

19 February 2019

Evaluation of the Luxembourg Institute of Health (LIH) – Synthesis Report on the Institute Level

Report by the external peer review committee

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technopolis _{group} February 2019

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Executive summary

This report presents the results of the peer review of the Luxembourg Institute of Health (LIH) and is part of an evaluation of the three Luxembourg Institutes (LI) (the former CRP's LIH, LISER and LIST) under the responsibility of the Luxembourg Ministry of Education, Science and Research (MESR). The evaluation covers the period 2014-2017 and considers scientific performance, relevance for society, including client and partner interaction, and the governance and organisation as requirements to sustain the ability to and suitability for promoting scientific performance and interaction with clients.

The audit was performed by an independent external assessment committee, consisting of five internationally renowned researchers in their fields, Professor Rudi Beyaert, Doctor Gabriele Anton, Professor Pierre Hainaut, Professor Patrick Rossignol and Professor Helle Ulrich. The first four of these committee members each also chaired one peer review of the departments of LIH, which took place in the months prior to this institute review, and the results of which are written up in separate reports. Fritz Ohler, Geert van der Veen, Anke Nooijen and Janna van Belle (Technopolis Group) acted as support for the peer review Committee.

The committee concludes that LIH has performed on a very good level during the current evaluation period (2014-2017). However, despite its clear excellence in basic research, the committee is of the opinion that LIH has only addressed parts of its stated goals and missions. Indeed, these missions were too broadly formulated and covered several aspects that LIH could not cover on its own. Thus, during the evaluation period, LIH has essentially conducted research activities that were largely similar to those of academic research institutions, e.g. universities, in both their scientific objectives (publications, academic impacts) and their management model (project-oriented, rather than program-oriented).

The committee welcomes the new mission statement formulated in the PC1821. The committee considers that this new statement has the dual merit of building on the foundation of excellence in research achieved under the previous contract, and of outlining a clear perspective for the realistic development of these strengths for the next 5-10 years. Specifically, the PC1821 identifies that the activities of LIH should be geared towards patient-centred translation and application to both public health and personalized medicine. It also clearly states that LIH has to better cooperate with other institutes and stakeholders in developing a thriving health sector in Luxembourg. Although the key mission statement is still very broadly formulated (to put Luxembourg at the forefront of biomedical research and create a translational hub in the heart of Europe), the specific initiatives that are presented as part of this mission of LIH for 2018-2021 are clearly defined and provide adequate focus for being used as a guide for defining priorities in the construction of the management structure, the prioritization of the work programme and the allocation of core resources.

This new model nicely showcases the two main dimensions of LIH (basic research and translational research). However, one concern the committee has is that it is not fully clear how some of LIH's activities related to population health fit or feed into this model. In particular, activities such as collecting data and maintaining registries, epidemiological surveillance, surveillance of risk factors, prevention, early detection, development of supportive care, etc. do not clearly appear as part of the new strategy.

The success of the newly proposed strategy will be strongly dependent on a more optimal, efficient and transparent use of the very generous block grant that LIH receives from the government. Therefore, the Committee fully endorses the foreseen shift in budget distribution and allocation from a bottom-up to a top-down approach and reserving a big fraction for long-term strategic initiatives. In addition, LIH will only be able to succeed in its new mission if it can collaborate systematically and more intensively with the health sector (Ministry of Health, the hospitals, the health institutions), who should be convinced to collaborate with LIH by the Board of Directors (which has so far been too passive in this).

The Committee additionally recommends the following actions to support LIH in the process of repositioning itself, the most important of which are:

- Establish an External Advisory Board (EAB) to provide scientific, strategic, medical and market advice to the CEO and LIH prior to implementing the new strategy.
- Give careful thought to defining the missions for IBBL, and its position within the LIH organizational structure.
- Reform budget distribution and usage and use the block grant to stimulate or award implementation of long-term programmes.
- Create incentives and support for scientists to apply for European grants and/or to become more successful in this.
- Redirect the activities of the Business Development Office (BDO) to have more impact on innovation and offer incentives for researchers to focus on TT.

The following recommendations are aimed specifically at the Board of Directors and MESR:

- Develop a master plan for building a suitably located “health campus” gathering LIH, academic stakeholders and a value creation/innovation ecosystem of spin-offs and start-ups in the biomedical field.
- Ensure that the Board of Directors is better connected to the government, with the ultimate goal to provide them a clear view on the vision of LIH and enable interaction and collaboration between LIH and the Luxembourg health system.
- Encourage the Board of Directors to play a more active role in supervising the performance contract.

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1 Introduction and background

1.1 LIH

The Luxembourg Institute of Health (LIH) was formed through the merger of the biomedical research institute “Centre de Recherche Public de la Santé” (CRP-Santé), created in 1988 and the research infrastructure and biobanking service provider, Integrated BioBank of Luxembourg (IBBL) founded in 2008. This merger is effective since the 1st January 2015. With the merger, LIH became a single legal entity, however within this structure IBBL functions as an autonomous structure, with its own Chief Executive Officer (CEO), and its own performance contract.

With its more than 373 employees, LIH is the largest public research institute dedicated to biomedicine in Luxembourg. Striving for excellence, its researchers, by conducting basic and translational research, aim to improve patients’ lives, diagnosis, treatment, and to support the development and implementation of personalized medicine.

The LIH is composed of three large thematic departments: Oncology (DONC), Infection & Immunity (DII) and Population Health (DoPH). Besides, IBBL exists as a semi- autonomous structure. This structure was designed to enable it to assume its specific role of biobanking infrastructure and service provider (source: LIH SAR).

1.2 This peer review

The peer review is part of an evaluation of the three Luxembourg Institutes (LI) (the former CRP’s LIH, LISER and LIST) under the responsibility of the Luxembourg Ministry of Education, Science and Research (MESR). The evaluation covers the period 2014-2017 and considers *scientific performance*, *relevance for society*, including client and partner interaction, and the *governance and organisation* as requirements to sustain the ability to and suitability for promoting scientific performance and interaction with clients. The evaluation has been assigned to Technopolis Group (www.technopolis-group.com).

The peer review of LIH consists of separate peer reviews of each of the three departments of LIH (DII, DONC and DoPH) and of IBBL with a focus on scientific quality and innovation impact. This peer review at institute level provides an additional, overarching focus on strategy, relevance, management, organisation and governance. The peer reviews at department level have all been performed by teams of independent, external experts with a scientific or management background in one or more of the areas of interest of the department, supported by three evaluation experts of Technopolis Group. The peer review at institute level was performed by the chairpersons from the three department and the IBBL level peer reviews, and one peer not previously involved in the review.

The results of these four peer reviews inform the evaluation of LIH as an institute and also feed into the evaluation of the role of three LIs in the Luxembourg science and innovation system at national level.

The results are intended for MESR to (re)define their relation to LIH; for LIH to help fine-tuning its strategy and improve its performance further and for other (mainly public)-stakeholders to use as they find suitable.

The peer review set-up has been designed by Technopolis Group, based on the Terms of reference from MESR. It aligns with good practices used in many evaluations.

1.3 Composition of the Committee, independence, data provided, and procedures followed

1.3.1 Composition of the Committee

The audit was performed by an independent external assessment Committee, consisting of five internationally renowned researchers in their fields:

- **Rudi Beyaert** (chair, also chair of DII evaluation), professor in Molecular Biology at the University of Ghent (Belgium) and Deputy Director of the Center for Inflammation Research at the VIB, Ghent, Belgium
- **Gabriele Anton** (chair of IBBL evaluation) is head of the biobank group at the Institute of Epidemiology at Helmholtz Center Munich, Germany
- **Pierre Hainaut**, (chair of DONC evaluation) professor of Cancer Biology, Université Grenoble-Alpes; Director of Institute for Advanced Biosciences, Grenoble, France.
- **Patrick Rossignol** (chair of DoPH evaluation), professor of Therapeutics, Nephrologist and Vascular medicine specialist, head of Nancy Plurithematic Clinical Investigation center (CIC)-Inserm, France.
- **Helle Ulrich**, executive director of the Institute of Molecular Biology (IMB), Mainz, Germany.

Short CV's from all Committee members are attached in o.

Fritz Ohler, Geert van der Veen, Anke Nooijen and Janna van Belle (Technopolis Group) acted as support for the peer review Committee, Fritz Ohler with specific attention for governance and organisation.

1.3.2 Independence

Any existing personal or professional relationships between Committee members and programs under review were reported and discussed in the Committee meeting to safeguard an independent assessment of the quality of LIH in an unbiased and independent way. The Committee concluded that there were no close relations or dependencies and that there was no risk in terms of bias or undue influence.

1.3.3 Data provided to the Committee

In preparation of the review the peers received the following information:

- A self-assessment report of LIH at institute level.
- The self-assessment reports of LIH at department and IBBL level.
- A background report for the peer review of LIH prepared by Technopolis Group, including amongst other things an analysis of the participation of LIH in FNR and EC research projects and a bibliometric analysis of the publications of LIH.
- The draft reports of the peer reviews of the departments of LIH and IBBL.
- Additional material provided by the Institute at the request of Technopolis Group, including additional information on the valorisation strategy, the performance management system and details on the performance contract with the ministry, as well as a more detailed overview of the annual accounts.

The LIH review took place in a context of rapid change in its managerial approach and strategic planning, following the recent appointment of a new CEO of LIH¹. As a result, the Review Committee had to consider two different contexts: the state of LIH so far, its achievements and its current management and budget structure (corresponding to activities developed under the 2014-2017 performance contract (PC1417)), and the new strategic development plan put forwards by the new CEO (corresponding to activities to be implemented under the new 2018-2021 performance contract (PC1821)). The documentation made available to the peers prior to the review, and for the Department

¹ Ulf Nehrbass: CEO of LIH excluding IBBL

reviews, were essentially corresponding to the former context, whereas information on the latter context was presented and discussed verbally during the site review meetings. This gives the Committee the uneasy task of commenting and making recommendations on a number of critical issues that have been presented only verbally and in PowerPoint slides. Nevertheless, the Committee will address in this report both contexts, underlining the strengths and weaknesses of the current situation, and will provide a general assessment of the appropriateness of the future strategy².

1.3.4 Procedure followed by the Committee

The final assessment is based on the documentation mentioned above and the site visit to LIH in Luxembourg on 16-17 October 2018 (programme of the site-visit in Appendix C). At the end of the site visit and interviews the Committee elaborated and discussed the conclusions and recommendations. Draft conclusions were presented to the management team of LIH and representatives of MESR and the Ministry of Health at the end of the visit.

A first version of this report was drafted by the peers in the weeks after the site visit to Luxembourg. The report was finalized through email exchanges. The result of these exchanges was presented to the Institute in December 2018. The reaction of LIH was discussed by email by the Committee and led to adjustments of some factual points. The final report was submitted to MESR.

² Described in section 5 of the LIH SAR, p 43-53.

2 Rationale and needs

2.1 Mission and strategy of the institute

The relation between MESR and LIH is laid down in a performance contract. The initial 2014-2017 performance contracts of CRP-Santé and IBBL were signed with the MESR before the merger of both institutes in 2015 into LIH. A new performance contract has been signed in January 2018 (PC1821). Thus, the two performance contracts are of relevance for the current evaluation; the former contract defines the framework for evaluating activities carried out during the review period, whereas the new contract defines a framework for assessing the strategic vision and future plans put forwards by LIH CEO and scientific leaders.

The missions of LIH as stated in the PC1417 was *'to deliver scientific, economic and societal value for Luxembourg by performing research, studies and developments in the fields of clinically-oriented biomedical research and public health'*. The former CRP-Santé had developed the following strategic goals for the organisation in the frame of the performance contract 2014-2017:

- to continue its excellence in biomedical and translational research which is recognized by the international scientific community, while at the same time creating economical and societal value for Luxembourg,
- to be the national leader in biomedical and clinical research, implementing new clinical trials and personalized medicine in our country in close collaboration with hospitals, health care providers and other national and international actors,
- to be the first supplier of public health information in Luxembourg, enabling public authorities to make decisions based on scientific data and to communicate validated data to international institutions,
- to be a reliable and active partner for training of young scientists and higher education in close collaboration with national and international universities.

According to this performance contract, the activities of LIH are geared towards the generation of new knowledge in disease mechanisms, epidemiology, diagnostics and treatments of human diseases, and towards improving the understanding of health determinants and of the financial structures of health care.

The mission of IBBL as stated in the PC1417 was *'to provide accredited biospecimen-related services and a biobanking infrastructure for applied medical research'*. IBBL's vision is to be an international centre of excellence in biobanking and a valued partner in developing better healthcare solutions. IBBL expressed three high level strategic goals within their PC1417:

- To support Luxembourg biomedical research (including LIH research goals)
- To grow collections and revenues
- To contribute to increasing Luxembourg's visibility on the world stage

The overall vision underpinning the PC1821 is *to put Luxembourg at the forefront of biomedical research and create a translational hub in the heart of Europe*. The key mission assigned in this new contract is *to conduct excellent medical research for the benefit of patients in Luxembourg and beyond*. This mission is conceived as an expansion and redirection of the former PC1417 mission, stating that *during the next 4 years LIH will expand on this [former] mission both by further improving on the scientific excellence of its research effort, and by moving closer to the patient*. Specifically, this key mission statement requires that *patient-centric and application-inspired research should become the distinguishing characteristic of LIH in the Luxembourg research landscape, advancing it further from its basic research efforts*.

Thus, compared to the PC1417, the PC1821 places a much stronger emphasis on translational and application research for the benefit of the patient, whereas it re-iterates the objective of excellence in

basic research. The overall thrust of this new vision and mission is to *help nucleate a thriving health sector in Luxembourg*.

The PC1821 identifies 3 key strategic initiatives for LIH research (excluding IBBL):

- Aligning the LIH activity portfolio with the strategic priorities of Luxembourgish research. In cancer, this will be reflected in an increased engagement in the area of immune-oncology. In the inflammatory research field, activities will extend to gut inflammation and neuro-inflammation, creating stronger synergies between Luxembourgish institutes (e.g. LIH-LCSB).
- Increasing and developing transversal programs addressing patients' unmet medical needs, with the primary goal connecting clinical with fundamental research work through patient-oriented *bed-to-bench-to-bed* cycles, supported by the implementation of patient-based disease modelling and novel approaches for personalized treatment choices.
- Improving the framework for patient-oriented work by promoting a closer alignment of IPR policies amongst Luxembourgish institutions, by exploring new funding tools which could help the drive for *tangible* therapies and by promoting the opportunities that a coordinated move towards digital health would hold for Luxembourg.

The PC1821 also specifies that LIH should place an emphasis on communication to the *Grand Public* in order to explain to Luxembourgers the value of fundamental and patient-centred medical research and to attract pupils and young students more into medical research.

For IBBL, the PC1821 does not identify any more distinct missions compared to its PC1417 mission statement. Its strategic domains defined in the PC1821 are somewhat closer aligned to those of LIH:

- Continue to support Luxembourg research by serving the current programs, and foster initiation of new ones in particular with translational aspects within LIH;
- Be a preferred European partner for accredited biospecimen related services and biobanking infrastructure.

2.2 Appropriateness of goals and missions

These missions were too broadly formulated and covered several aspects that LIH could not cover on its own. Thus, during the evaluation period, LIH has essentially conducted research activities that were largely similar to those of academic research institutions, e.g. universities, in both their scientific objectives (publications, academic impacts) and their management model (project-oriented, rather than program-oriented). With respect to the evaluation of the work performed under the PC1417, the committee is of the opinion that LIH has only addressed parts of its stated goals and missions.

The committee welcomes the new mission statement formulated in the PC1821. The committee considers that this new statement has the dual merit of building on the foundation of excellence in research achieved under the previous contract, and of outlining a clear perspective for the realistic development of these strengths for the next 5-10 years. Specifically, the PC1821 identifies that the activities of LIH should be geared towards patient-centred translation and application to both public health and personalized medicine. It also clearly states that LIH has to better cooperate with other institutes and stakeholders in developing a thriving health sector in Luxembourg. Although the key mission statement is still very broadly formulated (*to put Luxembourg at the forefront of biomedical research and create a translational hub in the heart of Europe*), the three specific initiatives laid out as the main thrust for the efforts of LIH for 2018-2021 are clearly defined and provide adequate focus for being used as a guide for defining priorities in the construction of the management structure, the prioritization of the work programme and the allocation of core resources.

The committee however notes that the key performance indicators as specified in the PC1821 fall short of the key mission and of its three specific initiatives. For example, the performance indicators include only:

- 5 patents or licence agreements with potential for value creation
- 1 clinical trial per year in which LIH plays a leading role (but not strictly as sponsor)
- 2 positions per year for clinician-researchers with joint affiliations at LIH and at one hospital in Luxembourg.

These numeric indicators are in line with the level and type of activities as developed under the former PC1417 but are not aligned with the scope and ambition of the mission of the new PC1821. It is therefore doubtful that fulfilling these indicators will be an adequate marker for the expected impact of LIH on patient-centred translational research. In particular, being involved in only 1 clinical trial per year is an extremely low objective, and does not reflect LIH's aim to develop an ambitious translational program, as depicted in the key initiative number 3 of the PCI1821: "Within *LIH, patient-oriented bed-to-bench-to bed cycles will be reinforced through the implementation of patient disease modelling, as well as through novel approaches allowing for personalized treatment choices in cancer*". By comparison, the annual portfolio of clinical trials developed by Clinical Investigation Centres in university hospitals within a 200 km radius of Luxembourg includes several dozens of trials. LIH's ambitious objectives cannot be met if the LIH is leader of only 3 trials in 3 years. Each of the selected diseases (each cancer type being by itself a standalone disease for instance) should be addressed by at least one or ideally 2 to 3 (ensuring consistency in the effort) trials led by the LIH in 2018-2021.

They should be the basis for 5-years resource programming, with anticipation of how the missions may evolve in an incremental manner over time. Careful thinking and planning should take place in defining the role for IBBL, and its position within the LIH organisational structure. The redefined LIH mission should be reflected in both the organisational structure of LIH and in the spending plans.

2.3 Mid/long-term goals and mission

Mid- and long-term plans were presented to the Committee in the form of a written report, which was vastly augmented, clarified and put into context by the oral presentation of the CEO's long-term vision and plans for repositioning. However, the full description of this vision and plan was not made available to the Committee ahead of the meeting and therefore the Committee is not in a position to provide the expected degree of in-depth reviewing of the strategy. The following general comments therefore present a partial appraisal of the mid/long-term plans.

2.3.1 Strategic vision

Overall, the Committee welcomes very much the ambition presented by the CEO to develop an integrated scientific and strategic vision for LIH as a whole. The vision and strategy are clearly well aligned with the mission statement of the PC1821 and its three key initiatives. The committee perceives well the coherence between the mission statement of the PC1821 and of the strategic vision, highlighted by the usage of the same catch-words and sentences in both documents. The essence of this vision relies on the reorganisation of the institute on the basis of its two core missions: basic research and translational research. In terms of organisation structure, it builds on the current organisation model by overlaying a transversal, translational programmatic approach onto the current vertical departmental structure. In other words, it re-designs the structure of LIH according to a 2D-matrix in which the departments are the vertical dimension and the translational programs the horizontal dimension. The horizontal dimension follows a clear translational logic, from bench to bedside and also incorporates a knowledge development model across Technology Readiness Levels (TRLs).

This new model nicely showcases the two main dimensions of LIH (basic research and translational research). It also provides an interesting framework for reallocating resources between these two dimensions and for increasing access to competitive external resources for both basic and translational research.

The coherence of the vision owes much to the managerial approach of the CEO. His presentation provides a clear narrative to which most (but not all) current research activities can easily relate. This narrative is a powerful motivational instrument to implement changes across the structure of LIH while

allowing key leaders to adhere, participate and contribute. The Committee notes that the vision is supported by department heads, who are taking it on board in their department agenda.

However, it is not fully clear to the Committee how some of LIH's activities related to population health fit or feed into this model. In particular, activities such as collecting data and maintaining registries, epidemiological surveillance, surveillance of risk factors, prevention, early detection, development of supportive care, etc. do not clearly appear as part of the new strategy. Likewise, it is unclear how the new strategy will incorporate (or not) the activities of DoPH and DII contributing to population health in the form of service contracts, research, surveillance, and membership of European public health networks.

2.3.2 *Scientific positioning of the strategic vision*

The strategic vision focuses on two target organ/tissues, gut and brain, and on specific diseases developing in these organs, including chronic immuno-inflammatory diseases and cancer. Keywords include immunity, microbiome, molecular mechanisms, patient-oriented approaches, biomarkers, disease models. This positioning captures many of the current scientific forces and areas of excellence of LIH (but not, importantly, cardiovascular research).

Whereas the CEO explained how his strategic vision could accommodate several parallel translational programs, the flagship programme appears to consist of an ambitious project for functional profiling of *in vitro* responses of patient-derived tissues to drugs in order to inform therapeutic decision. This approach is potentially applicable to cancer and neurodegenerative disease. The positioning of this approach is clearly aligned with the key initiatives as specified in the PC1821. However, with the limited information that is provided during a short presentation by the CEO, the Committee feels unable to fully assess the readiness of LIH to set up this specific flagship program and to make the difference at the international level. It clearly perceives its originality and merits but questions its feasibility and its capacity to actually deliver the expected translational value. Also, the Committee notes that implementing such a flagship programme will require heavy investment in several areas such as cell and tissue imaging, artificial intelligence and metabolomics. It is not clear how these investments will be leveraged.

To address these issues as well as to enable the development of other translational programs, the Committee recommends that prior to implementing this proposed new strategy, LIH establishes an External Advisory Board (EAB) comprising a small number of undisputed international experts in translational research and in public health and in which key local stakeholders could have an observer status. The terms of reference of this EAB will be to provide scientific, strategic, medical and market advice to the CEO and LIH management team on the development of the different translational programs. The EAB could operate as the critical "go/no-go" recommendation board in prioritizing translation projects and in pushing them forwards along the Technology Readiness Level (TRL) scale. Experts should be ready to commit an equivalent of about 10 days/year for this task. The EAB should be put into place for the duration of the entire programme cycle (5 years) and should not be just operating ad-hoc, but be integrated as part of the management structure of LIH.

With regard to research outside of the translational programs, there is a need to develop a vision on how some of the population health research taking place in LIH can be incorporated in the new translational strategy. In this context it is surprising that the PC1417 Key Performance Indicator (KPI) "*Develop a strategic plan on public health*" was considered not needed in PC1821. The same is true for the KPI "*New active engagements in EU public health networks*", which was not maintained in PC1821.

2.3.3 *Identified risks*

The Committee appreciates and supports the bold change in direction signalled by the strategy proposed by the CEO. They however identified a number of issues that, if not correctly anticipated, could jeopardize the strategy and also destabilise the structure of the organisation. These include the following risks, in order of the perceived threat they pose to LIH's mission and new strategy of LIH:

- Insufficient involvement of medical experts in Luxembourg itself and limited infrastructure for clinical trials in Luxembourg hospitals
- Difficulties implementing the strategy in the current, dispersed spatial infrastructure of LIH

- Development of an international programme that is disconnected from public health concerns in Luxembourg, therefore undermining its perception and its capacity to drive the development of the national health system
- Failure to implement translational programs due to insufficient buy-in by people who work within LIH
- Difficulties in aligning the translational and innovation strategies among different actors and stakeholders in Luxembourg
- Insufficient access to patient's samples due to lack of Luxembourg-based resources and of constraints on sharing and accessing specimens from international sources
- Inability to recruit high-quality experts, e.g. in artificial intelligence
- Insufficient reference investors/incubators who may assist in leveraging funds beyond Proof of Concept (e.g. EU marking for medical devices, clinical trials, market analysis, early adopters, etc.)
- Lack of adhesion and participation of LIH across all categories of staff
- Need for heavy investment in several expensive and competitive areas, including equipment (often rapidly outdated and coming with large maintenance contracts) and data management resources
- The destabilisation of translational programs due to mobility of PIs or key staff

2.4 Appropriateness of the proposed strategy

During the past 5 years LIH has done well in striking a balance between its broad mission and the necessity to focus its activities on a small number of “niches” corresponding to domains of excellence. The value of this approach is demonstrated by the overall quality of publications and academic impacts across departments. It is to be noted that this focusing effort has been achieved despite a certain lack of integration and communication across departments. Thus, each department has made its priorities independently of others.

Strengths that come up strongly across all departments include:

- Excellence in basic research, with significant achievements in each department, demonstrated by the overall bibliometric impact and by several high-profile scientific publications
- Quality and expertise of PIs, research and support staff
- International recognition and outreach through strong partnerships at regional and broader European level
- Capacity to recruit excellent scientists and attractiveness for students and postdocs
- Overall good working atmosphere
- Establishment of attractive PhD programs

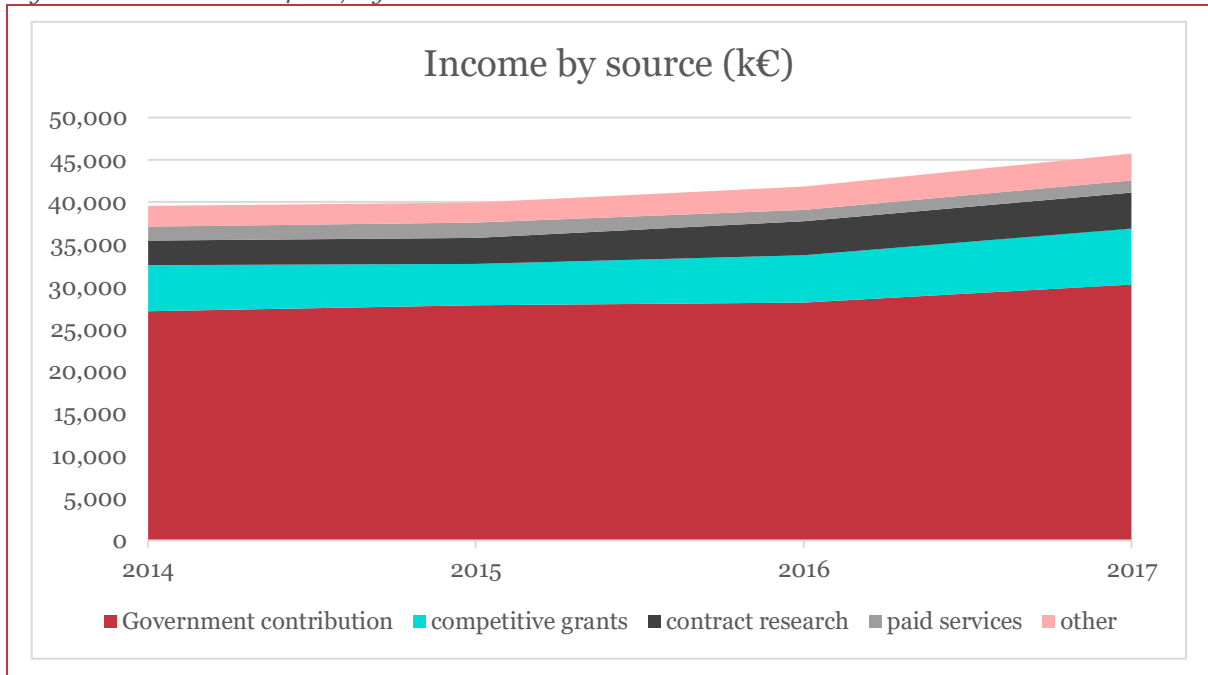
Common weaknesses across all departments include:

- Limited societal and economic impact in terms of translational and clinical outputs and of innovation/value creation (patents, start-ups)
- Lower-than-expected effectiveness in accessing international funding (e.g. H2020) and in obtaining competitive and internationally recognised status such as ERC grants
- Insufficient communication and exchange within units/groups in each department, between departments, and between departments and the LIH administration

2.4.1 Budget usage

In terms of actual budget resources, the peers note that, of the total consolidated budget of 45.7 M€, only 6.6 M€ (15%) comes from competitive grants³. Of those, EU grants (H2020, ERC, etc.) represent only 8% (1% of the total consolidated budget). Contract research (identified under the definition of “collaborative research”) brings in another 4.2 M€ (9%). It is not clear whether such “collaborative research” is covered at 100% by these contracts based on a full cost model (in other terms, whether part of the block grant is being used for funding “collaborative research”). Paid services represent 3% of the total budget (1.4 M€). **Error! Reference source not found.** shows LIH income by source.

Figure 1 Income LIH 2014-2017 by source

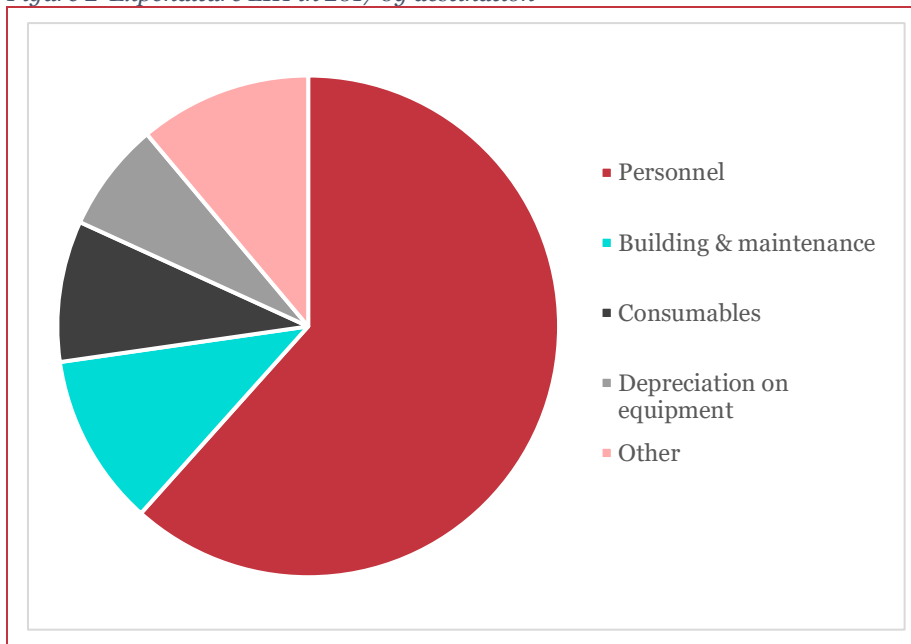


Source: LIH SAR

Personnel costs represents 61% of the total expense, and consumables for research 9%. Administrative, infrastructure and organisation costs represent about 28% of the total spending. A quick calculation indicates that the part of the block grant that is directly allocated to research departments and units amounts to about 45% of the total resources.

³ Source: LIH SAR

Figure 2 Expenditure LIH in 2017 by destination



Source: LIH SAR

Overall, the Committee notes that, while most of the research performed by LIH belongs to a type of research typically funded by competitive grants, the proportion of funding that comes from competitive grants is only 15% of the total.

Budget mechanisms appear to be unduly complex and not easy to understand for outside reviewers. The provision of a block grant of about 30M€/year and representing about 66% of the total income appears to be a very comfortable and healthy situation, which should in principle provide LIH with leverage for risk-taking and investment in innovative programs. However, in practice, most of this budget is committed to the salaries of permanent staff, thus effectively limiting the flexibility for reallocating budget across activities. This is compounded by the piecemeal approach in which the budget is being assembled. Thus, a reform in budget planning and in the mechanisms for constructing spending plans is needed.

The overall aim of such a reform should be:

- to better align actual spending with major milestones and deliverables of the scientific program
- to reduce budget and strategic fragmentation
- to provide stronger incentive to researchers for accessing internationally competitive funding
- to foster better transparency in resource allocation and prioritisation throughout the institution
- to enable strategic investments (e.g. recruitment of new PIs with unique expertise, implementation of new technological developments)

3 Scientific research and collaborations

3.1 Research agenda

Over the past 5 years, there has been no clearly defined LIH-wide research agenda. Partly inherited from the bottom-up organisation of research in the previous CRP-Santé, the strategy for the performance contracts (PC) 2014-2017 was based on input from department heads and leading PIs. The result in terms of research strategy was a focus on both **translational research in general** “*To enhance the translational aspects of CRP-Santé’s research activities transforming CRP-Santé over the next 4 years in a genuine translational biomedical research organisation able to lead the implementation of personalized medicine in Luxembourg*”, **clinical research** “*to take a leadership role in clinical research in close collaboration with other national partners (hospitals, university, IBBL ...) and become recognised in this domain at an EU level*” and **public health research** “*to develop a sound strategy for a state-of-the-art public health research firmly implemented in the EU context and serving the needs of the country*”.

This broad scope was reinforced by a departmental policy to focus and streamline existing research domains, strengthen the existing departments and allow them to reach critical mass to excel in their respective areas of expertise. As a result, research within LIH currently consists of a large number of good, but rather unconnected and sometimes overlapping research projects, which appear primarily driven by departmental strategies.

For researchers this fragmentation leads to a lack of critical mass working on the same topic in some areas of LIH research. Here a clear focused and well-communicated research strategy would support researchers in (re-)positioning themselves, allowing them to build up critical mass in areas relevant to LIH’s strategy. The Committee notes that the new strategy proposed by the CEO potentially addresses this issue. The Committee strongly recommends that the consequences of LIH’s new strategic direction for existing research are made as concrete as possible and communicated in a continuous fashion to the LIH research staff, enabling them to be actively involved in the dynamics of change. LIH plans to focus on diseases of the brain and gut, which are programs that can be thematically shared between departments and partner institutions to productively link up to clinical partners. Importantly, this will require the reorganization or reorientation of several groups that are now working on other tissues and diseases (e.g. cardiovascular disease).

In terms of research quality, as documented in each of the department’s reviews and in the review of IBBL, LIH has consistently performed in delivering good to excellent research. Over the past 5 years, LIH has built a strong, coherent and visible portfolio of complementary research activities, which collectively have placed Luxembourg in a visible position on the European map. It has also achieved remarkable success in recruiting excellent young team and group leaders, providing a strong backbone for future developments. Whereas the main focus of these activities has been on basic research, it is fair to state that LIH has fulfilled the part of its missions that are within its range of skills and expertise.

In contrast with its successes in basic biomedical research, LIH has so far achieved only relatively modest outputs in providing national leadership in translational and clinical research. Similarly, LIH has only to a limited extent implemented new clinical trials and personalized medicine in the country in collaboration with hospitals, health care providers and other national and international actors. As explained above, LIH in its current structure does not have the resources and leverage to fully deliver in this respect. In order to progress in fulfilling these missions, major developments will need to be made in the medical and healthcare systems, providing bridges for translating the expertise of LIH scientists into clinical trials and progress in the development of personalized medicine.

The assessment of research quality at the department level has been in part based on numeric indicators for (1) the impact and (2) the number of scientific publications. Other factors taken into consideration were originality, coherence, scientific positioning and leadership.

Results from the PC1417 show that LIH outperformed the targets which were set in terms of impact factors, apart from the KPI “% of publications with $IF \geq 2$ with 1st or last author from LIH”. In PC1821 this KPI has been replaced by the KPI ‘Number of joint peer-reviewed publications with other national

research institutions”. Although an increase in collaborative efforts is crucial for the success of LIH’s new translational strategy, the number of publications led by LIH (i.e. publications with a 1st or last author from LIH) as formulated in the PC1417 KPI remains important for the international visibility of LIH, and it is recommended to keep this as a KPI.

In terms of the number of publications, LIH has easily reached the target set for research productivity, which was set as 0.7 publications with $IF \geq 2$ per FTE researcher. For the PC1821 this target has been increased to 1, which is close to the 2017 achievement of 0.99. In order to avoid any tradeoff between quantity and quality, the Committee recommends emphasizing high quality research outputs (e.g. impact on the field, reflected by citations, new collaborations...) over purely numeric indicators of research productivity, and to have this reflected in the KPIs.

As for the IBBL, it is a strong player in the international biobanking field (both at the processing and storage level) and among the best in the world with regard to its engagement in biospecimen quality and method standardisation. Considerable investments have been made with regard to equipment and personal efforts which should be widely used by the Luxembourg research community, not only by LIH. Unfortunately, the use of the IBBL within Luxembourg is rather low, because the IBBL has targeted mainly international collaborations, although it should be noted that MESR in the performance contract 2014-2017 specifically asked IBBL to develop this external visibility by getting Horizon 2020 funding and signing contracts with third parties. Also, the lack of clinicians, and clinical research plays a role in the low use of IBBL in Luxembourg research. LU and LIH researchers could benefit a lot more from working together with the IBBL to improve biospecimen quality and to make use of the IBBL’s international visibility and should be encouraged to do so. Currently the IBBL already provides some support to LU research, but besides large NCER-PD (funded by FNR) and Cancer collections, these are most small-scale projects and not really visible or communicated extensively. An important opportunity that could benefit both LIH and the IBBL would be common grant proposals, both on national as on European level. In the light of the new translational approach of LIH, the IBBL should serve not only as biomaterial but as data centre for LIH that collects all kind of data related to patient samples, e.g. clinical, pre-analytic and analytic data and makes these data available for research projects. It should encourage and coordinate analysis of the precious samples and take care of secure storage of and controlled access to the data.

3.1.1 *International cooperation and networks*

To assess LIH’s position within the international research community the Committee has used the number of international research projects and the number of co-authored international publications as indicators.

As mentioned in section 2.4, with respect to the number of international research projects, LIH has a lower-than-expected effectiveness in accessing international funding (e.g. H2020) and in obtaining competitive and internationally recognized status such as ERC grants. During the period of evaluation, LIH successfully submitted four H2020 projects (2016 and 2017), always as partner: two projects in research departments and two in IBBL. According to the Interim Evaluation of H2020 (2017), average success rate across Europe was 11,6%. With 4 projects out of 41, LIH lies close to this score. However, two of the successful projects are held by IBBL (out of 10 submitted), providing research infrastructure with the biobank rather than specific research expertise or leadership. This means that for the rest of LIH, research-active departments have only received two out of 31 projects which is below the average success rate and presents an overall poor level of performance. That 41 projects were submitted ascertains a good visibility at the international level, however, visibility of LIH definitely need to be based on a higher success rate in international grant applications in which LIH research (and not only supporting infrastructures like IBBL) play a key role. In this context, initiatives should be taken to encourage (e.g. by co-funding or other incentives) and support (e.g. training, feedback from peers, ...) PIs to participate in H2020 funded networks and apply for prestigious ERC Starting/Consolidator/Advanced grants.

With respect to the number of co-authored international publications it is noted that LIH is very successful in collaborative research. This is illustrated by table 1, which shows the distribution of LIH’s international co-publications over 4 citation classes. The four classes stand for ‘poorly cited’ (CSS 1), ‘fairly cited’ (CSS 2), ‘remarkably cited’ (CSS 3) and ‘outstandingly cited’ (CSS 4) papers. Papers in class 3 and 4 can be considered highly cited. As a reference, the standard distribution within a comparable organisation is 70% (Class 1), 21% (Class 2), 6%–7% (Class 3) and 2%–3% (Class 4). The distribution of LIH papers indexed in the Web of Science (WoS) clearly deviates from the above rule, the share of poorly cited papers is distinctly below the reference standard, while the share of papers in all other classes lies above the corresponding reference value. Usually, the papers in Classes 3 and 4 are considered highly cited and their share amount to about 9% in the total reference population. The corresponding share for LIH reaches 15.7%, which is much higher than other organisations of its size.

Table 1: LIH’s international co-publications over 4 citation classes

Department	CSS 1		CSS 2		CSS 3		CSS 4	
	Papers	Share	Papers	Share	Papers	Share	Papers	Share
DII	95	57.2%	43	25.9%	20	12.0%	8	4.8%
DONC	59	44.0%	44	32.8%	21	15.7%	10	7.5%
DOPH	111	51.4%	70	32.4%	21	9.7%	14	6.5%
IBBL	10	66.7%	1	6.7%	3	20.0%	1	6.7%
LIH	271	52.0%	157	30.1%	62	11.9%	31	6.0%

From the data above, the Committee notes that there is a discrepancy between the position of LIH in publishing internationally co-authored papers (which is excellent) and its actual success rate in accessing international grants such as H2020 (which is poor). The Committee interprets this as suggesting that developing a more aggressive strategy for accessing international grants should provide higher returns, compatible with the actual level of scientific excellence.

3.1.2 National cooperation and networks

In recent years, LIH has intensified collaborative efforts with the other research organisations in Luxembourg in order to address organisational aspects touching all actors of public research. LIH is an active participant of the 3LIU group, a regular working group of the leaders of the 3 research institutions (Luxembourg Institute of Science and Technology - LIST, Luxembourg Institute of Socio-Economic Research - LISER, LIH) and the University of Luxembourg (UL) to discuss topics of common interest. Numerous research projects at LIH are supported by the FNR (CORE, AFR, ATTRACT, PEARL, etc.). LIH is a key actor together with UL, LNS and hospitals in two major research initiatives: the National Centre of Excellence in Research on Parkinson’s disease (NCERPD) and Plan Cancer.

The interaction with the UL in the past period has been increased. In particular in recent years, LIH has established a productive work relationship with the Luxembourg Centre for Systems Biomedicine (LCSB), with whom it also shares certain core facilities like the mouse facility of LCSB. The UL-LCSB plays an important role for LIH in building translational capacity. In this context, a collaborative effort between LIH and LCSB on patient-based disease modelling (using isogenic patient iPSC derived disease models) financed by a recently approved FEDER grant is a nice example. Long-term research and training partnerships have been built with the UL via joint appointments (e.g. PEARL Neuropathology) and PhD supervision right agreements for researchers at LIH. The FNR PRIDE programme has been key to stimulate the process of creating joint PhD training programmes between LIH and UL and ensuring the set-up of a more structured doctoral education as defined in the National Quality Framework for Doctoral Training defined in 2015/2016. Two PRIDE programs coordinated by LIH are

currently financed, NextImmune and CANBIO. To streamline the competencies of the LIH researchers with the translational programs of LIH, the development of research-oriented training & higher education activities in close collaboration with the UL (e.g. involvement in PhD school and in the training programme of the planned medical school, training of young researchers) and other partner universities will be needed.

It will be important to promote a strong relationship with the hospitals, especially the Centre Hospitalier Luxembourg (CHL). In this context, the research strategy proposed by the CEO will play a central role in the implementation of a ‘Personal functional profiling’ (PFP) programme for glioblastoma and gastrointestinal cancers, where LIH’s platform of organoids and PDX mouse models will be integrated and where IBBL will serve to bank patient biopsies and collect a range of data. This approach, which incorporates LIH, Luxembourg hospitals, LCSB and LNS, will become a strategic pillar of LIH and will be followed-up in a multicentre application for a National Centre of Excellence in Research in Oncology.

The planned Luxembourg Centre for Clinical and translational Research (LCTR) with CHL will, if successful, result in a reorganisation of clinical research within LIH. Promising governance links with the medical sector have also been announced; the scientific steering committee (SSC), the translational steering committee (TSC), and the shared research director of the LCTR (between CHL and LIH) are examples of this and will reinforce collaboration and consistency in the implementation of clinical research implementation. However, the majority of information with regards to these plans has been communicated during the review visit, and the Committee has not been presented with all documents supporting these declarations of intent.

In spite of these prolific interactions in the Luxembourgish context it is fair to state that owing to its institutional evolution, 2014-17 has been more inward looking for LIH, establishing performant research structures inside the institution. In view of its new mission and focus on patients, LIH will need to be more focused on cooperation and shared strategies and goals with other Luxembourgish institutes and hospitals. As discussed in section 2.2, the presented KPIs clearly do not sufficiently target clinical research, with only 1 study sponsored per year by LIH set as a target during the four-year period (2018-2021). During the LIH assessment visit it was explained that the KPIs were negotiated with the Ministry in 2017, prior to the new LIH policy emphasizing translational research consideration. A reappraisal of KPIs is therefore warranted.

For the future of LIH, and a coordinated translational effort with LIH’s collaborating institutions in Luxembourg, a close and productive interaction with IBBL is absolutely essential. Also, the translational capacity of LIH cannot be fuelled by national projects only but needs to attract outside collaborations. Additional platforms and capacities have to be built up. International collaboration will also be needed to have access to sufficient patients.

In this context, the collaboration with Ksilink, a French-German Translational Research Centre in Strasbourg, has been initiated, which gives LIH access to a network of hospitals and cancer patients as well as new translational technologies. Ksilink is also founded by and headed by the present LIH CEO. Here is a very high risk of a perception by outsiders of a conflict of interest, and the peers therefore recommend that the LIH CEO steps down from his position in Ksilink for transparency reasons. As it is understood that the LIH CEO will step down from his role as CEO of Ksilink at the end of Q 1, 2019, it is hoped and expected that for the intermediate period both the BoD and the EAB, which is recommended by the peers, will prevent any conflict of interest.

The Committee also noted that there is still room for improved collaboration between LIH and LNS. For example, it was mentioned to the Committee that 17 pathologists are working in LNS, while only 1 is present at IBBL. In addition, there is 1 neuropathologist who has a shared position (LIH-DONC and LNS). LIH should start to make full use of the proximity of LNS, most importantly by starting a collaboration with LNS on a generic tissue collection as has been foreseen in the Plan Cancer Collection- This will benefit medical research within Luxembourg as a whole. Implementation, however, has yet to be initiated. Obstacles preventing it should be identified and removed by all partners involved to enable a start as soon as possible.

3.2 Innovation

Until today, the economic benefits of research in LIH have remained underexploited for Luxembourg, mainly because there has been too much focus on academic research, and science has been too much dispersed. So far, only a very small number of patents were filed (e.g. 2 in 2017; KPI target of 4/year was not achieved) and the number of public private partnerships (PPPs) steadily decreased from 2014 to 2017. With revenues of 116k€, in 2017, it is clear that these PPPs do not generate much income. By repositioning towards its clinical roots and putting patients in a central position through translational bed-to-bench-to-bed cycles, LIH is however well positioned to put Luxembourg at the forefront of biomedical research and create a translational hub in Europe. By addressing a bigger agenda, LIH could also play a bigger role for public health in Luxembourg. However, this will require a change in culture of LIH scientists and showing that translational research and basic research provide equal publication opportunities. In this context, clear communication to LIH employees about the new strategy and expectations, as well as more training efforts in technology transfer (TT) related activities, will be essential, together with proper incentives for researchers to focus on TT.

The panel is a bit surprised that the KPI for ‘number of filed patent applications’ is reduced from four per year (in 2014-17) to 5 in four years (in 2018-21) in the new (2018-21) 4-year performance contract concluded with the Government of Luxembourg. Moreover, other KPIs corresponding to ‘number of public-private partnerships (PPPs)’, ‘number of « wet lab » PPPs’, ‘revenues from « wet lab » PPPs’, and ‘creation of spin-offs’, have been abandoned. The exact difference between the KPI ‘number of PPPs’ (e.g. 31 in 2017) and ‘number of wet lab PPPs’ (4 in 2017) is also not clear to the panel. The new KPI (‘number of filed patent applications or licence agreements’) is now the only remaining KPI regarding economic value creation, which does not fully fit the new plan/vision of LIH to focus on translational research. The Committee recommends that new KPIs reflecting the translational and economic innovation goals of LIH are added, reflecting the expected impact of the translational strategy proposed by the CEO (e.g. number of PPPs and revenues from PPPs).

LIH runs its own Business Development Office (BDO; previously named Research Knowledge Transfer Office (RKTO)), which was created in 2010 with the mission to foster a corporate culture of IP management and Knowledge Transfer within LIH. In 2015, LIH went one step further by restructuring RKTO through the integration of the Project Management Office, thereby covering the entire value chain of research, from project set-up all the way to the evaluation of results. In 2017, it has been decided to step down this approach and to create the BDO. Currently, the BDO’s main tasks are to help researchers identifying projects that can be valorised (e.g. the BDO has regular meetings with scientists with translationally relevant projects and screens abstracts of manuscripts and meetings), to establish policies and procedures, to establish agreements (between 100 and 200 per year, including collaboration agreements, MTAs, license agreements), to manage the patents portfolio, to detect and select business opportunities, and to provide training related to TT. The BDO currently comprises 5 FTE, which should be sufficient for the size of LIH. Collaboration of the LIH-BDO with IBBL is focused on reviewing IBBL agreements, but can be expanded on request (IBBL acts independent for business matters). LIH initiated an endeavour to create a national technology transfer platform for biomedicine but stopped this in 2015 as the UL-LCSB developed its own technology transfer office.

The panel is of the opinion that some of the activities of BDO may have to be redirected to have more impact. When well trained, PIs may be equally well (or even better) placed than BDO to identify projects with potential (avoiding the need for abstract screening by BDO and freeing up time for other tasks). BDO is not giving input when selecting the research programs at early stage. However, to make the difference, BDO may consider playing a role in developing a portfolio based on real assets (e.g. allocated tech transfer budget) and using these assets to support experiments that strengthen selected patent applications or to set up new projects that allow to build patent families that are attractive to companies or investors. Such a policy should be conducted in close contact with the department directors and SSC and TSC and take into account the requirements from the government and Luxembourg health system. A smooth transition of translational research towards applications will also require extra support in obtaining early proof-of-concept for findings with translational potential. This may need the establishment of a proof-of-concept fund within LIH, organized by BDO. Again, this may be enabled by

repurposing part of the core funding. The panel also realises that developing new strategies and PPPs that go beyond service activities may require additional funding from the government or changes in the grant portfolio of other national funding agencies like FNR. The panel learned during the discussions that FNR already supported one proof-of-concept project for preclinical research. Also, specific instruments for supporting public-private-partnerships in research should be further developed (e.g. the FNR AFR-PPP programme for PhD students and postdocs). Finally, the expected growth in TT activities and number of patents to keep will require the development of a long-term financial plan for BDO.

The committee also supports LIH's plans for an unified IPR regulation with other CRPs and UL, and where the lead would be with the BDO that initiates collaboration/service with outside partners.

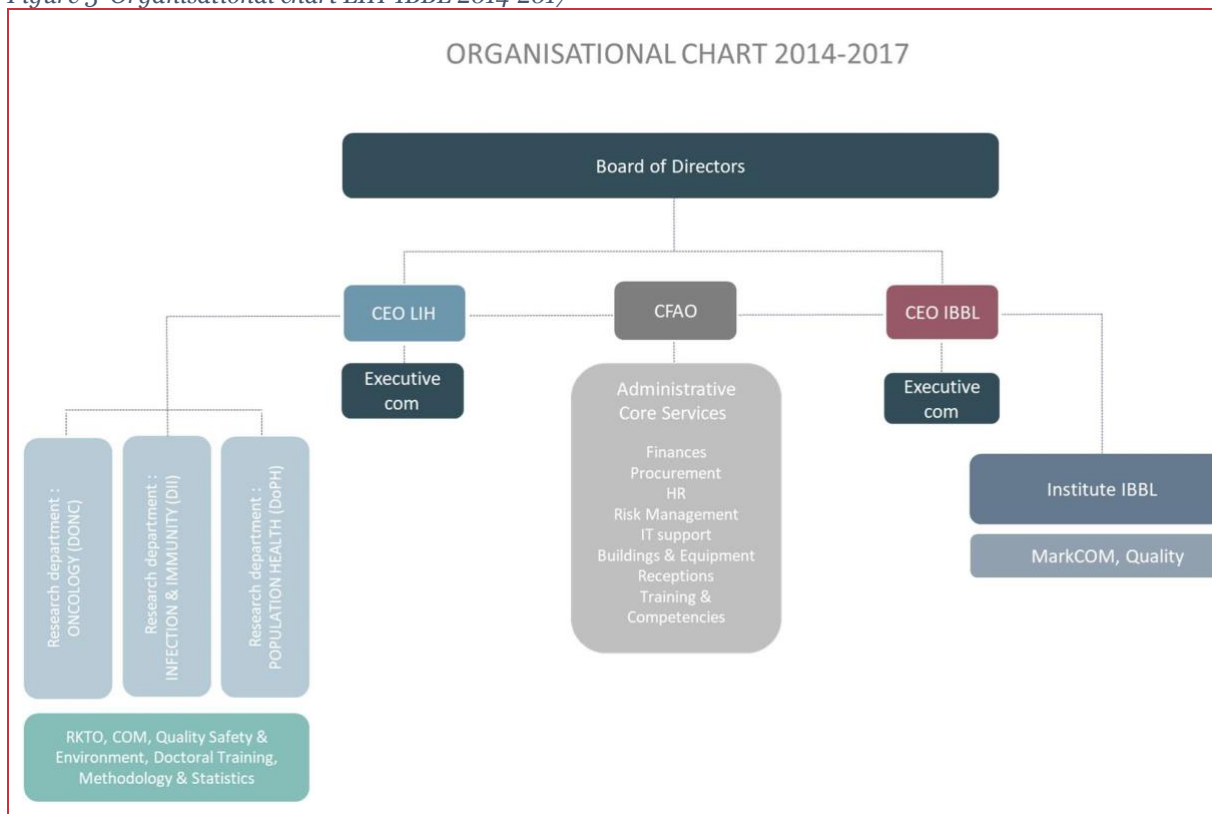
4 Organisation and management

4.1 Administrative management and finance

4.1.1 Functioning of the organisation structure

The LIH is a hybrid organisation since the integration of IBBL in 2015. On the one hand it is a public research organisation, representing a rather traditional academic culture and research practice. Examples of this are the way that LIH is person-centred rather than agenda-centred, works with projects rather than programmes, bottom-up specification of projects rather than specification of a broader mission-oriented research agenda, valorisation of results mainly through publications in academic journals and opportunity-driven filing of patents or stimulating a start-up. On the other hand, LIH is a research-supporting infrastructure, as it is running the Integrated Biobank of Luxembourg (IBBL) as well as several platforms. While being a single legal entity, with one budget, one CFAO and one administrative support system, the research part of LIH and the IBBL are managed by two independent CEOs, who report to the same Board of Directors see Figure 3.

Figure 3 Organisational chart LIH-IBBL 2014-2017



LIH SAR

Although unusual, in practice this division appears to work, mainly due to the fact that LIH receives a generous share of block grant (60% of total income; for IBBL this is even 80%) and the fact that research was and is primarily oriented at winning grants and attracting so-called ‘collaborative projects’, labelled ‘contractual research’ or ‘research contracts’ outside Luxembourg.

If LIH is perceived as an ‘Institute of Health *in* Luxembourg’, thus if the mission of LIH is to perform project-based research to contribute to the stock of knowledge, published in academic journals and related conferences, there is no good reason to change the organisational set-up of LIH, all the more as the departments as well as the IBBL have found their niches in the national and international communities. However, if LIH is understood as the ‘Institute of Health *of* Luxembourg’ in charge of

contributing to the health system in Luxembourg, the question arises, whether the (formal) organisational structure is adequate or should be re-arranged.

Here, with respect to the organisational structure, the key question is whether or not the IBBL should (i) remain the same as it is at present, (ii) be fully integrated as the fourth department within LIH under a single CEO, (iii) be turned around as a fully-fledged research infrastructure within LIH, performing the function of a core facility with a leadership that is subordinate to the LIH CEO, or (iv) as a separate legal entity. In all cases, consideration should be given to the question to what extent IBBL should not only deal with human clinical samples, but also with cohorts, clinical studies, with other biorepository resources (veterinary, agriculture), not least having a knowledge and operational capacity in the field of regulatory and ethical issues including open data.

Another consideration in this respect is that IBBL has the structure and potential to serve larger purposes than LIH research. Indeed, IBBL may evolve into a structure that serves as the Biobank for Luxembourg, providing service to hospitals, academy and private sector across a broad range of health, agriculture and industrial applications. Therefore, it may be appropriate to re-think the positioning of IBBL as an entity with a broader governance and financial basis than LIH itself.

Thus, the question, whether LIH has a well-functioning organisational structure, should be replaced by the question of the mission of LIH and IBBL. This is all the more relevant as at present, IBBL 'eats the largest piece of the cake' from the block grant. The answer to this question depends to the lesser extent on the two CEOs, the Board of Directors, and the MESR, but much more on the institutional environment and related actors in the health sector (ministry, hospitals, doctors, regulatory actors) and their practiced commitment.

4.1.2 Use of its institutional funding

In the past and current structure, the Committee notes that the relationship between the work programme and budget allocation is not evident. The budget seems to be built in a bottom-up manner, by assembling and putting together the budget requests of multiple independent projects. The Committee has noted that the current LIH project portfolio contains more than 400 contracts, at an average value of 70-80 k€, showing a tendency towards excessive fragmentation (such small contracts correspond to about 4-6 month's work for one person, considering salary, consumables, infrastructure and administrative costs). Such small budget-size projects do not fit a more programme-based strategy of LIH and are obviously incompatible with the initiation of clinical trials. The way the institutional funding is currently used also makes it difficult to decipher the coherence between the thematic scope at the scientific level and the actual spending.

LIH has no explicit and deliberate top-down policy which decides upon the use of the block grant and this results in an inefficient use of this resource. In the self-assessment report, when asked to describe and justify the use of the block grant, the following, in fact blurring answer has been given by LIH⁴:

Over the whole performance period 2014-2017 and until now, the **block grant usage per project** is based on the cost allocation defined in the yearly budget, which was created in a bottom-up process over several rounds – first in the departments and then on the LIH institutional level including the executive management. For final approval, the yearly budget is submitted to the LIH Board of Directors. This procedure is in line with the performance contract, as only the eligible costs are considered for the performance indicators calculation.

The implementation of the use of the block grant can be observed during the business year (01. January to 31. December) through the financial tools embedded in the business administration software Odoo, which has been in use at LIH since 2015. The LIH budget is defined by multiple individual projects using a detailed full-cost model for each project. From an accounting point of view, the final block grant allocation is part of the year-end closing process, and ideally shows minimal deviation from the original budget allocations. It is the responsibility of the Chief Financial and Administrative Officer (CFAO) of LIH to guarantee an equilibrated year-end closing budget every year to the LIH Board of Directors. Until 2015, the bottom-up budget-

⁴ SAR LIH, p15

building process of LIH left enough freedom and buffer to still take strategic investment decision that were important to further develop the institute LIH.

More recently – partially due to more success of LIH, which resulted in additional budgetary commitments – a larger fraction of the block grant had to be pre-assigned, thus leaving a lower fraction free for strategic investments. For the future, LIH has to develop a more performance-oriented financial allocation of the block grant to avoid paralysis and missing investment opportunities into novel cutting-edge technologies and high-level scientific talents.

As can be seen from table 2, LIH has never achieved the >40% share of income from outside, thus from grants and contracts (that is the target in the Performance agreement). These sources of income can be seen as indicators of scientific quality (grants as a proxy) and of relevance (contracts as a proxy).

Table 2: Use of block grant by LIH 2008-2017

	2008-10		2011-13		2014		2015		2016		2017	
	MEUR	%	MEUR	%	MEUR	%	MEUR	%	MEUR	%	MEUR	%
Total	69,8	100 %	91,1	100 %	37,1	100 %	37,6	100 %	39,1	100 %	42,6	100 %
Block grant	48,8	70%	61,6	68%	27,1	73%	27,8	74%	28,1	72%	30,3	71%
Contract revenue	13,0	19%	14,4	16%	4,5	12%	4,9	13%	5,4	14%	5,7	13%
Competitive funding	8,0	11%	15,1	17%	5,4	15%	4,9	13%	5,6	14%	6,6	16%

The main unclarity in the use of the block grant is at the top level of LIH. The Committee observed that across the entire system (CEOs, heads of department, Board of Directors, MESR) there is a lack of robust knowledge about the allocation of, and rationale behind, the use of the block grant. At the same time, a focused supervision of the use of the block grant, in particular by the Board of Directors is absent.

Within the given framework (the endowment with a generous block grant, the focus on external funding via grants and contracts), LIH performs well. However, considering the suboptimal use of block grant, together with the profile of IBBL acting as a comprehensive research infrastructure (cf. above), LIH is far away from a productive use of its institutional autonomy. A productive use would include the existence and active implementation of a small number of larger research programmes ideally aligned with the Luxembourg Public health priorities, agreed and actively implemented with key stakeholders in the Luxembourg health system.

Aside from improving understanding and transparency with regards to the use of block grants, there is therefore a clear recommendation that there should be clear and transparent guidelines on the budget strategy, allowing PIs to develop proposals within the framework of this strategy. The block grant should be used to stimulate implementation of long-term programmes, which in turn will result in improved attraction of grants and contracts, and improve internal and external collaboration, both with peer institutions, but in particular with health organisations.

4.1.3 Obstacles to increasing LIH's revenues from external funding

LIH, not unlike the other Luxembourg Institutes (LISER, LIST) enjoys a luxurious endowment with block grant. Moreover, they all benefit from a rather generous national research council, the FNR. Taking these two factors into account and also considering the fact that the block-grant is a non-performance-based payment (i.e. the amount is not dependent on performance against the PC1417 KPIs,) there is little incentive to gain for additional external funding. In this regard the poor incentive to strive for external income can be considered the main obstacle, thus mainly home-made.

Further, the unclear, even opaque use of the block grant must be considered as another – internal – obstacle. If the block grant was systematically used for the establishment of a small number of internally funded and governed research agendas and programmes, these could and would act as a guidance for the attraction of grants, contracts and partners. This would then allow a better integration into the national health system (access to data, samples, patients, testing in general, but also taking up of problems and challenges), not least being an attractive partner for international collaboration. Here, the so-called ‘multilateral programmes’ can be considered an opportunity for tailored international collaboration.

Thus, the key obstacle to go out for more grants, contracts and partners is to a large extent home-made: thinking, planning and acting in terms of projects rather than of programmes or agendas, non-focused use of the block grant, poor incentives for growth, not least a poor anchoring in the national health system.

LIH should step out of the comfort zone. (Minor) parts of the block grant should be allocated in dependence of external income. Major parts, however, should be invested in long-term, strategic programmes, including investment in infrastructure (in a broad sense, thus not only specialised equipment, but also data, access to patients, cohorts- including clinical trials cohorts, ethical and regulatory standards etc.). Therefore, the Committee fully endorses the foreseen shift in budget distribution and allocation from a bottom-up to a top-down approach and reserving a big fraction for long-term strategic initiatives. By emphasizing the focus of LIH on ‘real-world’ health issues rather than on academic research, this approach would make LIH more attractive for partnering with Luxembourgish health institutions and allow a better partnering with the international research community.

After having achieved the establishment of a performing local environment, Luxembourg has the potential to become an attractive partner, particularly in multinational research programmes (JPI, JTI, KIC)⁵.

4.2 Human Resources

LIH has been successful in recruiting good staff with a good proportion of international students and postdoctoral researchers, representing 36 nationalities. The staff distribution reflects a good gender balance across most career stages; the share of 35% female employees at the senior executive level could be seen satisfactory when compared to other institutions internationally, although the objective of 50% should be actively pursued. LIH has managed to attract a number of high potential scientists, for example via FNR’s ATTRACT and PEARL schemes. Beyond these special funding schemes, opportunities to influence the institute’s research direction via strategic recruitments are unfortunately rather limited, mainly due to the country’s inflexible employment regulations, which result in high employment cost, but also because of inefficient use of the block grant. It would be desirable, however, if a general recruitment plan aligned to the overall research strategy would be in place for those occasions where an open hiring is possible.

In order to attract excellent clinical researchers, coordination with local hospitals to offer an attractive associated clinical position would be highly desirable. To ensure the full operability of the CRC, LIH should keep in mind that it will require well educated staff, not only clinicians, but also on the level of nurses and information specialists.

LIH has reacted to the recommendations of a previous review to install a PhD programme by setting up two programmes, NextImmune and CANBIO, via the FNR-funded PRIDE scheme. This is highly appreciated by the Committee and impressive. More work is needed to unify and simplify the administrative regulations and requirements for students who are affiliated with different or even multiple institutions (e.g. with the University of Southern Denmark). The PhD students form an engaged and enthusiastic group of researchers who are generally happy with the quality of their supervision and

⁵ JPI= European Joint Programming initiatives; JTI= Joint Technology initiatives; KIC= Knowledge and Innovation Communities.

seem to be successful in interacting at the department level. PhD affairs are supervised by a coordinator who is doing an outstanding job at keeping track of and providing individual support for each student. Although PhD students are employees of LIH and have a representative, there seems to be no real structure that represents the interests of the PhD students. Mentoring and coaching of PhD students about career perspectives in science could be improved, as PhD students do not always appear to be fully aware of potential career paths. At present PhD students and postdocs have different contracts from the rest of the staff. They are also treated differently, e.g. in regard to the appraisal procedure. This is perceived as an imbalance by the staff delegation and should be addressed by the LIH administration.

The HR department is well aware of the need to invest in staff development. They are in the process of generating and implementing a programme to support the personal development of competencies at all career stages from PhD student to PI. HR also offers employees the opportunity to receive individual training from an external coach. HR is actively participating in the EURAXESS⁶ network and has achieved an Excellence label from this scheme. Their procedures are accredited by ISO certification. Development of leadership qualities in junior PIs is being actively encouraged and facilitated by providing the opportunity to attend externally offered courses (e.g. by True Colours), which are appreciated and perceived as very helpful by the staff whom the Committee met during the peer review.

Although communication of HR with the staff in general has improved with the new CEO, staff representatives still voiced some dissatisfaction with the management on how new regulations or procedures are being implemented in a top-down manner. This has been most severe in the case of the new salary system, where staff did not feel involved in the discussion and had the impression that management was making decisions without considering the benefit of the staff. Constructive discussion with the CFAO was reported to be problematic or even impossible. Overall, this has left some staff with the feeling of not being able to make a difference. It is important to note that the statements above are based on feelings expressed by staff representatives, and cannot be verified.

4.3 Physical infrastructure and working conditions

LIH does not possess a spatial organisation that reflects its mission. It is currently fragmented on four sites and some of the departments are housed in suboptimal conditions. The costs for the rental of buildings are high.

This spatial fragmentation is definitely a serious obstacle for the success of the integrative translational strategic vision proposed by the CEO. It should be fully realized that a specific selective advantage of LIH compared to national institutes of health of most other EU countries is the possibility to have all its members in a single place, enabling them to operate as a well-integrated community fostering interactions and joint strategies.

In particular, LIH departments have rapidly growing needs for accessing shared technological resources such as platforms (proteomics, genomics, biobanking), know-how (bioinformatics and molecular modelling) and for developing access to Artificial Intelligence (AI). The most efficient way to implement these developments is to enable the entire community of users to share their expertise on a single integrated site. While this is very difficult to achieve in many larger countries -due to distributed resources over territory and/or federal structure, this may be feasible in Luxembourg.

The Committee strongly recommends that Luxembourg develops a master plan for building a suitably located “health campus” gathering LIH together with hospital and academic stakeholders and a value creation/innovation ecosystem of spin-offs and start-ups in the biomedical field. Such a campus would place LIH research in an extremely favourable position for delivering its full potential and for fulfilling its missions, including in particular impacting on personalized medicine and value creation.

⁶ <https://euraxess.ec.europa.eu/>

The building situation of IBBL is different, since the new building of IBBL is very well equipped and functional for the needs of IBBL, and the proximity to the LNS is an asset. These circumstances speak in favour of not relocating IBBL.

The general working conditions at LIH are very good and at international standard. However, the international competitiveness of the research may in some cases not be good enough to keep highly qualified personnel. There is also the problem of an under-critical mass of researchers working on the same topic. To attract and keep highly qualified personnel, flexible career possibilities should be enabled.

It is planned to organize the management of the core facilities outside of the research departments in the future. Care should be taken to keep a close connection between the core facilities and the research departments, though. This ensures that core facilities stay at the forefront of technological advance and know about the specific research needs at LIH. It also helps to recruit highly qualified personnel with sufficient research experience. Also, access fees for LIH researchers should be kept to a minimum.

4.4 Research and innovation culture

LIH adopts the principles of Responsible Research and Innovation by involving society in science and innovation ‘very upstream’ in the process of research and innovation to align its outcomes with the values of society. This involves multiple aspects, including public engagement, open access, gender equality, science education, ethics, and governance. In this context, the LIH Communication Department (5 people, which is a lot for an institute the size of LIH) plays an essential role. The panel learned from a discussion with the communication manager that 15% of the time spent goes to internal communication, while 85% goes to external communication. There is a communication plan in place that supports the strategy of the institute, whose main target groups are the lay audience at national level, professionals (Luxembourg hospitals, patient organisations, international scientists) and LIH staff. Major activities include content writing, events management, school visits, digital communication, social media.

The fact that LIH has no strong self-identity remains an issue. The many different research directions sometimes hamper clear and effective communication. LIH could play a bigger role in communication about health risks, environmental issues and disease prevention. Personal engagement of scientists and/or FNR-sponsored activities are great initiatives in communication and outreach (e.g. by giving talks at schools or specific events for the lay public), but real LIH visibility will require certain incentives at the institute level. In this context, the fact that the number of projects or events to promote scientific culture to the young (<20 years) has been taken up as a new KPI clearly illustrates the commitment of LIH. The communication manager also sees the need to move towards more modern and digital communication such as videos, TV screens, virtual reality.

During the period 2014-17, LIH has not articulated an Open Science strategy. Open access publications started to be monitored in the year 2017 and amount up to 35%. Presently, LIH is working with the other research institutions and the FNR to develop a nationwide Open Science strategy, primarily focused on Open Access and on building an open repository for publications for Luxembourg. The discussion will need to be expanded to include other aspects of Open Science such as open data. The Communication Department is already working with LIH-DoPH on open data registries.

Internal communication is suboptimal due to the distribution of physical infrastructure, and an underdeveloped intranet. The Committee learned that intranet is in the process of being redeveloped, which needs high priority as this was also raised as a serious concern during the departmental evaluations. The panel advises to involve more the scientists (what are their expectations), to apply for funding related to communication from other organisations, and to work together with the MESR on education where possible.

5 Governance

Given the rather broad mission of LIH (cf. chapter 2.1) and the frequency of changes of the legal framework, the organisational structure, and, not least, of key staff during the last years, the governance model and its practical implementation and handling has to be considered a key factor in the long-term performance of LIH. Moreover, given the mixed, even limited performance in various key areas of LIH (limited societal and economic impact, poor performance in accessing international funding, insufficient communication, exchange and collaboration within and across units, groups and departments, cf. section 2.4), not least unclarity in the use of the block grant (cf. section 4.1.2), the governance model and its handling is thus challenged. The relevant key actors are here the MESR, the Board of Directors, and the CEO, their main instruments are the performance contract and the block grant and its use.

As this holds to a large extent true also for the two other institutes (LIST and LISER), the LIH is not only a research institute, but also a research infrastructure with both national as well as international outreach. Due to the rather substantial size and related funding requirements, particularly in the use of the block grant, IBBL serves and requires a separate discussion.

5.1.1 *The role of the MESR*

The governance relation between the MESR and LIH is multifaced. The most relevant reference, however, is the performance contract. It is – in formal terms – a binding agreement between the Government on the one hand, and the LIH on the other hand, represented by the Board of Directors. From a formal point of view, this is a design fault. The natural candidate for negotiation on the side of LIH should be the CEO, thus the executive. The Board of Directors, by contrast, should supervise and finally approve the performance contract. The Board of Directors thus should act as a supervisor (or honest broker) in order to ensure a fair deal in the negotiation and an effective / efficient implementation of the contract. In practical terms, however, it is the CEO who negotiates the performance contract which is then agreed by the Board of Directors, prior to the submission to the MESR.

All in all, the actual role perception and acting of the MESR and the Board of Directors can be seen an expression of goodwill and there is no need to re-think this overall governance framework as long as the respective roles and responsibilities of the executive and of the board are clear and accepted by all stakeholders.

There is one, however, relevant exception, and this should deserve highest attention in the future as it will not be sufficient to only demonstrate goodwill. In the past, but also at present, LIH is fluctuating between the mode “**an** Institute of Health **in** Luxembourg” and “**the** Institute of Health **for** Luxembourg”. As outlined throughout this review, the mission of being “the Health Institute for Luxembourg” can and should be understood as the main prerequisite for being an excellent research institute. However, this requires a substantial piece of work to persuade the Ministry of Health, the hospitals, and not least the health institutions to act as partners in long-term collaborations, positioning Luxembourg as role model for mission-oriented research (cf. Horizon Europe).

5.1.2 *Role of the Board of Directors*

The Board of Directors is the most powerful actor in the overall governance structure of LIH, at least in formal terms: it is nominated by the MESR and installed by the Government (i.e. the Council of Ministers), it negotiates the performance contract with the MESR and it supervises the LIH and its executives, not least the implementation of the performance contract. Even when taking into account the fact that the factual role of the Board of Directors is rather passive, and refraining from the various role conflicts and the absence of any ‘checks and balances’, a key element to assess the performance of the Board of Directors, is its access to the Government and related institutions. In the case of LIH this means access not only to the MESR, but also to the Ministry of Health and to health relevant institutions. Thus, the Board of Directors can and should be seen as a door opener, a mediator, an honest broker, and as a game changer in outlining and implementing new strategies.

In practice, however, this does not work, mainly due to the following reasons: the Board of Directors is not fully aware of this role and of its far-reaching implications; even if it would be aware, its power would be limited due to insufficient resources in terms of days per year. Not the least, the Board of Directors lacks sufficiently strong push (from LIH) and pull (from health policy and health care institutions). When it comes to lobbying, the burden is mainly on the shoulders of the LIH executives and managers rather than on the agenda of the Board of Directors.

Overall, there is an opportunity to re-think the role and degree of involvement of the Board of Directors, changing its attitude and degree of involvement from passive, supportive and facilitating to active, brokering, strategically planning and promoting change. The next couple of years can be used as an experimental setting in order to create a new, and much more systematic approach to specify the performance agreement. On the side of LIH, it will be key to think and act in terms of collaborative research programmes with distributed roles between the LIH and stakeholders in the health research system.

Notwithstanding the difficulties to achieve this more active, strategically oriented role for the Board of Directors, there is one other essential duty of the Board of Directors, namely to supervise the use of the block grant. In the past, neither the CEO nor the Board of Directors, not to mention the MESR, have provided or received systematic information about the use of the block grant. This ‘blind spot’ is substantial, as the block grant amounts to 60% of the overall financial resources and its use is under the full autonomy of the CEO vis-à-vis the Board of Directors. Furthermore, the absence of data and information and related debate co-occurred, at least during the period of the evaluation, with the absence of an overall core strategy and related research agenda.

In the future, the use of the block grant and related strategy and research agenda should be the main topic in the interaction between the CEO and the Board of Directors. While grants and contracts are mainly governed by grant agencies or clients in terms of quality, relevance, completeness, timeliness, performance etc. the block grant and thus the use of 60% of overall budget is governed, managed, supervised etc. entirely within the institute.

5.1.3 *IBBL*

With the IBBL, the LIH maintains an excellent research-supporting and research infrastructure that offers not only biobanking but also method and specimen validation, which is of wider interest in Europe and whose international visibility is very high. From the point of view of the IBBL the integration has been successful, and the current governance structure works well. The support in administrative topics provided by LIH is highly appreciated by the IBBL and it would be a waste of money to have own administrative structures for IBBL alone. On the other hand, it is important that IBBL is perceived as autonomous within and outside Luxembourg as it serves not only LIH, but also other Luxembourg research institutes, the university, and has a number of international clients, both private and academic. There is a strong identity perceived internally and internationally around IBBL branding. A tighter connection to LIH could theoretically be interpreted as IBBL not being “neutral” with regard to sample access, project selection and participation in EU consortia.

However, the position of IBBL in the LIH organisation structure needs specific attention. The Committee sees four possible scenarios (as already addressed in section 4.1.1.): IBBL (i) remains the same as it is at present, (ii) is fully integrated as the fourth department within LIH under a single CEO, (iii) is turned around as a fully-fledged research infrastructure within LIH, performing the function of a core facility with a leadership that is subordinate to the LIH CEO, or (iv) as a separate legal entity. The current situation, with LIH and IBBL being one single legal entity, with one budget and one administrative support system, but two independent CEOs who report to the same Board of Directors seems a bit odd and is not benefiting the visibility of each. With the CEO of IBBL retiring in two years, discussions and plans related to a new organization structure should start now.

In support of option 2, to integrate IBBL as the fourth department within LIH, is the fact that IBBL can play a pivotal role in the implementation of the new LIH strategy, as it would offer LIH an in-house infrastructure to run large population or clinical cohorts. On the other hand, in favour of option 4, to set

IBBL up as a separate legal entity, is the consideration of the Committee that IBBL is a serious budget and strategic liability for LIH because it is the nature of biobanks to increasingly consume more budget and resources. From this point of view, it may be better to move it out of LIH and establish it as “the biobank of/for Luxemburg”, jointly supported by a broader range of stakeholders than LIH.

The BoD should make a decision on the relation between IBBL and (the rest of) LIH, based on the vision on the Luxembourg Health research landscape, the desired position of LIH/IBBL therein and the re-defined strategies of LIH and IBBL.

6 Conclusions and recommendations

6.1 Conclusions

In the evaluation period 2014-2017, LIH performed on a very good level. It has been successful in recruiting good staff and the overall working conditions are good and at international standards. Despite the broad scope of research and little integration between research projects (partly due to lack of a common strategy and a fragmented physical infrastructure), so far, the organisational strategy has resulted in excellence in basic research, with important achievements in each department. However, while LIH has fulfilled the basic research part of its mission, achievements in providing national leadership in translational and clinical research are still modest.

The Committee therefore fully supports the new CEO's strategic vision and plans to reorganize the institute according to a 2D-matrix model in which horizontal transversal translational programs overlay the vertical dimension of the different departments and welcomes the new mission statement formulated in the PC1821. The Committee considers that this new statement has the dual merit of building on the foundation of excellence in research achieved under the previous contract, and of outlining a clear perspective for the realistic development of these strengths for the next 5-10 years.

Nevertheless, the new mission and goals are still defined in a rather vague manner and do not always take into account certain weaknesses and risks that lay outside LIH. The success of the newly proposed strategy will strongly depend on a more optimal, efficient and transparent use of the very generous block grant that LIH receives from the government. Therefore, the Committee fully endorses the foreseen shift in budget distribution and allocation from a bottom-up to a top-down approach and reserving a big fraction for long-term strategic initiatives. In addition, LIH will only be able to succeed in its new mission if it can collaborate systematically and more intensively with the health sector (Ministry of Health, the hospitals, the health institutions), who should be convinced to collaborate with LIH by the Board of Directors (which has so far been too passive in this respect).

In recent years, LIH has intensified collaborative efforts with the other research organisations and with hospitals in Luxembourg. In particular the increased collaboration with the University of Luxembourg, both in terms of research (especially with LCSB) and educational training is a big step forward. Nevertheless, in view of LIH's new mission and focus on patients, more coordinated efforts with the IBBL and Luxembourgish and international hospitals or centres will be needed. Also, despite several good research outputs in terms of scientific publications and collaboration with national and international laboratories, LIH (except for IBBL, and individual research groups) still lacks international visibility. The fact that LIH has no strong self-identity certainly is part of this problem as it also prevents effective communication. Moreover, the very generous block grant for LIH also creates a too comfortable situation for LIH researchers, who may not feel the need to coordinate or participate in international grant applications (e.g. from the H2020 program). This is also reflected in the failure to achieve targeted income from grants/contracts of 40% or more of the total budget.

The relation between the MESR and LIH is laid down in a performance contract that outlines the mission, vision, overall and departmental strategic objectives, and key performance indicators. However, one can observe limited attention to this most relevant governance instrument, both in terms of available information about the use of the block grant as well as in terms of actual decision making. Clear and ambitious KPIs related to the new mission of LIH are lacking and consequences of under-achievement are not defined. Also, here the BoD (and MESR) seem to be rather passive and do not handle this powerful governance contract with sufficient rigour.

6.2 Major recommendations for LIH

Based on the findings from this peer review, the committee recommends:

1. **To establish a clear and pragmatic link between precisely defined missions, organizational structure and budget spending.** Whereas the missions as defined in the previous PC1417 were too broad, the new PC1821 is better tailored to the realistic capabilities of LIH. However, missions should be defined carefully, with realistic impact expectations and considering interdependencies with external factors such as the development of clinical research in hospitals throughout Luxembourg and the expansion of an innovation/investment ecosystem supporting start-ups and value creation. Moreover, the missions as defined by the PC should be usable as a guide for management and budget decisions, including prioritization of investments and recruitments.
2. **To enable the development of different translational programmes, the Committee recommends that LIH establishes an External Advisory Board (EAB)** comprising a small number of undisputed international experts in translational research and Public health, and in which key local stakeholders could have an observer status. The main role of the EAB should be to provide scientific, strategic, medical and market advice to the CEO and LIH upstream the new strategy implementation.
3. The Committee recommends **a reform in budget distribution and usage**, which is more flexible, less fragmented, better aligned with the overall mission of LIH, and which allows strategic initiatives at the institutional level. The block grant should be used to stimulate or award implementation of long-term programmes. The CEO should have the ‘ownership’ and thus the key responsibility for its use.
4. Unfortunately, the use of IBBL within Luxembourg is rather low, in part because IBBL has targeted mainly international collaborations, and in part because there is a lack of clinical researchers to drive clinical research using IBBL. The Committee recommends that IBBL and LIH **develop initiatives that enable a more intensive use of IBBL by LIH and other researchers in LU and consider opportunities for increasing the number of clinical researchers working with and in LIH.**
5. The Committee recommends that **the activities of the Business Development Office (BDO) are redirected to have more impact on innovation.** Financial assets should be foreseen for TT activities supporting experiments or even new projects that allow to strengthen certain patents (e.g. by showing proof-of-concept) or to build certain patent families.
6. The move of LIH to more translational research will require a change in culture of LIH scientists and showing that researchers can still do basic research with a translational output, allowing them to publish. The Committee recommends **a clear communication about the new strategy and expectations**, as well as the implementation of more **training efforts in TT related activities.** Also, proper **incentives for researchers to focus on TT** should be discussed.
7. The Committee recommends **developing a clear business plan** to assess costs and opportunity of the translational portfolio considered by the new strategy. Prior to its implementation, LIH will need to seek the advice of its EAB and to secure additional MESR independent funding sources for translation, including outside translational funds (e.g. from the European Investment Bank).
8. The committee recommends **creating incentives and support for scientists to apply for European grants and/or to become more successful.**
9. Careful thinking and planning should take place in defining the **roles for IBBL, and its position within the LIH organisational structure.** As this can also have an impact on the new strategy and mission of LIH as put forward by the new CEO of LIH, he should have a important voice in this.
10. For reasons of transparency and independence, **the LIH CEO should step down from any position in Ksilink** and withdraw any potential share he may still own.

6.3 Major recommendations for the BoD and MESR

11. The **Board of Directors should connect better to the government and related institutions**, with the ultimate goal to provide them a clear view on the vision of LIH and enable interaction and collaboration between LIH and the Luxembourg health system.
12. The **Board of Directors should play a more active role in supervising the negotiation and implementation of the performance contract including the use of the block grant.** Although the KPI system is not a perfect system, it enables the detection of under-achievement. Also, consequences of under-achievement should be anticipated and contingency plans defined.
13. The Committee strongly recommends that **Luxembourg develops a master plan for building a suitably located “health campus”** gathering LIH, academic stakeholders and a value creation/innovation ecosystem of spin-offs and start-ups in the biomedical field.
14. The Committee recommends **redefining some of the presented KPIs**. Clearly, they do not sufficiently target clinical research, with only 1 study sponsored per year by LIH set as a target during the four year period (2018-2021). Also, a KPI on the number of publications led by LIH (i.e. publications with a first or last author from LIH) as formulated in the PC1417 KPI, but no longer in the PC1821 KPI), should be maintained as this reflects the scientific impact and international visibility of LIH. Also, KPIs reflecting the translational and economic innovation goals of LIH should be added (e.g. number of PPPs and revenues from PPPs).

Appendix A Members of the Assessment Committee

6.4 Rudi Beyaert (Ghent, BE)

Rudi Beyaert is full professor at the University of Ghent (Belgium) and Deputy Director of the Center for Inflammation Research at the VIB, a life sciences research institute in Flanders. He is heading the Unit of Molecular Signal Transduction in Inflammation, whose mission is to study the molecular mechanisms that regulate inflammation and immunity. Prof. Beyaert's scientific research is situated at the borderline between molecular biology and medicine, and makes use of a variety of modern biochemical, molecular and cellular approaches combined with mouse gene targeting and mouse models of human inflammatory disease. So far, he has supervised 37 PhD students and more than 30 postdocs, of whom several now hold professor positions while others made their careers in industry, public health, clinical reference laboratories, etc. Prof. Beyaert has published over 250 research papers that received more than 17 000 citations, which is also reflected by a h-index of 69, and he is inventor on >10 patent applications. His work has been recognized by a number of awards, including the five-yearly Prize of Fundamental Medical Sciences of the Belgian Royal Academy of Medicine.

6.5 Helle Ulrich (Mainz, DE)

Helle Ulrich obtained her PhD in Chemistry from the University of California, Berkeley, USA, in 1996. After postdoctoral work at the University of Heidelberg and the Max Planck Institute for Biochemistry in Martinsried, Germany, she established an independent research group at the Max Planck Institute for Terrestrial Microbiology in Marburg, Germany. She moved to the United Kingdom in 2004 to take up a group leader position at the Clare Hall Laboratories of the Cancer Research UK London Research Institute. In 2013, she became a Scientific Director and Full Professor of Biology at the Institute of Molecular Biology (IMB) in Mainz, Germany. Helle Ulrich has been awarded the BioFuture award of the German Ministry for Education and Research (2001-2006), an EMBO Young Investigator Award (2003-2006), has been elected to EMBO membership (2008) and has obtained Advanced Investigator and Proof-of-Concept Grants from the European Research Council (2013, 2018). Her research focusses on how posttranslational modifiers of the ubiquitin family modulate genome stability. In particular, she is interested in the pathway of DNA damage tolerance, which facilitates the processing of DNA lesions during genome replication.

6.6 Pierre Hainaut (Grenoble, FR)

is PhD in Biology, University of Liège, Belgium, 1987. After postdocs in France and in the UK (Nice, Cambridge, York; 1988-1994), he joined the International Agency for Research on Cancer (IARC, World Health Organisation) in 1994, where he held the post of head of Molecular Carcinogenesis from 1999 to 2011. In 2012, he joined the International Prevention Research Institute as Research Director. Since 2014, he is Professor of Cancer Biology and Chair of Excellence in Translational Research at Université Grenoble Alpes (UGA), France. Since 2014, he is Director of the Institute of Advanced Biosciences (<https://iab.univ-grenoble-alpes.fr/institute?language=en>), a multi-thematic research centre supported by Inserm, CNRS and UGA, dedicated to Epigenetics, Chronic Diseases and Cancer (19 research teams, 300 staff). He is also responsible for Cancer Molecular Diagnosis at the University Hospital Grenoble Alpes (CHUGA). His research focuses on TP53 mutations and on biomarkers of transition from chronic diseases to cancer. From 1994 to 2011, he has led the development of the international IARC database of TP53 mutations, a source of information on the causes and consequences of mutations affecting the p53 suppressor protein in cancer. His current research focuses on the roles of p53 in cell bioenergetic metabolism and epigenetics, with applications to prevention and early cancer (Li-Fraumeni Syndrome).

Pierre Hainaut is author of over 435 publications and 50 book chapters (32,000 citations; h-index 93, Google Scholar; 81, research gate). He has co-edited two books on p53 ("25 Years of p53 Research" 2005, 2007, Springer, "p53 in the Clinics", 2011, Springer), a textbook of Molecular Epidemiology ("Molecular Epidemiology: Principles and Practice", IARC Press, 2011), and a textbook on biobanking ("Human biobanking: Principles and Practice", Springer, 2017). He is senior editor (with Paolo Boffetta) the

3rd Edition of the Encyclopaedia of Cancer (Elsevier, 2018). He is editor of the section “Cancer Biology” for Current Opinion in Oncology (since 2011).

6.7 Patrick Rossignol (Nancy, FR)

Patrick Rossignol, MD, PhD, is professor of Therapeutics, Nephrologist and Vascular medicine specialist, head of Nancy Plurithematic Clinical Investigation center (CIC)-Inserm, France. He has participated/is participating in several EU FP6-7 programs (Ingenious Hypercare: Coord A; Zanchetti; MEDIA: Coord: W. Paulus; HOMAGE & FIBROTARGETS: Coord F. Zannad, Nancy CIC). He is coordinating a French network of excellence endorsed by F-CRIN (French Clinical research Infrastructure Network, the French affiliate of ECRIN/ERIC: Cardiovascular and Renal Clinical Trialists (INI-CRCT www.inicrct.org) since 2014. He is coordinating the University Hospital “French Government Investment for the Future” Fighting Heart Failure programme (2016-2020). He is the PI of the ongoing double blind (spironolactone vs. placebo) cardiovascular outcome randomized controlled trial in hemodialysis (ALCHEMIST: ClinicalTrials.gov Identifier: NCT01848639) and carotid barostimulation in resistant hypertension trial (ESTIM-rHTN NCT02364310), and steering committee member of several international randomized clinical trials. He is serving in several DSMCs and event adjudication committees. He is a EURECA-m (cardiorenal working group of ERA-EDTA: The European Nephrology Dialysis Transplantation Association) member since its creation in 2009 and got elected as board member (2013-2016). Since 2016 he is a Heart Failure Association of the European Society of Cardiology “Translational” and “Cardiorenal” board member. He currently participates in the ASN KHI. He is the co-founder of CardioRenal.

6.8 Gabriele Anton (Munich, DE)

Dr Gabriele Anton is head of the biobank group at the Institute of Epidemiology at Helmholtz Center Munich. The biobank is a major resource for researchers working in the fields of prevention, diagnosis and therapy of complex diseases and collects biosamples since more than 30 years. Currently the group is establishing the Core Facility HMGU Biobank that will offer services around biobanking to all institutes at Helmholtz Center Munich and collaboration partners.

Gabi received her PhD from the Ludwig-Maximilians-University (LMU) Munich in 2000. Her postdoctoral work focused on infection research. Today she is involved in national and European projects in the field of biobanking, for example within the German Center for Infectious Diseases, in the German Biobank Alliance and in BBMRI-LPC (Biobanking and BioMolecular resources Research Infrastructure – Large Prospective Cohorts).

Appendix B : Table with the full evaluation questions for LIH, copied from the terms of reference

LIH
<p>1. Mission, goals and strategic plans of LIH: The evaluation shall review the mission and goals of LIH and how the CRP lives up to these. The mid- and long-term plans shall also be evaluated regarding their existence, their ambition and whether they can be reached. The <i>scope</i> of LIH shall also be analysed; i.e. the actual and potential outreach beyond the small Luxembourg home ground, as discussed in the following topics 2. to 4.</p>
<p>2. Research performance: The evaluation shall assess first the clarity, uniqueness and ambition of the research agenda. In a next step it shall evaluate the quality, output and impacts of the research being performed in the departments and units of LIH and put these into perspective with the record of comparable socio-economic research centres in Europe. Further, the evaluation shall assess how and how strongly LIH is participating in mission-oriented research and is able to contribute to the tackling of societal challenges on national and international level. The appraisal of critical size of research activities shall be included here also; as well as progress being made towards joint publications, stronger research intensity and improvements in FNR (e.g. PEARL) and EU (e.g. ERC) grant record. This topic is in close relation to the relevance criterion (topic 3.). The evaluation of the research output, the impact and the ability to renew the knowledge base shall be done for each research unit and department and be rated clearly in an appropriate way.</p>
<p>3. Innovation performance: The evaluation shall assess all the different forms of innovation and value creation activities of the centre, including applied research work, contract research, provision of public data, membership in international committees, transfer activities, services, attractiveness of the physical infrastructure and related topics. This evaluation task also encompasses policies and support actions like strategies for the dissemination of results to companies and society and other action. Again, the evaluation shall analyse the mission orientation, quality, output and impacts of the innovation activities on all levels of LIH and it shall put them into perspective with the record of comparable socio-economic research centres in Europe.</p>
<p>4. Role as a national and European evidence provider: The evaluation shall assess the specific role and performance of LIH as a national and – where applicable – European data and expert study provider for evidence-based policy. The evaluation shall rate the quality of the underlying databases and data banks, see also para. 9.</p>
<p>5. Users, networks and user access: The evaluation shall further assess whether the “real world” contacts of LIH are substantial, yielding and resilient. This includes an analysis of the relevant international networks of the centre and the embeddedness in European consortia. In this context and given the small size of Luxembourg this includes the analysis of the relevant markets, i.e. whether LIH is more a local or an international player.</p>
<p>6. Collaboration with Luxembourg research actors: The evaluation shall describe and appraise the research collaboration patterns with the other two CRPs and the University of Luxembourg (UL), both quantitatively and qualitatively. The evaluation shall use the Common Strategy Paper 2016-2025 of the three CRPs and UL as one important source for the assessment of intensified collaboration patterns. The evaluation shall further review the positioning of LIH with regard to the growing and now sizeable university UL, including the complementarity of research approaches. Past achievements and challenges shall be evaluated as well as future potentials.</p>
<p>7. Human Resource (HR) policy and performance: The evaluation shall include a review of recruitment and career policies and the performance of key staff. The issue of PhD training (together with UL and other organisations) shall be evaluated, as well as matters of internal and external training and the supply of life long learning courses for industry and society.</p>
<p>8. General working conditions and infrastructure: The evaluation shall consider if LIH offers its researchers the intellectual, organisational and material working conditions that are internationally competitive and can be justified to the taxpayer. This includes also the infrastructure as well as the general support structures of the centre. Regarding infrastructures, the evaluation shall also review the business model, operating modes, responsibilities and user access, further the existence and functionality of core facilities (for internal use and as external services).</p>
<p>9. Campus: The evaluation shall review whether the LIH premises are appropriate but also well used and supportive to intra- and inter-organisational collaboration. This is especially important for the new location in Belval.</p>
<p>10. Governance: The evaluation shall analyse the relevant governance structures, both within the centre and in relation to MESR and the government. This includes also funding matters, the level of achievement regarding performance indicators and the dealing in case of underperformance. In this topic the evaluation shall also review and discuss the ability of LIH to contribute to national priority setting.</p>
<p>11. Management and organisation, incl. budget: In this broad evaluation task a number of topics shall be evaluated, including the management structure, the quality of decision making processes (including management in case of a crisis), the use of the granted financial and organisational autonomy according to the law, the budgeting processes, the financial record and sources of income, the installation of proper quality management systems and related points. Another topic</p>

to be evaluated is the appropriateness of the inner structure of the centre and the leadership performance on all levels, i.e. centre, departments and units. The evaluation shall review the capability (on all levels) to implement and develop the research agenda of LIH.

12. **Research and innovation culture:** The evaluation shall take into account questions of research and innovation culture like RRI, open science and innovation, public and community engagement, ethics, public understanding of research and comparable activities.

13. **Overall assessment:** An overall assessment shall be provided.

Appendix C : Glossary

3LIU:	reference to 3 research institutions LIST, LISER, LIH and UL
BDO:	Business Development Office
BoD:	Board of Directors
CEO:	Chief Executive Officer
CFAO:	Chief Financial and Administrative Officer
CHL:	Centre Hospitalier Luxembourg
CRP-Santé:	Centre de Recherche Public de la Santé
DII:	Department of Infection & Immunity
DONC:	Department of Oncology
DoPH:	Department of Population Health
EAB:	External Advisory Board
EC:	European Commission
FNR:	Luxembourg National Research Fund
FNR AFR-PPP:	Industrial Fellowships programme
FTE:	Full-time Equivalent
IBBL:	Integrated BioBank of Luxembourg
IPR:	Intellectual Property Rights
KPI:	Key Performance Indicator
LCSB:	Luxembourg Centre for Systems Biomedicine
LCTR:	Luxembourg Centre for Clinical and Translational Research
LI:	Luxembourg Institutes: joint reference to LIH, LIST LISER 3LIU
LIH:	Luxembourg Institute of Health
LISER:	Luxembourg Institute of Socio-Economic Research
LIST:	Luxembourg Institute of Science and Technology
MESR:	Luxembourg Ministry of Education, Science and Research
PC1417:	2014-2017 performance contract
PC1821:	2018-2021 performance contract
PFP:	Personal Functional Profiling
PPP:	Public-Private Partnerships
SAR:	Self- Assessment Report
SSC:	Scientific Steering Committee

TSC: Translational Steering Committee
TRL: Technology Readiness Level
UL: University of Luxembourg

Appendix D Site visit programme

6.9 Peer review programme (institute level) – October 16 and 17

Day 1 – October 16

Time	Programme	By
11.30/12.00	Arrival at airport/train station	
12.00 - 13.00	Transfer to institute	
13.00 - 14.30	Over sandwich lunch: <ul style="list-style-type: none"> Recap of department evaluations findings Identification of main discussion points (based on Technopolis note) Reporting format; Work distribution among peers 	Peers and Technopolis only Peers: <ul style="list-style-type: none"> - Pr Helle Ulrich (Institute of Molecular Biology) - Pr Geraldine Thomas (Imperial College London) - Pr Patrick Rossignol (Centre d'Investigation Clinique Plurithématique Pierre Drouin) - Pr Pierre Hainaut (Institute for Advanced Biosciences) - Pr Rudi Beyaert (VIB Inflammation Centre Universität Gent) Technopolis: <ul style="list-style-type: none"> - Anke Nooijen - Geert Van der Veen - Janna van Belle - Fritz Ohler
14:30 - 15.00	Group discussion on valorisation of research results and organisation of PPPs	Relevant staff <ul style="list-style-type: none"> - Dr Fabrice Mouche, Head of BDO - Dr Fabienne Roussel, TT&IP Officer (BDO) - Patrizia Maters, Legal Officer (BDO) - Dr Frank Glod, Head of SO - Dr Sylvie Delhalle, Scientific Advisor and Project Coordinator (DII) - Dr Cristina Maximo, Departmental Grant Administrator (DONC) - Dr Isabelle Ernens, Sr Project Coordinator (DoPH)
15.00 - 15.15	General Q&A about Administrative Core Services	- Mr Karl-Heinz Dick, CFAO
15.15 - 15.30	Tea/coffee	
15.30 - 16.00	Discussion on HRM policy and issues (including Performance Management)	HRM director <ul style="list-style-type: none"> - Ms Valérie Gavroy, HR Director - Mr Karl-Heinz Dick, CFAO
16.00 - 17.00	Discussion on Institute Finance and mechanisms for distribution of block grant, including a discussion on institute overhead and the role of the administration.	Finance director (may be accompanied by institute director) <ul style="list-style-type: none"> - Mr Karl-Heinz Dick, CFAO - Ms Nancy Bechoux, Finance Manager - Dr Ulf Nehrbass, CEO - Dr Catherine Larue, CEO IBBL
17:00 – 18.30	Discussion about performance and strategy with Institute Board of Directors	Representation of Institute Board, including Government Commissioner: <ul style="list-style-type: none"> - Dr Gregor Baertz, President of the Board - Dr Nadine C Martin, Vice-president of the Board - Ms Patrizia Luchetta - Mr Xavier Poos, Government Commissioner
18.30 - 19.00	Recap/Draft conclusions on the first day	Peers only
19.00 – 20:00	Transfer to hotel, Free time	

20:00-...	Dinner	<p>In presence of institute management and (representation of) Institute Board:</p> <ul style="list-style-type: none"> - Dr Gregor Baertz, President of the Board - Ms Patrizia Luchetta - Dr Ulf Nehrbass, CEO - Dr Catherine Larue, CEO IBBL - Mr Karl-Heinz Dick, CFAO - Dr Frank Glod, Head of SO - Prof Dr Markus Ollert, Director DII - Pr Laetitia Huiart, Director DoPH - Pr Rolf Bjerkvig, Director DONC - Pr Simone Niclou, Deputy Head DONC
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Day 2 – October 17

Time	Programme	By
08:30 - 8:45	Transfer to institute	
08.45 - 10.30	Discussion on institute strategy, past and future (and relation to institute mission performance contract with the Ministry)	<p>Institute director, executive committee</p> <ul style="list-style-type: none"> - Dr Ulf Nehrbass, CEO - Dr Catherine Larue, CEO IBBL - Mr Karl-Heinz Dick, CFAO - Dr Frank Glod, Head of SO - Prof Dr Markus Ollert, Director DII - Pr Laetitia Huiart, Director DoPH - Pr Rolf Bjerkvig, Director DONC
10.30 - 10.45	Tea/coffee	
10.45 - 11.45	Group discussion with Staff Delegation	<p>(Representation of) Staff Delegation</p> <ul style="list-style-type: none"> - Wim Ammerlaan - Sylvie Delhalle - Coralie Dessenne - Brian De Witt - Fred Fack - Jonathan Turner - H�el�ene Agostinis
11.45 - 12.15	Discussion about communication policy (internal and external communication, including science communication and PR)	<ul style="list-style-type: none"> - Juliette Pertuy, Communication Manager
12:15 - 13:00	(simple) Lunch	Peers and Technopolis only
13:00 - 14:45	Time to draft preliminary conclusions	Peers and Technopolis only
14:45 - 15:00	Tea/coffee	
15.00 - 16.00	Presentation of preliminary conclusions and discussion on possible recommendations	<p>To institute management and client (MESR)</p> <ul style="list-style-type: none"> - Dr Ulf Nehrbass, CEO - Dr Catherine Larue, CEO IBBL - Mr Karl-Heinz Dick, CFAO - Dr Frank Glod, Head of SO - Prof Dr Markus Ollert, Director DII - Pr Laetitia Huiart, Director DoPH - Pr Rolf Bjerkvig, Director DONC - Pr Simone Niclou, Deputy Head DONC
16.00	End of programme, transfer to train station/airport	

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