forces; however, we are making sure that there is a good balance between scientific production using existing data, and logistical aspects that are requested when setting up this new study with a trans-generational approach.

The Committee rightly emphasized that "the true integration of epidemiology and biological processes is becoming viewed as increasingly important and the group is actively involved in the process of integrating genetics and biomarkers" ; however, the Committee considers that we" have not yet fully capitalized on these techniques" . We feel sorry that we did not succeed in conveying clearly enough how much we already invested in such bio-epidemiological approaches, using our biobank (we have originated specific platforms, such as a lipidomic platform to further understand breast cancer development) as soon as the number of relevant events is large enough for specific E3N studies, alternatively participating in EPIC bio-epidemiological studies. Indeed we obtained and devoted important financial resources to set up our biobank and we already used them in many studies using lipidomics, metabolomics or genetics. Being aware of the importance of genetic and epigenetic studies, we recently collected saliva in 47,000 women to complete our biobank for genetic projects, and recruited two senior researchers in genetic and epigenetic epidemiology, for setting up new studies in this area.

The Committee rightly emphasized how important it was for our team to recruit personnel on permanent positions, in order to ensure continuity of our research, and especially recruitment of "young seniors" and of junior researchers; we set up the optimal conditions for such recruitments (including Marie Curie fellowships, or high rank positions for foreign researchers) and we hope that these recruitments will soon become effective. The Committee's recommendation that we should develop our own research but also collaborations is in full agreement with what we are setting up, both within CESP and at an international level.

We fully agree with the Committee regarding the need for increasing the number of PhD students, they are six at present, through increasing the number of researchers with an HDR (i.e. who can supervise PhDs). Five members of the team will candidate for an HDR within the next twelve months, which will enable us to more than double the number of PhD students, since only three of us have an HDR at the moment.