

SIRIC PROGRAMME 2018-2022- MID-TERM REPORT (2020) EVALUATION FORM

Project number	SIRICEval20-011
Name of the SIRIC	CARPEM
Name of the SIRIC Director	LAURENT-PUIG Pierre
Name of the Reviewer	3

General information

The SIRIC designation aims to offer new opportunities for conducting translational cancer research, thus helps optimising, accelerating and disseminating the production of new knowledge and its application to cancer care. The SIRIC programme should increase the link between the different dimensions of research (basic, clinical, public health, epidemiology, and human and social sciences), by concentrating a critical mass of experts (physicians, researchers, engineers, healthcare workers and patients).

The role of a SIRIC is to make big improvements in the quality of research organisation, knowledge production, transfer of innovation into practice and care organisation, and new outcomes dissemination to all potential beneficiaries.

The SIRIC programme is a French National Cancer Institute's policy in research structuring initiated in 2011. The importance and priority of this flagship programme have been reinforced in the 2014-2019 Cancer Control Plan with a second call for designation, launched in 2017.

This second (2017) call for designation was open to previously designated sites and to new applicants. It has resulted in the designation of 2 new SIRICs (CURAMUS and ILIAD) and the renewal of 6 SIRICs (BRIO, CARPEM, CURIE, LYriCAN, MONTPELLIER and SOCRATE 2.0) for a 5-year designation period (2018-2022). It is addressing specific challenges related to anticipated needs, in order to fight cancer more effectively.

The current mid-term evaluation aims at obtaining a first scientific assessment of the progresses and achievements made by the 8 SIRICs during the 1st period (from January 2018 to June 2020) in order to make recommendations to them on scientific objectives and/or strategies for the 2nd period (July 2020-December 2022).

The mid-term report will be evaluated using 13 criteria (see below).

Each criterion should be scored from 0 to 5 as follows:

0: null ; 1: very weak ; 2: weak ; 3: good; 4: very good; 5: excellent.

1. SIRIC governance and management structure with executive and scientific committees

- Adequacy of the governance organisation for the scientific, administrative and financial management of the SIRIC
- Director of the SIRIC: appropriateness of his/her commitment for the SIRIC organisation, administrative and financial management
- SIRIC managerial and scientific committees: adequacy, role and responsibility of the members
- Respect of the gender equality within the governance
- Commitment of the partner institutions in the SIRIC organization and shared resources
- Adequacy of the scientific management of the SIRIC: progress of the integrated research programmes, inter-programme exchanges, national and international collaborations, dissemination activities
- Appropriateness of the SIRIC administrative services: oversight of shared resources, budget management and accounting processes

Comments on criterion 1:

Since 2018 a restructuration has been created to structure and improve clinical activities, research and teaching in the field of oncology and foster the integration between research and clinics for better care of cancer patients. With now more hospitals included the new Paris Cancer Institute CARPEM led by P. Laurent-Puig was created. The Institute's first challenge is to obtain European accreditation as a "Comprehensive Cancer Center".

The gender equality is the rule among CARPEM structures. The director is committed to oversee the scientific strategy, the financial management of the CARPEM as well as all the items that might have an incidence on the management of the CARPEM.

The scientific advisory board (SAB) has been enlarged, but has only met once (in 2020) to assess achievements and scientific plans of CARPEM.

Specific recommendations for the 2nd period of the SIRIC designation:

SAB should meet at least once a year. However, SAB hold 9 members which makes it difficult to arrange.

Support the plan of European accreditation by OECL as a comprehensive cancer center.

2. Establishment of shared resource facilities to support the SIRIC integrated research programmes

- Development or creation of efficient and operational transversal platforms (genomics, imaging, animal models, etc)
- Development or creation of shared facilities and joint services (methodology, biostatistics, bioinformatics, regulatory and ethical procedures, etc)
- Establishment or development of high-quality biobanks with linkage to clinical and follow-up data and subsequent sharing
- Contribution of the transversal platforms and shared facilities and services in the integrated research programmes

Comments on criterion 2:

Shared resources are of priority with potential for synergies in the area of cancer genomics and immunotherapy and the data warehouse activities.

The translational research platform (TRP) is the flagship platform of CARPEM as an essential transversal tool for all CARPEM members.

CARPEM aims at providing clinicians and researchers with semi-automated dynamic prospective cohorts, using data integration, Natural Language Processing and Artificial Intelligence methods.

The first automated prospective cohort focuses on patients treated by immunotherapy.

A common biobank supported by CARPEM is dedicated to clinical diagnosis and research.

Specific recommendations for the 2nd period of the SIRIC designation:

Consider building master observational trials (MOT), as CARPEM members are strongly involved in SeqOIA and are co-leaders of some national indications for genome sequencing in cancer. This requires massive funding

3. Commitment to support the emergence of research projects (e.g., pump-priming grants)

- Implementation of SIRIC call for projects for emerging/high risk projects funding
- Follow-up and support of these projects' maturation into more ambitious grant applications
- Support for the creation of emerging research teams with integrated research programmes

Comments on criterion 3:

CARPEM supports emerging, innovative and collaborative, involving at least two CARPEM teams or at least 1 CARPEM team and 1 labelled platform within the framework of a CARPEM technological development. 32 projects were submitted until 02/2020 and 11 have been funded so far, for a planned total of 420 000 €.

Specific recommendations for the 2nd period of the SIRIC designation:

(Please feel free to use as much space as needed)

4. Commitment to a training programme in translational and integrated research

- Enlargement and reinforcement of the training opportunities on the specificity and constraints associated to the translational and integrated research (quality insurance, ethical and regulatory affairs, transversal management, etc)
- Programmes/activities proposed to scientists for training in the medical environment and programmes/activities proposed to clinicians for training in a scientific environment (bridges between basic science and clinical practice, and vice versa)
- Programmes/activities proposed to foster the continuum of research and integration of all disciplines, specially human and social sciences, epidemiology and public health

Comments on criterion 4:

CARPEM organizes a call of proposal in the form of a thesis or Masters for MDs, PharmDs or biological, biomedical or informatics engineers intending to complete their training with a PhD. To date, CARPEM has received 13 applications and funded 4 PhDs. In addition, CARPEM funds post-doctoral researchers for one year.

Specific recommendations for the 2nd period of the SIRIC designation:

So far, focus has been on translational research, cancer immunology, cancer hematology and cancer endocrinology), and additional focus on social sciences, epidemiology and public health is encouraged, and more programs could be funded.

5. Progress of the SIRIC multidisciplinary integrated programmes

For each integrated research programme, consider:

- Overall scientific quality and relevance of the programme
- Quality and quantity of the 1st achievements, the outstanding performances and the successful developments
- Robustness of the action plan for the 2nd period
- Anticipated outcomes in terms of production and dissemination of knowledge and practice
- Impact of the SIRIC label on the integrated research programme
- Joint actions with the other SIRIC research programmes

INTEGRATED RESEARCH PROGRAMME 1

Comments:

The IRP1 explores epidemiological relationships between aberrant metabolism and incidence, molecular subtype, outcome and therapeutic response of several major cancers.

This has been executed as planned, meaning that no deviations from the work plan have occurred. with a number of relevant publications in medium and high-ranked journals, including Science, Nature Medicine, British Medical Journal, Cancer Cell, Cell Metabolism as well as to multiple high-impact factors specialty journals and directly led to 46 publications during the 2018-2020 designation period with first and/or last authors from CARPEM.

Specific recommendations for the 2nd period of the SIRIC designation:

A recommendation of the scientific advisory board is the creation of a specific cancer-dedicated bioinformatics platform, which is now in process.

INTEGRATED RESEARCH PROGRAMME 2

Comments:

	<p>The Integrated research program 2 (IRP2) consists in understanding the role of tumor heterogeneity in the mechanisms of tumor resistance to both targeted therapeutics and immune response modifiers.</p> <p>It is divided into 3 work packages (WP) WP3 to WP5. WP3 is devoted to the development and improvement of new technologies to understand the heterogeneity of cancers, WP4 is devoted to preclinical models to address scientific concerns related to host and tumor heterogeneity, and WP5 is devoted to the validation of biomarkers.</p> <p>IRP2 has made it possible to strengthen national and international collaborations involving different types of cancers and biomarkers.</p> <p>IRP2 has led to 65 publications during the 2018-2020 designation period with 20 publications made in journals with an impact factor superior to 10, including 10 in journals with an impact superior to 15 and 5 in journals with an impact superior to 20. IRP2 indirectly led to 38 publications during this period and IRP2 directly led to 13 patents since 2018.</p>
	<p>Specific recommendations for the 2nd period of the SIRIC designation:</p> <p>IRP2 will further develop new technologies that provide high dimensional profiling on a single cell basis while preserving the three-dimensional structures of the tumor microenvironment. This has been recommended by SAB</p>

INTEGRATED RESEARCH PROGRAMME 3

	<p>Comments:</p> <p>The IRP3 addresses the legal, ethical, and human barriers encountered in modern translational research, which they term ‘ethical vigilance’. The main objective was to explore the acceptance and the feasibility of the implementation of the concept of dynamic consent (DC) for the purpose of translational research in the “real life” context of CARPEM. Almost all the teams have been or will be implicated in this integrated program.</p> <p>However, both the legal and the regulatory framework for research practices are under revision in France since 2016. Thus, the establishment of the guidelines for the CARPEM DC platform has been held up. In addition, there was a great change of members in the Advisory Translational Ethics Board (ATEB), which also delayed the program.</p> <p>Still, IRP3 has enabled implementing within the NutriNet-Santé study platform a specific interface for each of the CARPEM-LYNCH and CARPEM-CANCER cohorts by taking advantage from the simplicity and flexibility of the NutriNet-Santé platform in adding new protocols and questionnaires. It represents a unique platform for multidisciplinary collaborations.</p> <p>The integrated program of research 3 will contribute to the production of new knowledge concerning patients’ expectations and fears towards their participation to specific research cohort, but also concerning the sharing and the linkage of their data.</p>
	<p>Specific recommendations for the 2nd period of the SIRIC designation:</p> <p>CARPEM has decided to increase the scale of this dimension by reinforcing the</p>

	place of patients and their representatives through the development of the “patient experience” approach into both clinical and medical practices. This is strongly supported.
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6. Availability of a sufficient patient population to support bench to bedside studies in all integrated research programmes

- Adequacy of the cancers/topics targeted in the integrated research programmes with the medical activity (sufficient number of patients)
- Sufficient rate of patient recruitment in the integrated research programmes : collection of biological samples, inclusion in clinical trials, etc

Comments on criterion 6:

CARPEM included several Paris hospitals and a large population, covering many common and rare tumor types. The organization facilitates the collection of an appropriate volume of biological samples and clinical data, and CARPEM is considered a relevant candidate as OEI comprehensive cancer center.

Specific recommendations for the 2nd period of the SIRIC designation:

Since more hospitals are now included in the new structure, the collaboration should now be consolidated.

7. Effective integration between basic and applied scientists (e.g., clinicians, population scientists)

For each integrated research programme, consider:

- Experience and involvement of the programme leaders (scientific/medical expertise, management of teams, commitment to the programme, meetings organisation, etc)
- Relevant and justified selection of the members of the programme, representativeness of the multidisciplinary
- Quality of the Intra-SIRIC collaboration (active participation, regular meetings, other animation activities), added-value of the multidisciplinary and integrated organisation of the programme
- Commitment of the multidisciplinary research team to achieve translational goals

Comments on criterion 7:

The steering committee brings together clinicians, researchers, epidemiologists, human and social science researchers and patients. In order to encourage interactions between CARPEM teams, the emergence program makes it compulsory for at least two different CARPEM teams to interact. The steering committee is extremely attentive in its project selection to this aspect.

Structuring the interactions between epidemiologists, geneticists, immunologists, physicians dedicated to nutrition and oncologists is part of the programs. It allowed potential identification of new targets for therapy which will be implemented in clinics

Specific recommendations for the 2nd period of the SIRIC designation:

(Please feel free to use as much space as needed)

8. Commitment to develop and integrate human and social sciences, epidemiology and public health studies

- Strategy to develop and integrate human and social sciences, epidemiology and public health studies in the overall SIRIC objectives as well as in each research programme
- Activities effectively implemented by the SIRIC for the development and integration of the human and social sciences, epidemiology and public health studies and associated results

Comments on criterion 8:

IRP1 integrated public health by exploring epidemiological relationships between aberrant metabolism and incidence, molecular subtype, outcome and therapeutic response of cancers.

Also new nutritional and metabolic risk factors are being identified, controlling tumor progression. This is also part of IRP3 which addresses the legal, ethical, and human barriers encountered in modern translational research. It allows the newly created university hospital groups to strengthen their links with Universities, territories and partners and thus enhance the quality of care and research for all patients.

The translational research platform TRP explores two additional directions: first, on adding geographical data in order to be able to link clinical and omics data with social determinants and exposome information available as open data.

Specific recommendations for the 2nd period of the SIRIC designation:

Further development of TRP

9. Involvement of patient advocates

- Consultation of patients' representatives for the SIRIC strategic decisions (governance and management structure)
- Involvement of patients' representatives in the research integrated programmes
- Participation of patients' representatives in activities related to the dissemination of knowledge and practice to the patients and the public

Comments on criterion 9:

Patient representatives are part of the steering committee that has the responsibility for the dissemination of knowledge, web-site etc. However, the involvement of patient in the scientific programs is unclear.

IRP3 addresses the legal, ethical, and human barriers encountered in modern translational research, named 'ethical vigilance'. Its main objective was to explore the acceptance and the feasibility of the implementation of the concept of dynamic consent for the purpose of translational research in the "real life" context of CARPEM.

Specific recommendations for the 2nd period of the SIRIC designation:

(Please feel free to use as much space as needed)

10. National and international synergistic collaborations as well as public-private partnerships

In each integrated research programme, quality of the extra-SIRIC collaboration:

- Effective national collaborations (including inter-SIRIC joint actions): regular meetings or teleconferences, operational exchanges, common publications
- Integration within the regional network: interaction and joint actions with the Cancéropôle (regional cancer hubs) or other regional structures
- Active international collaborations: regular meetings or teleconferences, operational exchanges, common publications
- Public-private partnerships (existence of collaborative contracts, licensing, creation of spin-off, etc)

Comments on criterion 10:

ExtraSIRIC collaborations in the framework of IRP1 are directly and indirectly linked to CARPEM integrated research program 1. Indeed, most of the participating teams developed collaborations with national and international partners.

Also, extraSIRIC collaborations in the framework of IRP2 are directly and indirectly linked to CARPEM integrated research program 2. This analysis showed a large level of collaboration through the world.

Also for IRP3, the inclusions within the CARPEM-LYNCH cohort will be extended to other medical follow-up centers for Lynch Syndrome patients. These centers are members of the PRED-IdF network, a regional network dedicated to patients with hereditary predisposition to digestive cancers.

Specific recommendations for the 2nd period of the SIRIC designation:

(Please feel free to use as much space as needed)

11. Dissemination of new knowledge and good practices resulting from the research towards health professionals and patients, incitation in technology transfer for economic development

- Appreciation of the networks supporting the dissemination programmes: public research institutions, public and private hospitals, charities, private companies, etc
- Efficiency of the activities performed for dissemination of knowledge and good practices towards professionals: information on new scientific knowledge, training on new practices (for screening, diagnosis, and treatment), knowledge transfer in management of quality of life, observance, inequalities, etc
- Efficiency of the activities performed for communication, dialogue and meetings towards patients and the public in order to share experience and progress expected before, during or after the disease
- Support and incentive measures in technology transfer for economic development of the research outcomes

Comments on criterion 11:

200 reviews were published in the last 2 years to diffuse the knowledge acquired by CARPEM. Several members of the CARPEM participate in establishing recommendations of good practices in different cancers and spreading the implication of genomics, immunology and metabolism disorders in the occurrence of cancers. Meetings are organized to upgrade knowledge of oncologists and pathologists, medical residents and fellows in the field of immunotherapy and targeted therapy. Animated supports are developed for explaining to patients the SIRIC CARPEM programs and the new therapeutic practices.

Specific recommendations for the 2nd period of the SIRIC designation:

(Please feel free to use as much space as needed)

12. Ability to leverage funding and/or resources obtained as a result of an “excellent” designation

- Capacity of the SIRIC managerial structure to gain local and regional public funding (or equipment, facilities, etc)
- Capacity of the integrated research programmes to acquire other national or European important co-fundings
- Capacity of the SIRIC operational platforms and joint services to obtain innovative equipment or the associated funding

Comments on criterion 12:

New large projects beyond the integrated research programs have been constructed. Several CARPEM members coordinate large national translational studies in the framework of national or international therapeutic trials (PEATCC08, IDEA) as well as within the French cooperative groups in hematology (GRAALL, GFM). The results of CARPEM second period research form the basis of biomarkers guided large clinical trial (CIRCULATE, amended PEMBROSARC, BIONIKK). Finally, the SIRIC CARPEM has a strong leverage effect, the different CARPEM teams have been able to raise up to 12 M€ during the last 2 years.

Specific recommendations for the 2nd period of the SIRIC designation:

The secretary general was trained to fundraising and built a partnership with Foundation AP-HP to collect donations. CARPEM can now receive donation from private people including former patients and families or firms. Information is available on the website or at the hospitals where leaflets are distributed. CARPEM has already collected 50 K€.

13. Global vision of the SIRIC, scientific directions, goals and perspectives for the 2nd designation period

- General understanding of the definition and objectives of the SIRIC designation
- Adequacy of the SIRIC activities with the initial objectives and workplan submitted in the application dossier for the designation in 2017
- Integration of the designation scientific committee recommendations
- Added-value of the SIRIC designation for the site and the local organisation
- Appropriateness of the SIRIC workplan and perspectives for the 2nd period of the designation
- Global expected impacts of the SIRIC at the end of the designation period regarding the 2 main objectives: improvement of integrated research and dissemination of knowledge
- Long-term vision beyond the end of the current designation (after 2022)

Comments on criterion 13:

A new construction with more hospitals included has created the opportunity to structure and improve clinical activities, research and teaching in the field of oncology and foster the integration between research and clinics for better care of cancer patients. Under the auspice of APHP.Centre – Université de Paris hospital, they created the Paris Cancer Institute CARPEM led by P. Laurent-Puig. The Institute's first challenge is to obtain European accreditation as a "Comprehensive Cancer Center".

The objectives of this new organization are:

- a) To structure the offer of cancer care within APHP.Centre-Université de Paris
- b) To increase the quality of care, research and care/research interactions
- c) To improve the national and international visibility in a competitive field
- d) To participate in a European network and be able to apply as a Centre, to calls for tenders.
- e) 28 programs in oncology have been defined in which the clinical part, the research part (CARPEM), and teaching side are integrated.

CARPEM fosters large research projects involving academic and industrial partners in genomics, immunology and AI which will reinforce its national and international visibility. To this end, they have established a common and unique data warehouse in order to generate new integrated knowledge. A significant number of significant publications has been created moving science ahead.

Specific recommendations for the 2nd period of the SIRIC designation:

Funding is a challenge, and more focus on fundraising is suggested.

SAB should meet more often.

Continue efforts for OECl accreditation

Financial report 2018-2020

- Adequacy of the 2018-2020 financial plan with the SIRIC workplan
- Adequacy of the allocated budget to the general SIRIC managerial services
- Appropriateness of budget allocation between the different categories of expenses: staff, operating costs, equipment, etc
- Appropriateness of budget allocation between the integrated research programmes, the transversal platforms and the dissemination activities

Comments on the financial report:

Well presented. Appropriate with regard to the workplan

Specific recommendations for the 2nd period of the SIRIC designation:

(Please feel free to use as much space as needed)

General comments and recommendations

General comments on the SIRIC mid-term report and final recommendations for the 2nd period of the designation

Recommend continuation. A new and larger center has been established, creating science of high quality. Well-presented and relevant research programs and appropriate platforms and infrastructure