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## iPLESP - Institut Pierre Louis d'épidémiologie et de santé publique

Rapport Hcéres

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

Department for the evaluation of  
research units

AERES report on unit:

Pierre Louis Institute of Epidemiology and Public Health

Under the supervision of  
the following institutions  
and research bodies:

Université Paris 6 - Pierre et Marie Curie

Institut national de la santé et de la recherche  
médicale



January 2013



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

Research Units Department

President of AERES

**Didier Houssin**

Research Units Department

*Department Head*

**Pierre Glaudes**



## Grading

Once the visits for the 2012-2013 evaluation campaign had been completed, the chairpersons of the expert committees, who met per disciplinary group, proceeded to attribute a score to the research units in their group (and, when necessary, for these units' in-house teams).

This score (A+, A, B, C) concerned each of the six criteria defined by the AERES.

NN (not-scored) attached to a criteria indicate that this one was not applicable to the particular case of this research unit or this team.

**Criterion 1 - C1:** Scientific outputs and quality;

**Criterion 2 - C2:** Academic reputation and appeal;

**Criterion 3 - C3:** Interactions with the social, economic and cultural environment;

**Criterion 4 - C4:** Organisation and life of the institution (or of the team);

**Criterion 5 - C5:** Involvement in training through research;

**Criterion 6 - C6:** Strategy and five-year plan.

With respect to this score, the research unit concerned by this report and its in-house teams the following grades:

- Grading table of the unit: **Pierre Louis Institute of epidemiology and public health**

C1	C2	C3	C4	C5	C6
A+	A+	A+	A	A+	A

- Grading table of the team: **Surveillance and Modelling of communicable diseases**

C1	C2	C3	C4	C5	C6
A+	A+	A+	A+	A	A+

- Grading table of the team: **Epidemiology of influenza and viral hepatitis: risk, Prognosis and therapeutic options (EPINHEP)**

C1	C2	C3	C4	C5	C6
A+	A+	A+	A+	A+	A+

- Grading table of the team: **Clinical epidemiology of HIV infection: Therapeutic strategies and co-morbidities**

C1	C2	C3	C4	C5	C6
A+	A+	A+	A	A+	A+

- Grading table of the team: **Resistance to antiretroviral drugs**

C1	C2	C3	C4	C5	C6
A	A	A+	A	A	A



- Grading table of the team: **Epidemiology of allergic and respiratory diseases**

C1	C2	C3	C4	C5	C6
A	A	A+	A+	A	B

- Grading table of the team: **Epidemiology and Evaluation of Musculo-skeletal and Systemic Diseases**

C1	C2	C3	C4	C5	C6
A	A	A	A	B	B

- Grading table of the team: **Hospital epidemiology, quality and organization of healthcare**

C1	C2	C3	C4	C5	C6
A	A	A	A	A	A

- Grading table of the team: **Socio-territorial determinants and inequalities in health**

C1	C2	C3	C4	C5	C6
A+	A+	A+	A	A+	A+



## Evaluation report

Unit name:	Pierre Louis Institute of epidemiology and public health
Unit acronym:	
Label requested:	UMR-S
Present no.:	UMRS-707, UMRS-943, team 11 of UMR S 1018 (Epidemiology of occupational and social determinants of health) of the Centre for Epidemiology and Population Health, UPMC Clinical Research group 08
Name of Director (2012-2013):	Mr Guy THOMAS, Ms Dominique COSTAGLIOLA, Mr Bruno FAUTREL
Name of Project Leader (2014-2018):	Ms Dominique COSTAGLIOLA

## Expert committee members

Chair:	Ms Claire JULIAN-REYNIER, Aix-Marseille Université, France
Experts:	Mr Peter BURNEY, Imperial College of London, UK
	Mr Jean-Claude DESENCLOS, Institut de Veille Sanitaire, France
	Ms Stéphanie GENTILE, Université Aix-Marseille, representing CNU
	Ms Maria GLYMOUR, Harvard School of Public Health, USA
	Mr Jean-François GUEGAN, Institut de Recherche pour le Développement, representing Inserm
	Mr Christian JORGENSEN, Université de Montpellier 1
	Ms Terese KATZENSTEIN, University Hospital Rigshospitalet, Copenhagen, Denmark
	Mr Pascal ROY, Université Lyon 1
	Mr Jean-Claude SCHMIT, Centre de Recherche Public de la Santé, Luxembourg
	Ms Colette SMITH, University College of London, UK

### Scientific delegate representing the AERES:

Ms Valériane LEROY



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

Mr Francis BERENBAUM, Université Paris 6

Ms Christine GUILLARD, Inserm



## 1 • Introduction

### History and geographical location of the unit:

The Pierre Louis Institute of epidemiology is a research centre that will be formed by the merging of two INSERM/UPMC units (UMR S 707, and UMR S 943); of part of Team 11 (Epidemiology of occupational and social determinants of health) from the Centre for Epidemiology and Population Health (UMR S 1018 based in Villejuif, Paris South University) and a UPMC Clinical Research Group 08 in rheumatology.

The Institute will be mainly located at the Pitié-Salpêtrière Hospital (welcoming the team from Villejuif) and partially at Saint Antoine Hospital.

### Management team:

Ms D. COSTAGLIOLA will be the director of the Institute and Mr G. THOMAS the deputy director.

### AERES nomenclature:

SVE1\_LS4 Physiology, physiopathology, medical systems biology

SVE1\_LS6 Immunology, microbiology, virology, parasitology

SVE1\_LS7 Epidemiology, public health, clinical research, biomedical technologies

SHS1\_1 Economics

SHS2\_4 Sociology, Demography

### Unit workforce:

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
<b>N1:</b> Permanent professors and similar positions	22	31	29
<b>N2:</b> Permanent researchers from Institutions and similar positions	9	13	13
<b>N3:</b> Other permanent staff (without research duties)	25	31	19
<b>N4:</b> Other professors (Emeritus Professor, on-contract Professor, etc.)	19	26	18
<b>N5:</b> Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	7	9	6
<b>N6:</b> Other contractual staff (without research duties)	80	82	16
<b>TOTAL N1 to N6</b>	162	192	101

Percentage of producers	<i>(2014-18 project producers (N1+N2)/ number as at 01/01/2014</i> <b>95%</b>
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<b>Unit workforce</b>	<b>Number as at 30/06/2012</b>	<b>Number as at 01/01/2014</b>
Doctoral students	37	
Theses defended	30	
Postdoctoral students having spent at least 12 months in the unit*	6	
Number of Research Supervisor Qualifications (HDR) taken	9	
Qualified research supervisors (with an HDR) or similar positions	26	32



## 2 • Assessment of the unit

All the members of the committee agreed with the following points:

### Strengths and opportunities:

- The overall scientific aims of the research centre are outstanding:
  - o The coherence of the four more consolidated teams around communicable diseases and of the social epidemiology research team is clearly a major strength of the overall project.
  - o The multi-disciplinary and complementary nature of the research groups involved (biostatistics/biomathematics, clinical epidemiology, social epidemiology, virology, clinical expertise, public health, evidence-based medicine) is original and relevant.
  - o The wish of the head of the centre and of senior researchers from the most consolidated teams to help the development of the new emerging Institute teams from other clinical fields, for which the attached hospital departments are well-known, is fair and clearly a strength of the overall centre.
- The reputation of the proposed leader of the centre is exceptional, and her ability to organise the overall scientific and administrative management of the structure is a guarantee of the success of the new institute.
- The planned organisation and grouping of these 8 research teams as a future centre was considered to be excellent. The creation of this centre by the grouping of previously and well-known INSERM teams will increase the international visibility of epidemiology in France.
- The capacity of the research teams to raise external funds is impressive.
- The increase in the number of PhD students and post-doctoral fellows because of the Institute will allow the organisation of more relevant initiatives in their direction. The dynamics of the overall group will clearly be improved.
- The overall atmosphere of the centre appears to be very good. Furthermore, the meeting with doctoral/postdoctoral students convinced the subgroup of the committee who audited them that the dynamics of the overall research centre were excellent.

### Weaknesses and threats:

- Presently there are 3 different locations for the 8 teams (Hôpital Saint-Antoine, Pitié-Salpêtrière and Villejuif). The acquisition of 700m<sup>2</sup> on the Pitié-Salpêtrière site will allow the Villejuif group and some of the Saint-Antoine groups to co-locate but not all. Having a common location for the centre is essential to optimise scientific exchanges between people and the overall dynamics of the project.
- The head of the institute should take care not to be overwhelmed by too many time consuming activities and responsibilities and will have to make sensible choices.
- The size heterogeneity of the research teams could be an issue for the internal team dynamics, recruitment and resource allocation.

### Recommendations:

The administrative workload of the management of 192 people (not including the 37 PhD students) has clearly to be considered with caution and should not be under-estimated. The need for collective management by the researchers and through permanent or contractual positions for high level administrative staff is highlighted, in particular for the management of people and for the contracts.

Such a research centre will need to have a specific plan for internal communication of information on professional development for both technical staff and for the doctoral and post/doctoral fellows.



Inter-group exchanges are planned via internal seminars (PhD student seminars, Methods seminars). The committee highlights the need to nominate specific persons to be responsible for not only the seminars but also for facilitating knowledge transfer across the teams (on statistical methods in particular, and potentially also for other areas). This will help to structure cross-team dialogue and aid the future development of the research teams, in particular for those which are smaller in size or which appear to be more fragile (for whatever reason).

To ensure the continuation of the scientific excellence demonstrated by this institute, maturation of high level leadership profiles has to be kept in mind.

The attractiveness of the centre should be an incentive for increased leadership in international projects.



### 3 • Detailed assessments

#### Assessment of scientific quality and outputs:

Major breakthroughs in the field of epidemiology have been achieved, in all sub-disciplines of clinical, population and social epidemiology, as well as in pharmaco-epidemiology, biostatistics and statistical and mathematical modelling. There has been outstanding scientific production from the fusion of two INSERM/UPMC units, a team from UMR S1018 and a new clinical research group from UPMC. In terms of publications, the team has been outstanding both quantitatively (more than 600 papers during the last five years with leaders from the group and more than 1000 for all articles) and qualitatively, reaching the highest international standards (high impact factor journals such as Nature, NEJM, JAMA, Lancet, Lancet Oncology, Lancet Infectious diseases, Ann Intern Med, PNAS, BMJ, ...). Seven researchers belong to the Top 1% of scientists (ISI, Web of Knowledge). The institute is a world leader in the field of communicable diseases in particular influenza, HIV infection and viral hepatitis. Discoveries and tools (e.g. national cohorts, such as the ANRSO4 which contains information on more than 120000 HIV-infected persons managed in 69 hospitals) that have been developed in the institute are and may become the leading references, facilitated in particular by the collaboration with the clinical domain. The Centre includes a data management and statistical analysis centre for both ANRS clinical studies and the "Sentinelles network".

#### Assessment of the unit's academic reputation and appeal:

Researchers from all teams have been invited to communicate at leading international events (example: team 3: International AIDS Society [IAS] 2010, Interscience Conference on Antimicrobial Agents and Chemotherapy [ICAAC] 2011, the European Aids Conference 2011 and the Conference on Retroviruses and Opportunistic Infections [CROI] 2012). Prestigious International and National Awards such as ERC grants, Prix de l'Académie des Sciences (Louis Daniel Beauperthuy (Team 1), Prix Le Goff (team 2) have been awarded to the group. High-level foreign researchers have been recruited by the institute (Team 1, CR1 Inserm 2011). The centre includes many projects funded by the European Union (in particular through 4 networks of excellence; EUROCOORD (Team 3), NEAT (Team 3), CHAIN (Team 4), GA2LEN (Team 5), and through 8 other projects for teams 3, 4 and 5, for which the leaders are members of the scientific committees or leaders of work-packages). The institute is an internationally recognized leader in projects, networks and infrastructures in its field (Teams 1, 2, 3, 5 and 8). Team members are on editorial committees of national and international journals (Teams 1, 2, 3, 4, 5 and 8).

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

The majority of senior researchers have both internationally and nationally recognized expertise. They are members of the scientific committee of GDF Suez (Team 2), the WHO network for HIV guidelines (Team 2), the "Recommandations nationales sur la prise en charge des patients infectés par le VIH" (Team 3, Team 4, Team 8), the WHO Global Alliance on Respiratory Diseases initiative (Team 5). They also participate in media interviews (Le Monde, La Recherche, Le Figaro), radio talks (Europe 1, France Inter, France culture, Team 2; France Culture, team 5) and TV scientific shows (team 7, team 5) and journaux télévisés (team 5). They also have many contracts with the pharmaceutical companies (Teams 1, 4, 5); clinical practice guidelines (EULAR team 6, team 7, ARIA team 5), HCSP and ANSES expertise in the frame of permanent working groups (team 5), HAS expertise (team 7) and NGO exhibitions (team 8).

#### Assessment of the unit's organisation and life:

The centre's organisation appears to have been adequately planned. The current excellent governance of the two major funders of the centre is the base for the new structure. A scientific internal management board and an international advisory committee will be created. The current internal communication is very good. The entity has proven able to optimally manage conflicts, and situations of crisis or transition. Because of the high number of non-permanent positions, in particular for technological platforms, the link between administration and the centre has to be adapted with the creation of the new institute, particularly with the merging of the different sites.



### Assessment of the unit's involvement in training through research:

All students encountered during the visit appeared to be well integrated into the scientific activities of their team (through their authorship and co-authorship of articles, their attendance at international conferences, and their participation in internal seminars organized on a periodical basis (from weekly to monthly depending on the size of the teams). The future centre will organise regular specific seminars for students from all teams and external seminars with invited scientists. Students declared they were happy with their guidance throughout their professional experience. The centre is offering high-level, internationally renowned, diverse courses and research seminars at doctoral level. The teams are involved in two doctoral schools (ED515 for virologists and ED393 for public health PhD, and the head of the centre is responsible for one of the doctoral schools (Pierre Louis doctoral school, ED393).

### Assessment of the five-year plan and strategy:

The overall project planned for the centre was considered as excellent by the panel. The program is ambitious and innovative. The program shows high feasibility in terms of impressive resources collected from external grants (adequacy of goals and means). The entity displays a very good knowledge of their environment, and a real ability for innovation through its open-minded attitude towards small emerging clinical teams in particular. There exists a clearly built strategy enabling a major breakthrough in the field of clinical, population and social epidemiology. The project is likely to maintain (or obtain) a leading international standing, both for its scientific construction and scope of expected results.



## 4 • Team-by-team analysis

**Team 1 :** Surveillance and Modelling of communicable diseases

Name of team leader: Mr Pierre-Yves BOELLE

### Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
<b>N1:</b> Permanent professors and similar positions	3	4	4
<b>N2:</b> Permanent EPST or EPIC researchers and similar positions	1	1	1
<b>N3:</b> Other permanent staff (without research duties)	2	2	2
<b>N4:</b> Other professors (PREM, ECC, etc.)	0	0	0
<b>N5:</b> Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	0	1	0
<b>N6:</b> Other contractual staff (without research duties)	10	9	0
<b>TOTAL N1 to N6</b>	16	17	7

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	6	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit	0	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	3	4



## • Detailed assessments

### Assessment of scientific quality and outputs:

Team 1 has produced an outstanding scientific production with overall 145 papers from which 84 are led by a researcher of the group (first or last author) and 61 are resulting from collaboration with national and international teams. Some leading papers were published in Nature (2008, impact factor [IF]=36.28) and Proceedings of the National Academy of Sciences (2009, 2010 IF=9.8), notably. During the last 5-year period (2007-2012) team 1 has produced important findings (i) in demonstrating the role of health professionals as important host carriers contributing to the spread of nosocomial infections, (ii) in showing the role of school closure to altering the course of childhood disease spread, and (iii) in pinpointing the importance of not-yet detected HIV cases in AIDS persistence and spreading.

Theoreticians and modellers from Team 1 are developing sophisticated up-to-date statistical/mathematical tools to unravel infectious disease transmission and spread, and to propose through scenario implementation the most appropriate or optimal solutions for decision-making in public health (eg. vaccination strategies, school closure, international airport closure).

Team 1 is becoming more influential internationally. It is now recognized as one of the leading groups in its field in France and Europe.

### Assessment of the unit's academic reputation and appeal:

The team members are regularly invited to speak at international conferences and meetings. They are currently participating in international networks and/or research programmes. The Surveillance and Modelling of Communicable Diseases team has demonstrated its attractiveness by being joined by two new senior researchers. Team researchers have received an award from the French Academy of Science and a highly competitive European Research Council (ERC) starting grant.

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

The research activity in modelling communicable diseases has significant social and economic impacts through allowing evidence-based decision making in public health at both the national and international level. It especially contributes to increasing the knowledge on spatial disease spreading and on the mechanisms of emergence/re-emergence of infectious diseases (e.g., the role of people not yet identified as HIV-infected in spreading the infection, the impact of super-spreading events in nosocomial infections). It also investigates the ways of assessing the effectiveness of disease control strategies such as vaccination (flu, measles), non-pharmaceutical measures (hand hygiene, school closure). In addition, this research activity has been extended to the analysis of livestock disease spreading through animal contact.

### Assessment of the unit's organisation and life:

The team has high-level standards of governance. It ensures also the management of the Sentinel Network and of three methodological axes: 1) Statistical Modelling of Communicable Diseases; 2) Large-Scale Mobility Models; and, 3) Statistical modelling of HIV infection.

The team has a constant involvement in subgroup animation and student supervision.

### Assessment of the unit's involvement in training through research:

The team is currently involved in training four master and seven doctoral students. It has also engaged one post-doc fellow.

The team organises the regular SaMMBA seminars (the monthly seminar at Pasteur Institute) and the seminars in Modelling in Biomedicine. It is also offering a two-week course in statistical modelling and another course in advanced statistical analysis in epidemiology (University Pierre et Marie Curie - Paris 6).



### Assessment of the five-year plan and strategy:

The team constitutes a promising research group on multi-scale models applied to disease transmission and has a leading role in developing this type of research for various infectious diseases.

#### Conclusion:

- Strengths and opportunities:

Major strengths of the team are a high level of expertise in statistical and mathematical modelling development, and a high level of interaction between its team members.

Participation into multidisciplinary collaborative networks at local, national, and international levels.

Important collaboration with members from notably Team 2, and high potentiality for collaboration with other teams notably 3 to 6.

Strong linkages between top-leading research and training through courses and lectures in the field.

High opportunity for generating new breakthrough and concepts in mathematical modelling of communicable diseases.

- Weaknesses and threats:

Need for recruitment of junior researchers.

The potential threat is that team 1 members may be used by other teams as computer scientists or data analysts when two-ways collaborations should benefit both.

- Recommendations:

The team 1 should work on increasing the dissemination of the methods developed for better exchanges with the international scientific community and for wider practical implementation.

Team 1 should also consider to integrate genomic information in the modeling of spread of infectious diseases in collaboration with Team 4 and to develop new interactions with Team 2 on HCV and HBV modelling.

Team 1 should benefit from the creation of the new Institute in developing internally interactions with other teams, in nationally interacting with the rare other research groups in the field, and in improving attractiveness for post-docs, young scientists, and top-leading visiting modellers.



## Team 2 :

Epidemiology of influenza and viral hepatitis: risk, Prognosis and therapeutic options (EPINHEP)

Name of team leader: Mr Fabrice CARRAT

## Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
<b>N1:</b> Permanent professors and similar positions	3	4	4
<b>N2:</b> Permanent EPST or EPIC researchers and similar positions	0	0	0
<b>N3:</b> Other permanent staff (without research duties)	2	5	1
<b>N4:</b> Other professors (PREM, ECC, etc.)	0	1	0
<b>N5:</b> Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	1
<b>N6:</b> Other contractual staff (without research duties)	36	29	0
<b>TOTAL N1 to N6</b>	42	40	6

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	4	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	3	3



## • Detailed assessments

### Assessment of scientific quality and outputs:

Team 2 has produced 191 papers (72 signed as first or last authors, with 4 papers in top 1% ISI Web of Knowledge). Leading papers were published in Lancet (1, IF=38.27), JAMA (1, IF=30.03), AIDS (23, IF=6.24), Antiviral Therapy (13, IF=3.16), J AIDS (7, IF=4.42), J Antimicrob Chemother (8, IF=5.06), J Hepatol (12, IF=9.26), J Viral Hepatitis (9, IF=4.08), and Gut (4, IF=10.11).

During the last 5-years period (2007-2012), Team 2 has produced breakthrough in several field areas such as the natural course of influenza infection, the effectiveness of hepatitis B vaccine in HIV infected persons. Several important papers have contributed to the improved knowledge on influenza epidemiology and prevention and hepatitis B-HIV co-infection.

Statisticians and modellers from Team 2 used or developed innovative tools and methods in their research area, including cross-checked population kinetics/population dynamics models, randomized and cluster randomized trials, individual centered modelling, integrative approaches in analysing complex data from cohorts with multiple data collection ("omics" approaches), statistical methods for analysing non binary gold standards.

### Assessment of the unit's academic reputation and appeal:

In the last 5 years, three team 2 senior members were invited to give numerous lectures in international conferences (2, 16 and 20, respectively) and many more in national meetings.

One senior researcher received a national award from the French Academy of Sciences, and another one is a leading member or chair of international task forces or foundations on HIV and hepatitis B and C/HIV co-infection research.

One senior researcher is a section editor (field: viral infection) for BMC infectious diseases (impact factor=3.1), and another one is associate editor for the scientific journal Clinic and Research in Hepatology and Gastroenterology.

The team is developing original trans-disciplinary approaches including (clinical, virological, genetic, immunological epidemiological, statistical, behavioural and social methods) in their main research themes (Influenza and Hepatitis B and C), with appropriate skills for integrative studies in epidemiology and public health.

The teams received several national grants from ANRS, ANR (including an ANR-EQUIPEX, investissement d'avenir). It led a work package in two EU consortiums on the epidemiology of SARS and influenza (FP6 INFTRANS and FP7 Flumodcont).

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

Team 2' senior researchers contributed intensively to expertise and decision-making through the French Public Health Council (Haut Conseil de la Santé publique) on influenza and pandemic influenza preparation, control and mitigation strategies, and influenza vaccine strategies.

For hepatitis B, C and HIV/HCV co-infection the team contributes to clinical expertise through the ANRS.

Members of the team participated in public debates and conferences on influenza at the national level.

The team is building, through the implementation of the Hepather cohort, a well-defined and structured collaboration and partnership with leading international drug companies that are developing new Hepatitis B and C antiviral drugs.

The data centre team of the unit has acquired an expertise in e-CRF development and comply to the FDA CFR21 part 11 (revised April 2011) with regards to procedures and controls designed to ensure the authenticity, integrity and the confidentiality of electronic records (encryption and Hashing of identity).



### Assessment of the unit's organization and life:

The team is well-structured with a clear functional chart that identifies the main research activities (with those in charge), the data centre and database management function (with the detailed functions: administrative, project management, quality control monitoring, data management and biostatistics) and the list of those involved in each of these activities. The role and activities of each staff member is clearly explained and well-balanced.

The animation of the team includes weekly scientific meetings and specific meetings regularly organized with PhD and Master Students. Relationships between scientific and technical staff members are faithful and professional, as expressed during the meeting with technicians and engineers.

Operational issues are discussed in a specific meeting three times a year.

The management of database including security and quality issues and the interactions between database project managers and researchers is described in details in the organization of the team.

### Assessment of the unit's involvement in training through research:

The team belongs to the school of Public Health Pierre Louis (Ecole Doctorale ED393) of UPMC.

The team is strongly involved in the supervision of PhD and Master 2 students (in epidemiology): between 2007 and 2012: 5 students completed a PhD and 12 a Master 2 in epidemiology (3 permanent researchers with HDR).

The follow up of the PhD trained in the team is extremely good: of the five PhD, one has been appointed a post-doctoral position in the team, three have been appointed a post-doctoral position in another research group and one is expected to be recruited as a professor of infectious diseases.

The follow up of PhD and Master 2 students is active (weekly meetings) and efficient.

The team is involved in many teaching activities at UPMC University (medical school, biostatistics, master of public health and epidemiology, infectious diseases, HIV and hepatitis management...).

Two senior members of the team are involved in numerous postgraduate courses in France, Eastern Europe and Africa.

One senior member of the team is an associated professor at the School of Public Health University, Minneapolis.

### Assessment of the five-year plan and strategy:

The project is innovative, excellent, coherent and ambitious in each of the four area of research planned by the team for the next five years: influenza, hepatitis B and C chronic infection, Hepatitis B screening strategies and HBV/HIV co-infection. The research five year-plan is based on either already existing cohorts with biological collection (Copanflu a population cohort for influenza infection; cohort of HBV/HIV infected patients in Cote d'Ivoire [VarBva project]) or that are underway (Hepather cohort).

The team has an extremely good knowledge of its thematics and of the research environment in each of the themes of their research in France and internationally, including Africa for HBV and HIV co-infection.

The strategy is clear, well designed and very coherent with the research objectives. It is based on a sustained expertise on epidemiology and biostatistics with strong collaboration with experts in virology, immunology, hepatology, epidemiology and social sciences at national and international levels.

Methods used are up-to-date: cohort studies with integrative (EVAS) approaches randomized interventional trials, innovative biostatistics.

The Copanflu cohort, which is unique world-wide, offers many strong research opportunities including epidemiological, virological, immune and social outcomes.

The Hepather cohort (largest prospective cohort on Hepatitis B and C chronic infection), will confer a leading international position to the team, with major expected results on the efficacy/effectiveness, tolerance, pharmacokinetics, pharmaco-epidemiology and compliance of new antiviral drugs under development.



The project on the effectiveness and efficiency of hepatitis B screening strategies (Optiscreen) is original with respect to the current international scientific literature. The method used including an intervention trial is innovative. It will provide new evidenced based strategies to improve the screening of hepatitis B chronic infection and earlier treatment.

The five year plan is feasible. Although the management of the ambitious hepather cohort has some risk-taking, the credibility of the scientific and institutional strategy, the wide experience of the team in managing cohort studies (study design, data monitoring, data base, information system...) and controlled trials, the amount of funding already obtained (Equipex funding from Investissement d'avenir, ANRS and funding mechanisms organized with the industry) should overcome this risk.

There is a great synergy between the projects of the team in terms of designs and methods (cohort study, clinical approaches, including treatment, epidemiological outcomes, innovative statistical approaches...) and public health/clinical outcomes.

The SWOT analysis made by the team was realistic and did not ignore any critical issue.

### Conclusion:

- Strengths and opportunities:

Scientific coordination of several major and large cohort studies,

Strong methodological and operational capacity in implementing large cohort studies, clinical studies and randomized control trials including cluster intervention trials,

Sustained funding of large cohorts,

Statistical expertise and development capacity to analyse the complex data that are collected,

Multidisciplinary collaborative network set up linked to the implementation of the different cohorts,

Future new scientific activities will arise and benefit from shared platforms within the Pierre Louis Centre and collaboration with Team 3 and Team 4 of the Centre, including questions regarding resistance to antivirals or methodological issues in the data analysis of large databases with clinical outcomes (causal models, comparative effectiveness...).

The Hepather cohort will allow for assessing many emerging clinical and public health research questions on chronic HBV and HCV infections.

For influenza the team foresees the development of intervention trials based on their current analytical research results.

There is a trusting atmosphere within the team, notably between scientists and the large team of technical staff members.

- Weaknesses and threats:

Modest number of senior researchers,

Some lack of attractiveness for external post-doc or young scientists,

Scarcity of operational staff with permanent position making that high turn-over could impact on research efficacy and sustainability.

The burden of logistic and operational activities and complex management of the Hepather cohort could undermine scientific activities, in particular the generation of new scientific concepts and idea.

Risk of conflict of interests and problems for intellectual property linked to the involvement of drug companies, which are developing new antiviral drugs, in the funding of the Hepather cohort.

- Recommendations:

For influenza, consider to move from explanatory research to interventional research.



Use the opportunity of the creation of the Pierre Louis Research Institute to:

- Develop new interactions with Team 3 and 4 (HCV and HBV treatments, resistance to antivirals, causal models, comparative effectiveness...)
- improve international attractiveness for post-docs and young scientists
- mutualize technical expertise on data collection and database management with the Team 3

Although the management of the partnership with the private sector has been carefully designed and secured (contractual issues regarding intellectual property, strict rules and procedures for mocked up studies) the team and their institutional public stakeholders (ANRS, INSERM transfert...) shall pay a particular attention to prevent potential conflicts (including conflict of interest) that may arise with the development and marketing of new competitive antiviral drugs for hepatitis B and C treatment.



### Team 3 :

Clinical epidemiology of HIV infection: Therapeutic strategies and co-morbidities

Name of team leader: Ms Dominique COSTAGLIOLA and Ms Christine KATLAMA

### Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
<b>N1:</b> Permanent professors and similar positions	2	3	3
<b>N2:</b> Permanent EPST or EPIC researchers and similar positions	2	2	2
<b>N3:</b> Other permanent staff (without research duties)	14.5	16	9
<b>N4:</b> Other professors (PREM, ECC, etc.)	5	4	4
<b>N5:</b> Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	2	2
<b>N6:</b> Other contractual staff (without research duties)	22	22	9
<b>TOTAL N1 to N6</b>	48.5	49	29

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	4	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	4	4



- Detailed assessments

#### Assessment of scientific quality and outputs:

The publication list for the team is impressive. Over the past five years they have published 191 articles where the team has led the research projects and a further 127 to which they have participated. Their group has published in high impact factor journals like Lancet (IF=38.27), PNAS USA (IF=9.68), Arch Intern Med (IF=10.63), Ann Intern Med (IF=16.73) and numerous publications in the major journals within the field of HIV and infectious diseases like AIDS (IF=6.24), J AIDS (IF=4.42) and Lancet Inf Dis (IF=17.39). Thirteen papers are in top 1% of publications. The group has conducted studies exploring new ART combinations, with both positive and negative findings helping defining ART strategies.

#### Assessment of the unit's academic reputation and appeal:

The team leaders have both been invited to give lectures at the major HIV conferences (Conference on Retroviruses and Opportunistic Infections [CROI], International AIDS Conference [IAS], European AIDS Clinical Society [EACS] and Interscience Conference on Antimicrobial Agents and Chemotherapy [ICAAC]). One team leader is a member of the governing board of EACS and participates in writing of guidelines. The other is member of the executive committee of the ART Cohort Collaboration, cohort COHERE and EUROCOORD, member of the Steering Committee of the International Workshop on HIV Observational Databases (IWHOD).

Both are involved as PIs of a number of French multicentre Clinical Randomised Trials.

One team leader is a member of the working group "Towards an HIV Cure" initiative launched by the International AIDS Society (co-organiser) as well as the co-organiser of a workshop on complications and comorbidities among HIV patients, and subject that the group has focused on both in their previous research and current research activities.

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

Group leaders are opinion leaders in the HIV field at an international level.

Late presentation of HIV is commonly occurring, in France as well as in many other developed and developing countries. Finding strategies to circumvent this is an important clinical issue and likely to have major clinical implications: for instance, results of a study regarding screening and earlier HIV diagnosis likely to lead to public health benefits.

Team members are collaborating with AIDS patient association at the national level.

#### Assessment of the unit's organisation and life:

Monthly meetings are held between team groups both to discuss the results of scientific projects conducted in one of the teams but also think tank meetings with participation of immunologists. The interaction between epidemiologist, clinicians and immunologists enables the group to address scientific questions from several angles.

The younger scientists in the group (Ph.D. students and Post docs) report easy access and fruitful discussions and collaborations with their supervisors. They regularly participate in meetings and conferences and are given the opportunity to present their data, both as abstracts and manuscripts.

An international student has been recruited.

There is evidence of excellent external communication and collaboration with others within France and internationally.



### Assessment of the unit's involvement in training through research:

One of the team leaders created the EACS HIV advanced course in 2003 and still co-ordinates the course yearly. Likewise, she has created the European Clinical Research Course (ECRECO). Short clinical research courses within AFRAVIH have been conducted in Bamako and Abidjan. The other team leader is head of the Public Health Pierre Louis Doctoral School.

### Assessment of the five-year plan and strategy:

The research strategy is ambitious with an excellent knowledge of the research field. Extensions of studies of complications of long-term HIV infection / long-term ART have been planned. With the French Hospital Database on HIV (FHDH), the group has excellent possibilities for investigating these questions in lieu of the size and completeness of the database as well as the possibilities to link to other databases.

- Excellent feasibility in terms of resources - good track record of completion of projects. Future planned work are based on pre-existing structures already implemented by the team so very high probability of successful completion (e.g. FHDH)

- Among the newer research questions are: Can HIV DNA level be used to evaluate if ART can safely be stopped? Can purging of HIV-infected cells be used to minimize/eradicate this reservoir? Can (even) simpler ART regimens be constructed?

### Conclusion:

#### ● Strengths and opportunities:

The unit is a long-term very productive collaboration between researchers with different backgrounds as statistician/epidemiologist and clinician, respectively. Both team leaders have developed extensive networks, nationally as well as internationally, and participate in several national and international collaborations.

Furthermore, there has been a year-long collaboration with the immunologists at Pitié-Salpêtrière.

A new team member seems to have a different back-ground with most publications within the field of other infectious diseases including tropical diseases, which will enable the group to broaden their research interests.

#### ● Weaknesses and threats:

Though the questions related to possible long-term toxicities / complications / co-morbidities among long-term treated HIV-patients are of major importance and the group has good conditions for investigating these, many other cohort studies are investigating the same issues. Therefore, maintaining the novelty and uniqueness of the groups' work in this area, as has been done to date, will be important.

The group has successfully attracted researchers for PhD projects, but it has been more difficult to recruit senior researchers.

#### ● Recommendations:

Build on the strong foundation of collaborative research. The group has previously investigated alternative ART combinations / strategies and this line of research is encouraged to be maintained or even extended.



**Team 4 :** Resistance to antiretroviral drugs

**Name of team leader:** Ms Anne-Genevieve MARCELLIN and Mr Philippe FLANDRE

**Workforce**

<b>Team workforce</b>	<b>Number as at 30/06/2012</b>	<b>Number as at 01/01/2014</b>	<b>2014-2018 Number of project producers</b>
<b>N1:</b> Permanent professors and similar positions	3	3	3
<b>N2:</b> Permanent EPST or EPIC researchers and similar positions	1	1	1
<b>N3:</b> Other permanent staff (without research duties)	3,5	5	5
<b>N4:</b> Other professors (PREM, ECC, etc.)	1	1	1
<b>N5:</b> Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	0	0	0
<b>N6:</b> Other contractual staff (without research duties)	2	3	2
<b>TOTAL N1 to N6</b>	10.5	13	12

<b>Team workforce</b>	<b>Number as at 30/06/2012</b>	<b>Number as at 01/01/2014</b>
Doctoral students	2	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	4	
Qualified research supervisors (with an HDR) or similar positions	4	4



- Detailed assessments

#### Assessment of scientific quality and outputs:

During the last five years, 173 peer reviewed publications of which 133 as leaders have been published mainly in the top journals of the speciality in J Inf Dis (IF=6.41), AIDS (IF=6.24), Antimicrobial Agents and Chemotherapy (IF=4.84).

On the other side there have been no publications in general, top level scientific journals (e.g. Nature, Science...). Some of the publications by the group have influenced clinical guidelines and have therefore a direct impact on clinical care.

#### Assessment of the unit's academic reputation and appeal:

The team has been participating for some years already in the 7FP Chain project as a work package leader for WP1 (large work package) and as contributors to 2 other work-packages. This gives international visibility to the team. Some members of the team have been invited as speakers to international high-level conferences (i.e. CROI and similar). The team is able to recruit students internationally.

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

The team has submitted over the last five years two patents related to novel antiretroviral drugs. Several team members are active in national drug resistance guidelines committees (mainly the ARNS drug resistance algorithm). This involvement has a direct impact on clinical care. The team has a sustained collaboration with some African partners (knowledge transfer). The team also collaborates with pharmaceutical companies on drug resistance to novel drugs.

#### Assessment of the unit's organisation and life:

Based on the interviews with researchers, PhD students and support staff, the committee had the impression that there is a good involvement of all level of employees in the decision process of research. The team holds regular weekly meetings. Some members of the team are also involved in the safety/security process of the centre.

#### Assessment of the unit's involvement in training through research:

7 PhD students have completed successfully their training during the last five years. 3 Master students have been in the team. Currently 6 PhD students and 2 post-docs are in training for 4 persons with a HDR. The students seem to be adequately followed by their supervisors and have regular opportunities to exchange on their research results.

#### Assessment of the five-year plan and strategy:

The project is primarily the continuation of past, successful work adding some more innovative aspects (e.g. the clinical relevance of minority species or the influence of gag cleavage site mutations on drug resistance algorithms) although other international high level groups are pursuing similar research. The impression is that the proposed project does not take all possible advantages from the proposed creation of a public health institute and there might be additional opportunities for innovative research in collaboration with other teams.



## Conclusion:

- Strengths and opportunities:

The virology group is a well-established and highly productive team. It benefits largely from the close collaboration with the clinical team 3, which is a motor in driving their research agenda. It has currently access to novel technologies such as next generation sequencing and attempts to apply these to clinical problems (e.g. role of minor species). Due to the close link with ANRS cohorts and clinical trials, it is one of the only teams - if not the only - worldwide which can validate clinically the proposed drug resistance algorithms. This opportunity for further research has to be preserved and even developed in the coming years.

Other opportunities arise from the proposed institute on public health which makes new competences more easily available to the team (e.g. modelling by team 1 or 2, access to chronic viral hepatitis data and samples by team 2). From the proposed project, it is not clear if there has been already an extended reflection on how to take advantage of these new opportunities.

- Weaknesses and threats:

One major threat to the group - and to all groups working in HIV drug resistance - is that HIV drug resistance is a "dying science" as current drug regimens become increasingly powerful and drug resistance therefore is less and less an issue in clinical care. There remains for sure an interest in characterising drug resistance profiles to newer drugs; however, the clinical impact of this research is constantly decreasing.

A second threat is that the group is investing increasingly efforts into drug discovery. This is per se an interesting topic; however, it does not fit so well with the objectives of a public health research institute. Even if there are no doubts that there are good reasons why a virology laboratory should be part of a public health institute, putting too much emphasis on drug discovery activities might be criticised as a divergence from the primary objectives of the institute and a strategic misfit.

- Recommendations:

Build on past competences and on unique capabilities of the team (such as the clinical validation capabilities of drug resistance algorithms). These should be further developed.

Develop real cross-fertilisation with other teams especially with Teams 1 and 2. There might be high opportunities for innovative projects. This will open new fields of research to the team, largely compensating for the decreasing interest in HIV drug resistance per se.

Reconsider to which extend the discovery of novel drugs fits with the objectives of a public health institute and if this activity could not be more appropriately pursued in another context.



**Team 5 :** Epidemiology of allergic and respiratory diseases

**Name of team leader:** Ms Isabella ANNESI-MAESANO

### Workforce

<b>Team workforce</b>	<b>Number as at 30/06/2012</b>	<b>Number as at 01/01/2014</b>	<b>2014-2018 Number of project producers</b>
<b>N1:</b> Permanent professors and similar positions	3	9	7
<b>N2:</b> Permanent EPST or EPIC researchers and similar positions	1	1	1
<b>N3:</b> Other permanent staff (without research duties)	0	0	0
<b>N4:</b> Other professors (PREM, ECC, etc.)	1+1	4+5	2+3
<b>N5:</b> Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	0
<b>N6:</b> Other contractual staff (without research duties)	2	2	0
<b>TOTAL N1 to N6</b>	9	22	13

<b>Team workforce</b>	<b>Number as at 30/06/2012</b>	<b>Number as at 01/01/2014</b>
Doctoral students	4	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	5	7



- Detailed assessments

Assessment of scientific quality and outputs:

The group has been involved in a wide range of collaborative projects resulting in a large number of joint publications. Out of the 432 publications of the team, 241 papers have been led from the Team 5, with several in the Journal of Allergy and Clinical Immunology (IF=9.17) which is the Journal with the highest impact factor for allergy and others in Thorax (IF=6.84) which is the highest impact factor for respiratory disease that regularly accepts epidemiological papers.

Assessment of the unit's academic reputation and appeal:

One of the senior researchers provides leadership at a European level in the field of drug hypersensitivity; the team leader has provided national leadership in the international Study of Asthma and Allergies in Childhood, which is the largest epidemiological study of asthma and allergies in children ever undertaken (ISAAC study). Both have taken leading roles in European Societies (European Respiratory Society [ERS] and European Academy of Allergy and Clinical Immunology [EAACI]).

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

There is evidence of influencing policy at the European level in collaboration with various societies. Specifically related to the group's research on school environment, there is a European document recommending environmental standards for schools.

Assessment of the unit's organisation and life:

The group is well managed and has a strong collegial atmosphere with high morale.

Assessment of the unit's involvement in training through research:

The training environment is excellent and the programme has regular MSc students and currently has 4 PhD students. The jury was impressed by the fact that the students shared the task of presenting the work to the jury, and that this was done to a high standard. While being questioned on their own the students expressed a particularly high level of satisfaction with the support that they received from the team leader.

Assessment of the five-year plan and strategy:

The panel saw a good case for an external senior physician-researcher joining the group but were yet to be persuaded of the practicality of his commuting between Paris and Montpellier. The jury felt that the future plans for this group required further development and a more focused programme aligned to the skills of the wider research centre.

Conclusion:

- Strengths and opportunities:

This is a well organised group with high morale and a particularly supportive training environment. It is also very well connected through its director with the wider world outside France. It has taken full advantage of this by joining multicentre European projects and this has led to a number of opportunities to co-author papers.

The extension of the work of the Unit by the addition of a clinical scientist from a University hospital in the south of France was seen as being very positive, and adding other possibilities of clinical links in a University with a strong respiratory team.



The main interests of the principal scientists are the respiratory effects of air pollution (team leader), developmental aspects of respiratory disease, and drug hypersensitivities. There are excellent opportunities to develop very high level programmes of work in these areas in collaboration with other proposed members of the Institut Pierre Louis. For instance, working with team 8's expertise in geographical techniques to improve exposure assessment for studies of air pollution in urban environments, working with Team 8 leader to develop and extend their expertise in studies of life course epidemiology, and working with Team 1 leader to use the Sentinelle network or Team 7 to use the hospital systems to extend their studies of adverse events to drugs. The proposed move of a young researcher to the Unit would strengthen all these opportunities.

The commitment of the Institute director to this group is also a strength and very important.

- Weaknesses and threats:

This group is well connected internationally, but could have produced more primary research papers over the last period. The current plans also seem not to have taken fully into account the potential for strengthening their contribution by working more closely with new members of the Institute. The plans provided look too diffuse and unfocused and too opportunistic. The jury expressed reservations on how one of the proposed new investigators would be able to contribute fully to the Institute while holding a responsible clinical position in Montpellier.

- Recommendations:

1. To ask for a revised forward plan that takes clearer advantage of the new grouping;
2. To look at the best ways of engaging the senior physician-researcher from Montpellier with the Unit.



**Team 6 :** Epidemiology and Evaluation of Musculo-skeletal and Systemic Diseases

**Name of team leader:** Mr Bruno FAUTREL

**Workforce**

<b>Team workforce</b>	<b>Number as at 30/06/2012</b>	<b>Number as at 01/01/2014</b>	<b>2014-2018 Number of project producers</b>
<b>N1:</b> Permanent professors and similar positions	2	2	2
<b>N2:</b> Permanent EPST or EPIC researchers and similar positions	0	0	0
<b>N3:</b> Other permanent staff (without research duties)	0	0	0
<b>N4:</b> Other professors (PREM, ECC, etc.)	5+4	5+4	7
<b>N5:</b> Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	0	0	0
<b>N6:</b> Other contractual staff (without research duties)	0	0	0
<b>TOTAL N1 to N6</b>	11	11	9

<b>Team workforce</b>	<b>Number as at 30/06/2012</b>	<b>Number as at 01/01/2014</b>
Doctoral students	2	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	0	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	2	3



- Detailed assessments

#### Assessment of scientific quality and outputs:

There was a good scientific production improving in the last year (2011/2012): during the last five years, 67 peer reviewed publications of which 38 as leaders have been published. Publications in speciality journals (including Arthritis & Rheumatism (IF=7.86) 2009, 2011, Ann Rheum Dis. (IF=8.72) 2012), with the best impact factor in the speciality. No higher impact paper.

#### Assessment of the unit's academic reputation and appeal:

The team leader is involved in the working group of the "European League Against Rheumatism (Eular)". Senior researchers are invited speakers at international conferences (Eular), and involved in recommendations for clinical care in rheumatic diseases.

No FP7 fundings.

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

The team is a young but dynamic team involved in clinical research in rheumatology, with broad activities (social impact of low back pain, epidemiology of rare systemic diseases, societal impact of rheumatoid arthritis [RA] and ankylosing spondylitis [AS]). They have obtained several industrial contracts. They have contributed in establishing cohorts of patients with rare diseases, which is a large unmet need. The team also contributed in 2012 to Eular clinical practice guidelines for RA and for national Consensus for the French High Health Authority [HAS] concerning local injections.

#### Assessment of the unit's organisation and life:

This is small team, with good interactions, and weekly meeting planned with PhD students. Interactions with other teams in the institute are clear and productive. Good interactions with clinical department.

#### Assessment of the unit's involvement in training through research:

The team is involved in teaching (rheumatology) and has supervised 2 PhD students as well as master students. The team leader is involved in Eular annual international course. No responsibility yet for course work in Master or doctoral School.

#### Assessment of the five-year plan and strategy:

The project presented is proposing an assessment of the societal impact of rheumatic disease including RA, AS, lowback pain. The second objective is to define criteria to optimize therapeutic strategies in systemic disease, including RA. This will include self-assessment and a predictive matrix to define patients at risk for structural damage. A further interesting part is dedicated to the epidemiology of rare disease (Systemic Lupus Erythematosus, Erdheim Chester disease) using the SNIRAM data base.

The project appears well structured and feasible for this group, but would benefit from a clearer and narrower focus. Moreover, methodology and medico-economic assessment should be better defined; integration within the Institute and stronger interactions with team 8 will help.



### Conclusion:

- Strengths and opportunities:

The team is dynamic and active in clinical research in rheumatology, with broad activities (low back pain social impact, epidemiology of rare systemic diseases, societal impact of RA and AS). The proposed programme of work would 1) assess the societal impact of rheumatic disease including RA, AS, lowback pain; 2) define criteria to optimize therapeutic strategy in systemic disease, including RA, and 3) establish a project in the epidemiology of rare systemic diseases, which is currently an unmet need.

- Weaknesses and threats:

The team is small, supported by 2 PUPH, with no full time Inserm scientist. The project would benefit from a clearer and narrower focus and the methodology and medico-economic assessment should be better defined.

- Recommendations:

Stronger interactions with team 8 will help to structure the research.

Integration in the Institute will improve the scientific value.



**Team 7 :** Hospital epidemiology, quality and organization of healthcare

**Name of team leader:** Mr Gilles HEJBLUM

**Workforce**

<b>Team workforce</b>	<b>Number as at 30/06/2012</b>	<b>Number as at 01/01/2014</b>	<b>2014-2018 Number of project producers</b>
<b>N1:</b> Permanent professors and similar positions	3	3	3
<b>N2:</b> Permanent EPST or EPIC researchers and similar positions	1	1	1
<b>N3:</b> Other permanent staff (without research duties)	0	0	0
<b>N4:</b> Other professors (PREM, ECC, etc.)	2	1	1
<b>N5:</b> Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	0	0	0
<b>N6:</b> Other contractual staff (without research duties)	0	0	0
<b>TOTAL N1 to N6</b>	6	5	5

<b>Team workforce</b>	<b>Number as at 30/06/2012</b>	<b>Number as at 01/01/2014</b>
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	3



## • Detailed assessments

### Assessment of scientific quality and outputs:

- The team published 90 publications in the last five years, including 51 as lead authors.
- They published in journals, which have high impact factor level, eg: Arch Int Medicine (IF=8.0), Crit Care Med (IF=6.33), Chest (IF=6.22), Lancet (IF=38.28).
- Their publications focused on the team's research domain.

### Assessment of the unit's academic reputation and appeal:

Team Members have relevant scientific involvement in international editing: one is member of 3 journal editorial boards (Am J Respir Crit Care Med, Annals of Intensive Care and Reanimation, and In Care Unit). Several members are reviewers for high impact factor international journals (i.e. BMJ, JAMA, Intensive Care Unit, BMC Anaesthesiology...). One member is the President of the College of Intensive Care Database Users (CUB REA)]. Team members were invited to do 77 oral communications at international congresses over the last five years.

3 PhD candidates were recruited during the last five years.

They have several national, European and international collaborations in the domain of intensive care (i.e. work groups within the European Society of Intensive Care, and with a group from Pittsburgh University).

The international collaborations mainly concern 6 studies, which resulted in 6 international publications.

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

Research was conducted in the topic area of intensive care regarding the modification of guidelines for CXR prescription in ventilated patients. Results were published by the "Haute Autorité de Santé" (HAS), which is the national organization that defines guidelines in France. The team's field of research is closely related to medical practices. The results will therefore be easily transferred in clinical practices.

### Assessment of the unit's organisation and life:

- It is a small team with only 3 permanent members and two PhD candidates currently.
- They organize two meetings per month when students present the advancement of their work.
- The PhD candidates are satisfied with the monitoring of their work. The mood of the team seems very satisfactory.

### Assessment of the unit's involvement in training through research:

Team members have many teaching responsibilities: Diploma of medical pedagogy

- Head of the modules of Master "Evaluation, gestion et éthique" (Evaluation, Management and Ethics).
- Co-Head of module "Statistiques appliquées à la biologie" (Applied Statistics in Biology).
- Recruitment of two new PhD candidates in 2012, Two PhD defended their thesis in 2010 and 2011.
- Supervision of many Master 2 Internships for public health students every year.



### Assessment of the five-year plan and strategy:

The team will work first in the field of intensive care through two well-funded research projects. One is on elderly patients admitted in ICUs multicentric project (PHRC) and the second on the prescription of chest X-Rays in mechanically ventilated patients in ICUs (RARE Study).

Second they plan to develop research in the field of pharmacology quality assurance (partly funded), through first the use of the pharmaceutical computer record in the medication reconciliation, impact on the rate of adverse events (granted by the PHRC), and second on the decrease of the prescription of hypnosedative drugs in elderly patients.

The third research axis is in the field of risk management (projects presently financed) considering two empirical projects. First on "Sentinel patients" and the assessment of the quality of the hospital stay (SENTIPAT project). (Granted by the PHRC) and second through a research of the continuity of nursing care after hospital discharge (Granted by PHRI, 1 PhD).

One of the objectives is to develop the Virtual Hospital project, which proposes to analysing/modelling/improving health care processes. They wish to develop an agent- based plate-form.

### Conclusion:

#### ● Strengths and opportunities:

- The research programme of the team is well structured around projects funded for the most part;
- High quality of publication;
- Large network of clinical partnership.

#### ● Weaknesses and threats:

- Small size;
- Should be cautious about not being overwhelmed by too many research orientations.

#### ● Recommendations:

- This small team is likely to be in a more favourable situation inside the centre: this will help visibility and collaborations;
- We recommend discussions with other research teams of the centre to enlarge their research focusing to other domains besides intensive care;
- We recommend increasing looking for PhD students recruitment in particular for Pharmacist researchers involved.



**Team 8 :** Socio-territorial determinants and inequalities in health

**Name of team leader:** Mr Pierre CHAUVIN

### Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
<b>N1:</b> Permanent professors and similar positions	3	3	3
<b>N2:</b> Permanent EPST or EPIC researchers and similar positions	3	7	7
<b>N3:</b> Other permanent staff (without research duties)	3	3	2
<b>N4:</b> Other professors (PREM, ECC, etc.)	0	1	0
<b>N5:</b> Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	4	3
<b>N6:</b> Other contractual staff (without research duties)	8	17	5
<b>TOTAL N1 to N6</b>	19	35	20

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	12	
Theses defended	13	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	5	7



## • Detailed assessments

### Assessment of scientific quality and outputs:

This group includes international leaders with respect to spatial modelling of social exposures, cross-nested models, integrating causal inference into social epidemiology, and intergenerational transmission of health disadvantage. They contributed breakthrough work with initiation of offspring cohort (TEMPO) including links to detailed occupational data on GAZEL cohort parents. Work on spatial modelling and data collection for activity space is internationally cutting edge for this research area. Over the last 5 years, team members led 151 publications, plus 93 as collaborators, in leading epidemiology/public health journals: J Natl Cancer Inst (IF=13.75), Annu Rev Public Health, (IF=5.45), Mol Psychiatry (IF=13.66), Diabetes Care (IF=8.1), Soc Sci Med (IF=3.47), ....

### Assessment of the unit's academic reputation and appeal:

The unit recruits students internationally with strong training and post-doctoral training programs. Researchers are invited for international presentations and have established fruitful, productive collaborations with respected international colleagues. Team members have been recognized with national awards. Achievements of the unit are manifest in the impressive collaboration generated with the new unit, created by recruiting a large group of excellent researchers from another centre.

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

The work of this unit has important influences on other researchers in many areas, prompting recognition and incorporation of social inequalities measures into other research topics. Their findings have succeeded in drawing attention to inequalities, e.g., with respect to migrant and homeless populations. Team members participate in social/cultural activities and policy efforts such as council on providing access to care. Spatial modelling tools developed in the unit have been developed into a software package that will be widely used. Researchers collaborate with regional health agencies, NGOs and international foundations (e.g., Wyeth and others).

### Assessment of the unit's organisation and life:

The team has good collegiality, enthusiastic students, and regular seminars to promote lively intellectual life. The larger group may benefit from more specific management/ clarification of management plan to continue excellent record of mentoring and collaborations. Of critical importance is the availability of tools and resources to remove administrative obligations from the task list of researchers. Such support would probably improve research productivity/quality even further.

### Assessment of the unit's involvement in training through research:

This team has a flourishing student body and several post-docs. In the last 5 years, 13 PhD students defended with approximately 5 PhD directors available. They generally also have a group of 5-6 masters' students per year. Notably, they have mentored junior trainees (previously doctoral students) into INSERM positions in the unit. Researchers teach at Paris 11 and other French universities, plus some international teaching re on HIV, global health, psychosocial epidemiology.

### Assessment of the five-year plan and strategy:

The proposal includes excellent research on social inequalities, social determinants of health, and underserved/vulnerable populations. The proposal includes valuable descriptive work to inform social policy. These address very important topics in France. The proposal indicates that the unit will also continue as a centre of excellence in place effects on health/geographic modelling, mobility studies and incorporation of causal inference tools into social epidemiology. The proposal includes a valuable integration of occupational health and social determinants, including psychosocial aspects of work, and mental health outcomes. The unit is working on cutting edge representative studies of underserved populations. It is remarkable to achieve such representative samples in hard-to-reach populations and the findings will translate directly into health policy. Opportunities include incorporating newer directions for methodological development and theoretical underpinnings (e.g., biological foundations) to understand mechanisms creating social inequalities that will persist across time.



## Conclusion:

### ● Strengths and opportunities:

The scientific quality of the research, the commitment to training of junior researchers, and the innovative methodological approaches taken within the unit are clearly strengths.

The strengths of the proposal include integration of occupational health, social determinants, psychosocial aspects of work, and mental health outcomes as well as cutting edge representative studies of underserved populations. Opportunities include important methodological development and testing alternative theories on mechanisms linking social conditions and health and generating social inequalities.

By combining the already existing team in Saint-Antoine with the new team coming from Villejuif, Team 8 will be the largest research team on social epidemiology in France integrated in a research centre with an excellent potential for methodological development, cross-fertilization and breakthroughs.

The opportunity for these researchers to sit together is an important strength. The larger organization of the team in the future could help individual researchers. For example, if the collaboration provides opportunities to improve administrative support and protect researchers' time for research, this is a tremendous opportunity and will provide valuable efficiencies.

A key opportunity would include more frequent communication with individuals in other fields, exposure to new methods and data to enhance research within the unit, and better administrative support for researchers. Achieving real collaboration across units will not be automatic; mechanisms to promote this might include joint seminars and preferential support for funding applications that are joint across units.

### ● Weaknesses and threats:

The most important threat is that this excellent team of researchers will be distracted from their core research mission. This could happen, for example, if researchers need to spend too much time on administrative rather than research related activities. Further, the team will face numerous other demands, including helping other teams with measures or research approaches for studying social inequalities and time-sensitive policy response needs. There is no easy answer about how to handle this; there is a tension because the collaborations are valuable, and helping integrate social inequalities perspectives into other fields is part of the mission of social epidemiology, but researchers need to be sure they have protected time for their specific research agendas.

Because the unit is very large, decision making processes may be unclear and ultimately slow down researchers. When setting up an organizational structure, it is important to minimize the bureaucratic layers. A threat in the new organization is the potential for a large organizational structure to increase bureaucratic layers that hinder research instead of facilitating it. For example, some large organizations require researchers to proceed through longer approval process in order to initiate such new projects.

The research of the team focuses on descriptive and analytical approaches. Based on the previous work and experience of the team with many stakeholders, moving into interventional approaches is a legitimate opportunity to consider.

### ● Recommendations:

- Need to Increase capacity for administrative support;
- Clarity on organisational structure, emphasizing a structure with minimal bureaucracy, fostering independence of researchers, and minimising competition between teams;
- Promote communication/collaboration between teams with formal structures;
- Consider to bridge explanatory research with interventional research approaches.



## 5 • Conduct of the visit

### Visit dates:

Start: 10<sup>th</sup> of January 2013, at 8:30 am

End: 11<sup>th</sup> of January 2013, at 6:00 pm

Visit site(s): on 10<sup>th</sup> January 2013

Institution: UPMC Saint Antoine

Address : 75012 Paris

Second site: on 11<sup>th</sup> January 2013

Institution: Hopital la Pitié Salpêtrière

Address: 75013 Paris

### Conduct or programme of visit:

#### Day one - January 10<sup>th</sup> 2013

- |             |  |
|-------------|--|
| 8:30        | Welcome (closed-door meeting): Visiting committee with the AERES scientific advisor  |
| 9:15        | Plenary session<br>AERES representative: the role and procedures of AERES  |
| 9:30        | Director of the Unit, D. COSTAGLIOLA (30' presentation, 15' discussion): General strategy  |
| 10:15       | Team 1 - Monitoring and modelling of communicable diseases (30' talk + 25' discussion)   |
| 11:10       | Team 2 - Epidemiology of viral hepatitis and influenza: risk, prognosis and therapeutic strategies.<br>(30' talk + 25' discussion) |
| 12:05       | Team 3 - Clinical epidemiology of HIV infection: treatment strategies and comorbidities.<br>(30' talk + 25' discussion)            |
| 13:00       | Lunch  |
| 14:00       | Team 4 - HIV resistance to antiretrovirals (30' talk + 25' discussion)   |
| 14:55       | Team 5 - Epidemiology of Allergic and Respiratory Diseases (30' talk + 25' discussion)   |
| 15:50       | Coffee break   |
| 16:10       | Team 6 - Epidemiology and Evaluation and Systemic Inflammatory Osteoarticular Diseases (30' talk + 25' discussion)                 |
| 17:05       | Face-to-face meeting of the visiting committee with the head of each team (1, 2, 3, 4, 5, 6):<br>6*5'=30'                          |
| 17:35-19h30 | Debriefing closed-door visiting committee  |



**Day two - 11th of January 2013**

8:30	Team 7 - Hospital Epidemiology, quality and organization of care (30' Talk + 25' discussion)
9:25	Team 8 - Social Epidemiology (30' Talk + 25' discussion)
10:15	Face-to-face meeting of the visiting committee with the head of each team (7,8) and debriefing closed-door visiting committee (10')
10:25	Coffee break
10:45	Three parallel meetings with personnel without head, team leaders, or managing bodies Discussions with engineers, technicians, administrative Discussions with staff scientists Discussions with students and post-docs
11:45	Discussion with the representatives of managing bodies (45')
12:45	Lunch (private meeting of the visiting committee and in presence of the aeres scientific advisor (45'))
13:30	Discussion with the direction committee: head alone (20') + all (30')
14:20	Private meeting of the visiting committee (in presence of the AERES scientific advisor)
17:00	End of the visit

**Specific points to be mentioned:** The programme was perfectly respected and the visit was carried out in excellent conditions.

## 6 • Statistics by field: SVE on 10/06/2013

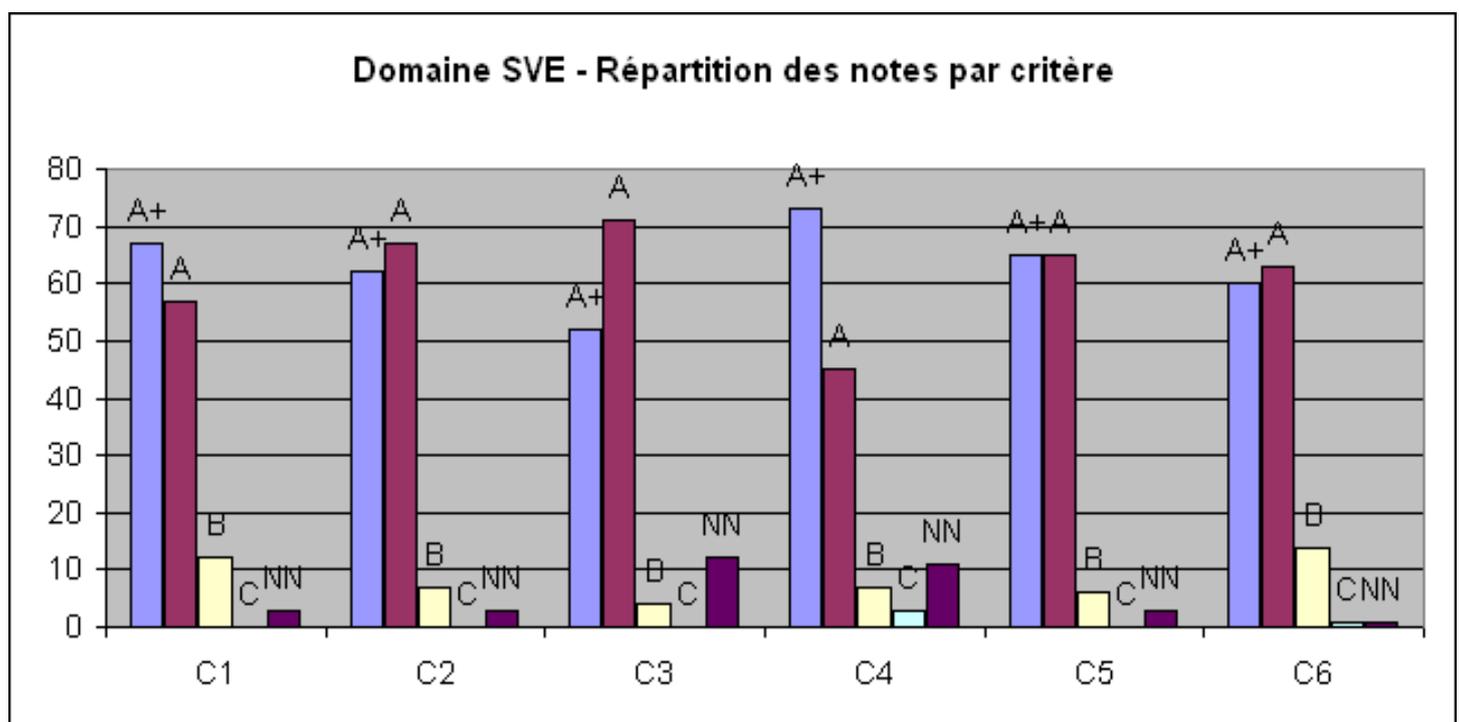
### Grades

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	67	62	52	73	65	60
A	57	67	71	45	65	63
B	12	7	4	7	6	14
C	0	0	0	3	0	1
Non Noté	3	3	12	11	3	1

### Percentages

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	48%	45%	37%	53%	47%	43%
A	41%	48%	51%	32%	47%	45%
B	9%	5%	3%	5%	4%	10%
C	0%	0%	0%	2%	0%	1%
Non Noté	2%	2%	9%	8%	2%	1%

### Histogram





## 7 • Supervising bodies' general comments

Paris le 22 04 2013

Le Président  
Didier Houssin  
Agence d'évaluation de la recherche  
et de l'enseignement supérieur  
20 rue Vivienne - 75002 PARIS

M. le Président,

Nous avons pris connaissance avec le plus grand intérêt de votre rapport concernant le projet de l'Institut Pierre Louis d'Epidémiologie et de santé publique, porté par Mme Costagliola. Nous tenons à remercier l'AERES et le comité pour l'efficacité et la qualité du travail d'analyse qui a été conduit.

Ce rapport a été transmis à la directrice de l'institut qui nous a fait part en retour de ses commentaires que vous trouverez ci-joint. Nous espérons que ces informations vous permettront de bien finaliser l'évaluation du laboratoire.

Restant à votre disposition pour de plus amples informations, je vous prie de croire, M. le Président, à l'expression de mes salutations respectueuses.

Le Vice -Président Recherche et Innovation

Paul Indelicato



## **Comments on the AERES report for the Pierre Louis Institute of Epidemiology and Public Health**

We would like to take this opportunity to thank the visiting committee for fruitful interactions during the visit and for the thorough evaluation of our project. We don't have any comments on the general assessment of the unit. We have listed below some comments by team and some technical comments

### **Team 1**

In joint projects developed with other teams of the institute (especially 2, 3 and 4), we pay attention to balance intellectual and technical inputs of all partners.

### **Team 4**

We would like to comment on the point that HIV drug resistance is a "dying science". Although HIV drug resistance prevalence is decreasing in resource-rich countries, there is still a need for centres of excellence working in this area as:

- There are several new drug classes that are currently being developed (maturation inhibitors, attachment inhibitors, LEDGF inhibitors, ...) for which mechanisms of resistance are unknown.
- Despite drug regimens becoming increasingly powerful, around 12% of treated patients in France still present virological failure, mainly due to / associated with antiretroviral resistance.
- HIV drug resistance is an increasing problem in resource-limited countries, where the prevalence of resistance is now rapidly increasing. Our group is fully involved in this area and we have implemented a research laboratory in Bamako (west Africa, Mali). We intend to apply with University College of London and Tor Vergata University of Roma to EU grants Horizon 2020 in this area.

As recommended by the committee, we will share our expertise about resistance to antivirals with Teams 1 and 2, for modelling hepatitis viruses resistance.

Drug discovery is a very innovative aspect of our research that is fully encouraged both by INSERM and UPMC. We started from our accumulated knowledge on resistance to design new antiviral agents targeted to overcome resistance. Indeed, our first compound is under license with a Biopharma in Canada.

### **Team 5**

As a general comment, the members of team 5 were surprised to see that the Environment-Health topic was never mentioned in the report.