PERMIT – PERsonalised MedicIne Trials

Advisory boards report

Work Package 1 - Deliverable 1.2

Deliverable no	1.2
Deliverable Title	Report of Advisory Board
Contractual delivery month	M15 (March 2021)
Responsible Partner	ECRIN
Author(s)	Paula Garcia

Executive summary

The PERMIT project is supported by two advisory boards that provide insight and council for the good conduct of the project. The Scientific Advisory Board (SAB) and the Ethics Advisory Board (EAB) of the PERMIT project gathered in a joint meeting on January 20, 2021 and provided feedback on the findings of the first year of the PERMIT project. They also provided suggestions for the second and final year of the project, recommending field experts that could provide insight across the different work packages. The board members considered the developments of the first year of PERMIT highly relevant and encouraged the consortium to continue its efforts.

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Document log

Issue	Date (yyyy-mm-dd)	Comment	Author/partner
1	2021-03-31		Paula Garcia -ECRIN
2	2022-11-07	Added footer with reference to grant number	Paula Garcia -ECRIN
3	2022-11-08	Removed "summary of discussions" pg8	Paula Garcia -ECRIN

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Background – Advisory Boards' Mission

The PERMIT project is supported by two advisory boards that provide insight and council for the good conduct of the project. These boards were constituted in April 2020 for the Scientific Advisory Board (SAB) and June 2020 for the Ethics Advisory Board (EAB). The SAB advises the PERMIT consortium on the approach, the methodology and the scientific content of the project and the EAB provides insight on all the ethical aspects related to the PERMIT project.

Approach – Joint meeting of the boards

The advisory boards of the PERMIT project had each met once during 2020. During the first meeting of each board the project was presented in detail to the board members, and the members then provided advice and suggestions for the initial stages of the project (see Deliverable 1.1 – Advisory boards report).

The first year of the PERMIT project focused solely on conducting a series of scoping reviews to map the methods used throughout the personalised medicine (PM) research pipeline and to identifying gaps and outline existing needs for standards and methodological guidelines. The scoping reviews culminated in a joint Gap Analysis Workshop, where the findings of each of the four scoping reviews and the main gaps were discussed with the consortium. This workshop took place on December 2-3, 2020.

On January 15, 2021 the General Assembly gathered for a virtual meeting, and the results of the Gap Analysis Workshop were presented, as were the work plans for the year 2021. The members of the SAB and EAB were invited to join the General Assembly, so they could also listen to the presentations of the gap analysis and the envisioned work plans for each work package. Following the General Assembly, a joint meeting of both boards was held on 20 January, 2021 to allow members to discuss amongst themselves and to provide feedback on the findings of the first year suggestions for the second year of the project.

Results – joint EAB & SAB meeting

Through the discussion, the members of the SAB highlighted the important distinction that must be made when speaking of validation, between the validation of the final machine learning model, and the validation of the model building approaches. Also on the topic of validation of the stratification, the interest of replicating the stratification through a biological model was highlighted as an option for external validity. This can be particularly challenging, and in some cases it is simply not possible to find a biological model for the replication. For these cases it was suggested to apply supervised clustering. Even if partial, it can also provide external validation. The importance of maintaining the quality of the data, and ensuring homogeneity when collecting data from different sources was also highlighted as a key recommendation.

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Regarding the questions on sample size calculation, SAB members provided references on sample size calculation that can be applied for certain statistical models. Their application will depend on the volume and type of data, as well as the response that is being assessed. They highlighted that a simulation or pilot study can help to define the sample size as well.

From the ethical standpoint, the EAB highlighted the importance of submitting clear and concise evidence to competent authorities and ethics committees that presents a full picture of the clustering and the process that was followed for its validation. Ethics committees need to have sufficient evidence outlining a clear benefit for patients from the clustering and subsequent treatment of follow-up, in order to approve clinical trials or further studies.

After the meeting, several board members provided suggestions to the Coordinator of field experts that could be invited to the working sessions and workshops that will be organized in 2021 for the different work packages.

Discussion and Conclusions

Both the SAB and the EAB are now fully familiar with the PERMIT project and engaged in its successful development. The board members considered the developments of the first year of PERMIT highly relevant and encouraged the consortium to continue its efforts. The members provided encouraging recommendations and voiced their disposition to be consulted during the recommendation drafting process. The suggestions provided by the board members on field experts will be taken into consideration and the experts will be invited to the workshops and working sessions organized by the different work packages in 2021.

Next Steps

It is foreseen that the General Assembly meet again during the summer of 2021, and it will determine the need to gather the boards for consultation again before the end of the project. If the General Assembly or Steering Committee consider that one or both boards must gather sooner, an extraordinary meeting will be organized. Were the General Assembly to determine that there is no need to gather the board members, they will all be invited to the project's final meeting.

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Appendix I - Meeting minutes of joint SAB & EAB meeting

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PERMIT SCIENTIFIC AND ETHICS ADVISORY BOARD MEETING MINUTES

20 January, 2021
Microsoft Teams

Participants:

- Jacques DEMOTES (JD) – ECRIN
- Paula GARCIA (PG) – ECRIN
- Christine KUBIAK (CK) – ECRIN
- Mihaela MATEI (MM) - ECRIN
- Annalisa BARLA (AB) – SAB member
- Lars HULSTAERT (LH) – SAB member
- Martin POSCH (MP) – SAB member
- Virginie PIRARD (VP) – EAB member
- Simone NICLOU (SN) – EAB member
- Chiara GERARDI (CG) - IRFMN
- Florence BIETRIX (FB) – EATRIS
- Emanuela OLDONI (EO) – EATRIS
- Vibeke FOSSE (VF) – UiB/EATRIS
- Teresa TORRES (TT) – PSSJD
- Enrico GLAAB (EG) – Elixir-Lu
- Tamas BERECZKY – EAB member
- David PEROL – EAB member

Apologies:

- Raphaël PORCHER – UPD
- Rita BANZI (RB) – IRFMN
- Irene SCHLUENDER - TMF

Objectives of the meeting:

- Present and discuss the findings of the first year of the PERMIT project
- Discuss potential missed gaps and opportunities for recommendations
- Identify potential experts for the future working sessions and workshops
- Present the deliverable on the inventory of ethical and data protection issues in PM research

Overview of the presentation

- The first year of the PERMIT project focused on a series of scoping reviews mapping the existing methods for personalised medicine (PM) research throughout the research pipeline, and identifying the existing gaps and

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opportunities for recommendations and standards. It culminated in a Gap Analysis Workshop.
- A survey on industry practices for PM preclinical research was also carried out.
- The gaps that were identified for each of the four stages of the PM research pipeline and those gaps that were transversal were also highlighted (see attached slides).
- During 2021 PERMIT aims to draft the recommendations that will address these gaps. In order to achieve this, a series of working sessions and workshops has been planned from February to September. In the working sessions, consortium members will meet with external field experts to address the different questions and gaps and discuss potential recommendations. Then a draft of the recommendations will be produced, and will be discussed in dedicated workshops with all key stakeholders, again associating the external experts.
- Once recommendations have been published, training material will be developed to facilitate their implementation will be produced.
- A series of questions regarding regulatory gaps were raised by the PERMIT project to the CTFG, who provided preliminary responses (see slides attached). These were discussed with the attendees.
- Deliverable 1.3 was briefly discussed. The preparation of this deliverable will be led by Mihaela Matei from ECRIN and Irene Schluender from TMF. For this deliverable an inventory of ethical and data protection issues arising along the PM research pipeline will be made. In order to convey the main ethical issues, representatives of patient associations will be associated to the process, as well as representatives from ethics committees. EAB members will also be consulted for input.

Summary of discussion

- The important distinction of the validation of the final machine learning model, and the validation of the model building approaches was made by MP.
- The interest of replicating the stratification through a biological model was highlighted for external validity. But in some cases this is not possible for which the suggestion of using supervised clustering, at least partially, was raised.
- AB highlighted that ensuring that the data used is of the best possible quality is therefore key, as is ensuring that data collected from different sources keeps the same data standards.
- VP pointed to a key aspect in terms of presenting results of the clustering and of its validation to competent authorities and ethics committees. Ethics committees need to have sufficient evidence outlining a clear benefit for patients from the clustering and subsequent treatment of follow-up, in order to approve clinical trials or further studies.
- Regarding the definition of sample size for the machine learning models, MP pointed out that for statistical models some literature is available, but much will depend on

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the volume and type of data, as well as the response. A simulation or pilot study can help to define the sample size as well.

Conclusions
- The boards made constructive contributions on the findings of the scoping reviews and the preliminary guidance of the CTFG, that will help to raise the right questions during the working sessions and workshops. - Board members also provided suggestions of external experts from diverse fields who could be invited to the working sessions and workshops. - The General Assembly of the project will gather in autumn and will assess the need for a final consultation of the boards.

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