

BBMRI-ERIC GRANT AGREEMENT NO 676550

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REPORTS FROM THE INTERNATIONAL ADVISORY COMMITTEE

Executive Summary

The International Advisory Committee was set up to ensure the scientific excellence of the work and to provide visions for the structuring and operation of the activities of ADOPT BBMRI-ERIC. The committee consisted of international leaders of the scientific community, namely Dr. Isabel Fortier (Montreal, CA), Prof. Rongxing Gan (Shanghai,CN), Dr. Deborah Mascalzoni (Uppsala, SE), Dr. Jim Vaught (Washington DC, USA) and Eero Vuorio (chair, Turku, Finland). Since the start of ADOPT Project as of 1st October 2015, the International Advisory committee has commenced twice to reflect upon the work carried out. This report presents the reports from the committee provided in April 2016 and in March 2017.



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Document log

Issue	Date	Comment	Author/partner
D1.1-Rev1	2017-08-16	Inclusion of EU funding recognition to comply with Grant Agreement art. 29.4. Updates on Deliverable Template.	Outi Törnwall



Report of the first meeting of the International Advisory Committee (IAC) of ADOPT BBMRI-ERIC in Valletta, Malta on March 16-17, 2016

Members of the IAC, **Dr. Isabel Fortier** (Montreal, CA), **Prof. Rongxing Gan** (Shanghai, CN), **Dr. Deborah Mascalzoni** (Uppsala, SE), **Dr. Jim Vaught** (Washington DC, USA) and **Eero Vuorio** (chair, Turku, Finland), met for the first time in Valletta, Malta on March 16-17, 2016 for a joint meeting of ADOPT BBMRI-ERIC Management Committee and IAC. All IAC members were present for the entire program, which was preceded by a concise introduction to BBMRI-ERIC by the Director General Jan-Eric Litton, as well as members of the Headquarters staff and Common Service representatives.

The **background material** provided to IAC members for this first meeting of the IAC comprised the 177-page project proposal of the ADOPT BBMRI-ERIC (dated January 14, 2015). The project is funded by the European Commission with approximately 5 MEUR for a 3-year period starting in Oct 2015. The chair of the IAC reminded panel members that according to the Grant Agreement the IAC is expected to advise ADOPT BBMRI-ERIC in all relevant matters “to ensure scientific excellence as well as compliance with the needs of industry and society” and to provide a vision for the structuring and operation of activities of ADOPT BBMRI-ERIC within the approved Grant Agreement. He also reminded the IAC members that they should not propose changes to the approved Grant Agreement. The IAC is scheduled to meet once a year and produce a report (deliverable D1.5) at months 7 and 19 of the project (April 2016 and April 2017).

In the absence of other introductory material, the observations summarized in this report reflect the opinions of IAC members based on presentations and discussions during the Malta meeting against the project proposal, including the deliverables and milestones therein.

Recommendation 1: For the next IAC meeting in Spring 2017, the IAC members should be provided with short structured reports on progress in each Work Package at least one week before the meeting.

1. Relationship of the ADOPT BBMRI-ERIC project with the BBMRI-ERIC Research Infrastructure

The IAC commended BBMRI-ERIC for adopting for the ADOPT BBMRI-ERIC project the same governance structure that already exists for the Infrastructure, thereby avoiding creation of additional governance/administrative layers (with the exception of the IAC itself). Both the Director General of BBMRI-ERIC (Jan-Eric Litton) and the IAC chair reminded IAC members that targeted INFRADEV-3 funding for the pan-European biobanking infrastructure was a result of a favorable evaluation of BBMRI (-ERIC) in September 2013 by an independent Assessment Expert Group (AEG) appointed by ESFRI (the European Strategy Board for Research Infrastructure). In this evaluation of all the Research Infrastructures on the 2010 ESFRI Roadmap, ELIXIR (European Life-Science Infrastructure for Biological Information) and BBMRI were identified as the most advanced Research Infrastructures in the Life Sciences (Biological and Medical Sciences) domain, and were “awarded”



by specific targeted calls for proposals by the European Commission (EC). As the aim of the targeted funding was to support the implementation and development of these the infrastructures, the decision not to establish additional layers of governance in ADOPT BBMRI-ERIC was well justified.

The IAC also commends the ADOPT BBMRI-ERIC project for basing its Work Package (WP) structure on the recommendations and challenges identified in the ESFRI evaluation report of 2013 and the subsequent 2014 ESFRI document (Prioritisation of Support to ESFRI Projects for Implementation); thereby demonstrating their willingness to tackle the points raised in the evaluation report.

For the IAC, the overlap of BBMRI-ERIC Work Program funded by the Members States and the ADOPT BBMRI-ERIC project funded by EC presents a challenge as the activities of the Infrastructure and the ADOPT BBMRI-ERIC project cannot really be separated. However, the IAC did not really consider this a problem, as the advice and recommendations provided in this report will hopefully also be considered by BBMRI-ERIC. The IAC takes note that the membership of BBMRI-ERIC has continued to increase since the writing of the application. This achievement can probably not yet be credited to ADOPT BBMRI-ERIC funding.

BBMRI-ERIC has been successful in obtaining additional external funding from the EU through its participation in other projects that have received funding. The IAC also takes note that the number of samples in BBMRI-ERIC biobank catalogue has continued to increase considerably.

2. Progress within WPs

From the oral reports of the WPs supported by PowerPoint presentations the IAC concluded that work within most Work Packages has started as planned. However, in some cases the WP reports gave essentially the same information that was written in the ADOPT BBMRI-ERIC application dated January 14, 2015. This could be justified by the first deliverables and milestones still half a year ahead. As very few deliverables have been scheduled for the first 6 months of the project, it is somewhat difficult for the IAC to judge how well the individual subprojects have progressed. However, the IAC notes that for a three-year project all partners should have **a sense of urgency from the very beginning of the project** in order to meet the deadlines and milestones without delays

The IAC noted that the **risk analysis** of the ADOPT BBMRI-ERIC proposal was quite optimistic and no high risks were identified. The IAC feels that both the time and effort needed to meet the milestones may be underestimated. Experience from other projects has demonstrated that access to samples and data, implementation of data infrastructures, and data harmonization and integration processes are generally much more time consuming than originally expected. In addition, the availability of colon cancer samples of adequate quality, the extraction of data from patient records, and creating a common service for rare diseases are among the issues which may pose more significant risks than noted in the table. The IAC also notes, that the original ADOPT BBMRI-ERIC proposal discussed at length the **performance indicators**, but this topic was not really covered in the presentations.

Recommendation 2. The IAC recommends that all ADOPT BBMRI-ERIC participants make use of the time available before first deliverables are due in order to detail their plans and prepare for the deliverables. This is particularly important for the cross-cutting nature of the major deliverable such as the colorectal cancer project, as a delay in one WP may actually also lead to delays in the other WPs.



Recommendation 3. The IAC recommends more interaction between the WPs, (e.g. access; identity confirmation issues) as tools that already exist should be used rather than duplication of tool development.

Recommendation 4. Work on the **performance indicators** should be started quickly. The IAC expects to hear information on the specific indicators to be used in the next IAC meeting.

3. Awareness of developments in other projects in EU and globally

The IAC was somewhat disappointed that in some WP reports there was an apparent lack of awareness of coordination and harmonization efforts made elsewhere, in other EU-funded projects (e.g. BioSHaRE, RD-Connect, including large cluster projects like BioMedBridges and the on-going CORBEL) and in global consortia (P3G, Maelstrom). A number of organizations have developed, implemented and tested methods, software and other resources that can leverage the research potential of BBMRI-ADOPT and facilitate the achievement of the project. Maybe this information is known to the WPs, but just did not receive attention in the reports. It is very important for ADOPT BBMRI-ERIC to build its coordination and harmonization activities on the results of previous projects, to learn from their errors and achievements, adopt their useful results and avoid duplication of work done elsewhere.

The IAC sees the current situation as an opportunity for Research Infrastructures, particularly BBMRI-ERIC and ELIXIR, but also other life science infrastructures, to adopt an important role in storage and distribution of samples and data produced by research projects.

Developing this as a service function could be an important step towards sustainable funding of the infrastructures.

A positive example of interactions of ADOPT BBMRI-ERIC with ELIXIR/EBI was reported by the rare disease WP; the two Research Infrastructures had worked on the division of tasks and the WP had also been in contact with the different national, European and global Rare Disease organizations. The use case on Osteogenesis Imperfecta has been started, but thus far focuses primarily on one country (Italy). As already planned, this WP will foster adoption of a pan-European aspect following earlier positive models, e.g. the example of the neuromuscular disease community in collaboration with the respective patient organizations.

Recommendation 5. All WPs involved in development of standards, access rules and software solutions towards interoperability of different datasets should closely study progress made in earlier and ongoing EU-funded and global consortia, and thereby avoid duplication of efforts.

4. The cross-cutting core project on colon cancer is an excellent idea as it will drive the entire ADOPT project. Therefore, clarification of the goals is very important. During the long and relatively unstructured discussion on the variables and definitions of data to be included in the biobank data repository, the goal of the core project (biomarker development vs generation of a database) was never agreed upon. As the mandatory/recommended/voluntary nature of variables is dependent on the goal and the mandatory status will influence selection of the 10 000 colorectal tumor samples, it is important to decide on the primary and possibly



secondary goals. It is also important to select and clearly define a limited number of core variables to be included in the final database. Tumor sample selection and all data integration procedures depend on the generation of this core list of variables.

The IAC feels that discussions on the variables to be included as mandatory or voluntary should carefully consider the expert opinions of clinical and basic researchers and the needs of potential users of such a valuable resource. As this represents the first BBMRI-ERIC –wide disease database, it is important that all key stakeholders can accept the proposed core variables. In an ideal situation, such a collection could create a global recommendation of key data to be integrated and made available through participating biobanks (with a possibility to include additional optional data if readily available). The easiest way to obtain a dataset of 10 000 cases is to initially contact a few large biobanks and take into account the information available in these biobanks to help define the core dataset to be generated. However, to be truly cross-cutting, the project should also include samples from smaller biobanks. During the discussion, a word of warning was also raised: development of detailed list of core variables for one disease group is unlikely to suit other disease entities without modifications.

The IAC was surprised that the discussion focused solely on existing colorectal samples, for which only a limited amount of harmonization can be achieved retrospectively. It became obvious that heterogeneity of existing sample variables is likely to be a major challenge of the core project; yet, prospective sample collection was not discussed, although this would simplify harmonized/standardized collection of samples and core data.

Recommendation 6. It is important to decide on the scientific goal(s) of the colon cancer project and thereafter decide on the variables and definitions of data to be used as mandatory and recommended/voluntary. The IAC recommends that earlier work on colon cancer cohorts (e.g. International Cancer Genome Consortium, The Cancer Genome Atlas and IARC) and international professional organizations are consulted with an aim to reach global consensus on data variables.

5. Integration of ELSI and IT with the core project was considered very important and challenging. Information of the colorectal cancer cohort must also contain data on what can be done with the samples, on access policy and on identification of users of secure access. Moreover, it is extremely important to ensure that limitations of use set by the specific cohort, or by the consents in the different countries, or special requirements are “attached to the data”. This means that scientists will be able to search the databases without unwittingly violating legal or ethical constraints. Harmonization of samples from the ELSI perspective is highly relevant, but heterogeneity of practices in different countries is a major challenge. A certain standard is needed. It is also relevant to establish beforehand a policy of return to the bio- resources, that afterwards can apply their local policy on return (or not return) of relevant results.



6. Internationalization in the context of ADOPT BBMRI-ERIC is primarily relevant to dealing with expanding the membership in Europe but also for other continents. At the EU level this is a well justified political goal and should be encouraged. Together with the BBMRI-LPC project BBMRI-ERIC has been successful in establishing connections to most EU “Widening” countries. However, interactions at the scientific level with biobanks in other continents receives much less attention, although members of the IAC are aware of the participation of BBMRI-ERIC in such networks.

7. Funding

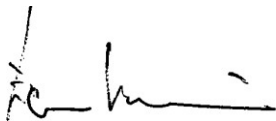
Unlike most life science Research Infrastructures BBMRI-ERIC has been successful in obtaining a **large number of short-term funding** streams as partners or coordinators in 11 EU-supported projects. While this support helps BBMRI-ERIC to extend its activities, the IAC is concerned that the relatively small staff of the Headquarters may be spreading themselves too thin with so many projects, deliverables and milestones which may even be overlapping between projects.

Considering the large contribution of ADOPT BBMRI-ERIC funding to the total BBMRI-ERIC budget, sustainability of the infrastructure in October 2018 when the ADOPT project ends should be a concern from the beginning. This is obviously an area where the IAC is willing to give its support towards increased sustainable funding of BBMRI-ERIC.

Finally, the IAC commends the leadership of ADOPT BBMRI-ERIC for their achievements during the first years of the Infrastructure. We trust that the observations presented in this report, together with the recommendations given, will help the ADOPT BBMRI-ERIC project to achieve its major goals and thereby support BBMRI-ERIC in becoming a World-leading biobanking infrastructure.

On behalf of the International Advisory Committee of ADOPT BBMRI-ERIC,

Turku, April 15, 2016



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Report of the second (and last) meeting of the International Advisory Committee (IAC) of ADOPT BBMRI-ERIC in Trondheim, Norway on March 7-8, 2017

Members of the IAC, **Dr. Isabel Fortier** (Montreal, CA), **Prof. Rongxing Gan** (Shanghai, CN), **Dr. Deborah Mascalzoni** (Uppsala, SE), **Dr. Jim Vaught** (Washington DC, USA) and **Eero Vuorio** (chair, Turku, Finland), met for their second meeting in Trondheim, Norway on March 7-8, 2017 for a joint meeting of ADOPT BBMRI-ERIC Management Committee and IAC. With the exception of Deborah Mascalzoni all IAC members were present for the entire program. Dr Mascalzoni participated in the IAC discussion through a teleconference.

The meeting was hosted by Biobank Norway and included a visit to HUNT Biobank in Levanger. Professor Kristian Hveem gave an excellent presentation of the large, well- functioning HUNT biobank and on the scientific achievements already made. The possibility to link molecular data obtained from the biobanked samples with extensive national registries and electronic health records presents an excellent model for all BBMRI-ERIC National nodes and biobanks.

The background material provided to IAC members for the second meeting of the IAC comprised the 26-page text of the ADOPT BBMRI-ERIC Annual Report (Reporting period: from 01/10/2015 to 30/09/2016). The chair of the IAC reminded panel members that according to the Grant Agreement the IAC is expected to advise ADOPT BBMRI-ERIC in all relevant matters “to ensure scientific excellence as well as compliance with the needs of industry and society” and to provide a vision for the structuring and operation of activities of ADOPT BBMRI-ERIC within the approved Grant Agreement. He also reminded the IAC members that their task is not to propose changes to the approved Grant Agreement.

The first report of the IAC was based on the ADOPT BBMRI-ERIC meeting in Valletta, Malta on March 16-17, 2016 contained a number of observations and recommendations, and can also be considered background material for the Trondheim meeting.

Finally, and most importantly this report is largely based on presentations and discussions during the Trondheim meeting against the project proposal, including the deliverables and milestones therein. The presentations obviously focused on progress of the ADOPT project achieved since the previous IAC statement.

1. General Comments

The IAC commends Professor Jan-Eric Litton, PI of the ADOPT project and Director General of BBMRI-ERIC, and his ADOPT team for addressing the recommendations made by IAC last year. This includes the recommendation that each Work Package provides a short report on their progress to IAC members before the next meeting. The IAC received the First Annual Report of ADOPT BBMRI-ERIC for EC with the meeting documents, which fulfilled this request.



The IAC also acknowledges the very friendly and open atmosphere of the Trondheim meeting.

2. Relationship of the ADOPT BBMRI-ERIC project with the BBMRI-ERIC Research Infrastructure

During the presentations in Trondheim the IAC members were pleased to note that the integration of the ADOPT BBMRI-ERIC project and BBMRI-ERIC had progressed very well. The ADOPT funding was clearly being used to support the implementation and development of BBMRI-ERIC without any additional layers of governance. The IAC also took note of a change in the Management Committee (National node director) of BBMRI-ERIC and an analogous change in the WP leadership. This was a wise decision considering the close links between the ADOPT project and BBMRI-ERIC. A new situation will emerge later in 2017 when the Director General leaves office. It will be important to offer the new Director General a key position in the ADOPT project to maintain this close link.

The IAC takes note that the membership of BBMRI-ERIC has continued to increase during the past year, which is a strong signal of widespread trust in the infrastructure. It is a particularly positive sign to see such a large number of Eastern European ("Widening") countries as Members and Observers of BBMRI-ERIC.

3. Progress within WPs

In 2016, the IAC recommended that all ADOPT BBMRI-ERIC participants make use of the time available before first deliverables are due in order to detail their plans and prepare for the deliverables. From the reports of the WPs supported by PowerPoint presentations the IAC concluded that work within all Work Packages had made progress. However, the IAC still noted differences in the level of rigor between the WPs. Underspensing of funds granted were also noted. Delays in starting some WPs probably explain why in the Resource review for the first Annual Report only 11 % of total funds had been used during the first 12-month period. Despite this low spending (or reporting?) rate, the IAC notes that almost all of the Milestones had been reached and Deliverables produced according to the Grant Agreement. The IAC also observed an increased number of **interactions between the WPs** as was recommended in 2016.

In 2016 the IAC stated that the **risk analysis** of the ADOPT proposal was quite optimistic and no high risks were identified. By the Trondheim meeting these estimates had been appropriately revised with more medium/high risk aims, possibly after recognition of the unexpectedly high complexity of data harmonization and integration, European languages, access to samples and data, and the overall implementation of the data infrastructures. In addition, processes are generally much more time consuming than originally expected. It is not yet clear how well the inclusion criteria for biobanked samples will work in the pilot for colon cancer cohort.

The IAC notes that its recommendation on the **performance indicators** had been taken up by BBMRI-ERIC, a logical step to take, as the Member States expect such indicators for their own use.



4. Awareness of developments in other projects in EU and globally

Last year the IAC noted in some WP reports an apparent lack of awareness of coordination and harmonization efforts made elsewhere, in EU-funded and other projects (e.g. BioSHaRE, RD-Connect, including large cluster projects like BioMedBridges and the on-going CORBEL, or National Cancer Institute, P3G, Maelstrom Research). Many contacts to these projects and organizations were made in the current presentations. Yet, the IAC feels these efforts could be strengthened. One such area is the interaction of the rare disease WP (WP7) of ADOPT BBMRI-ERIC with RD-Connect and EuroBioBank which still appear as separate entities with similar goals. As stated already in 2016, the use case on Osteogenesis Imperfecta should be enlarged to cover other countries than Italy to demonstrate its usefulness in the pan-European and global context.

5. The pilot project on colon cancer

The IAC continues to maintain a very favorable view concerning this pilot, as it will drive the entire ADOPT project. A lot of effort had been put into identifying the core variables to be generated based on different consultations. One goal of the pilot is to serve as a testbed for the evaluation of the feasibility to: (1) generate **all** the core variables in an integrated database, and (2) build a **high quality** dataset supporting innovative research. The IAC discussed the potential challenges to be faced in achieving data integration and consider important that the ADOPT investigators continue pursuing the implementation of a scientifically based approach to support decision making and rigorous data processing. For example, it is essential that the manual data entry and semi-automated exercise (processing data under a compatible format) use consistent decision making rules to generate the core variables (e.g. same rules to code open text data or to deal with missing values and outliers). In addition, data processing rules across biobanks must be consistent. It could thus be important, for manual data entry, to provide the biobanks with the specific algorithms they need apply to generate the core variables.

The IAC feels it is important to start expanding on the concept of the type of scientific questions the colon cancer cohort should be used for. Biomarker development emerged as one potential area where the cohort could be very useful.

6. ELSI activities

WP5 and the Common Service CS-ELSI of BBMRI-ERIC had seen a number of changes in their operational plans during the past year. These included a revised concept for the Stakeholder forum under BBMRI-ERIC headquarters, establishment of an Engagement officer for the Stakeholder forum and joining of existing ELSI tools (hSERN, LAT and legal Wiki) into a single, more user-friendly and sustainable service. The IAC views these changes as simplifications and commends WP5 and CS-ELSI for these improvements. Yet, heterogeneity of ELSI practices in different countries remains a major challenge. The establishment of the ELSI help desk should be very helpful for different users. The functionality of the ethics check will be tested with the colon cancer cohort. This will help in identifying gaps or problems, fixing them and providing a tested tool for further usage.



The collaboration with RD-Connect on Surveys with the Stakeholders is also welcomed as a concrete effort to maximize results across EU funded projects.

7. Internationalization

Together with the BBMRI-LPC and ADOPT projects BBMRI-ERIC has been successful in establishing connections to nearly all “Widening” countries in Europe and is among the most successful research infrastructures also in this respect. Potential new Members had again been identified, although final applications for Membership were still pending.

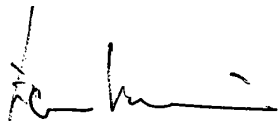
8. Funding perspective

In 2016, the IAC noted that the contribution of ADOPT BBMRI-ERIC funding to the total BBMRI-ERIC budget was very high and expressed a concern for the sustainability of the infrastructure after October 2018 when the ADOPT project ends. This is obviously also a concern for the Member States who must be responsible for the sustainable funding of BBMRI-ERIC.

Finally, the IAC commends the leadership of ADOPT BBMRI-ERIC for their achievements to date. Recognizing that this will be the last IAC report, we hope that the observations and comments presented in this report will help the ADOPT BBMRI-ERIC project to continue its support to BBMRI-ERIC. Overall, the IAC feels that the ADOPT project has been successful in this task, but further financial support is needed to implement and pilot the tools being developed for BBMRI-ERIC.

On behalf of the International Advisory Committee of ADOPT BBMRI-ERIC, Trondheim, March 8,

2017



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