

Returning Clinical Trial Data to study participants within a GDPR compliant and approved ethical framework

All information regarding future IMI Call topics is indicative and subject to change. Final information about future IMI Calls will be communicated after approval by the IMI Governing Board.

Topic details

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| Action type | Research and Innovation Action (RIA) |
| Submission and evaluation process | 2 stages |
| IMI2 Strategic Research Agenda - Axis of Research | Adoption of innovative clinical trial paradigms |
| IMI2 Strategic Research Agenda - Health Priority | Other |

Specific challenges to be addressed by public-private collaborative research

A large amount of high-quality health data is collected during clinical studies (interventional and non-interventional), but, beyond the immediate objectives of the study, these valuable data are not used to the extent they merit. Subject to appropriate legal grounds, these data could be used to enrich patients' healthcare records to improve clinical decision-making and reduce duplication in procedures/investigations. In addition, returning clinical trial data to patients could allow them to contribute their data for additional scientific research (e.g. patient-powered research), in particular for rare diseases where treatments and data are scarce or unavailable. Finally, the lack of transparency and sharing of clinical trial data could contribute to the lack of patient willingness to be involved in studies, delays in clinical study set up and conduct, and delays in conducting health research in Europe to the detriment of vulnerable patients and public interest in general.

Some of the main barriers to returning clinical trial data to study participants include:

- Complexities of determining acceptable common data format, processes or infrastructure;
- Complexities of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), Good Clinical Practice (GCP) and EU Clinical Trial Regulation (CTR) (e.g. including study integrity, privacy and confidentiality); and
- Lack of harmonisation of the national legal framework related to processing of health-related data across Member States and need for additional guidance on some practical aspects of the implementation of the General Data Protection Regulation (GDPR), whether for primary and/or secondary use of individual clinical trial data (personal data).

At the same time, there is an increasing awareness that greater transparency and engagement with study participants are needed in clinical research, and that the return of study participants' clinical trial data can address those needs.

In order to tackle these challenges, a multi-national public-private partnership including many of the actors involved in clinical trials processes is necessary:

- Collaboration of **industrial and academic clinical trial sponsors** to develop EU-wide standards for (i) data return to individual study participant and (ii) secondary use of clinical data, as well as to propose and agree on those common standards with ethics committees and personal data protection authorities;
- Collaboration with both **healthcare providers and relevant Electronic Health Record (EHR)/clinical trial technology vendors** to develop the process for returning these data electronically to the patient (directly through an EHR system where possible, or through other means (either electronic or non-electronic) where such a system is not possible), taking into account ongoing and previous activities on European interoperable EHR exchange in alignment with the European Electronic Health Record exchange format (EEHRxF) as set out in Commission Recommendation C(2019) 800¹;
- Inputs from various **EU regulators** will be essential to the success of this project and required to develop common, validated usability and privacy standards. Involvement of **legal counsels and ethics, and data protection experts** will be crucial as data return will have to be compliant with GDPR as well as with local legal and ethical requirements.
- Substantial, focused input from **study participants, patient organisations and healthcare professionals** to fully understand what data would be the most important to return to them, what data would be acceptable for being shared with researchers, and how such data may best be returned and/or shared.

Scope

This project has two main objectives, which are equally important:

- The first one is to align local and pan-European implementations and best practice for handling personal data protection regulations in order to foster the harmonisation of the legal framework applicable to medical research in the Member States;
- The second one is to deliver a pan-European prototype process to return clinical trial data to study participants, building on previous and ongoing EU-level activities on citizen-centric access to health records. This prototype process will be delivered as part of the project alongside a robust business plan to ensure its sustainability.

To support these objectives, the project will:

- Define harmonised rules for complying simultaneously with data protection regulations, regulatory requirements and ethical standards in Europe. These rules are to be endorsed by appropriate regulatory bodies and patients;
- Define which, when and how clinical trial data should be returned to study participants, including for integration in, or interconnection with, patients' individual health records management files or applications and, where they exist, national and/or hospital EHR systems (for clarity, no 'lay summaries' or other expert analyses are within the scope of this project) and EHR standards such as EEHRxF;
- Define data governance models for cases where individual clinical trial data is (or can be) utilised for both healthcare decision making and future research, taking into account previous and ongoing EU-level activities on data governance in these fields;

¹ <https://ec.europa.eu/digital-single-market/en/news/recommendation-european-electronic-health-record-exchange-format>

- Ensure that the whole process, from collection of data to its destruction or anonymisation, including sharing of individual personal data, is aligned with the study participants' expectations and the authorities and ethics committees' standards and procedures, and documented in binding and/or approved standards or guidance documents.

Expected key deliverables

The overarching project deliverable is a working prototype demonstrating how study participants can visualise (directly or indirectly with a healthcare professional), query and share the clinical trial data returned to them. It should cover the following:

- A test version of the prototype process, agile enough to be interoperable in most countries, should be delivered by mid-term, with the final version delivered by month 42 to allow for implementation of the business plan in the final six months.
- For at least one "real" study (type and medical area to be proposed by participating EFPIA companies) the prototype process should demonstrate within a proof of concept mechanism how relevant clinical trial data can be:
 - Either integrated or interconnected with at least two existing repositories (e.g. data in national or hospital patients' EHRs or in other
 - System/application directly accessible to patients); and
 - Can be re-used in further medical health research or clinical studies.
- The working prototype process must be delivered alongside a robust business plan to ensure it is mature enough to pave the way for the development of a sustainable and effective platform after the end of the project.

In addition, the project will have to produce the following key deliverables:

- At least three different decision committees established:
 - One in charge of defining reasonable expectations of researchers, and involving technical experts (including for the anonymisation of health data), healthcare professionals (HCPs)/principal investigators (PIs), and experts in genetics counselling (made up of members of the consortium and external/invited members);
 - One in charge of defining legal and ethical acceptance of proposals, and involving data protection authorities (DPAs) and ethics committees (ECs/International Review Boards (IRBs)) from at least five of the top 10 European countries conducting the most significant number of clinical trials (made of external/invited members); and
 - One in charge of representing patient expectations and involving patient associations (made up of members of the consortium and, if needed, external/invited patient association members).
- Published aligned position papers from the above decision committees, including the proposed regulatory standards and guidance documents. They should include an official opinion of the regulators (e.g. of the European Data Protection Board (EDPB)), where possible;
- Workshops organised with the aim to foster harmonisation of the health data processing provisions across Member States. Decision positions should, where possible, include an official opinion of the regulators (e.g. EDPB) at the end of the project;
- Proposed harmonised standards to be applied to personal data by operational stakeholders, such as sponsors' and investigators' study teams. These documents will have to be discussed with and agreed upon, as much as possible, by decision committees. The proposed standards and documents must at least specify:
 - Which exact data elements and which categories of studies would be suitable and useful for both for being returned to study participants and for further research;

- How to make individual clinical study data available for return to study participants;
- How to allow the processing of individual clinical trial data for re-use in further clinical research projects, including guidelines (a) for consent, either initial (whether for interventional or for non-interventional studies) or for returning data; (b) for selecting the most appropriate legal basis; (c) for clarifying their consequences on patients' rights as granted by the GDPR, in particular their right to be informed and to object; and (d) for establishing contractual agreements among parties conducting trials (in particular between sponsors and investigators/investigational sites using decision trees or other tools to assign appropriate role to each party – i.e. controller, processor, joint-controllers or co-controllers).
- Proposed harmonised standards on how to transform personal clinical data into fully anonymised health data (which are no longer subject to GDPR and other local data protection regulations);
- Proposed harmonised technical standards necessary to handle the data, and including:
 - The analysis of existing standards for securely hosting and exchanging health data;
 - The selection of preferred standards for such activities including definition of type/timing;
 - The assessment of interoperability of clinical trial data with patients' individual health records management files or applications and/or, where existing, national or hospital EHR systems.
- Public release of final harmonised, acceptable technical requirements derived from the above deliverables and position papers, including at least those that allow:
 - Data retrieval and upload;
 - Study participants' access to data, and ability to know what their personal data is being used for and solutions to object/opt-out for any or all further uses of their personal data (preferably in a centralised, multilingual cross-country and cross-sponsor platform);
 - Delivering the data or enabling the patient to handle the data, with the option for the patient to donate the data once for all for scientific research.
- Public release of final harmonised and approved (by data protection authorities and ECs) standards and guidance documents as implemented in industry-wide approach such as a GDPR code of conduct, defining:
 - How to return individual clinical trial data to study participants in Europe (including for study participants to make such data available in EHR or other systems and for further research); and
 - When and how (considering data quality) to deliver which data or annotations of data, specific to the stakeholder (e.g. patient, healthcare professional, sponsors, etc.).

Expected impact

In their proposals, applicants should describe how the outputs of the project will contribute to the following impacts and include, wherever possible baseline, targets and metrics to measure impact:

- **For patients:** the project results should **empower patients** by returning their clinical trial data to them and to their medical records. Data acquired during clinical trials will aid better shared medical decision-making and reduce duplication in procedures/investigations;
- **For healthcare professionals:** enriched healthcare data obtained during clinical care should **aid better clinical decision** making and reduce duplication in patient procedures/investigations;
- **For EU research:** giving patients control of their clinical trial data will **open possibilities for ethical data re-use** e.g. if the patients opt in to donate their data to a common data sharing platform;
- **For pharma:** returning clinical trial data to study participants during study conduct has the potential to **improve adherence** to study procedures and **improve overall patient retention. Facilitate conduct and**

setup of clinical studies as well as access to health data for research. Doing this in a meaningful way will further help to educate patients and in doing so empower them to be equal partners in the management of their disease;

- **For regulators:** it is an opportunity to exchange opinions with counterparts from other countries and researchers to propose informed workable aligned positions;
- **From a societal perspective:** the project will **increase the transparency** of clinical study and therefore increase the **trust** of patients in clinical research. At a time where clinical trials are increasingly complex, this may help with recruitment for studies and **improve oversight by patients and regulators** on clinical data re-use.

In their proposals, applicants should outline how the project plans to leverage the public-private partnership model to maximise impact on innovation, research & development; regulatory, clinical and healthcare practices, where relevant. This could include a strategy for engagement with patients, healthcare professional associations, healthcare professionals, regulators, ethics committees, HTA agencies, payers etc., where relevant.

In addition, applicants should describe how the project will impact the competitiveness and growth of companies, including SMEs.

Moreover, in their proposals, applicants should outline how the project will:

- Manage research data and adhere to ethics requirements² ;
- Disseminate, exploit, and sustain the project results. This may involve engaging with suitable biological and medical sciences research infrastructures³.
- Support the improvement of the interoperability of EHRs by aligning with the EEHRxF.

Communicate the project activities to relevant target audiences.

Potential synergies with existing consortia

Synergies and complementarities should be considered with relevant national, European and non-European initiatives (including suitable biological and medical sciences research infrastructures) in order to incorporate past achievements, available data and lessons learnt where possible, thus avoiding unnecessary overlap, and duplication of efforts and funding.

To tackle challenges and ambitious objectives, the project should leverage outcomes of past IMI JU and EU or other programmes. The selected consortium is expected to acknowledge and integrate the following resources:

- Harmonised consent forms and guidance documents for clinical trials and secondary use of data and biological samples¹ as outcomes of the IMI DO-IT decision committees;
- BBMRI Code of Conduct for health research, when available;
- ECRIN European Clinical Research Infrastructures Network;
- EUCROF Code of Conduct for clinical trials, when available;
- Relevant insights and work from the complementary Patient Data Return Initiative (PDAI) founded in 2017 by a group of Pharmaceutical companies. Though that ongoing initiative does not focus on legal or

² Guidance on data management is available at http://ec.europa.eu/research/participants/docs/h2020-funding-guide/cross-cutting-issues/open-access-data-management/data-management_en.htm

³ <http://www.corbel-project.eu/about-corbel/research-infrastructures.html>

regulatory requirements of EU Member States, its progress on the data sharing process (e.g., technical insights), insights from stakeholders (such as patient groups and sponsors) on the value of returned data, and insights from completed data sharing pilots (best practices) are expected by PDAI to be available for this project by its commencement;

- Particular attention should also be paid to the initiatives piloting decentralised clinical trials, aligning clinical study data with EHRs, implementing blockchain and federated technology for secure infrastructures, aligning on data sharing with patients and/or HCPs.

Industry consortium

The industry consortium is composed of the following EFPIA partners:

- Sanofi (Lead)
- Medidata (Co-Lead)
- Abbvie
- Astra Zeneca
- Bayer
- Janssen
- Pfizer
- Servier
- Takeda

The industry consortium will contribute the following expertise and assets:

- Expertise in conducting studies (data management, study/trial operational management, biostatistics);
- Expertise in the relevant legal framework (GDPR and CTR);
- Experience in networking with EU and local healthcare and data protection regulators;
- Expertise in sensitive data exchange and in building digital infrastructure;
- Expertise in data security and data anonymisation;
- Expertise in data protection and transparency;
- In addition, the industry consortium will act as a liaison with the patient data return initiative (PDAI).

Indicative duration of the action

The indicative duration of the action is 48 months.

This duration is indicative only. At stage 2, the consortium selected at stage 1 and the predefined industry consortium may jointly agree on a different duration when submitting the stage 2 proposal.

Indicative budget

The financial contribution from IMI2 JU is a maximum of EUR 3 260 000.

The indicative in-kind and financial contribution from EFPIA partners is EUR 4 930 000.

Due to the global nature of the participating industry partners, it is anticipated that some elements of the contributions will be non-EU/H2020 Associated Countries in-kind contributions.

Expertise and resources expected from applicants at stage 1

The stage 1 applicant consortium is expected, in the submitted short proposal, to address all the objectives and key deliverables of the topic, considering the expected contribution from the industry consortium which will join at stage 2 to form the full consortium.

The stage 1 submitted short proposals should include suggestions for creating a full proposal architecture which could be in line with the suggested architecture described below, though this architecture is only a suggestion.

This may require mobilising, as appropriate the following expertise:

- Academic clinical trials sponsors from at least five different European Member States (including at least one central/eastern European Member State);
- Robust legal, ethics and data protection expertise (including for clinical studies);
- Proven expertise in working/collaborating with ethics committees and personal data protection authorities, as advice from various EU regulators will be essential to the success of this project and required to develop common, validated usability and privacy standards;
- Healthcare professionals;
- Participants with robust expertise in health and clinical data interoperability and secured exchanges, in EHR and in clinical trial databases, and including those operating in a commercial environment;
- Study participants and patient organisations.

It would also be crucial to include relevant SMEs. SMEs could, for example, be beneficial in the legal and data protection areas as well as interoperability of data and framework for their secured exchanges.

The size of the consortium should be proportionate to the objectives of the topic while ensuring its manageability. Ethics committees and regulators will have to be invited afterwards. They are not expected to be part of the applicant consortia.

Considerations for the outline of project work plan

In their stage 1 proposal applicants should:

- Give due visibility on project management, data management and ethics; dissemination, exploitation and sustainability; and communication activities. This should include the allocation of sufficient resources for these tasks, which will be further developed in stage 2 proposal;
- Consider including a strategy for ensuring the translation of the project results into drug development, regulatory, clinical and healthcare practices and/or decision-making processes.

Suggested architecture

Work Package 1 – Legal and Regulatory Framework

The goals of this work package are to:

- Align IMI DO-IT harmonised consent form (http://bd4bo.eu/wp-content/uploads/2019/03/DO-IT_WP4_D4.10_Level3_Clinical-ICF.docx) and supporting guidance documents (<https://bit.ly/3a7yARK>) with recent updates in EU laws and in line with EDPB standards, as well as local regulatory body opinions;
- Work locally with selected countries in order to get those documents officially approved by the appropriate authorities;

- Develop additional template and guidance documents necessary for primary and secondary use of clinical data in compliance with GDPR, referencing variations between and/or within Member States (including for managing privacy notices and rights/choices for secondary use through a patient portal) as well as for contracting with individual investigators/institutional investigation sites;
- Manage adequate experts' committees of patients, authorities and experts in personal data protection to review, discuss and take position on proposed guidance documents.

Work Package 2 – Standards

The goals of this work package are to:

- Review and elaborate upon standards and guidance documents;
- Provide recommendations;
- Develop new standards when necessary;
- Submit standards (in particular regulatory ones) for approval to appropriate governing authorities/regulators.

Work Package 3 – Technology Framework

The goals of this work package are to:

- Develop a technology framework that can be based on existing technologies or on new potential tech development;
- Isolate and handle potential technical issues;
- Set-up the process that will be deployed in WP4.

Work Package 4 – Working Prototype process

The goals of this work package are to:

- Deploy a working prototype process to establish viability, and to suggest overall direction, as well as provide feedback. It should at least provide study participants (or their chosen physician) with direct access to the individual clinical data or documents, and where possible, in an interoperable electronic format to comply with the GDPR portability right;
- Integrate with EHR/other system;
- Facilitate future research.

Work Package 5 – Communication, Dissemination & Stakeholder engagement

The goals of this work package are to:

- Establish a website and all appropriate tools for communications purposes;
- Establish a communication structure and implement it on project basis (training webinars, stakeholder engagement meetings);
- Conduct surveys with patients, HCPs, etc;
- Establish and organise dissemination of project results;
- Build adherence of relevant stakeholders.

Work Package 6 – Business Plan and Sustainability

The goals of this work package are to:

- Establish, early in the project, a robust business plan to sustain the projects results
- Implement the business plan, including marketing of the solutions to relevant end-users.

Work Package 7 – Project management and overall coordination

Additional considerations to be taken into account at the stage 2 full proposal

At stage 2, the consortium selected at stage 1 and the predefined industry consortium jointly submit the full proposal developed in partnership. The full proposal is based upon the selected short proposal at stage 1.

In the spirit of the partnership, and to reflect how IMI2 JU call topics are built on identified scientific priorities agreed together with EFPIA beneficiaries/large industrial beneficiaries, these beneficiaries intend to significantly contribute to the programme and project leadership as well as project financial management. The final architecture of the full proposal will be defined by the participants in compliance with the IMI2 JU rules and with a view to the achievement of the project objectives. The allocation of a leading role within the consortium will be discussed in the course of the drafting of the full proposal to be submitted at stage 2. To facilitate the formation of the final consortium, until the roles are formally appointed through the consortium agreement, the proposed project leader from among EFPIA beneficiaries/large industrial beneficiaries shall facilitate an efficient negotiation of project content and required agreements. All beneficiaries are encouraged to discuss the project architecture and governance and the weighting of responsibilities and priorities therein.

Data Management

In their stage 2 proposal, applicants should give due visibility to data management including use of data standards. A full 'data management plan' (DMP) as a distinct deliverable must be delivered within the first 6 months of the project. The DMP needs to be kept up to date with the needs of the project and as such be updated as necessary during its lifetime.⁴ The DMP has to reflect on the legal, regulatory and ethical guidance from work packages 1 and 2.

Dissemination, exploitation and sustainability of results

In their stage 2 proposal, applicants must provide a draft plan for dissemination and the exploitation, including sustainability of results. A full plan as a distinct deliverable must be delivered within the first 6 months of the project.⁵, and updated during the project lifetime and could include identification of:

- Different types of exploitable results;
- Potential end-users of the results;
- Results that may need sustainability and proposed sustainability roadmap solutions.

Sufficient resources should be foreseen for activities related to dissemination and exploitation, including the plan for the sustainability of the project results. This may involve engaging with suitable biological and medical sciences Research Infrastructures (RIs).⁶

⁴ Guidance on data management is available at http://ec.europa.eu/research/participants/docs/h2020-funding-guide/cross-cutting-issues/open-access-data-management/data-management_en.htm

⁵ As an additional dissemination obligation under Article 29.1 of the [IMI2 Grant Agreement](#) will apply.

⁶ <http://www.corbel-project.eu/about-corbel/research-infrastructures.html>

Communication

The proposed communication measures for promoting the project and its findings during the period of the grant should also be described and could include a possible public event to showcase the results of the project.

Indicative text