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SMASH
HCM

DELIVERABLE

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Abstract (for dissemination)	This document presents the governance framework, structure, and procedures established for the effective management and coordination of the project "Stratification, Management, and Guidance of Hypertrophic Cardiomyopathy Patients using Hybrid Digital Twin Solutions – SMASH-HCM". The report specifies decision-making processes and project-related bodies' members.
Keywords	Project Governance

Statement of originality

This deliverable contains original unpublished work except where clearly indicated otherwise. Acknowledgement of previously published material and of the work of others has been made through appropriate citation, quotation or both.

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List of Abbreviations

AE	Affiliated Entity
AI	Artificial Intelligence
AP	Associated Partner
BEN	Beneficiary
CA	Consortium Agreement
COOR	Coordinator
D	Deliverable
GA	Grant Agreement
HCM	Hypertrophic cardiomyopathy
PEB	Project Executive Board
UCD	University College Dublin
WP	Work Package

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Executive Summary

This document presents the governance framework, structure, and procedures established for the effective management and coordination of the project "Stratification, Management, and Guidance of Hypertrophic Cardiomyopathy Patients using Hybrid Digital Twin Solutions – SMASH-HCM" funded under Horizon Europe. The report specifies decision-making processes and project-related bodies' members.

1 SMASH-HCM Project overview

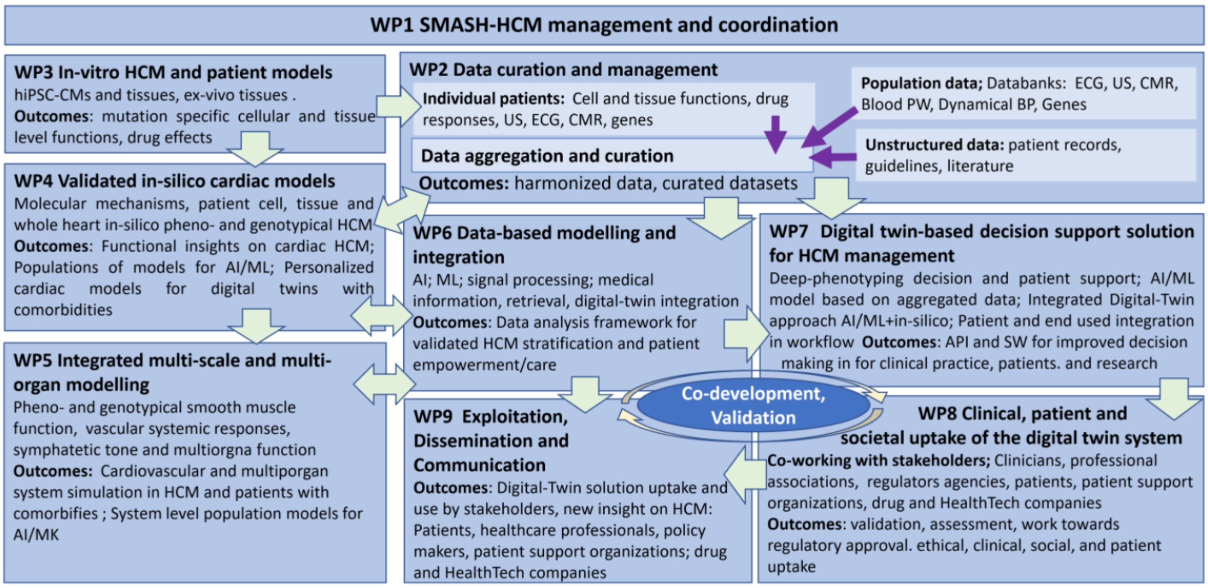
Hypertrophic cardiomyopathy (HCM) is the most common inherited heart disease (prevalence 1:200 - 1:500), manifested by thickening of cardiac walls, increasing risks of arrhythmia, and sudden cardiac death. HCM affects all ages, and it is the leading cause of death among young athletes. Comorbidities due to gene mutations include altered vascular control, and, caused by HCM, ischemia, stroke, dementia, or psychological and social difficulties. Multiple causal mutations and variations in cellular processes lead to highly diverse phenotypes and disease progression. However, HCM is still diagnosed as one single disease, leading to suboptimal care.

SMASH-HCM will develop a digital-twin platform to dramatically improve HCM stratification and disease management, both for clinicians and patients. Multilevel and multiorgan dynamic biophysical and data-driven models are integrated in a three-level deep phenotyping approach designed for fast uptake into the clinical workflow. SMASH-HCM unites 8 research partners, 3 hospitals, 3 small and medium-sized enterprises, and a global health-technology corporation in collaboration with patients to advance the state of the art in human digital-twins: including in-vitro tools, in-silico from molecular to systemic level models, structured and unstructured data analysis, explainable artificial intelligence - all integrated into a decision support solution for both healthcare professionals and patients.

SMASH-HCM delivers new insights into HCM, improved patient care and guidance, validated preclinical tools, and above all, a first HCM stratification and management strategy, validated in a pilot clinical trial, and tested with end users. Thus, it provides a cost efficient and effective solution for this complex disease. SMASH-HCM develops a strategy towards fast regulatory approval. In reaching its goals, SMASH-HCM serves as a basis for future digital-twin platforms for other cardiac diseases integrating models and data from various scales and sources.

The project is carried out in nine work packages (WPs).

Figure 1. Organisation of SMASH-HCM work through 9 WPs.



2 Governance Structure & Members of Decision-Making Bodies

The governance structure of SMASH-HCM is designed to ensure transparency, accountability, and efficient decision-making throughout the project lifecycle. The following key stakeholders comprise the governance framework. The composition of the stakeholders is detailed in the Sections 2.1-2.4

- Project Coordinator
- Project Partners
- Project Executive Board
- Project Management Support Team
- General Assembly
- External Ethics and AI Data Governance Advisory Board
- SMASH-HCM Advisory Board

Project Coordinator

SMASH-HCM is coordinated by Tampere University (TAU), i.e., Tampereen Korkeakoulusäätiö Sr. in Finland. The project is led by Prof. Jari Hyttinen.

Project Partners

Table 1. List of SMASH-HCM Partners

Number	Role	Short-name	Legal name	Country
1	COOR	TAU	TAMPEREEN KORKEAKOULUSAATIO SR	**FI**
2	BEN	POLIMI	POLITECNICO DI MILANO	**IT**
3	BEN	UNIBO	ALMA MATER STUDIORUM - UNIVERSITA DI BOLOGNA	**IT**
4	BEN	EMP	EMPIRICA GESELLSCHAFT FUR KOMMUNIKATIONS UND TECHNOLOGIEFORSCHUNG MBH	**DE**
5	BEN	UNIFI	UNIVERSITA DEGLI STUDI DI FIRENZE	**IT**
5.1	AE	AOUC	AZIENDA OSPEDALIERO-UNIVERSITARIA CAREGGI	**IT**
6	BEN	UKE	UNIVERSITAETSKLINIKUM HAMBURG-EPPENDORF	**DE**
7	BEN	UCD	UNIVERSITY COLLEGE DUBLIN, NATIONAL UNIVERSITY OF IRELAND, DUBLIN	**IE**
8	BEN	UNIVREN	UNIVERSITE DE RENNES	**FR**
8.1	AE	INSERM	INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE	**FR**
9	BEN	CHUR	CENTRE HOSPITALIER UNIVERSITAIRE DE RENNES	**FR**
10	BEN	MDT	MEDTRONIC BAKKEN RESEARCH CENTER B.V.	**NL**
11	BEN	IST	INSILICOTRIALS TECHNOLOGIES S.P.A.	**IT**
12	AP	UOXF	THE CHANCELLOR, MASTERS AND SCHOLARS OF THE UNIVERSITY OF OXFORD	**UK**
13	AP	PHARM	PHARMATICS LIMITED	**UK**

Project Executive Board (PEB)

The Project Executive Board (PEB) consists of the Coordinator and representatives of the SMASH-HCM partners. The Executive Board members are nominated by the corresponding partners, and appointed to the Board by the General Assembly. At the time of the submission of this Deliverable (D1.1), the General Assembly has not yet convened, hence the members of PEB have not been officially appointed yet. The General Assembly has tentatively been planned for autumn 2024, to be held in connection with another Consortium meeting. It is preferred that PEB is kept compact, and PEB members shall be mainly Work Package (WP) leaders if those are part of the Partner team. In other words, partners are encouraged to suggest people with access to fast day-to-day monitoring and action taking as PEB members.

Project Management Support Team

SMASH-HCM is supported by the Project Management Support Team of three permanent members Prof. Jari Hyttinen, Dr. Annariina Koivu and Dr. Antti Ahola (all from Tampere University) ensuring comprehensive project management and oversight. Additionally, the Team may call upon other members or experts to contribute to specific meetings based on their relevance and expertise.

General Assembly

The General Assembly shall consist of one representative of each partner. At the time of the submission of this Deliverable (D1.1), the General Assembly has not yet been appointed.

External Ethics and AI Data Governance Advisory Board

UCD as the Lead of WP2 will convene an External Ethics and AI Data Governance Advisory Board (hereinafter: Ethics Advisory Board). At the time of the submission of this Deliverable (D1.1), the Ethics Advisory Board has not yet been appointed. The members will have expertise relevant to ethics and data management, AI, and data protection compliance.

SMASH-HCM Advisory Board

SMASH-HCM Advisory Board (hereinafter: SMASH Advisory Board) brings complementary expertise into the project. Advisory Board members will have a comprehensive portfolio of different expertise areas and skills; tentatively these include, Dr. Michelle Michels (Erasmus MC, The Netherlands), Dr. Fady Malik (Cytokinetics), Dr. Loredana Guidolin (Amicus), Dr. Rob MacLeod (University of Utah). There will be a representation from patient organisations including the Finnish Heart Association, Cardiomyopathy UK, and CRY (Cardiac Risk in the Young), as well as representation from social sciences. The members not mentioned by name here, and possible alternate board members, will be appointed at the first General Assembly meeting.

3 Roles and Responsibilities

Project Coordinator

In its Coordinator role, TAU as the legal entity, acts as the intermediary between the SMASH-HCM partners and the European Commission. TAU, in addition to its responsibilities as a partner, performs the tasks assigned to it as described in the Grant Agreement (GA) and Consortium Agreement (CA). It is responsible for establishing the project-internal bodies including General Assembly, PEB, and Management Support Team.

TAU is responsible for carrying out the tasks planned for WP1:

- i) will ensure effective project coordination, action planning and follow-up, project internal communication, and administration;
- ii) implement timely financial and scientific, technological and management reporting;
- iii) continuously assess risks and implement mitigation measures;
- iv) manage data, intellectual property to promote innovation and ensure legal compliance,
- v) align the project with complementary research initiatives.

TAU's further responsibilities:

- monitoring compliance by the partners with their obligations under the CA and the GA.
- keeping the contact information list of the partners and other contact persons updated and available.
- collecting, reviewing to verify consistency, and submitting reports, other deliverables (including financial statements and related certifications) and specific requested documents to the European Commission.
- transmitting documents and information connected with the project to any other parties concerned.
- administering the financial contribution of the European Commission and fulfilling the financial tasks described in Section 7.2 of the CA.
- providing, upon request, the partners with official copies or originals of documents that are in the sole possession of the Coordinator when such copies or originals are necessary for the partners to present claims.
- providing a copy of the GA and its annexes to the Associated Partners.

Project Partners

To the extent applicable, the project partners are bound by the GA (beneficiaries) and CA (beneficiaries and associated partners) which means that they must follow the Agreement rules as well as provisions of EU, national and international law. In addition, they have full responsibility for implementing the project properly.

Beneficiaries' further responsibilities:

- Provide their input for the communication with the European Commission.
- Prepare requested documentation for the Coordinator's revision.
- Provide input for deliverables and prepare their deliverables for the Coordinator's revision.
- Spend their budget according to the Horizon Europe rules.
- Prepare their own financial statements.

Project Executive Board (PEB)

The Project Executive Board (PEB) acts as the supervisory body for the execution of the project. It reports to and be accountable to the General Assembly. The PEB shall prepare the meetings, propose decisions, and prepare the agenda of the General Assembly. The PEB shall seek a consensus among the partners. It is responsible for the proper execution and implementation of the decisions of the General Assembly. To fulfil its roles and responsibilities, the PEB will have official quarterly meetings, as well as additional regular monthly meetings when needed to follow the progress in each WP, including deliverables and milestones. The PEB continuously seeks opportunities and means to enhance collaboration in the project. In comparison to General Assembly, the focus of the PEB is more towards the detailed planning, execution, and management of the tasks and activities assigned to WPs. They are responsible for ensuring that the objectives of WPs are achieved within the allocated resources and timeline.

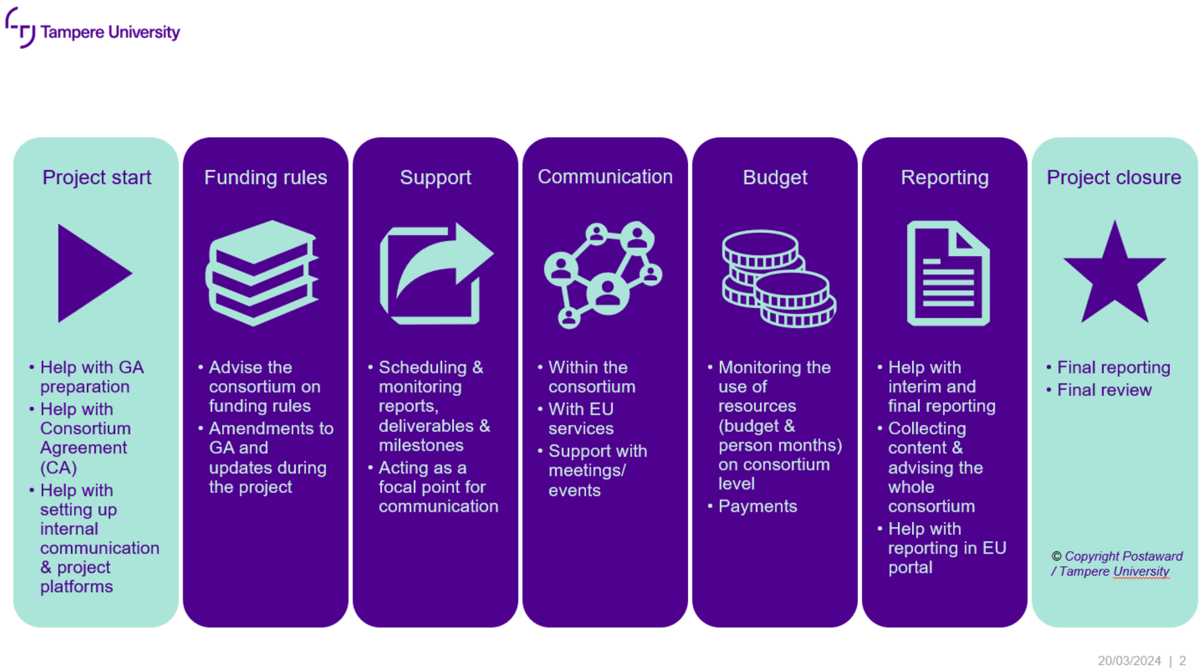
Further responsibilities of PEB:

- monitoring the effective and efficient implementation of the project, including quality assurance and risk management.
- collecting information at least every 6 months on the progress of the project, examine that information to assess the compliance of the project with the consortium plan and, if necessary, propose modifications of the consortium plan to the General Assembly.
- supporting the Coordinator in preparing meetings with the European Commission and in preparing related data and deliverables
- preparing the content and timing of press releases and joint publications by the consortium or proposed by the European Commission in respect of the procedures of the GA Article 17 and Annex 5 Section “Communication, Dissemination, Open Science and Visibility” and of Section 8 of the CA.
- In the case of abolished tasks as a result of a decision of the General Assembly, advise the General Assembly on ways to rearrange tasks and budgets of the partners concerned.

Project Management Support Team

SMASH-HCM Project Management Support Team’s support is essential for delivering project successfully and achieving desired outcomes. It has various responsibilities throughout the project lifecycle, and they may vary depending on the project stage (Figure 1). The Team’s responsibilities may relate to a range of project management topics including project planning, resource allocation & budget management, scheduling and time management, risk management, communication, team leadership, and quality control.

Figure 2. Project Management Team's responsibilities (example on the approach of TAU as a coordinator. Copy rights: TAU/ Postaward).



General Assembly

The General Assembly is the ultimate decision-making body of the SMASH-HCM consortium. Overall, the General Assembly serves as a forum for collaboration, coordination, and decision-making, and enabling the successful execution of the research project.

External Ethics and AI Data Governance Advisory Board

The Ethics Advisory Board will advise on ethical concerns and data protection compliance for sharing patient imaging, clinical and genetic data. It will provide ethical guidance on data management and data transfer. It will support the AI implementation and guide consortium members on Z-inspection (http://z-inspection.org/) best practices for mapping ethical issues and tensions onto EU guidelines for trustworthy AI.

SMASH-HCM Advisory Board

SMASH Advisory Board provides independent advice and specialised expertise and guidance in fields relevant to SMASH-HCM, offering insights that complement the skills and knowledge of the project team. It helps to organise dissemination and patient awareness events involving patients.

4 Decision-Making Processes

Project Coordinator

The Project Coordinator applies systematic, evidence-based, and consensus-based decision-making in the project. Relevant consortium-level decisions and discussions will be documented and disseminated to all project partners to ensure transparency and accountability. The Project Coordinator chairs

- all meetings of the General Assembly, unless decided otherwise in a meeting of the General Assembly.
- all meetings of the PEB, unless decided otherwise by a majority of two-thirds.

It is the responsibility of the Project Coordinator to convene, give notice, prepare the agenda, and record the minutes for the above meetings.

Project Partners

Project partners are encouraged to use structured, systematic, and inclusive processes in the decision-making to ensure legitimate and transparent decisions in their internal and collaborative meetings.

Project Executive Board (PEB)

Table 2. Overview of PEB meetings.

	Ordinary meeting	Extraordinary meeting
Timing of the PEB meeting	At least quarterly, can be monthly	At any time upon request of any Member of the Executive Board
Notice of the PEB meeting	14 calendar days	7 calendar days
Setting of the agenda for the PEB meeting	7 calendar days	N/A
Making the PEB meeting minutes available	10 calendar days	10 calendar days
Voting	Decisions shall be taken by a majority of two-thirds (2/3) of the votes cast.	

Minutes of PEB meetings, once accepted, shall be sent or otherwise made available by the Coordinator to the General Assembly Members for information. All pertinent documentation will be on designated SMASH-HCM Teams platform as the official way of making information available. The PEB prepares the meetings and proposes decisions and agenda of the General Assembly.

Project Management Support Team

Project Management Support Team implements or supports the implementation of the project Coordinator's responsibilities regarding decision-making processes. Project Management Support Team has also regular internal meetings.

General Assembly

Table 3. Overview of General Assembly meetings.

	Ordinary meeting	Extraordinary meeting
Timing of the General Assembly meeting	At least once a year	At any time upon request of the Executive Board or 1/3 of the members of the General Assembly
Notice of the General Assembly meeting	45 calendar days	15 calendar days
Setting of the agenda for the General Assembly meeting	14 calendar days	10 calendar days
Voting	Decisions shall be taken by a majority of two-thirds (2/3) of the votes cast.	

The partners agree to abide by all decisions of the General Assembly but may exercise their veto rights. The CA determines the issues that need to be taken to the General Assembly. The Associated Partners are excluded from voting on and vetoing the decisions in certain cases listed in CA.

External Ethics and AI Data Governance Advisory Board

The Ethics Advisory Board will meet at the start of the project and annually thereafter. UCD is responsible for convening the meeting; giving notice of the meeting; setting agenda; and taking minutes of the meeting and making them available.

SMASH-HCM Advisory Board

SMASH Advisory Board will meet periodically. It will be invited to General Assembly yearly and preferably in the relevant consortium meetings. TAU as a Coordinator is responsible for convening the meeting; giving notice of the meeting; setting agenda; and taking minutes of the meeting and making them available.

5 Conclusions

The Governance Report outlines the governance framework and procedures established for SMASH-HCM. By adhering to these guidelines, the project aims to ensure effective management, coordination, and oversight to achieve its objectives and deliverables within the Horizon Europe research program.