IMI2 GA853989 - ERA4TB
European Regimen Accelerator for Tuberculosis (ERA4TB)

WP8 – Management, Outreach and Sustainability

D8.1 Project Handbook

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V1.0	20/03/2020	First Draft
V1.1	27/03/2020	Comments from WP8 main contributing partners
V1.2	03/04/2020	Comments from SC
V1.2-Final	06/04/20	Final Version

LIST OF ACRONYMS

ACRONYM	DESCRIPTION
AMT	Asset Management Team
CA	Consortium Agreement
DAT	Data flows Assurance Team
DoA	Description of Action
EAB	Ethics Advisory Board
EC	Executive Committee
EFPIA	European Federation of Pharmaceutical Industries and Associations
ERA4TB	European Regimen Accelerator for Tuberculosis
GA	General Assembly
GTA	Grant Agreement
IMI2 JU	Innovative Medicines Initiative Joint Undertaking
PDC	Pipeline Development Committee
PL	Project Leader
PMO	Project Management Office
PMT	Pipeline Management Team
SAB	Scientific Advisory Board
SC	Steering Committee
WP	Work Package
WPL	Work Package Leader

ABSTRACT

The present document aims at providing an overview of the management and administrative procedures and principles that will ensure an efficient execution of the ERA4TB Project and contribute to the production of high-quality project results.

The main objective of the Project Handbook is to make available to the project participants a quick reference 'manual' that points out, in an understandable way, the management structure, tasks, responsibilities, and procedures on all levels of project execution. All the general principles are defined in provisions of the Grant Agreement (GTA), the Description of Action (DoA) and the Consortium Agreement (CA), but it also draws from best practice, IMI2 rules and accepted project management standards. The procedures set up in this document have to be understood as a starting point and may be adjusted as the project evolves.

This document specifically covers the following areas:

a. Overall working principles and procedures for compounds' progression.

b. General project management processes that ensure tight coordination of the project activities resulting in high quality Deliverables.

c. Administrative project management processes that ensure accurate legal and financial management, reporting and justification of the work being carried out.

d. An internal communication strategy that ensures clear and effective communication between the Participants and that allows for the early escalation and the timely resolution of management and technical issues.

e. An overview of the methods and procedures undertaken by the Consortium to identify, analyse, assess, and monitor risks affecting the project or its results, and the development and monitoring of associated mitigation and contingency plans aiming at mitigating the potential negative effects and therefore maximising the potential benefits of risks.

PROJECT BASIC INFORMATION

- Project full title: EUROPEAN REGIMEN ACCELERATOR FOR TUBERCULOSIS
- Project Acronym: ERA4TB
- Grant Agreement Nº: 853989
- IMI Call topic: IMI2 Call 15-Topic 8
- Project start date: 01/01/2020
- Project end date: 31/12/2025
- Project budget: 207,963,891€
- IMI-JU Contribution: 89,815,600€
- EFPIA beneficiaries in-kind contribution: 118,148,291€
- Number of beneficiaries: 31

1. OVERALL WORKING PRINCIPLES AND PROCEDURES FOR COMPOUNDS' PROGRESSION[1]

The ultimate objective of ERA4TB is to enact a progression pipeline that leverages research excellence and resources in Europe to be able to undertake preclinical and clinical development activities for individual compounds and combinations. Such pipeline has been conceived as a modular system in which each module is uniquely numbered to represent a type of assay/study (DoA, pages 5 and 6) following the typical progression sequence in pharmaceutical development.

To better match the work packages in the work plan, the pipeline is divided into two big blocks: 'preclinical profiling' (WP 2, 3, 4-Fig.1) and 'portfolio and early clinical development' (WP6 and 7-Fig.2), with WP5 (modelling) somewhat bridging the two.

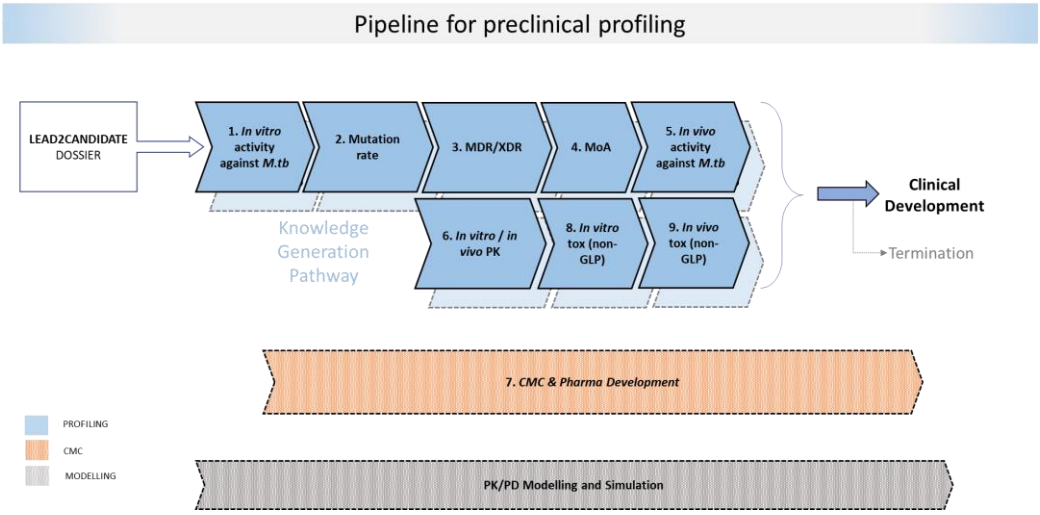


Figure 1. ERA4TB's Preclinical profiling progression pipeline

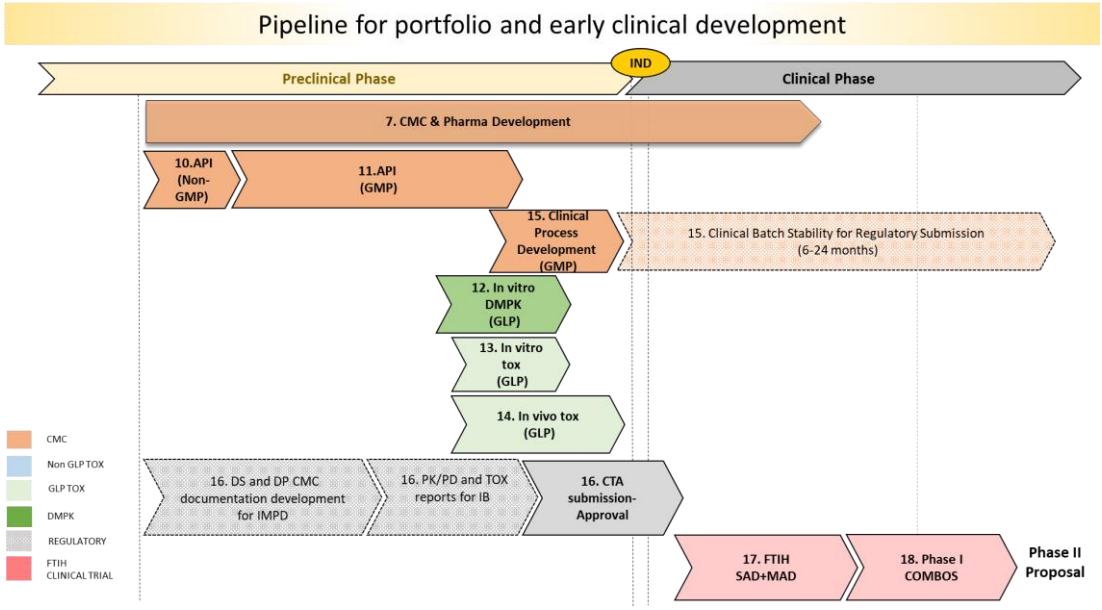


Figure 2. ERA4TB's detailed portfolio progression pipeline

[1] The overall working principles and procedures will be regularly updated according to the needs emerging from the project implementation.

- **Modules specification**: Each of the modules (the uniquely numbered boxes in the diagrams above) in the pipeline will have a complete specification, based on the research capacity available at the Consortium via its academic/SME partners or subcontractors. Such specification will include:

    - scientific and technical details about the corresponding assay
    - operational sites (currently available as well as foreseen)
    - standard lead times
    - estimated costs per compound or assay, as defined.

The latter are especially important in the cases of modules belonging to WP3, WP6 or WP7, as these have a large flexible fund that will be dynamically allocated as needed by the compounds.

The pipeline will not be static; it is expected to evolve and expand as the project progresses, for example increasing scope with new assays or increasing capacity with new labs capable of performing. However, it is of the utmost importance to have absolute clarity of what the ERA4TB platform can reliably undertake at any point in time.

- **Services contracted externally**: The work in some modules will be necessarily performed, partially or totally, by external vendors (e.g. CRO, CMO, etc.). To this end, ERA4TB will preferably set up framework contracts with a list of vendors, considering past experience and taking into account the compound owners´ needs and preferences to accelerate delivery and ensure data quality. Such a list may be enlarged as the project progresses so that a variety of vendors can be offered to compound owners. The selection of any vendor will always have to be compliant with IMI guidelines and the "best value for money" principle (see section 7 for more details). Compound owners may always choose to contract a specific study or assay directly if they need or have a strong preference for a specific supplier whose selection would not align with IMI funding requirements.

Modules will evolve as needed depending on performance, scientific advances and the experience acquired as the project develops in terms of assays and studies that best represent the state-of-the-art. Similarly, the ERA4TB pipeline will strive to adapt its research capacity to be able to reliably deliver and tackle expected compounds, based on past performance, estimated attrition rates and the interest expressed by EFPIA and Associated Partners. This dynamism may therefore involve adding or changing labs and service providers undertaking the different modules, be it partners or external vendors.

The Asset Progression Plans (APPs)

A molecule may enter the ERA4TB platform at any point in the progression pipeline, and the owner may want to use all or only a few of the modules. This will be formalised in an Asset Progression Plan (APP).

The underlying philosophy is that, for each specific compound or combination, a number of modules will be enacted by agreement between the compound owner(s) and ERA4TB. Some assays may have been already undertaken by the compound owner, or they may not be available in the platform, or it may be decided by the compound owner that they will undertake them in parallel outside the ERA4TB platform for whatever reason.

By default, modules will be executed as defined in the module specification, which may differ

from similar assays undertaken by the compound owners or by other institutions outside ERA4TB.If needed, different requirements for a module in the APP will be discussed and incorporated whenever feasible.

Upon expressing interest in entering a molecule into the ERA4TB platform[2], the owner(s) will initiate an APP and then meet the ERA4TB team (which members will be representatives of specific WPs appointed by the PMO on a case by case basis depending on the progression needs of a specific molecule or combination) to discuss and collegiately agree on a final APP. This will naturally involve examining the profile and results obtained to date for such molecule, examining the current availability of modules within the pipeline, and deciding which ones will be enacted.

An APP (see template in Annex I) will therefore contain:

- Which modules will be activated for the compound, and any relevant scientific or technical specification of those (e.g. where protocols or experiments can be adapted to the specific needs of the compound).
- Which partner labs and vendors from within the ERA4TB 'roster' is proposed to be used for each selected module.
- Overall timelines based on standard lead times, availability of the selected modules and requirements of the vendors selection process (alternative quotes, validation, etc).
- Overall cost to the project based on standard costs per module, fine-tuned depending on the specifications agreed for each module.
- Whether, what and how legacy data pertaining to the compound will be uploaded to the ERA4TB platform.
- Which combinations are suitable with such a molecule and, if applicable, which restrictions are set to specific combinations with other molecules. Those combinations not affected by restrictions can be tested in the ERA4TB platform after prioritisation, if required (see below).

APPs will be shared among the compound owners via the **Pipeline Development Committee** (PDC, defined in section 2.2) to avoid potential overlaps. Additionally, availability of APPs for all compounds entering the pipeline will allow ERA4TB to dynamically monitor the pipeline status – this is expected to be facilitated through a dashboard-like tool that will graphically represent where compounds are in the pipeline in relation with their respective APPs, alert about potential bottlenecks, etc. It will also provide a transparent view on resources already committed to the different compounds, with particular attention to the flexible funds of WP3, 6 and 7 and their committed use – these funds are naturally depletable and therefore their use has to be carefully decided with a long-term perspective that considers a) the compounds already in the ERA4TB pipeline; b) their expected progression according to typical attrition rates; and c) the prospects of new molecules entering the platform, and at which point in the pipeline.

Operational and governance considerations[3]

Once the APP is sufficiently defined, the PDC will approve or reject the compound for entering the pipeline. Each APP will be sanctioned by the PDC, which decides on the entrance and progression of molecules or combinations. The project Steering Committee will then validate the resources allocation needed.

2 EFPIA and Associated Partners have already expressed interest in doing so for a number of molecules through the Asset Map described in the DoA.

[3] Description and composition of each governing body is included in section 2

Once an APP is defined, the derived work plan for the compound will be agreed between the compound owner and ERA4TB representatives appointed for that specific compound. Monitoring and management of such workplan will be a responsibility of an **Asset Management Team** (AMT), in close collaboration with the overall **Pipeline Management Team** (PMT) of ERA4TB, which is in charge of ensuring that all the modules in the whole pipeline work adequately and as expected.

The APP is expected to be updated regularly, e.g. because the activation of specific modules will be dependent on data generated in others, or because not all assay specifications can be defined at the time the molecule enters the platform. Major changes in an APP (e.g. if additional modules are requested, or any module is no longer needed, or in case major deviations in costs are detected/anticipated) will need re-assessment and approval by the PDC, and subsequently if needed by the Steering Committee.

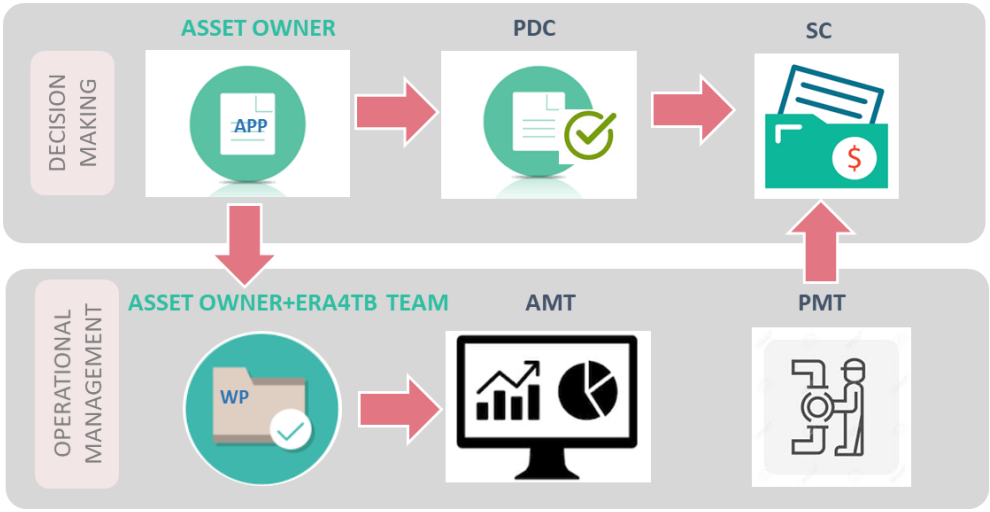


Figure 3. Overview of the operational and governance implications of the asset's progression process

Modelling of combinations: **WP5** will define at project start a minimum set of information required for testing all combinations. Based on that information set, WP5 is expected to produce a ranked list of combinations as unbiased as possible. Then, the PDC will make the decision on which combinations to pursue and in what order/sets. This decision will be revisited every time an updated ranked list of combinations (from new data available) is produced.

APP for combinations: Following the same approach, the compound owners will jointly define an APP and then refine it with the module owners. The APP will then be approved/rejected by the PDC.

SUMMARY of steps to follow - COMPOUND OWNERS:

- Define first version of APP
- Discuss and complete with ERA4TB team
- For each compound approved for entering the platform, define the representative(s) that will be part of the Asset Management Team

SUMMARY of steps to follow - ERA4TB platform team:

- Define each module's specification and send to PMO at an early stage of the project.
- For each compound entering the platform, receive first version of the APP and discuss with the compound owner potential adjustments needed in any modules and complete APP for consideration by the PDC
- For each compound entering the platform, nominate representative for Asset Management Team

2. MANAGEMENT STRUCTURE

As outlined in Figure 1 below, the ERA4TB project governance has a double structure:

- One conceived **to manage the project and the consortium** dynamics efficiently and according to IMI requirements (blue and grey boxes of Fig. 4). It revolves around a multi-level structure, with representation of different stakeholders and competencies at all levels that cover the four following key aspects of project management:
  - Decision-making for handling strategic and contractual issues
  - Operational management for preparing and implementing strategic decisions taken by the ERA4TB Government bodies and performing day-to-day management
  - Scientific/technical management for driving the work
  - Advice concerning the evolution of the Project
- Given the particularities of ERA4TB, additional governance structures are set up to decide on the entrance and progression of a molecule and **to specifically manage and monitor the drug development pipeline** (orange boxes of Fig. 4).

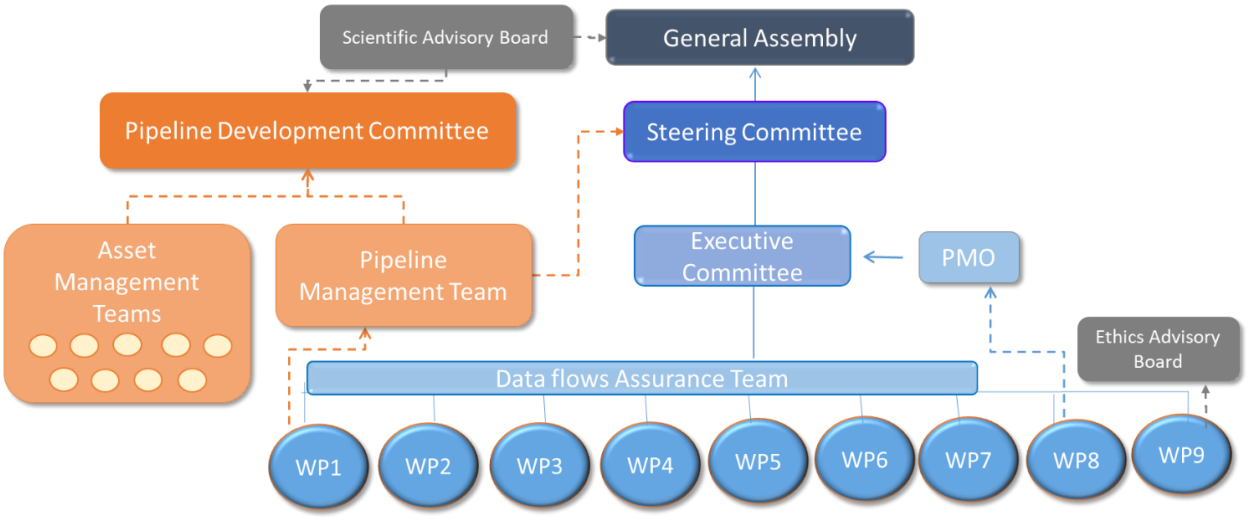


Figure 4. ERA4TB Governance Structure

2.1. Management structure to manage the Consortium

Project leadership

Scientific Leader: **Prof. Stewart Cole (IPP)** in charge of the overall scientific coordination of the project and alignment of the different tasks to be performed.

Technical Coordinator: Prof. Juan José Vaquero (UC3M) in charge of the technical coordination of the action and acting as official contact point with IMI2 JU for all administrative and technical requirements regarding the project implementation.

Project Leader: **Dr. David Barros (GSK)** in charge of the overall scientific and Action related governance, in close collaboration with the Scientific Leader and the Coordinator.

General Assembly (GA)

Scope of decision-making: The GA has the ultimate decision-making responsibility in matters affecting the overall project strategy and composition of the Consortium. The GA shall be responsible for the determination of policies in relation to the overall management of the Action and the finding amicable solutions for any unresolved disputes between the Beneficiaries relating to the execution of the Action.
Composition: Body composed of all partner institutions participating in the project. One representative per partner for voting purposes. See members in table 1 below.
Quorum: For a General Assembly meeting to be quorate there shall be present no fewer than 75% of the partners (designated GA representatives or their delegates with voting capacity).
Meetings and voting: The GA will meet at least once per year and will adopt decisions by simple majority (each partner having a vote), except in cases where unanimity is required according to IMI2 rules (e.g. new partners, major changes in scope, etc.). For the simple majority, the votes of the attendees will be balanced to be representative of non-EFPIA Beneficiaries and EFPIA Beneficiaries

PARTNER	GA REPRESENTATIVE
UC3M (Chair/Co-Chair)	Juan José Vaquero
IPP	Stewart Cole
UNIZAR	José Antonio Aínsa (primary)/Santiago Ramón García (secondary)
IPL	Alain Baulard
SYNAPSE	Carlos Diaz
FZB	Prof.Dr.Ulrich E. Schaible
IM4TB	Gabriel Clerc
C-PATH	Richard Liwski
CNR	Filippo Castiglione
CEA	Roger LE GRAND
SERMAS	Alberto M. Borobia
UU	Ulrika Simonsson
PHE	Sally Sharpe
EPFL	Neeraj Dhar
UHC	Jan Rybniker
UNIPD	Riccardo Manganelli
UPV	Maria Rosalia Pasca
NICE	Páll Jónsson
IBT	David Bonnel

SCI	Samira Boarbi
IOS	Osvalds Pugovics
BAR	Cyril Guyard
QPS	Wim Tamminga
LUND	Leif Bjemer
GRIT	Claus Stie Kallesøe
GSK (Chair/Co-Chair)	David Barros (Joel Lelievre - replacement)
EVT	Jean Michel Culouscou
JANSSEN	Alex Pym
BMGF	Peter Warner
TBA	Anna Upton
DDU	Paul Wyatt

Table 1. Official members of the GA

Steering Committee (SC)

Scope of decision-making: The SC is responsible for the overall execution of the Action, alignment across all Work Packages, decision making and the initial finding of amicable solutions for any disputes between the Beneficiaries relating to the execution of the Action. It will ensure the smooth operation of the Action and guarantee that all efforts are focused towards the Action Objectives, Deliverables and Milestones.
Composition: Representative appointed as Project Leader, the Representative appointed as Scientific Leader, the Representative appointed as Coordinator, a Representative of each of the Work Package Leaders, one Representative of each of the EFPIA and each Associated Partners and a Representative of the Project Management Office (the latter if established shall have no voting rights). See SC members in Table 2 below.
Quorum: 75% of the members need to attend for an SC meeting to be quorate.
Meeting and voting: The SC will meet at least quarterly and each SC Representative has one vote in the SC. Decisions will be taken by qualified majority (75% of attending members), the Chair having a casting vote.

PARTNER (role)	SC REPRESENTATIVE
UC3M (Coord) (Chair/Co-chair)	Juan José Vaquero
UC3M (WPL4)	Arrate Muñoz-Barrutia
IPP (Sc. Leader)	Stewart Cole
IPP (WPL3)	Roland Brosch
UNIZAR (WPL2)	Santiago Ramón-García (primary) / José Antonio Aínsa (secondary)
SYNAPSE (WPL8)	Carlos Diaz
IM4TB (WPL6)	Gabriel Clerc
C-PATH (WPL1)	Patrick O'Meara
CNR (WPL5)	Oscar della Pasqua (Filippo Castiglione deputy)
SERMAS (WPL7)	Alberto M. Borobia
SERMAS (WPL9)	Antonio J. Carcas
GSK (Proj. Leader) (Chair/Co-chair)	Joel Lelievre (David Barros – replacement)
EVT	Christine Roubert
JANSSEN	Benny Baeten
BMGF	Katrine Thor Andersen
TBA	Anna Upton

DDU	Paul Wyatt
PMO (no voting rights)	Elena del Rey, Elena Lopez, Patricio Lopez

Table 2. Official members of the SC

Executive Committee (ExCom)

Scope of decision-making: The Executive Committee shall be responsible for the preparation of decisions with respect to policies and decision making in relation to the overall management of the Project, the day-to-day operations and the initial arbitration of any disputes between the Beneficiaries relating to the execution of the Project. It will ensure the smooth operation of the Action and guarantee that all efforts are focused towards the objectives (including effort/budget reassignment within a specific WP at the request of the corresponding WPL).
Composition:
Representative appointed as Project Leader, the Representative appointed as Coordinator, the Representative appointed as Scientific Leader, a Representative of the leader of WP8, two Representatives of the EFPIA and IMI2 Associated Partners that are not already represented with minimum 1 representing the Associated Partners and a Representative from the Project Management Office (the latter non-voting). See EC members in table 3 below.
Quorum: At least 75% of the members and one of the leaders (Scientific Leader, Technical Coordinator or Project Leader) need to attend for the meeting to be quorate.
Meeting and voting: The ExCom will be in constant communication and meet at least bi-weekly by teleconference. Decisions are expected to be made by consensus. In case that voting is needed, decisions will be made by simple majority.

PARTNER (role)	ExCom REPRESENTATIVE
UC3M (Coord) (Chair/Co-chair)	Juan José Vaquero
IPP (Sc. Leader)	Stewart Cole
SYNAPSE (WPL8)	Carlos Diaz
GSK (Proj. Leader) (Chair/Co-chair)	Francisco Rubio (Joel Lelievre – replacement)
EFPIA/AP 1	Nathalia Murillo (EVT)
EFPIA/AP 2	Anna Upton (TBA)
PMO (no voting rights)	Elena del Rey, Elena Lopez, Patricio Lopez

Table 3. Official members of the ExCom

Project Management Office (PMO)

Team composed by project managers from SYNAPSE, UC3M and GSK dealing with the day-to-day management of the project, including work plan follow up, reporting coordination, financial management, administration, legal and risk management as well as quality control procedures on project deliverables. The PMO will report directly to the project leaders and the ExCom, who are entitled to require the PMO to produce any reports needed in order to fulfil their role.

PARTNER (role)	PMO MEMBER
UC3M	Cristina Velasco, Patricio López
SYNAPSE	Elena del Rey
GSK	Elena Lopez

Table 4. Members of the PMO

Data flows Assurance Team (DAT)

Team devoted to ensuring that the data flows work smoothly at the operational level for both data generators and data consumers. This team will be composed by technical staff of partners involved in relevant WPs where data are of critical importance, especially WP1 and WP5, and led by SYNAPSE.

PARTNER (role)	DAT MEMBER
SYNAPSE (DAT lead)	Carlos Diaz
Partner TBD (WP1 technical staff)	Patrick O'Meara (C-Path) Jesús Carreterro (UC3M)
Partner TBD (WP5 technical staff)	Paolo Tieri
Other members of WP2,3,4,6,7 to be appointed	

Table 5. Members of the DAT

2.2. Management structure to manage the pipeline

Pipeline Development Committee (PDC)

Scope of decision-making: The PDC will evaluate and decide on the entrance and progression of molecules (or combination regimes) along the ERA4TB pipeline. Such decisions are expected to be taken by the PDC with the help of pre-specified go/no go criteria and on the basis of data collected at the different steps of the pipeline.
Composition: The PDC will be made up of the Representatives of each of the EFPIA partners (GSK, EVT, JANSSEN) and IMI2 Associated Partners (BMGF, TBA, DDU), as well as 6 representatives of academic partners who are experts in TB drug development (IPP, UC3M, SERMAS, IM4TB, UNIZAR, CNR).
Quorum: 75% of members need to attend for a PDC meeting to be quorate.
Meeting and voting: The PDC will meet as needed to evaluate on the compunds progression and, at least every six months at venues to be agreed. Supporting documents for a PDC meeting will be circulated with at least one week in advance by the PMO. Decisions will be taken by a majority of seventy-five (75) percent of the PDC members, except where a decision is related to the progression of a specific compound. In those cases, the EFPIA, APs and only 2 of the representatives of academic partners (IPP and UC3M) will have voting rights. The Chairperson of the PDC will have a casting vote.

PARTNER (role)	PDC MEMBER
UC3M	Juan José Vaquero
IPP (PDC Chair)	Stewart Cole
UNIZAR	Santiago Ramón-García (primary) / José Antonio Aínsa (secondary)
IM4TB	Farizade Moulfi
CNR	Oscar della Pasqua
SERMAS	Antonio J. Carcas
GSK	David Barros (Joel Lelievre – replacement)
EVT	Florian von Groote

JANSSEN	Alex Pym
BMGF	Peter Warner
TBA	Nader Fotouhi
DDU	Paul Wyatt (Kevin Read – replacement)
Secretariat	PMO

Table 6. Official members of the PDC

Asset Management Teams (AMT)

Scope of action: One Asset Management Team will be appointed to specifically monitor and supervise the progression of each molecule or combination of molecules throughout the pipeline.
Composition: Each AMT will be composed by at least two members: one representative from the asset owner, and one from ERA4TB academic partners, to be appointed specifically for each molecule or combination. To progress in its tasks the AMT may ask for specific meetings that might include representatives of those WPs relevant for their respective Asset Progression Plan. The team dedicated by the asset owner to its development will be allowed to be also involved in the AMT meetings and discussions.

Pipeline Management Team (PMT)

Scope of action: The PMT manages and monitors performance of the modules along the pipeline. It is responsible of ensuring that the technical performance of the pipeline works appropriately, including hand-off between modules, capacity planning, bottleneck resolution, etc. The PMT will be allowed to suggest budget reallocations to the SC to preserve the efficient functioning of the pipeline and will report to the PDC and SC as needed.
Composition: 5-7 members from Consortium partners, with expertise in pre-clinical in vitro assays, animal studies, portfolio/CMC development, FTIH studies, and modelling activities. Representatives of SYNAPSE, UC3M, IPP, UNIZAR, IM4TB, SERMAS and CNR will compose the PMT.

PARTNER (role)	PMT MEMBER
UC3M (PMT chair)	Patricio López
IPP	Michel Perez
UNIZAR	Ainhoa Lucía Quintana (primary) / Santiago Ramón-García (secondary)
SYNAPSE	Carlos Diaz
IM4TB	Farizade Moulfi
CNR	Oscar della Pasqua
SERMAS	Alberto M. Borobia

Table 7. Members of the PMT

2.3. How and when the project bodies meet?

The chair of each governing body, supported by the PMO, is responsible for convening meetings of the management and scientific bodies complying with the minimum of frequency of ordinary meetings as defined in the ERA4TB Consortium Agreement summarized in table 8 below. WPL hold the responsibility of calling meetings within their respective WP contributing partners as needed.

MEETING FREQUENCY	GOVERNANCE BODIES	SCHEDULE
Biweekly	Executive Committee (EC) - TC	Every 2 weeks starting on 25 Feb 2020
Quarterly (at least)	Steering Committee (SC) - TC/F2F	Monthly TCs
Every 6 months (at least)	Pipeline Development Committee (PDC) (TC/F2F)	Fixed PDC meetings every 6 months + ad-hoc as needed.
Yearly	General Assembly (GA) (F2F)	*to be defined*
	Scientific Advisory Board (SAB) (F2F)	Jointly with GA meetings
Regularly	Work Packages (WP)- TC/F2F	Up to each WPL and WP Team to decide

Table 8. Overview of project meetings

2.4. What are the Participants' main responsibilities?

Beneficiaries must use all reasonable endeavours to perform and fulfil, promptly, and on time, all of their obligations under the GTA and the CA, to accomplish the purpose and objectives of the ERA4TB project and act in cooperation and mutual trust. Beneficiaries shall also provide their respective contributions to deliverables, information, and reports as required by the WPL, the GA, the EC, the PMO, and the Coordinator, so as to help these bodies to fulfil their obligations.

In lay terms, each Participant must, essentially:

- Do the work assigned to it in the Description of Action, and any other detailed work plan derived from it, on time and with an appropriate level of quality.
- Collaborate with all other Participant as required by the tasks, including contributing to relevant deliverables.
- Not hinder the work of others or delay it unnecessarily.
- Attend and contribute to the meetings and teleconferences as required.
- Notify promptly the relevant governance body of any potential issue affecting performance. The normal chain of reporting would be, in this order: WPL -> PMO -> EC -> SC -> GA
- Notify the PMO about any risk that may be detected in the course of the work, and that may affect future performance.
- Fulfil the administrative and financial reporting obligations according to IMI2 rules – spend the budget foreseen only for the work expected in the project and report it faithfully.

2.5. How are internal conflicts resolved?

In the event that an internal conflict arises at a given time, the project coordination and the management structure is formulated to support a bottom-up approach with respect to its resolution.

- Conflicts amongst Participants in any given activity will be discussed at the Work Package (WP) level with the help of the respective Work Package Leads (WPLs).
- If unresolved, the issue will escalate to the EC, which with the help of the PMO, will use mediation and expert advice to objectively aim to solve the issue.
- Ultimately, the EC may also opt to refer the issue to the SC or the General Assembly, for wider consultation.

3. KEY LEGAL ASPECTS

3.1. The Grant Agreement (GTA)

The GTA is the main legal document underpinning the project's execution – effectively, a contract between the participants and the IMI2 JU. It is first signed by the IMI2 JU and the Coordinator. Each Participant then accedes to the GTA by executing an accession form. The GTA mainly provides information on the grant (parties, duration, start date, budget, etc.), obligations of the Participants towards the IMI2 JU (such as reporting requirements), as well as the intellectual property framework and other legal conditions. The GTA is dated of 12th Dec 2019 and has number 853989.

The **GTA** core document includes a standard text (i.e. it is essentially the same for any IMI2 project) describing the general rules and regulations governing IMI2 projects, including financial rules (e.g. which costs are acceptable, how payments are handled, etc.), Intellectual Property Rights (IPR) (who owns the results, how access to such results is enabled, etc.) and other general conditions applicable to IMI2 projects. These generic provisions can be supplemented (but not contravened) with project-specific provisions via a Consortium Agreement (see section 3.3 below), which enables projects to set out their specific IPR detailed rules, governance mechanisms, etc.

Beyond its core terms and conditions, mostly standard text, the Grant Agreement also includes the following annexes, which form an integral part of the contract:

Annex I. Description of the action.

The most extensive and important Annex to the GA is the Description of Action (DoA), which comprises the technical description of the work to be undertaken in the project (work packages, tasks, deliverables, milestones), the description and roles of the different partners, allocated efforts in person-months, and budget details. The DoA is derived from the original proposal submitted to the IMI JU for evaluation and approval, and it is the benchmark against which project progress will be judged. Compared to the rest of the Grant Agreement and annexes, which are mostly model texts, the DoA is specific for each project. It is important to remember that the DoA is an integral part of the Grant Agreement, and therefore it is a contractual commitment of all participants

Annex II. Estimated Budget for the action.

This Annex refers to the overall budget for the project and includes the budget details for all project participants. This document is automatically generated by the Participant Portal system.

Annex III. Accession form for beneficiaries

This form is required to be signed by all the project participants to formally accede to the ERA4TB GA. If a new participant joins the project, they will also be requested to sign this form.

Annex IV. Financial statement

This form refers to the summary of costs to be reported by those partners receiving IMI funding for each reporting period. Please see section 7 (How must financial statements to be submitted?) for more details.

Annex V. Model for the Certificate on Financial Statements

This Annex is required for those partners that request a total IMI JU funding of EUR 325 000 or more, as reimbursement of actual costs calculated on the basis of its usual cost accounting practices. Please see section 7 (How must financial statements to be submitted?) for more details.

Annex VI. Model for the Certificate on the Methodology

Partners may submit to IMI, for approval by the Commission, a certificate on the methodology to state that that their usual cost accounting practices comply with specific conditions (e.g. "unit costs" instead actual costs). Once the certificate is approved, costs declared in line with this methodology will not be challenged subsequently, unless the beneficiaries have concealed information for the purpose of the approval.

The Grant Agreement and all its Annexes are available in ERA4TB internal repository (link)

3.2. Changes to the Grant Agreement

The Grant Agreement can and must be changed whenever any important project parameter changes: partnership, duration, budget, etc. Implementation of such changes must follow a specific procedure called 'Grant Agreement amendment'. Most changes that trigger Grant Agreement amendments relate to updates in the DoA (e.g. changes in tasks and deliverables, changes in efforts allocated, changes in partner's teams, budget transfers across participants, etc.). These can be relatively minor, in which case they tend to be grouped and implemented together in one go, or major, which might trigger an amendment on their own, especially if it is urgent that the change is officially entered into the contract.

As consequence of this procedure, the amended provisions become an integral part of the Grant Agreement, while all other provisions remain unchanged and have full effect. For further details on policy on amendments see Article 55 of the ERA4TB Grant Agreement.

An amendment is necessary when one or several of the following changes applies:

- Changes involving beneficiaries and linked third parties
- Changes involving the coordinator/principal beneficiary
- Changes affecting the project or its implementation
- Changes involving the financial aspects of the grant

As said before, the Grant Agreement may be affected by other types of minor changes which do not constitute an amendment, but which must be communicated to the consortium or to the

IMI2 JU through an information procedure. In any case, participants should contact the PMO to confirm the procedure to follow for any modification needed. Some example of changes which do not require an amendment process *per se* are:

- Certain budget transfers[4] (see Table 9)
- If the name or address of a beneficiary, linked third party or coordinator changes
- If there is a change in the name of the bank or the address of the branch where the coordinator has an account, or in the name of the account holder.

Budget transfers and re-allocation	Amendment needed?
From one beneficiary to another	**NO**
From one budget category to another	**NO**
Addition/removal of tasks in Annex 1 Re-allocation of tasks in Annex 1	**YES**
Transfers between different forms of costs (actual costs, unit costs, etc.)	**YES** if no budget was foreseen for the 'form of cost' receiving the transfer
New subcontracts, new in-kind contributions	**YES** (strongly advised)

Table 9. Budget transfers that requires an amendment

Grant Agreement amendments are submitted to the IMI2 JU by the Coordinator on behalf of the Consortium. This implies that the Consortium must be aware and approve of any proposed changes before the amendment is requested.

The PMO will be responsible for following-up on amendments to the Grant Agreement during the project.

The procedure is as follows:

1. The Project Management Office (PMO) will keep track of all needed amendments
2. Meetings and communications with the participants affected will enable to compile all the necessary information to support the changes.
3. The Coordinator will launch the amendment request.
4. The list of modifications will be circulated to the General Assembly for their information and approval.
5. The PMO will prepare a new version of the DoA with the modifications and/or other documents needed to request the modifications
6. The PMO will circulate the amended documents to the EC for validation. The approval by the General Assembly will be required for any Amendment to the Grant Agreement, as defined in the Grant Agreement article 55.2 (Amendments to the Grant Agreement – Procedure).
7. The PLSIGN of the Coordinator will electronically sign and submit the request for amendment

[4] Budget categories are explained in sections 7.3 of this document,

8. IMI will assess the amendment request (IMI)
9. IMI will make a decision (acceptance or rejection of the amendment)
10. The new version of the DoA will be also accessible in Sharepoint.

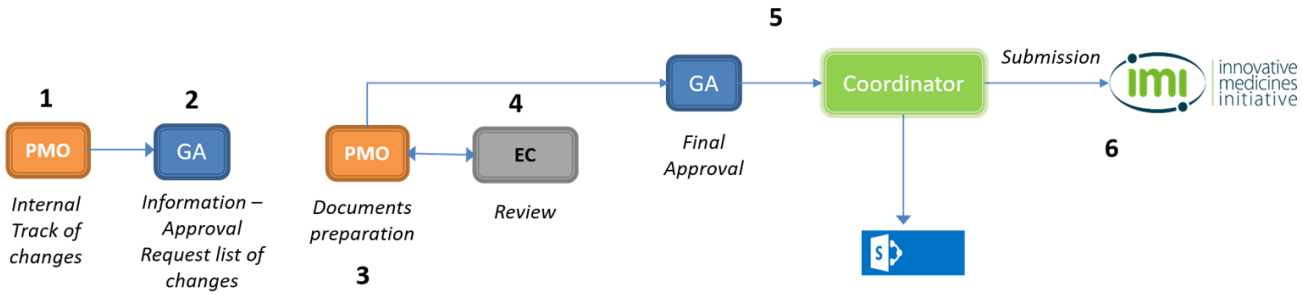


Figure 5. Changes to the Grant Agreement procedure

3.3. Consortium Agreement

The Consortium Agreement (CA) is concluded among the ERA4TB Participants in order to provide a legal framework for their collaboration within the boundaries of the Grant Agreement. The CA includes provisions on, for instance, governance, intellectual property, dissemination, and liability. The IMI2 JU is not a party to the CA. The signed version of the CA is accessible in ERA4TB internal repository (LINK).

Amendments to the CA may also be necessary in the course of the project, sometimes purely as a consequence of GA amendments. These CA amendments will be handled separately by agreement of all participants, under the coordination of the Coordinator and the Project Leader, with the support of the PMO.

3.4. Intellectual Property Rights

According to the Consortium Agreement (Articles 6 to 8), participants agree to respect their Individual Intellectual Property Rights and intend to cooperate with respect to the management of all matters relating to the protection and exploitation of all knowledge arising from the project and of the Intellectual Property Rights pertaining to such knowledge, with the view to promoting innovation.

Who owns the project results?

A **project result** (referred to as "Result" in the Grant Agreement and the Consortium agreement) is the property of the Participant that carries out the work that generates that result. The Participants remains free to transfer its ownership rights in results.

However, any single **IMP results**, even if they are owned by the beneficiary who generated such results, immediately following its generation, the full property of the result will be transferred to the IMP Owner. The same applies for any Combination of IMPs results.

What happens in case of joint ownership?

When several participants have generated a result and where it is not possible to distinguish their respective shares therein, the participants (co-owners) will jointly own this result.

In case of **joint ownership of results**, each Co-Owner may use the jointly owned results without restriction for Research Use, including the right to grant non-exclusive sub-licenses to its Affiliated Entities and to Third Parties, subject to the following conditions[5]:

- At least 45 days prior notice must be given to the other co-owner(s); and
- Fair and reasonable compensation must be provided to the other Co-owners, to be decided on a case-by-case basis

In case of **jointly-owned IMP results** (whether Single IMP results or combination of IMPs results), immediately following its generation, each such co-owning beneficiary automatically and in full transfers to the IMP Owner(s) concerned the full property of such results.

How should project results be protected?

Project results are the property of the participant(s) carrying out the work leading to them. When the results can be industrially or commercially applied, its owner must provide for adequate protection by means of IP rights, with due regard for its own legitimate interests (and the interests of the other participants).

The Participants may also determine the action to take when the owner of an IP asset is not interested in formally protecting a Result.

In connection with the statements above, as long as the Results -which can be industrially or commercially applied- have not been protected, no dissemination activities may be carried out either by the owner or by other participants (otherwise access to IP rights protection may be seriously jeopardised).

What are access rights?

Access rights are the licences or authorisation rights that permit to use the information owned by a participant of the project.

Participants in a project generally arrive at the project with their own knowledge, data, know-how, etc. (the so-called "**Background**" in the Grant Agreement and the Consortium agreement). Some elements of this background may have to be shared with other participants in order to carry out the project. Reciprocally, participants are in contact with information held by other participants. In addition, the project itself will generate new results which, in some cases, might be exploitable only with the background of certain participants or with the foreground that will be the property of certain participants.

It's worth noting that in ERA4TB, **data contributed as In-Kind** is not considered Background, and shall be treated as if they were Results, and the provisions of Access Rights to Results shall apply to them. They shall continue to be owned by the Beneficiary introducing them into the Action and shall be considered Confidential Information.

For IMP Results and for Results related to a Terminated IMP, Access Rights will be granted subject to a separate written bilateral agreement between the IMP Owner and the Beneficiary requesting Access Rights.

For detailed information on Access Rights, please refer to Article 8 of the Consortium agreement.

[5] ERA4TB Consortium agreement, article 7.2

4. DELIVERABLES

The overall quality control of the project results includes the quality-review coordination of every step of the project implementation, including processes for deliverables, prior to their submission to the IMI JU. It is crucial for the project to ensure that deliverables, as official results of the project, are reviewed and checked for quality.

The present document is only focused on the general methods implemented to ensure quality of written materials delivered to the IMI JU. A document produced in a project generally aims to provide information concerning the work, its progress or the derived results. Each and every document should thus be carefully drafted with rich content, a clear structure and a professional presentation. In ERA4TB, the three basic aspects for building quality into project documents are content, appearance and timing.

The complete list of ERA4TB due deliverables is included in Annex II.

IMI deliverable's template adapted to ERA4TB is available at Sharepoint (link)

4.1. How are project deliverables reviewed?

4.1.1. Quality criteria

Deliverables in ERA4TB are reviewed following a mandatory step for each deliverable generated within the Project. In the process, the following quality criteria should be used as reference:

As regards to content:

- **Completeness:** Information provided in the deliverable report must address all aspects related to the purpose for which the information is produced. On the other hand, redundancy of information must be avoided, as it obscures the clarity of documents. All information used should be provided to the depth needed for the purpose of the document.
- **Accuracy:** Information contained in the document must be reliable and must correspond to reality. This means that all background information used in the reports should be appropriately supported by references. Foreground information should be sufficiently supported so that misinterpretation is avoided. Use of statistically validated objective data is to be prioritised.
- **Relevance:** Information used in the document should be focused on the key issues and be written in a fashion that takes into consideration its target audience.
- **Depth:** all information should be provided to the depth needed for the purpose of the report and the project.

As mentioned in section 6, periodic reports should clearly state whether the deliverable complies with the overall objectives of the project; the specific objectives of the Work Package; and with the activity description as specified in the Description of Action. If deviations occur, they should be clearly stated and justified.

As regards to appearance and structure:

- **Adherence to standards:** uniformity.

As regards to timeliness:

- **Punctuality:** The information must be provided in relation to the particular phase of the project's development and according to the Project Plan. If deviations occur, they shall be clearly stated and justified.
- **Timing**: no delays in the deliverable submission.

4.1.2. Internal review process

Within ERA4TB, the review process is coordinated by the PMO.

1. **Five weeks before the submission** deadline, the **PMO** shall send a **request** to the WPL/author(s) to produce the outline of the deliverable. The EC is informed of the request.
2. Within a maximum period of a week of the request, the WPL, or the deliverable Leader if different, shall submit and agree with the EC on an **outline of the deliverable report**. Absence of response from the EC will be understood as no objection to the outline.
3. Upon approval by the EC and within a period of two-weeks maximum, the WPL/Authors shall generate the **draft** of the whole deliverable, previously agreed with the collaborating partners of the WP. This draft of the deliverable report shall be sent to the PMO.
4. The PMO shall distribute the draft to the **SC** for **review and feedback**. In the following week SC's comments, if any, are gathered by PMO and forwarded to the Author to address them properly.
   Optionally, the author can appoint up to three reviewers among the project participants for a peer review of the document. The review of the appointed reviewers will be made in parallel of the SC review.
5. The WPL/Author(s) shall incorporate the comments and send the **consolidated final version** to the PMO. If there are no substantial changes from the initial draft circulated for review (previous point 4), the Coordinator (or the PMO on his behalf) shall send the final version to the General Assembly for their reference (the document will be also uploaded in the Participant Portal and Share Point) and to IMI JU on the due date. If there are substantial changes from the initial draft, the EC can decide having an additional review of the SC for final approval.

During the whole process, it is recommended that there is one responsible author that acts on behalf of all authors and communicates with them for evolving the document.

The internal review process is depicted in the following diagram:

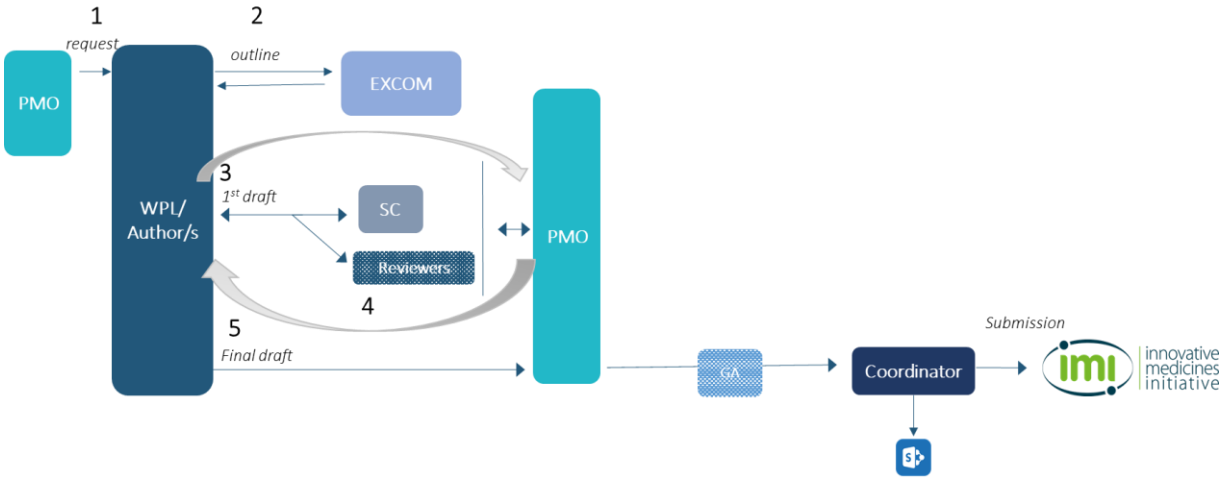


Figure 6. ERA4TB internal review of deliverables

Summarising, the information flow and the illustrative timeline in the review process for deliverables is:

1. PMO sends a **request** to the WPL/author(s) to produce the outline of the deliverable **(week -5).**
2. WPL/Author(s) sends and agrees upon the **outline** with the EC **(week -4).**
3. Within 2 weeks, the WPL/Author(s) generates a **draft of the document**, previously agreed with the collaborating partners of the WP.
4. PMO sends the draft to the SC (and potential reviews if appointed by the author) **(week -2)**; **SC's (and potential reviewers') comments,** if any, are gathered by PMO and forwarded to the Author to insert them properly **(week -1).**
5. WPL/Author(s) sends the **consolidated version** to the PMO and the Coordinator (or the PMO on his behalf) sends the final version to the GA (the document is also uploaded in the Participant Portal) and to IMI JU as official submission on **due date**[6]**.**

Fast-Track review process

In the case of periodic reports and also in the case of other management documents, and in consideration that the main authorship of these documents corresponds to the PMO members, the outline will be agreed with the EC and the review procedure will follow a simplified version of both steps. In this case, the process is depicted as follows:

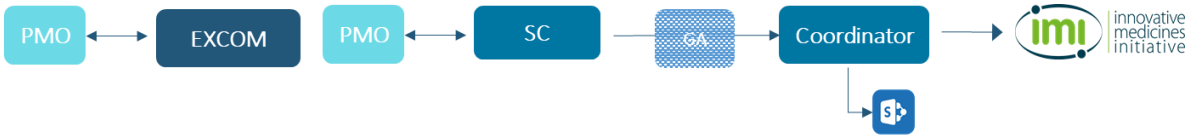


Figure 7. Review process for periodic reports and other management documents

[6] The timelines described in the DoA as "expected delivery date" mean that the deliverable must be submitted by the end of that month.

5. INTERNAL COMMUNICATION

5.1. Internal Communication Processes

Large projects such as ERA4TB require intensive communication exchange and tends to generate a lot of documentation. Clear internal communication guidelines must be respected to ensure efficient vertical downward and upward communication flows, as well as lateral and diagonal communication within the project:

- Communication should be based on needs, target audience, and feedback received.
- Coordinate communication with project milestones, events, activities, and results.
- Emails should not be overused but strategically used.
- Ensure that messages are sent in a timely manner.
- Take advantage of existing communication vehicles and opportunities.

5.2. How should Participants communicate internally?

To ensure that communication within the project complies with the principles listed above, the Consortium will adopt the following approach in that respect:

- Use of electronic mail as the main tool for communication within the Consortium.
- Documentation of discussions, agreements and decisions made by phone is encouraged. Specifically, phone conferences should always have agenda and minutes, which should be made available through SharePoint (See section 5.2.1).
- Several distributions lists have been initially created which can be used by any participant depending on the subject of the message. Additional lists may be created as the project evolves, if necessary. The PMO will be responsible for updating the above-mentioned lists with the information received from Participants. When a list is used, care has to be taken by Participants to use the "reply to all" feature only when relevant. The table below shows the distribution lists created by the time of publishing this Handbook:

ERA4TB MAILING LISTS	
all@era4tb.org (All project members)	ga@era4tb.org (General Assembly representatives)
wpl@era4tb.org (Work package Leads)	sc@era4tb.org (Steering Committee representatives)
wp1@era4tb.org (WP1 members)	excom@era4tb.org (ExCom representatives)
wp2@era4tb.org (WP2 members)	pmo@era4tb.org (Project Management Office)
wp3@era4tb.org (WP3 members)	dat@era4tb.org (Data flows Assurance Team)
wp4@era4tb.org (WP4 members)	pdc@era4tb.org (Pipeline Development Committee)
wp5@era4tb.org (WP5 members)	amt@era4tb.org (Asset Management Teams)
wp6@era4tb.org (WP6 members)	pmt@era4tb.org (Pipeline Management Team)
wp7@era4tb.org (WP7 members)	legal@era4tb.org (Legal representatives)
wp8@era4tb.org (WP8 members)	mt@era4tb.org (Management Team)
wp9@era4tb.org (WP9 members)	communication@era4tb.org (Communication Team)

Table 10. Available distribution lists for ERA4TB

- A Share point space has been created for ERA4TB to be used as a repository of relevant information and files which facilitates the exchange of documents within the Consortium (i.e. meeting minutes, documents in progress, final versions and other relevant reports or announcements). The SharePoint platform also provides the possibility of discussion between participants through messages, maintenance of a calendar of meetings and events, upload of files, and tracking of important milestones and events at both the Project and WP level.

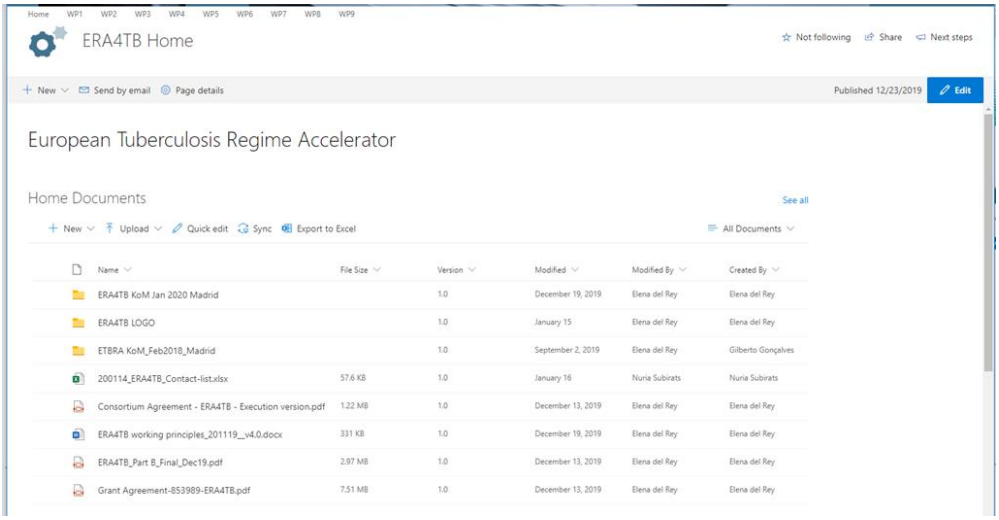


Figure 8. ERA4TB SharePoint home page

- Creation and maintenance of **updated participants' contact information** with clear information of who is included in every mailing list mentioned above. The latest version of the ERA4TB contact list is available at: *contact lists;*
- Use, when possible, of **de facto standards** based on MS Office-compatible files for electronic document exchange among participants. PDF format can alternatively be used to avoid excessive size of files when no editing is required;
- **Good practice** when using email is required. Participants must respond promptly to any email received. When that is not possible, at least acknowledgement of receipt of all messages is strongly recommended, especially when answering an explicit request. Carefully consider whether “reply to all” is required;
- All **emails** sent to any of the mailing lists created so far should preferably be labelled by default with “ERA4TB” in the subject section and senders should add the particular subject of the message. When individual messages between participants are exchanged, use of the same tag is strongly encouraged (e.g. ERA4TB GA meeting agenda);
- **Messages need to be clear**, especially when requests are made. Deadlines must be made explicit. No relevant issues for the work to be performed can remain unclear;
- **Security** of intra-Consortium emails may be reinforced by appropriate means as the project unfolds to ensure confidentiality and integrity of information exchanged, especially if specific, potentially sensitive data is to be exchanged.

5.3. Participant Portal system

In addition to the conventional communication channels already in place, the IMI JU will communicate with the Consortium through the Participant Portal, an internet tool within the Horizon 2020 Program with the aim of becoming over time the main channel of interaction between IMI projects' Participants and the IMI JU, covering the stages of the project life cycle from proposal submission to project completion.

5.4. Confidentiality

It is important to keep confidential any information labelled as such by any other Participants. Please see Section 10 of the Consortium Agreement for more detailed provisions on confidentiality, as well as a few exceptions.

6. PROGRESS REPORTING

6.1. IMI Periodic Reports

Throughout the entire project execution period (i.e. from 1st January 2020 until 31st December 2025), the Consortium is deemed to submit, in due time, six periodic reports and a series of deliverables to the IMI2 JU, according to the following overall planning:

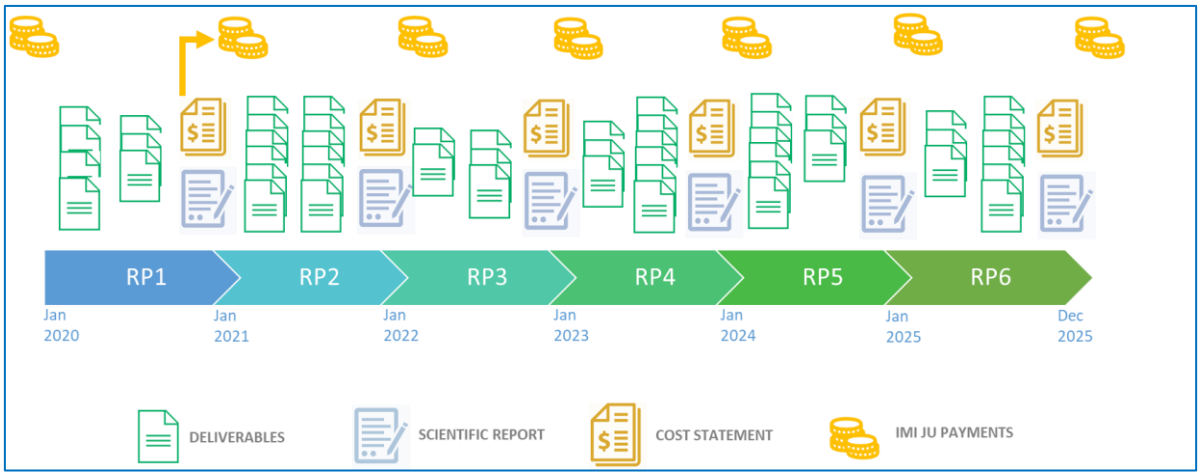


Figure 9. Reporting schedule

As depicted above, the project execution period is officially divided into 6 **periods** for both progress and financial reporting to the IMI2 JU:

- **RP1:** 1st January 2020 to 31st December 2020
- **RP2:** 1st January 2021 to 31st December 2021
- **RP3:** 1st January 2022 to 31st December 2022
- **RP4:** 1st January 2023 to 31st December 2023
- **RP5:** 1st January 2024 to 31st December 2024
- **RP6:** 1st January 2025 to 31st December 2025

Project deliverables are to be submitted at specific times stated in the DoA (*Part A Section 1.3.2 WT2 list of deliverables and Annex II of this document)*. Deliverables reflect the results achieved during the lifetime of the project, and they are important documents to assess the progress achieved.

In compliance with the rules specified in clause 20.3 of the ERA4TB Grant Agreement core document (Periodic reports – Request for interim payments), periodic reports have to be submitted to the IMI2 JU within 60 days after the end of each reporting period (e.g. the RP1 will be submitted by the end of February 2021).

The **periodic report** is divided in two main sections, which must include the following:

Part A

- Summary for publication:
  - Context and overall objectives
  - Work done in the period and achievements
  - Progress beyond state-of-the-art
  - URL of the project website and images (logo and other relevant information).
- Deliverables, Ethics, Data Management Plans, Other Reports.
- Milestones Achievement.
- Critical implementation risks and mitigation measures.
- Dissemination & Communication Activities.
- Scientific publications derived from the project.
- Innovation activities (if applicable): prototypes, clinical trials, testing activities, new products, process or methods in the market, private companies from the project who have introduced innovations due to the project.
- Patents - Registered Intellectual Property Right (*if applicable*).
- Impact on SMEs - Questionnaire to measure the impact of H2020 Programme on growth and job creation in participating SMEs. This will only apply for SME companies participating in the project.
- Training activities (*if applicable*).
- Questionnaire - Health Programme Indicators Instruments.
- EU Access and Benefit Sharing Regulation (NAGOYA Protocol) – *if applicable*.
- Gender of researchers and other workforce involved in the project.
- Financial Statement of all the beneficiaries receiving IMI JU Funding.

This section is completed in the Participant Portal – the online tool being used from IMI to report the project information during the project life. This part of the report will require the input from partners in most of the sections, but the gathering and entering of the information will be coordinated by the ERA4TB PMO, since this should be completed in the Participant Portal by the Coordinator (UC3M).

Part B

- Explanation of the work carried out by the beneficiaries and Overview of the progress
  - Objectives
  - Explanation of the work carried per WP – including contributions from all the beneficiaries (Academia + EFPIA).
  - Impact
  - Consortium management
  - Collaborations/synergies with other initiatives

- Financial contributions
- Update of the plan for exploitation, dissemination and sustainability of results.
- Update of the data management plan.
- Follow-up of recommendations and comments from previous review(s) (*if applicable*)
- Deviations from Annex 1 (DoA) and Annex 2 (Budget), tasks and resources. Unforeseen subcontracting or in-kind contribution from a third party against payment/free of charges.
- Summary of project outputs.

The current templates of the IMI2 Periodic Reports (revised January 2020) are available at: https://www.imi.europa.eu/resources-projects/project-reporting-documents

Each partner shall send, by e-mail, information about work performed in the corresponding period to the PMO[7], **within 30 calendar days** after the end of the reporting period. For accountability, beneficiaries are requested to keep track of their efforts at the activity level. This facilitates the linkage between effort and progress when reporting to IMI JU.

6.2. IMI Final Report

Within 60 days after the end of the project, and in addition to the periodic report for the last reporting period, the Consortium must also submit a final report to the IMI JU. This final report must include the following:

1) a 'final technical report' with a summary for publication containing:

a) an overview of the results and their exploitation and dissemination;

b) the conclusions on the action, and

c) the socio-economic impact of the action.

2) a 'final financial report' containing:

a) a 'final summary financial statement'[8], created automatically by the electronic exchange system, consolidating the individual financial statements for all reporting periods and including the request for payment of the balance and

b) a 'certificate on the financial statements'[9] for each beneficiary, if it requests a total contribution of EUR 325,000 or more, as reimbursement of actual costs and unit costs calculated on the basis of its usual cost accounting practices[10].

This final report will be prepared by the PMO and the Steering Committee with input from all partners.

7. FINANCIAL REPORTING

7.1. Basic documents and principles

As in any other IMI2 project, ERA4TB budgeting and financial flows are based on a few key concepts.

Each beneficiary has a budget, which comprises the estimated costs that will be incurred in due to the project. These costs can be covered with IMI2 funding, direct cash contributions from

[7] Specific additional tools/templates will be created and made available for the Consortium to facilitate the reporting.
[8] See Annex IV to the Grant Agreement.
[9] Drawn up in accordance with Annex V to the Grant Agreement
[10] See Article 5.2 and Article 6.2, Point A of the Grant Agreement

EFPIA partners, or both. Total funding received by a beneficiary cannot exceed its costs (i.e. it cannot yield a profit derived from participation in the project). EFPIA beneficiaries have planned costs, but they receive no funding; all costs are understood as in-kind contribution to the project.

IMI funding follows IMI reimbursement rules, which imply in IMI2 a maximum 100% of the costs reimbursed for research and development activities. IMI2 funding is paid in several instalments: an advance payment (pre-financing) at the beginning of the project, several annual interim payments reimbursing the costs reported and accepted in each Periodic Report, and a final payment of 15% of the total funding.

Direct EFPIA cash contributions are regulated by specific contracts between the paying EFPIA beneficiary and the beneficiary receiving the cash. At the time of the submission of this report, there is no EFPIA cash contribution foreseen within the ERA4TB budget.

Budgeting in ERA4TB has been carried out by using a Responsibility Assignment Matrix (RAM), which is indispensable to understand the beneficiaries' costs and expected funding.

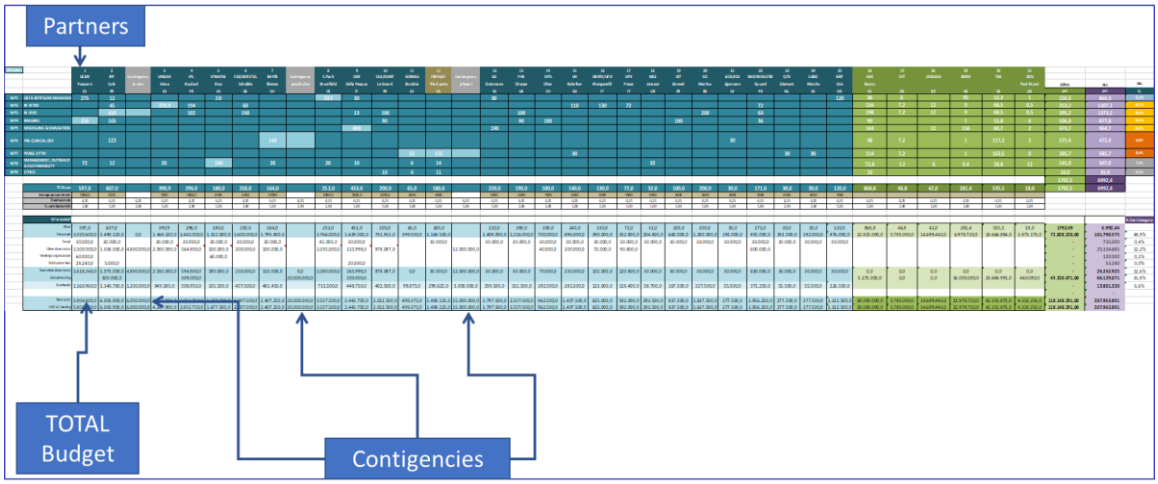


Figure 10. Responsibility Assignment Matrix

Efforts and costs are also displayed in the DoA. Budgets are flexible and can be adjusted during the project life if any unexpected need is raised. Please consult PMO.

7.2. ERA4TB 'Contingency' Funds

The ERA4TB Consortium has opted for a budgeting scheme in which most core partners responsible of modules in the pipeline have been assigned a "underlying" budget to cover the activities in their respective domains, and this is complemented by a "contingency fund" for each key pipeline phase that will be dynamically used according to the actual work required as expressed in the different Asset Progression Plans.

This dynamic allocation of resources will prevent pipeline clogging since the total available capacity in the Consortium has been dimensioned to be able to cope with the most complex scenarios, and in particular with the initial incarnation of the 'asset map' that has been foreseen by the EFPIA and Associated Partners. Estimated attrition rates will allow to foresee capacity needs downstream, and an open structure allowing the inclusion of supplemental capacity through a Network of Associated Centres will facilitate risk mitigation in cases where it is anticipated that capacity may be compromised. This very flexible and dynamic structure will enable reallocation of resources and expertise to the different molecules in the pipeline in real time, as a function of the project's needs.

There is a total of 41M Euro set aside as funding for specific earmarked activities allocated to the following beneficiaries:

- A provision of total budget of 20M Euro is planned within the subcontracting cost category for pre-clinical development expenses, and it will be managed by partner iM4TB in the framework of the activities to be carried out in WP6. According to the project needs, we will work with appropriate CROs and CMOs following the corresponding IMI financial procedures and ensuring the principles of transparency and best value for money in the selection processes (see tasks 6.1 and 8.3 within the DoA). These activities will be subcontracted following standards for late preclinical research in drug discovery and the need for specialized dedicated facilities.
- A total of 15M Euro will cover expenses related to Phase I/FTIH studies incurred by Clinical Trials Units and will be managed by partner SERMAS in the framework of WP7. This budget will be distributed among those beneficiaries that will be executing the Phase I/ FTIH studies according to the needs of the molecules entering the pipeline as agreed in the corresponding Asset Progression Plans. Such beneficiaries include Clinical Trials Units (CTUs): (i) SERMAS in Spain with a CTU (La Paz as Linked Third Party); (ii) UHC in Germany; (iii) QPS in The Netherlands; and (iv) LUND in Sweden. This capacity could be increased, if needed, by additional CTUs to be involved following the corresponding IMI rules.
- A total of 6M Euro has been foreseen to cover expenses of animal experimentation in WP3. This fund will be managed by partner IPP. This budget will be distributed to partners (transferring budget between IPP and the concerned beneficiaries) according to their participation into the different animal studies that will be required for the molecules entering the ERA4TB pipeline. These studies will be agreed with the corresponding compound contributors as part of the Asset Progression Plans, which will guide the assignment of this fund.

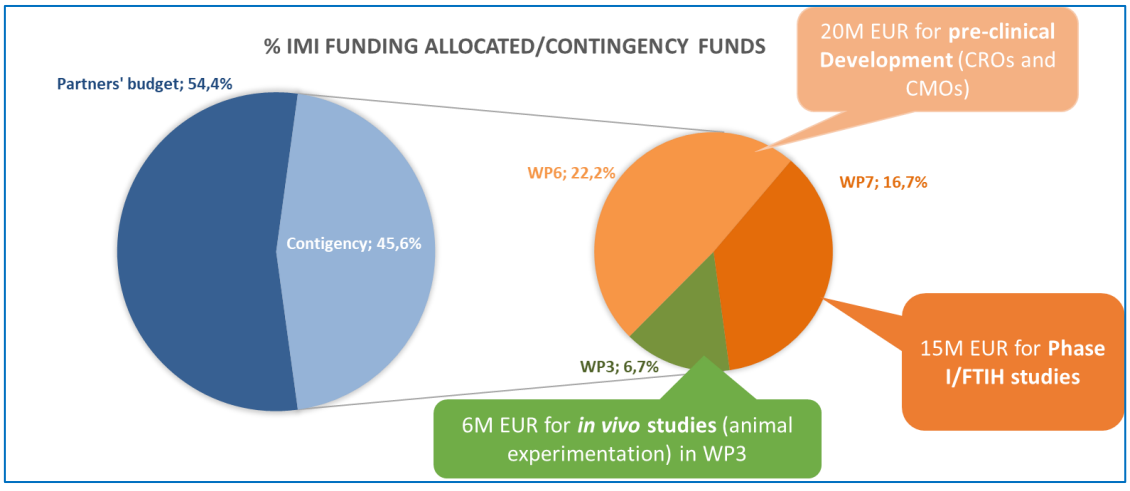


Figure 11. Contingency Budget distribution

Independent from these three provisions of budget, all partners eligible to receive IMI funding have also estimated their costs for the undertaking of activities. In cases where most of the costs will come from these funds (e.g. WP7), funding for partners is understood to cover only basic activities, and it will be supplemented during the project with these funds depending on the actual studies demanded. In other cases (e.g. WP2), mainly for 'Profiling' activities, the involved partners' funding is more substantial, as it relates more to creation of capacity rather than marginal costs of activities.

This budget structure is due to the necessity to have a dynamic and flexible resource assignment which will respond on the progress of the different molecules (and combinations) along the pipeline. The resource assignment distribution will be endorsed by the Steering Committee and it will be reflected within the RAM and the DoA through Amendments to the Grant Agreement as required.

The PMO will ensure transparency on the process of allocating and managing the budget. The usage of the contingency funds will be reported back to the Consortium and other stakeholders. The General Assembly Meetings will offer a good opportunity for the PMO to provide the update on the budget status, including the use of the contingency funds. The IMI Periodic Reports will also include specific section for this part of the budget.

7.3. Costs that can be claimed for reimbursement / accounted for as in-kind contribution

In order to consider project costs as eligible and therefore to get them approved by the IMI JU, they must fulfil the following general conditions:

- They must be incurred by the beneficiary;
- They must be incurred in connection with the action as described in the DoA and necessary for its implementation;
- They must be determined in accordance with the usual accounting principles of the beneficiary;
- They must be incurred during the duration of the project, except for costs relating to the submission of the periodic report for the last reporting period and the final report;
- They must be recorded in the beneficiaries' accounts;
- They must comply with the applicable national law on taxes, and social security;
- They must be reasonable, justified and must comply with the principle of sound financial management, regarding economy and efficiency;
- They must be indicated in the estimated overall budget in the DoA.

Beneficiaries should consider, in the day-to-day administration of the project, some practical advice that may facilitate their financial management:

- Need to be aware of their own budget distribution (please check ERA4TB RAM for detailed budget information);
- Need to coordinate their financial flows: budget, funding, expenditure, justification, payments;
- Need to avoid inconsistencies between efforts spent in the project (recorded in time sheets) and personnel cost justification.

Beneficiaries should note that '**budget'** means the costs that each partner is expected to incur, as declared in the DoA. The amount contributed by the IMI JU is called '**funding'** or 'IMI JU contribution' and corresponds to 100% of the eligible costs. A beneficiary has to justify its total budget in order to get the expected funding in full.

The actual costs incurred during the project (the 'practical' implementation of the planned budget) are what we call '**expenditure'**. These costs will conform to IMI2 JU rules and be therefore justifiable.

Lastly, '**payments'** refer to the actual amounts transferred to the partners' accounts during the project. These depend on the funding of each partner and the justification accepted by the IMI JU and cannot obviously exceed the total funding of each beneficiary.

Identification of **eligible costs**:

1. Personnel Costs. The IMI JU follows a policy of full cost justification for all beneficiaries. This means that the hours devoted by all the personnel involved in a project can be justified, irrespective of them being newly hired for the project or permanent staff.

For the justification of personnel costs in the periodic financial statement, beneficiaries must consider the efforts (expressed in person-months) reported for the same period so that these are consistent with the amounts justified. Personnel costs are understood to include salaries, social charges, etc. – all the actual costs that the person represents for the institution.

The personnel costs are normally calculated by the **hourly rate** multiplied by the number of actual hours worked for the project.

In addition, for personnel costs, the beneficiaries must keep time records for the number of hours declared for all actual work performed for the project. The time records must be in writing and approved by the persons working for the action and their supervisors, at least monthly.

Time records should include (see template provided in Annex III: ERA4TB Time Sheet Template, also available in the ERA4TB SharePoint):

- the title and number of the project, as specified in the Grant Agreement (GA);
- the beneficiary's full name, as specified in the GA;
- the full name, date and signature of the person working for the action;
- the number of hours worked for the action in the period covered by the time record; it is highly recommended that the number of hours is detailed per day (hours worked for the action in each day);
- short description of the work carried out during the month;
- the supervisor's full name and signature.

According to Article 18.1.2 of the Grant Agreement: "*as an exception, for persons working exclusively on the action, there is no need to keep time records, if the participant signs a declaration conforming that the persons have worked exclusively on the action"*. Nonetheless, institution rules need to be consulted first.

2. Other direct costs

Travel and subsistence costs

- Generally, common meetings expenses (caterings, meeting rooms, etc.) shall be paid and justified by the host partner/s in the corresponding reporting period under the "other direct costs" category.
- Travel costs must be needed for the work in the project, or for activities related to it (e.g. presentation of a paper explaining the results of the project in a conference). Travel costs related to a conference where no specific project-related work will be performed or presented by the beneficiary would not be eligible. Travel costs should be limited to the necessity for the project; any extension of the travel for other professional or private reasons is not an eligible cost.

- Each partner must apply the travel rules of their own organisation (i.e. some organisations are reimbursing flat rate allowance for meal expenses, other are reimbursing actual costs).

The depreciation costs of **equipment, infrastructure or other assets** (new or second hand) as recorded in the beneficiary's accounts are eligible, if they are purchased and written off in accordance with the beneficiary's usual accounting principles. The only portion of the costs that will be considered is that which correspondents to the duration of the action and rate of actual use for the action.

Costs of **other goods and services** (consumables, supplies, dissemination, protection of results, certificates on the financial statements, certificates on the methodology, translations, publications) are eligible if they are purchased specifically for the project.

3. Subcontracting costs. Regarding subcontracting costs, it is very important that the DoA includes a specification that enables approval by IMI. The current ERA4TB budget includes subcontracting costs, detailed in the DoA within the Resources section (sections 3.4 and 4.2), and labelled in the RAM as subcontracting.

Ground rule is that all partners must have the technical and financial resources needed to carry out the project themselves, but if it is necessary to implement the project, a beneficiary may call upon subcontractors to implement "action tasks" described in the Grant Agreement ("Subcontracting"; art. 13 GA).

4. Indirect costs. Indirect costs or overheads (e.g. heating, lightning, security, office supplies, etc.), which represent a fair apportionment of the overall overheads of the institution, are to be added to the above-mentioned categories. As they are indirect, these costs are not justified using invoices, etc., but simply stated in the financial statement (Form C), as a 25% of the direct costs explained above (except subcontracting and the costs of resources made available by third parties which are not used on the premises of the beneficiary, which bear no overheads). EFPIA beneficiaries might have their indirect costs included in the fully loaded FTE rate.

If any doubt arises with respect to project expenses or cost justification during the project life, beneficiaries are strongly encouraged to raise the issue to the PMO for guidance (pmo@era4tb.org)

7.4. Costs that cannot be claimed for reimbursement

Some costs cannot be considered as eligible and therefore their justification in the financial cost statement is not allowed, in particular:

1. Costs that do not comply with the conditions set out in Articles 6.1 to 6.4 of the Grant Agreement, in particular:
    - Costs related to return on capital.
    - Debt and service debt charges.
    - Provisions for possible future losses or charges.
    - Interest owed.
    - Doubtful debts.
    - Currency exchange losses.
    - Bank costs charged by the beneficiary's bank for transfers from the JU.
    - Excessive or reckless expenditure.

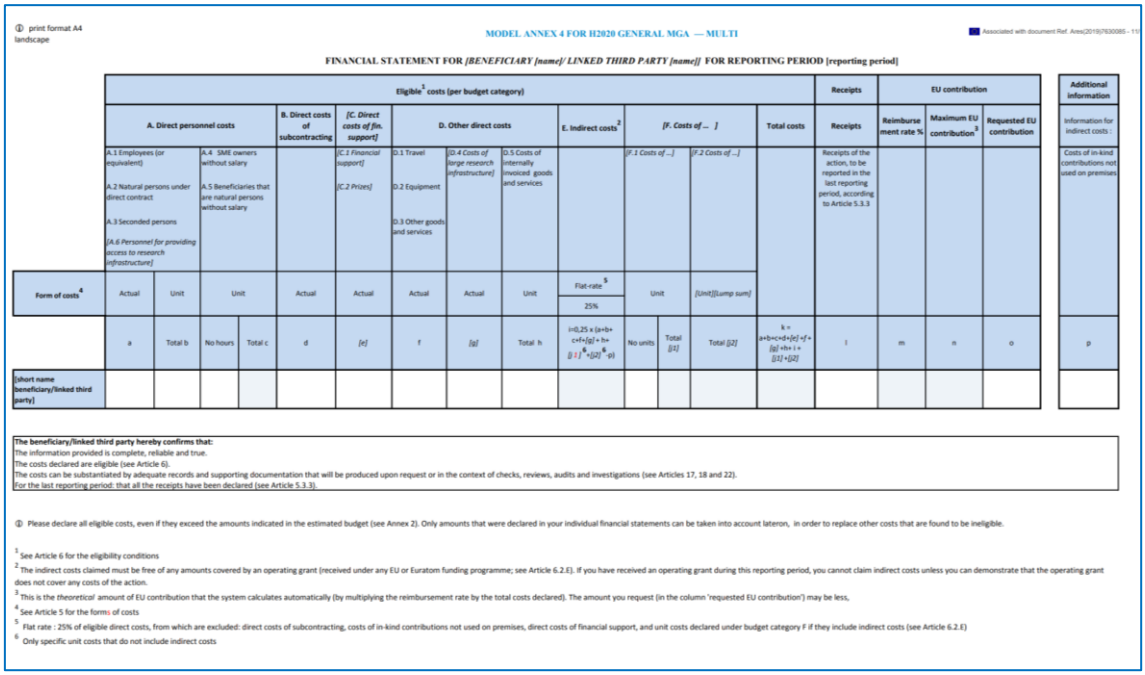
- Deductible VAT.
- Costs incurred during suspension of the implementation of the action.

2. Costs declared under another JU, EU or Euratom grant (including other grants awarded by the JU, grants awarded by a Member State and financed by the EU or Euratom budget and grants awarded by bodies other than the JU for the purpose of implementing the EU or Euratom budget); in particular, indirect costs if the beneficiary is already receiving an operating grant financed by the EU or Euratom budget in the same period.

7.5. How must financial statements be submitted?

Financial statements are specific documents in which each Beneficiary declares all the costs incurred during each reporting period and the funding requested to the IMI2 JU when applicable.

The justification of costs is done by means of an online application tool of the IMI2, called Participant Portal. The costs must be filled by each Consortium beneficiary through the system, which uses the Financial Statement model provided in the Annex IV of the Grant Agreement (figure below).



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MODEL ANNEX 4 FOR H2020 GENERAL MGA — MULTI

FINANCIAL STATEMENT FOR *[BENEFICIARY [name]/ LINKED THIRD PARTY [name]]* FOR REPORTING PERIOD [reporting period]

	Eligible[1] costs (per budget category)													Receipts	EU contribution			Additional information
	A. Direct personnel costs				B. Direct costs of subcontracting	[C. Direct costs of fin. support]	D. Other direct costs			E. Indirect costs[2]	[F. Costs of ...]		Total costs	Receipts	Reimbursement rate %	Maximum EU contribution[3]	Requested EU contribution	Information for indirect costs :
	A.1 Employees (or equivalent) A.2 Natural persons under direct contract A.3 Seconded persons [A.6 Personnel for providing access to research infrastructure]	A.4 SME owners without salary A.5 Beneficiaries that are natural persons without salary				[C.1 Financial support] [C.2 Prizes]	D.1 Travel D.2 Equipment D.3 Other goods and services	[D.4 Costs of large research infrastructure]	D.5 Costs of internally invoiced goods and services		[F.1 Costs of ...]	[F.2 Costs of ...]		Receipts of the action, to be reported in the last reporting period, according to Article 5.3.3				Costs of in-kind contributions not used on premises
Form of costs[4]	Actual	Unit	Unit		Actual	Actual	Actual	Actual	Unit	Flat-rate[5] 25%	Unit	[Unit][Lump sum]						
	a	Total b	No hours	Total c	d	[e]	f	[g]	Total h	i=0,25 x (a+b+c+f+[g] + h+ [j.1][6] +[j2][6] -p)	No units	Total [j1]	Total [j2]	k = a+b+c+d+[e] +f + [g] +h+ i + [j1] +[j2]	l	m	n	o	p
[short name beneficiary/linked third party]																		

The beneficiary/linked third party hereby confirms that:
The information provided is complete, reliable and true.
The costs declared are eligible (see Article 6).
The costs can be substantiated by adequate records and supporting documentation that will be produced upon request or in the context of checks, reviews, audits and investigations (see Articles 17, 18 and 22).
For the last reporting period: that all the receipts have been declared (see Article 5.3.3).

① Please declare all eligible costs, even if they exceed the amounts indicated in the estimated budget (see Annex 2). Only amounts that were declared in your individual financial statements can be taken into account lateron, in order to replace other costs that are found to be ineligible.

[1] See Article 6 for the eligibility conditions
[2] The indirect costs claimed must be free of any amounts covered by an operating grant (received under any EU or Euratom funding programme; see Article 6.2.E). If you have received an operating grant during this reporting period, you cannot claim indirect costs unless you can demonstrate that the operating grant does not cover any costs of the action.
[3] This is the *theoretical* amount of EU contribution that the system calculates automatically (by multiplying the reimbursement rate by the total costs declared). The amount you request (in the column 'requested EU contribution') may be less.
[4] See Article 5 for the forms of costs
[5] Flat rate : 25% of eligible direct costs, from which are excluded: direct costs of subcontracting, costs of in-kind contributions not used on premises, direct costs of financial support, and unit costs declared under budget category F if they include indirect costs (see Article 6.2.E)
[6] Only specific unit costs that do not include indirect costs

Figure 12. Financial Statement (Annex 4 Grant Agreement)

In addition, Non-EFPIA partners will be also asked to provide an explanation of the costs in a use of resources table that is included in the Part A of the Periodic technical report document (Financial Statement).

Specific guidelines for accessing the IMI Reporting tool will also be provided by the PMO in due time. These guidelines will include complete instructions and recommendations for adequate reporting.

Costs must be filled in the IMI online system **within 30 calendar** days after the end of the reporting period together with the use of resources explanation in the cost table. It is advisable that beneficiaries prepare in advance for reporting and liaise with any relevant financial or administrative department in their respective institutions at least one month in advance of the end of the reporting period.

Signature of the Financial Statement will be validated and signed through the Participant Portal. Specific instructions for these steps will be provided ahead of the Reporting timing.

7.5.1. EFPIA Reporting

Under the IMI2 framework, EFPIA and Associated Partners in kind contribution to IMI2 projects and SGG (Strategic Governance Groups) is to be reported by each company on an annual basis and on a portfolio level, independently of the project deadlines set in the Grant Agreement.

Financial statements must be reported by 31 January for the period running since the start date of the activity until 31 December.

The total contribution to be reported includes:

- in kind contribution to operational costs of the IMI2 JU Programme
- financial contributions, to the IMI2 JU or other beneficiaries (BRF), and
- contributions to IMI2 JU advisory groups (such as the SGGs) activities in which they were involved during the previous calendar year (n-1), if the establishment of such groups has been approved by the IMI2 JU Governing Board, and activities related to these groups have been foreseen in the IMI2 JU Annual Work Plan for the relevant year or accepted by the IMI2 JU Governing Board

The reporting period is 1 January– 31 December. The value of the contribution should be detailed at the level of each action (project), including both in kind (in kind EU/non-EU) and direct financial contributions. The contributions reported should be either actual or estimates (if actuals are not available).

In addition, total contributions to SGGs (Strategic Governance Group) where a company is involved should be reported. For Strategic Governance Group in kind contribution, costs shall normally be made of personnel costs and meetings travel costs, where representatives from EFPIA companies have participated/contributed.

The yearly report must be submitted to the IMI2 JU Programme Office no later than 31st of January of each year (n), together with adjustments to previous years, if applicable, through the reporting IT tool SOFIA. The information on the contributions to be submitted by 31st January may be indicative (e.g. can be reported under personnel (regardless of the category), if the breakdown per categories is not yet known). The actual costs including explanation of use of resources as outlined above should be submitted and certified annually at the latest by 30th April. Costs certified later will be considered as such in the following year's exercise. The guidelines for the in-kind contributions are available through this link.

7.6. Who needs to submit an audit certificate?

A certificate on the financial statement (CFS), also named audit certificate, is a statement from a competent auditor in which the correctness and compliance with IMI JU rules of a cost justification is certified.

A CFS must be submitted together with the corresponding financial cost statement at the end of the project by all beneficiaries if the beneficiary requests a total contribution of 325,000 Euro or more, as reimbursement of actual costs and unit costs calculated based on its usual cost accounting practices. This also applies for EFPIA/AP once the total costs claimed exceed 325,000 Euro.

Auditors eligible to deliver audit certificates must be “external auditors” or “public competent officers” who are “independent” and “qualified to carry out statutory audits of accounting documents”. It is highly recommended to determine an adequate auditor well before the end

of the reporting period to ensure his/her availability for a timely generation of the audit certificate.

As a guideline, Annex 5 of the Grant Agreement includes the terms of reference and independent report of factual findings for the certificate of financial statements. For EFPIA/AP the terms of reference are available through this link.

7.7. IMI JU funding Payments

The IMI2 JU funding is paid to the Coordinator (UC3M), who distributes it to the beneficiaries without unjustified delay.

The distribution of IMI JU payments is as follows:

Pre-financing

At the time of the signature of the Grant Agreement (December 2019), IMI JU transferred 11.67% of the IMI JU total funding of each partner. This amount was already distributed to partners who signed the Accession Form and provided the bank account information. This first payment was received by partners by mid-January 2020.

Following the kick-off meeting held on the 29th and 30th of January 2020, many partners expressed a serious concern about the pre-financing and the PMO raised the issue to IMI with the aim of finding alternatives to avoid potential cash-flow problems for partners.

As a result of this discussion, IMI generated in March 2020 a new version of the Grant Agreement to expand the pre-financing to 16.67% of total funding. This means a total increase of 5% which will be released once this extra amount is transferred to the Project Coordinator (UC3M).

Interim payments

The rest of IMI JU funding payments will be depending on cost justified and accepted, and distributed by the Project Coordinator after receipt from the IMI JU.

Final payment

A final payment will be released by the IMI JU corresponding to the costs accepted for the last reporting period plus any adjustment needed. Total payments during the project cannot exceed 85% of the total funding. 15% of the funding will only be paid after final reports are approved.

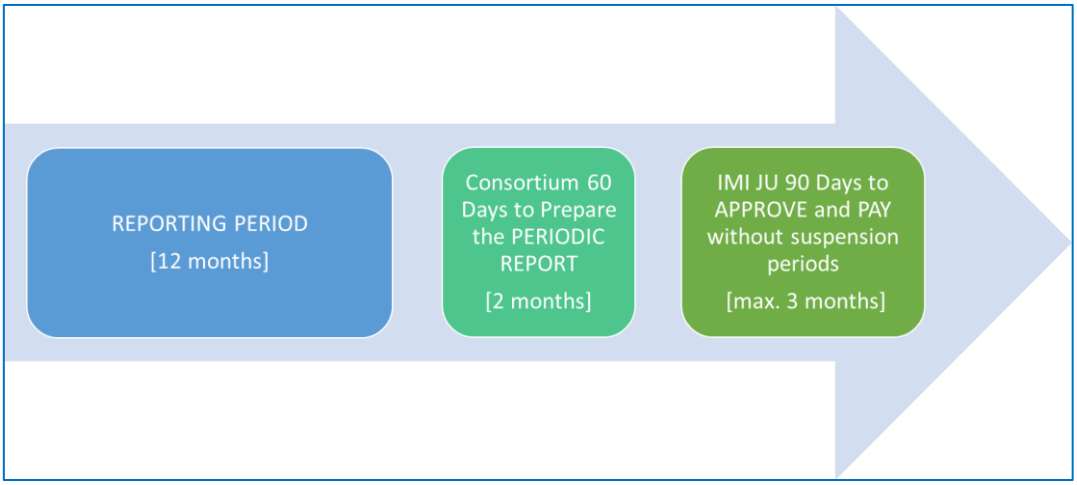

Figure 13. Timelines for reporting and IMI-JU payments

The most important notion for beneficiaries to bear in mind is that payments follow costs reported – and costs reported follow work done for the project. The Coordinator has the right to reject costs reported by any beneficiary if they are not in line with the work performed.

7.8. Receipts of the project

The receipts (in lay terms, 'income received due to the project') of the project would include:

1. **Financial contributions to the beneficiaries made by EFPIA companies/Associated Partners and/or their affiliated** entities. The financial contribution received by the beneficiary from EFPIA companies must be declared by the beneficiary as a 'financial contribution', in the Financial Statement of the last period. The EFPIA company must declare those costs in its Financial statement, when reporting yearly to IMI. The direct financial contributions are subjected to the bilateral agreements between the EFPIA and the beneficiary concerned.
2. Resources **made available by third parties to the partner** by means of financial transfers or contributions in kind which are free of charge:
    - Shall be considered a receipt of the project if they have been contributed by the third party specifically to be used on the project.
    - Shall not be considered a receipt of the project if their use is at the discretion of the beneficiary's management.
3. **Income generated by the project**:
    - Shall be considered a receipt for the beneficiary when generated by actions undertaken in carrying out the project and from the sale of assets purchased under the grant agreement up to the value of the cost initially charged to the project by the beneficiary;
    - Shall not be considered a receipt for the beneficiary when generated from the research use or direct exploitation of foreground resulting from the project

8. RISK MANAGEMENT

8.1. Why is risk management necessary?

Risks are inherent in any activity, especially when it is unique, as is the case of a project. The presence of risk increases dramatically when projects include a significant research component, due to its inherently exploratory nature and uncertain outcome. The inevitability of risks does not imply however the inability to recognise and manage risks to minimise the potential negative consequences while taking advantage of the opportunities for improving performance and results that may arise. Risk management in the ERA4TB project is the process that commences with the identification of risks and links this through to the resolution of individual risks. It encompasses the methods and procedures undertaken by the Consortium in order to identify, analyse, assess and monitor risks affecting the project or its results, and the development and monitoring of associated mitigation and contingency plans that aim at minimising the potential negative effects (for threat risks) and maximising the potential benefits (for opportunity risks).

8.1.1. Main objectives

The main objectives of the risk management task in ERA4TB are the following:

- To provide visibility and raise awareness of uncertainties that may affect the project development and/or results through a structured mechanism that ensures that both completeness and accuracy will be achieved in the process.
- To allow the project to focus on major risks by appropriate assessment and prioritisation according to risk exposure, a value that results of combining the estimated probability and impact values for any given risk.
- To proactively manage uncertainties that can affect the project performance, time schedule and/or budget, with proper feedback channels to project management, allowing for the development of contingency plans, mitigation and/or risk avoidance strategies.
- To continuously monitor the evolution of risks throughout the project, providing a framework to incorporate them in the work plan (as risks become issues) or disregard them (risks becoming pure concerns).
- To document risks, activities and decisions made so as to allow for capitalisation of the knowledge acquired with a view on facilitating planning and development of the post-project phase and future projects.

8.2. Risk Management procedures

The risk management procedures in ERA4TB have been adapted from lessons learnt in past projects by the Consortium, from guidelines produced by international standards bodies, and by recognised institutions such as the Software Engineering Institute (SEI).

Responsible for risk management within the project is the PMO. This facilitates straight forward and timely communication with the EC. However, risk management activities certainly benefit from the active participation of all involved actors, therefore an open structure that allows for contributions from all project partners is promoted. Taking into account the characteristics of the ERA4TB project, only the most appropriate procedures have been selected, giving priority to an extremely pragmatic approach that focuses on the project success and the fulfilment of the GA. As a consequence, the accent is put on risk identification processes that raise awareness on uncertainties and also on risk avoidance strategies. Qualitative analysis of risks is prioritized.

Four main steps conform the risk management process:

- Risk Identification
- Risk Assessment
- Risk Action Plan
- Risk Monitoring

The project management will make documentation available for this purpose upon request. Importantly, in a project like ERA4TB where sustainability in the long term is a core objective, and where the project activities serve to 'pilot' future ongoing activity, lessons learnt from managing risks during the project are of special importance.

8.3. Risk identification

Before risks can be managed, they must be identified. Identification raises awareness of risks before they become problems and adversely affect the project. The first phase of the risk management process deals with systematic research for threats to the successful achievement of the project objectives, or for opportunities that may be hidden therein, and their appropriate classification. This process relies heavily on the encouragement of project personnel to raise concerns and issues for subsequent analysis, as past experience has demonstrated that most risks are usually known by the personnel, who usually experience them as uneasy feelings, concerns or doubts about aspects of the project that wouldn't be defined as risks per se and thus remain hidden. The Risk Identification process must create and sustain a non-judgmental and non-attributive risk elicitation environment so that tentative or controversial views are not discouraged.

8.3.1. Activities for risk identification

In the ERA4TB project the following activities will be considered for risk identification:

- Structured and facilitated brainstorming sessions. These can be normally organised taking advantage of EC meetings to ensure availability of participants, management involvement and face-to-face interactions. However, complementary procedures such as online risk identification forms that can be freely submitted to the PMO are recommended.
- Structured interviewing. This method will normally be used to clarify details of risks, investigate new risks or for checking areas of the project that have been re-planned. One on one interviews or group meetings will be used depending on the issues to be discussed.
- Unstructured interview and informal reporting (at meetings, etc).
- Analysis of formal reporting by participants in the Interim and Periodic Progress reports.
- Analysis of critical path and WP interdependencies by the PMO and WP participants.

The outcome of the risk identification process will be the creation of a **Risk Documentation Form** (see template provided in Annex IV of this document) for each identified risk. A **Risk Registry** composed of the regularly updated Risk Documentation Forms will be maintained by the PMO.

Both opportunity and threat risks will be identified in the same way.

8.4. Risk Assessment

An initial risk assessment is normally carried out as a natural consequence of the identification process. Assessment turns risk data into risk decision-making information, and provides the basis for the Project Managers to work on the "right" risks. It aims at estimating the likelihood (probability) of a risk becoming a problem, the estimated impact ("damage" or "severity" in relation to the project objectives fulfilment) and an associated risk exposure, which is a consequence of the two former variables. In ERA4TB, a qualitative method will be initially used for estimation, ranking both probability and impact on a three-point scale (high, medium or low). In this simple scheme, risks having at least one dimension graded as "high" are always to be closely examined. However, quantification of the **risk exposure** is done by multiplying the

numerical values ascribed to each grade in the scale as follows:

	Impact	Low	Medium	High
Probability	*Values*	*1*	*2*	*3*
Low	1	**1**	**2**	**3**
Medium	2	**2**	**4**	**6**
High	3	**3**	**6**	**9**

Opportunity and threat risks are assessed in the same way, but threat risks have always priority over opportunity risks. Additionally, proximity in time is used to prioritize among risks with equal exposure.

It is important to take into account that interaction and inter-dependence between risks can occur, and that in some cases these complex situations should be treated as independent risks in themselves.

Risk assessment encompasses therefore a prioritisation of the risks that can be made according to exposure but that can also be filtered according to risk category or imminence in time. This phase also comprises a specification of the **Risk Owner,** understood as the partner in the best position to recommend mitigation strategies for the risk, develop and document a contingency plan and monitor the status of the risk. This normally corresponds to the partner responsible of the activity/WP to which the risk is ascribed. The partner being Risk Owner is responsible of closely following up the risk and report to the PMO, which acts as Risk Manager.

8.5. Risk registry and action plan

On the basis of the previous assessment, the planning phase turns risk information into decisions and actions (both present and future) to address individual risks. This phase comprises the **definition of mitigation approaches** (strategies to control, avoid, minimise or otherwise mitigate the risk, addressed to reduce risk probability and/or impact for threat risks, and the opposite for opportunity risks), identification of **trigger events** (conditions that indicate that the risk is turning into an issue) and configuration of **contingency plans** (actions to be taken to deal with the situation if the risk actually becomes a problem). All threat risks with "high" or "medium" probability or impact should have a mitigation strategy that must be immediately tackled and all risks having an **exposure equal or greater than 4 must have a contingency plan** prepared in ERA4TB. Additionally, a mitigation plan is required to be produced for all risks that can be easily mitigated, or that the PMO wishes to mitigate for strategic reasons. A mitigation strategy contains a plan for controlling either or both of the following:

- The risk cause/cause-impact relationship with the aim to reduce the impact probability of occurrence.
- The impact itself and/or its effect on the project.

Implementation of a mitigation approach is a responsibility of the **Risk Owner**, who will be supported by the Risk Management in the PMO when other partners are involved.

Contingency plans should identify the proposed management activity or alternative path to be

taken should the risk give clear indications (understood as occurrence of trigger events) that it cannot be avoided. Contingency plans implementation are Project Management issues and often have to be agreed with the IMI JU services to be entered into the work plan. Contingency plans and responsibilities for their implementation are agreed upon at SC level.

In summary, mitigation actions are what one does before the risk happens; once trigger events are detected, the risk becomes an issue and contingency plans are activated. If mitigation is successful, trigger events are de-activated and the risk is managed out or becomes irrelevant.

In all cases, risk avoidance strategies (which normally imply taking a lower risk path) have to be carefully considered provided that they do not endanger the GA fulfilment.

8.6. Risk Monitoring and updating

Risks and related actions undertaken have to be monitored and re-assessed continuously throughout the project until they are managed out. Previously identified risks with mitigation strategies and contingency plans need to be closely tracked to ensure that any consequential or residual risks are identified as early as possible, and that actions decided are duly carried out.

The PMO is responsible for maintaining the Risk Documentation Forms and following up risks and related actions with the respective owners, coordinating the re-assessment of risks if necessary and promoting the early identification and documentation of new risks. The PMO will support Risk Owners in the carrying out of mitigation actions that involve other partners as well.

The PMO is responsible for checking with the IMI JU services about the appropriateness of any contingency plans that have the potential to endanger the work plan fulfilment and the successful completion of the project.

ANNEXES

ANNEX I. ASSET PROGRESSION PLAN (APP) TEMPLATE

[TO BE COMPLETED BY THE ASSET OWNER]

Molecule/Combination Identification:

Owner of the molecule:

Is the molecule under any licence? If yes, please specify

Any relevant scientific or technical specification and results obtained from the molecule or combination:

From the modules proposed in Annex I, please indicate which modules should be activated for the molecule or combination:

Please indicate if there are any requirement in terms of labs and vendors services for the progression of the selected module or combination:

Whether, what and how legacy data pertaining to the compound will be uploaded to the ERA4TB platform:

In case of a single molecule, please indicate:

- suitable combinations with other molecules
- restrictions of combinations with other molecules, if any

[TO BE COMPLETED BY ERA4TB TEAM]

Proposed modules to be activated according to availability and technical suitability

Proposed partners, labs or vendors to be involved according to availability, technical and economic suitability

Expected timelines[11]

Overall cost to the project[12]

In case of a single molecule, proposed combinations (if applicable)

[TO BE COMPLETED BY THE PMO]

[11] based on standard lead times, availability of the selected modules and requirements of the vendors selection process (validation, etc).

[12] based on standard costs per module, fine tune depending on the specifications agreed for each module.

OPERATIONAL AND GOVERNANCE CONSIDERATIONS

ERA4TB Team appointed:

Asset Management Team (AMT) appointed:

Pipeline Development Committee (PDC) assessment (incl. date of validation):

Steering Committee (SC) assessment (incl. date of validation):

WORK PLAN OF MOLECULE XXX

Date of entry into the pipeline:

Selected modules:

Progression go/no-go points

Partners, Labs or vendors selected:

Resources allocated:

Specific Timeline:

Ex.

MOLECULE XXX	*Date*	*Date*	*Date*	*Date*	*Date*	*Date*	*Date*	*Date*	
ENTRY INTO THE PIPELINE									
MODULE A									
Specific test									
Specific test									
Specific test									
MODULE B									
Specific test									
Specific test									
Specific test									
MODULE C									
Specific test									
Specific test									
Specific test									

ANNEX II. LIST OF DUE DELIVERABLES

DELIVERABLES Follow up

Number	Deliverable name	Date	Due date
Year 1			
D1.1.	Full pipeline specifications	M3	31/03/2020
D8.1	Project Handbook	M3	31/03/2020
D9.1	Ethics plan	M3	31/03/2020
D1.2	Initial Data Management Plan	M6	30/06/2020
D1.3	Report on instantiation of EU-based Drug Development Information Management (DDIM) system	M6	30/06/2020
D8.2	Stakeholder and interdependencies mapping and engagement plan	M6	30/06/2020
D8.3	Draft framework for collaboration within the AMR Accelerator	M6	30/06/2020
D1.4	Initial Standardized templates for collection and reporting of clinical and preclinical data available to consortium members	M8	31/08/2020
D1.5	Consortium data contribution and distribution agreement reviewed and approved by Consortium members	M9	30/09/2020
D1.6	Availability of existing preclinical and clinical TB datasets	M12	31/12/2020
D1.7	First Report on DDIM system availability to Consortium members	M12	31/12/2020
D3.1	First Report on implementation of selected mouse models for in vivo evaluation of drug candidates	M12	31/12/2020
D3.2	Initial Report on knowledge on bioavailability and efficacy of selected drug candidates and regimens in various mouse models	M12	31/12/2020
D3.3	First Report on discovery and validation of predictive TB biomarkers	M12	31/12/2020
D3.4	First Report on molecular signatures of anti-TB drug treatment efficacy in the three animal models	M12	31/12/2020
D5.1	Initial Report on recommendations for design, dosing and sampling schedule for selected experimental protocols in WPs 2, 3 and 4.	M12	31/12/2020
D5.2	First Report on parameter estimates from drug-disease models along with the predicted dose rationale in humans for each compound in the portfolio	M12	31/12/2020
D5.3	First Report on recommendations for the design, dose and dosing regimen(s) to be evaluated	M12	31/12/2020
D8.4	Project communication plan and initial toolset	M12	31/12/2020
Year 2			
D1.8	Final standardized templates for collection and reporting of clinical and preclinical data available to consortium members	M16	30/04/2021
D3.5	Established marmoset model of TB	M18	30/06/2021
D4.1	Procedures for high throughput time-lapse widefield/confocal microscopy imaging	M18	30/06/2021
D9.2	First Report on Ethics and Data Privacy – including updates of ethics plan	M18	30/06/2021
D1.9	Second Report on DDIM system availability to Consortium members	M24	31/12/2021
D1.10	First Report on clinical and preclinical datasets standardized and integrated into the DDIM	M24	31/12/2021
D3.6	Second Report on implementation of selected mouse models for in vivo evaluation of drug candidates	M24	31/12/2021
D3.7	First Report on knowledge on bioavailability, PK/PD and efficacy of selected drug candidates and regimens in NHPs	M24	31/12/2021
D4.2	Efficient pipeline and logistic resources to image infected tissue	M24	31/12/2021
D4.3	Initial Molecular imaging systems, procedures and protocols to perform quantitative, dynamic PET/CT and NIR imaging studies in BSL3 conditions in mouse models	M24	31/12/2021
D4.4	Initial Molecular imaging systems, procedures and protocols to perform quantitative, dynamic PET/CT studies in BSL3 conditions in NHP models	M24	31/12/2021
D6.1	First Report on full Drug Substance CMC reports	M24	31/12/2021

Year 3			
D4.5	Platform for supervised and automatic image analysis	M30	30/06/2022
D2.1	Implementation of HFS-TB in a BSL3 setting in Europe	M30	30/06/2022
D8.5	Project Assessment	M30	30/06/2022
D1.11	Updated Data Management Plan	M36	31/12/2022
D1.12	Second Report on clinical and preclinical datasets standardized and integrated into the DDIM	M36	31/12/2022
D2.2	Full in vitro anti-tuberculosis profile for each candidate molecule	M36	31/12/2022
D3.8	Development and optimization of NHP models for TB drug efficacy evaluation	M36	31/12/2022
D5.4	Final Report on recommendations for design, dosing and sampling schedule for selected experimental protocols in WPs 2, 3 and 4.	M36	31/12/2022
D5.5	Initial Report on drug-disease models for the selection of compounds and companion drugs for combination therapy	M36	31/12/2022
D5.6	Second Report on parameter estimates from drug-disease models along with the predicted dose rationale in humans for each compound in the portfolio	M36	31/12/2022
D6.2	Initial Report on DMPK results reports in preclinical species	M36	31/12/2022
D6.3	Initial Report on full Drug Product development reports	M36	31/12/2022
D9.3	Second Report on Ethics and Data Privacy – including updates of ethics plan	M36	31/12/2022
Year 4			
D8.6	Initial Sustainability Plan	M40	30/04/2023
D1.13	Third Report on DDIM system availability to Consortium members	M48	31/12/2023
D1.14	Third Report on clinical and preclinical datasets standardized and integrated into the DDIM	M48	31/12/2023
D2.3	Comparison list of all promising candidate molecules using dynamic PK/PD HFS-TB model	M48	31/12/2023
D2.4	Development of a drug discovery platform to identify and characterize molecules interfering with *Mtb* host-pathogen interactions	M48	31/12/2023
D3.9	Third Report on implementation of selected mouse models for in vivo evaluation of drug candidates	M48	31/12/2023
D3.10	Second Report on knowledge on bioavailability, PK/PD and efficacy of selected drug candidates and regimens in NHPs	M48	31/12/2023
D3.11	Second Report on discovery and validation of predictive TB biomarkers	M48	31/12/2023
D3.12	Second Report on molecular signatures of anti-TB drug treatment efficacy in the three animal models	M48	31/12/2023
D3.13	Initial Report on delivery of a new potential TB drug or Pan-TB regimens ready for Phase I/II clinical trials	M48	31/12/2023
D5.7	Second Report on recommendations for the design, dose and dosing regimen(s) to be evaluated in Phase I/IIa studies for compounds in the portfolio	M48	31/12/2023
D6.4	Second Report on full Drug Substance CMC reports	M48	31/12/2023
D6.5	Initial Report on full GLP toxicology reports in selected rodent and non-rodent species	M48	31/12/2023

Year 5			
D8.7	Updated Sustainability Plan	M50	28/02/2024
D9.4	Third Report on Ethics and Data Privacy – including updates of ethics plan	M50	28/02/2024
D1.15	Report on analytics and machine learning tools generated and made available to consortium members	M60	31/12/2024
D2.5	Priority list of 2, 3 and 4-way drug combinations based on static *in vitro* profiling and integration with historical and newly generated pharmacological data	M60	31/12/2024
D3.14	Final Report on knowledge on bioavailability and efficacy of selected drug candidates and regimens in various mouse models	M60	31/12/2024
D5.8	Final Report on drug-disease models for the selection of compounds and companion drugs for combination therapy	M60	31/12/2024
D5.9	Third Report on parameter estimates from drug-disease models along with the predicted dose rationale in humans for each compound in the portfolio	M60	31/12/2024
D5.10	Open access modelling and simulation platform for evaluation of compounds beyond the duration of the consortium	M60	31/12/2024
Year 6			
D9.5	Fourth Report on Ethics and Data Privacy – including updates of ethics plan	M68	31/08/2025
D4.6	Final Molecular imaging systems, procedures and protocols to perform quantitative, dynamic PET/CT and NIR imaging studies in BSL3 conditions in mouse models	M70	31/10/2025
D4.7	Final Molecular imaging systems, procedures and protocols to perform quantitative, dynamic PET/CT studies in BSL3 conditions in NHP models	M70	31/10/2025
D1.16	Final Data Management Plan	M72	31/12/2025
D1.17	Final Report on data management platform implementation	M72	31/12/2025
D2.6	Comparison list of most promising drug combinations using dynamic PK/PD HFS-TB model	M72	31/12/2025
D2.7	Elucidation of the mode of action, resistance and drug interaction mechanisms of prioritized compounds and their combinations	M72	31/12/2025
D2.8	Identification of new anti-virulence compounds targeting Mtb HPI	M72	31/12/2025
D3.15	Third Report on knowledge on bioavailability, PK/PD and efficacy of selected drug candidates and regimens in NHPs	M72	31/12/2025
D3.16	Third Report on discovery and validation of predictive TB biomarkers	M72	31/12/2025
D3.17	Third Report on molecular signatures of anti-TB drug treatment efficacy in the three animal models	M72	31/12/2025
D3.18	Final Report on delivery of a new potential TB drug or Pan-TB regimens ready for Phase I/II clinical trials	M72	31/12/2025
D5.11	Third Report on recommendations for the design, dose and dosing regimen(s) to be evaluated in Phase I/IIa studies for compounds in the portfolio	M72	31/12/2025
D6.6	Third Report on full Drug Substance CMC reports	M72	31/12/2025
D6.7	Final Report on DMPK results reports in preclinical species	M72	31/12/2025
D6.8	Final Report on full Drug Product development reports	M72	31/12/2025
D6.9	Final Report on full GLP toxicology reports in selected rodent and non-rodent species	M72	31/12/2025
D8.8	Final Sustainability Plan	M72	31/12/2025
D9.6	Fifth Report on Ethics and Data Privacy – including updates of ethics plan	M72	31/12/2025

ANNEX III. TIME SHEET TEMPLATE

Time Recording for a IMI2 Action	Month:		Year:	

Title of the action (acronym):		**Grant Agreement Nº:**	
Beneficiary's / linked third party's name:			
Name of the person working on the action:		**Type of personnel (see Art.6.2A Grant Agreement)**	

DAY / Reference e.g. WP	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	Total
Total Hours																																

Short description of the activities carried out in the month:	
Signed (name of the person working for the action):	Signed (name of the supervisor):
Date:	Date:
ignature:	Signature:

ANNEX IV. RISK DOCUMENTATION FORM

Risk ID ([13]) Resolved ***Active*** *(4 and above)* ***Inactive*** *(below 4)*

RISK TITLE				
TYPE OF RISK	Threat	Opportunity		
CLASSIFICATION:				
WORK PACKAGE/ACTIVITY:				
DETECTION DATE		**RISK REPORTER**		
RISK OWNER[14]				
LAST UPDATE		**VERSION**		

Description
(Summarise the risk, indicating causes and consequences. Where possible identify the stakeholders that may be impacted). Indicate whether other Work Packages may be affected.)

Proximity in time:
Impact on project: (a)
Probability of happening: (b)
Exposure[15]: (a)*(b)

Mitigation Approaches[16]
(Actions to carry out before the risk happens to affect impact, probability or proximity)

Trigger Events
(Conditions that indicate that the risk is becoming an issue and trigger onset of a contingency plan)

Contingency Plans[17]
(Actions to carry out if the risk actually happens)

Notes

[13]Risk ID codes are completed by the PMO.
[14]The Risk Owner is the partner in the best position to recommend mitigation strategies, develop contingency plans and monitor the status of the risk.
[15]Exposure is the result of the impact multiplied by the probability (a*b)
[16]All threat risks with medium or high probability or impact should have a mitigation strategy.
[17]All risks having an exposure equal or greater than 4 should have a contingency plan in advance.