

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	4

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:

- SIRIC CARPEM has recently been through major restructuring with a new agreement between the partners signed as late as December 2019. Earlier in 2019 the two university partners merged into Université de Paris, and four AP-HP hospitals developed a new umbrella agreement. Although these developments are surely helpful from inter-institutional integrated research, this new organization is still young and must pose some early policy, governance and management challenges.
- The governance and management structure of CARPEM is now quite well designed with a superior Directorate interacting with a strong international scientific advisory board (SAB). Scientific strategy and administrative/financial management is handled by the Steering Committee with adequate representation including a patient representative, interacting with a CARPEM Council with all research team and platform leads as well as the ATEB (patient representatives, medical ethics). Curious that the Director does not appear to be part of the Steering Committee (should normally be the leader?), and that the committee only meets once every 2 months.
- CARPEM Director Prof. Laurent-Puig is also the Director of the related Canceropôle Ile-de-France. He is personally actively involved in many of the CARPEM research projects, but it is not specified how much time and dedication he is able to devote to CARPEM leadership.
- Degree of dedication to CARPEM from the individual partner institutions is not specified and may constitute a challenge due to other institutional priorities as indicated in paragraph 1.5 (p. 6).
- IRP 1 and 2 are progressing very well in terms of scheduled deliverables, and seem to consist of many high-quality projects, but with limited prioritization and interconnection. Individual IRP leadership and strategically prioritized collaborations therefore appears to be an issue, particularly in IRP 2. The progress in IRP 3 appears weak and this programme probably needs some re-design and a revised prioritized action plan.
- National and international collaborations are strong.
- The administrative management of CARPEM appears adequate, and is led by the Secretary General through the appropriate departments at the Georges-Pompidou Hospital.
- Gender equality in leadership appears good, except in the SAB (7/8 are males).

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

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

- A defined scientific leadership team for each research programme (IRP) should be considered as the three IRPs overseen by the common Steering Committee cover very heterogeneous topics, and CARPEM could thus benefit from more programme-specific team leadership. Such leadership could then feed into the Steering Committee to cover the overarching strategies and collaborations.
- Helpful with more frequent meetings in the Steering Committee, especially considering the challenges mentioned in paragraph 1.5 (p. 6)? Participation of the CARPEM Director?

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:

- CARPEM has at its disposal all relevant state-of-the-art methodological platforms supporting its very wide range of high quality research activities (as illustrated by the projects utilizing each platform).
- Animal housing especially designed for metabolic studies is available.
- All platforms are partly supported by CARPEM funds.
- One platform (Translational Research Platform – TRP) is created and funded by CARPEM and aims at data integration (data warehouse and AI) from clinical and laboratory resources.
- The platforms have their own management structures with annual reports.
- Several locations for platforms and research teams probably complicate platform access and collaboration.
- High quality prospective biobank samples (blood, cells, tissue) are abundant from all 3 hospitals, are subjected to an approved common broad donor consent, and appear to be prepared and stored under common accredited SOPs.
- An excellent link from the samples to patient data is secured through the TRP platform, where clinical data is captured and stored through the REDcap technology (currently on 40.000 patients...).
- Data in the report also show significant extraction of biobank samples for current research.
- The Phase I clinical trial unit at Georges Pompidou Hospital is a valuable resource for early clinical trials testing the clinical significance of CARPEM discoveries.

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

- As CARPEM's "signature platform", TRP seems marginally staffed (one postdoc and one bioinformatics engineer). Data warehouses are generally challenging structures, and TRP should probably be strengthened for daily management and further development. The report states that "all scientists participate" in this, but nevertheless a strengthened core team seems wise.
- The platforms also serve users outside CARPEM, and how platform access is prioritized and regulated is unclear. If not done already this should be well structured to secure optimal access and usage.
- It appears that biobanking is based on written consent. There are available technologies for the implementation of web-based electronic consent procedures for simplification and to secure consent filing. If not on board this should be considered.
- Not stated to what degree the Advisory Translational Ethics Board (ATEB – p. 5) interacts with the ETREs medical ethics team (p. 18), which may be related to the reported poor consistency of ATEB (p. 45). These should work closely together.
- An experimental (animal) imaging platform is not mentioned specifically. As animal studies are important especially in IRP 1, this could perhaps be an important development.

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:

- There is a defined emergence research program with funding calls twice yearly – directed to new projects connected to IRP 1 and 2. A valuable feature is that at least two CARPEM research teams need to be involved in the applications, promoting integrated research.
- Funded projects receive maximum €40 000 for one year, but there does not appear to be a follow-up funding for very promising projects.
- The 11 funded projects are heavily dominated by basic/translational topics, although 5 clinical teams are said to take part.

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

- Consider larger representation of clinical research projects.
- Establish some continued support beyond one year for the most promising projects, as supplement to other external funding.
- Support and give advice on expansion of research teams for the most promising projects.

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:

- The training activities are largely focused on partial funding of Ph.D. degrees, Master 2 degrees, and post-doc fellowships. Apparently no specific focus on intra-CARPEM training in multidisciplinary collaboration, transverse team leadership, translation to clinical implementation etc.
- Participation in an inter-SIRIC programme (SOCRATE, CURIE) on molecular medicine for clinicians, but no programme for the reverse aspect: clinical picture and challenges for basic/translational researchers. This would be very important considering the heavy basic/translational nature of IRP 1 and 2. Not stated how many CARPEM scientists have participated. Appears valuable but quite general in nature without specific focus on the challenges of integrated research?
- Apparently no training programme for IRP 3 topics (“ethical vigilance”): this is a novel area which is probably quite unfamiliar for IRP 1 and 2 scientists in the context of an integrated SIRIC CARPEM.

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

- Develop the training programme towards collaborative methodology and leadership, and to reciprocal training between clinicians and translational researchers within CARPEM to further facilitate integrated research in this SIRIC specifically.

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: Metabolism, genetics, immunity & environment**Comments:**

- The scientific quality and productivity appear quite excellent in both WPs. There are many excellent scientists, and some discoveries within epidemiological/dietary/serological risk factors and metabolomics/genomics/immunology are novel and may become of clinical importance. Others (particularly on HCC and pre-stage ploidy) are more modest expansions on established knowledge.
- Excellent publication list with several high impact papers and a total of 46 publications directly related to CARPEM IRP1 at mid-term.
- IRP1 has followed and delivered very well according to the original plan (0/15 deliverables reported as delayed), and will continue pursuing the scheduled deliverables without major amendments. Based on the results at mid-term the chances of success appear excellent. CARPEM leadership has followed the SAB advice to establish a dedicated bioinformatics platform, and this development seems very wise.

	<ul style="list-style-type: none"> • On p. 71 in the report only two clinical trials are listed as relevant to IRP1: one on the development of a diagnostic test for a mutated metabolic biomarker, and one (presumably) on predictors of response in a phase II immunotherapy trial (see below for suggestion going forward). • The programme for dissemination of knowledge from IRP1 is to a large degree concentrated around the scientific publications (including many reviews), seminars and teaching activities towards younger scientists (mostly on HCC topics). Dissemination to the general public appears limited to two videos on the website (on immunosurveillance of breast cancer and microbiota, metabolism and response to immunotherapy). • The general impact of the SIRIC designation on integrated research in and between the partner institutions is not well described in the report, but appears obvious from the scientific developments involving most integrated research teams. • Intra-SIRIC collaboration between the IRPs in CARPEM appears moderate to good (mostly between IRP 1 and 2), and is stimulated by the shared CARPEM Steering Committee. • There are specific collaborations with other SIRICS (particularly CURAMUS and SOCRATE), and wide collaborations nationally and not least internationally (CARPEM has world leading scientists with established wide collaborative networks). • Although there appear to be some improvement points, the quality of the science and the execution so far merits an excellent score for IRP1.
	<p>Specific recommendations for the 2nd period of the SIRIC designation:</p> <ul style="list-style-type: none"> • Increase the communication programme towards the public, particularly around relevant topics such as obesity/metabolism and cancer, its relationship to the immune system, effect of therapy etc. – “open public meetings”? • Increase the number of interventional clinical trials based on the novel research results within many parts of IRP1. This can form the basis of small early Phase I/II trials which should fit well into the dedicated early phase unit at hospital Georges Pompidou.
<p>INTEGRATED RESEARCH PROGRAMME 2: Cancer heterogeneity</p>	
	<p>Comments:</p> <ul style="list-style-type: none"> • The overall scientific quality and relevance is very good to excellent. • WP3 involves a large array of novel technologies linked to heterogeneity, resistance and prognosis. These appear developed by CARPEM researches, and the original list of deliverables is to a large degree followed (and some even appear to be ahead of time). The projects involve both liquid and solid tumours, single cell and tissue analyses, circulating and tissue tumour cell parameters, and interplay between tumour and the microenvironment. At this stage the large number of approaches appear somewhat disconnected from each other. • The report on WP4 (new preclinical models) is much more modest and does not

address all scheduled deliverables at this stage (although D4.5 is described under WP5). Task 4.1.3 on complement appears to describe findings in tumour material from patients rather than in a preclinical model.

- WP5 focuses on the clinical validation of prognostic and predictive biomarker combinations/signatures in selected tumour types, including important retrospective validations in large international clinical trials. Some of the findings are impressive (e.g. Immunoscore in manifest and early CRC, ct RAS mut. in CRC, Tertiary Lymphoid Structures in sarcomas). Several described projects involving biomarkers on autophagy, angiogenesis and epigenetics do not appear to be part of the original work plan on p. 31.
- Progress in IRP2 is generally very good considering the recent covid situation with only 2/30 deliverables being reported as delayed.
- General productivity is excellent with 65 full publications being regarded as directly related to IRP2 at mid-term, including 20 publ with IF>10 and 5>20 (not stated how many with first/last author from CARPEM).
- No major amendments to the original action plan are planned for period 2, but incorporation of 3 new technological platforms is planned (Nanostring, 3D cultures and multiplex immunohistochemistry software). The plan appears robust and the outlook for continued scientific quality and productivity are very good.
- Communication of strategy results is largely by very good scientific meetings (particularly on cancer immunology biomarkers), but activity towards the public appears to be limited.
- The SIRIC designation has led to important team accomplishments of international cutting edge quality, additional external funding (including from EU), and has contributed to the realization of prospective large national clinical trials (PEMBROSARC, CIRCULATE). Furthermore, the designation has inspired to planned integrated research beyond the CARPEM designation period.
- Inter-SIRIC-collaborations: Not extensive, but with SIRIC CURAMUS on an application for new instrumentation and in a project on relapse prognostication for colon cancer.

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

- A larger degree of research interplay between WP3 approaches could be wise. Prioritize which models in WP3 that have the largest potential for further CARPEM research towards clinical implementation and pursue these in a more concentrated and integrated effort.
- Move to more prospective clinical trials – like the national PEMBROSARC and CIRCULATE trials, but also smaller CARPEM-initiated trials testing discoveries prospectively and capitalizing on the phase I unit at the Georges Pompidou hospital.
- Downscale CARPEM efforts in WP4 due to modest progress? May give opportunity to re-direct resources.
- Increase the communications activity towards the public.
- Inter-SIRIC collaborations could be increased.

	<ul style="list-style-type: none"> All together the IRP2 gets a strong “Very good” rating.
INTEGRATED RESEARCH PROGRAMME 3: Dynamic consent and health democracy	
	<p>Comments:</p> <ul style="list-style-type: none"> The original design was innovative and very interesting; involving the patient perspectives on giving dynamic consent to broad participation in continuous translational research. Further to study the patient aspects of combining and sharing data, the design of a dynamic consent serving these purposes, and its testing in two selected cancer patient cohorts combining data from a clinical questionnaire with data from the large NutriNet-Santé study. However, the programme has run into serious startup difficulties due to need for major renewal of the instrumental ATEB board members and an ongoing revision of the appropriate national legislation from 2016. Some of these difficulties could have been foreseen and affected design and planning? Achievements thus appear limited to a very limited enrollment of Lynch syndrome and solid tumour patients, with an invitation for these to also join the NutriNet-Santé study. Unclear what the actual status of the development of the dynamic consent is right now. Progress has been limited with 7/15 deliverables being considered as delayed by this reviewer and only 8 publications directly related to IRP3 being listed. The action plan for period 2 does not seem to be altered so far, but a scheduled programme meeting this October will discuss and evaluate. Given the progress so far the further progress of IRP3 must be regarded as uncertain. No inter-SIRIC collaborations listed. The communications plan is aimed a lot towards the public, but has naturally been slowed down like the rest of IRP 3. The programme concept is interesting and valuable, but the design and progress so far appear weak. <p>Specific recommendations for the 2nd period of the SIRIC designation:</p> <ul style="list-style-type: none"> Carefully evaluate the programme and re-focus as appropriate. Prioritize further realistic deliverables and monitor progress carefully. Patient cohorts, target numbers and end points may need to be reviewed.

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:

- Patient volume for clinical research is as far as I can see not directly addressed in the report, but from the CARPEM website the HEGP and Cochin hospitals together have approx.. 8300 new cancer patients a year, and the Necker hospital has a significant number of haeme oncology patients and high clinical research activity (numbers not stated). The clinical part of CARPEM thus has a patient volume in the upper range of European Comprehensive Cancer Centres.
- Clinical trials are often multicenter national projects which of course helps adequate patient numbers.
- It is stated in the report that research interactions between clinicians and lab researchers are challenged by the many locations within CARPEM.

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

- The multiple locations issue needs active intervention through e.g. scientist exchange programs, particularly for clinical-lab interactions.

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:

- All IRPs appear to have an appropriate multidisciplinary composition given the topic of the programme.
- However, the actual specified tasks and contribution of the clinical partners in IRP 1 and 2 are unclear.
- No defined programme to educate lab researchers and clinicians in their reciprocal activities to aid integrated research.
- The numerous clinical and research locations are surely a challenge to optimal interaction.

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

- Better define the roles and responsibilities for the interacting scientist categories.
- Strengthen reciprocal education between lab and clinical collaborators.
- Ease the locations burden by periodic exchange of scientists.

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:

- Epidemiology and public health are prominent disciplines in IRP 1, and social sciences, public health and epidemiology are prominent in IRP 3.
- Results of these sciences are prominent in IRP 1 (epidemiology and cancer impact of obesity and nutrition, including identification of biomarkers). IRP 3 has so far problems in its general progression, but has established an integration of two patient cohorts with the large epidemiological Nutrinet-Santé study.
- These sciences are not an active part of IRP 2, which is a more mechanistic scientific programme on cancer heterogeneity and resistance mechanisms. In this context IRP 2 does not quite comply with all the overall intentions of the SIRIC call, and could have had a stronger epidemiological/social sciences component. However, as a more prioritized approach is recommended by this reviewer for IRP 2, adding new projects at mid-term seems unwise.

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

- No specific recommendations.

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:

- Active involvement of patients combined with a continuous discussion of ethical aspects of translational research is a strong feature of CARPEM, with its Advisory Translational Ethics Board (ATEB) interacting with the Steering Committee. Although the ATEB represents a splendid concept it has not had a consistent membership, and has needed extensive replacement of members over the first SIRIC period.

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

- No specific adjustments recommended.

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:

- CARPEM has extensive national and international collaborations, also helped by the strong international profile of several of its lead scientists. CARPEM scientists have lead roles in several large national clinical trials involving strong biomarker research.
- International collaborations appear to be mostly by project, without regular overarching CARPEM contacts.
- Strong national and international co-authorship in IRP 1 and 2 publications.
- Also collaborative activities with the regional Cancéropôle.
- Only moderate inter-SIRIC collaborations of IRP 1 and 2 with SIRICs CURAMUS and SOCRATE, and with CURIE in training of molecular medicine for clinicians.
- Public-private partnerships appear numerous and strong on the funding side (with companies, foundations), but more limited as regards direct research collaborations. Patents based on CARPEM discoveries are numerous, but no spin-off startup companies are listed

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

- Increase inter-SIRIC collaboration on a project basis where appropriate and promising.
- Promote and support spin-off company creation. Unclear whether there is an adequate infrastructure and support for spin-off formation – improvement 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:

- CARPEM has an excellent public website which appears informative and well updated for the scientific community and the public.
- In general the programme for dissemination of knowledge is extensive and very good towards the scientific community, with multiple seminars and teaching activities.
- Dissemination to the patient organisations and the general public is much more limited both in scope and volume (some information videos on the website etc.).
- Exposure in news/media not mentioned.

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

- Increase communication, information and discussions (seminars etc.) with the general public, not only regarding individual research activities, but also around CARPEM and its importance as a collaborative organisation.
- Actively seek media exposure, may also be beneficial for funding.

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:

- CARPEM has a quite long list of collateral funding obtained from a multitude of national sources (regional and national public bodies, institutional grants, foundations, private companies etc.). The funding achievements are probably realised both through the excellence of individual research groups and the SIRIC designation.
- However, it is unclear if some of this collateral funding is shared with other projects outside CARPEM. The report quite clearly states (p. 6) that current funding is insufficient for all the planned research activities.
- Only two EU grants are listed; this reviewer would have expected more.

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

- Increase the number of grants, particularly from EU. If not already present, develop a good support program and infrastructure for grant application writing, particularly for EU calls.

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:

- The scientific directions in the three IRPs are generally very good to excellent in relation to SIRIC programme objectives, and should be pursued with some suggested adjustments.
- Results at mid-term in relation to the list of the original deliverables in IRP 1 and 2 are very good, but inadequate for IRP 3.
- Some suggestions from the Scientific Advisory Board (SAB) are mentioned in the report and are being pursued for period 2.
- All three IRPs have potential and probability for delivery of high level integrated research and dissemination in period 2, including developments of importance for patient care and for the development of an optimal consent structure for dynamic translational research.
- CARPEM's long term vision following the designation period is both excellent and realistic: development towards OECl accreditation of a new Comprehensive Cancer Centre under the name "Cancer Institute of Paris CARPEM", securing continuation and further development of integrated cancer research in tandem with high quality clinical care. This process is already initiated and is strongly supported by this reviewer.

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

- IRP 2 is recommended to undergo some project prioritization within the CARPEM framework.
- IRP 3 needs some prioritization and re-structuring including and probably a revised realistic work plan.

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:

- The financial report is hard to understand: In general the mid-term report states lack of funding for planned CARPEM activities (section 1.5 p.6) , but the financial report seems to show an accumulated underspending of approx.. €1 100 000 by June 2020?

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

- No recommendations feasible.

General comments and recommendations

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

A few high level recommendations:

- The report is detailed and very informative, and also outlines some acknowledged challenges. Some descriptions of individual projects and accomplishments are too detailed. The specification of the relationship of project accomplishments to scheduled deliverables is very valuable.
- Funding challenges: prioritization of projects (particularly in IRP 2) and re-structure (IRP 3) can probably allow for re-allocation of resources. Also, strengthen grant writing.
- Geographical challenges / collaboration between many sites: establish scientist exchange programs, including for clinicians to labs. Co-locate activities and scientists if possible.
- Better define the roles, responsibilities and modes of interaction between lab researchers and clinicians/public health/epidemiology/social sciences, i.e. optimize the integrated research further through leadership and structuring of multidisciplinary: “not only take part, but how to take part”.