# DELIVERABLE

Project Acronym: **SMASH-HCM**

Grant Agreement number: **101137115**

Project Title: **Stratification, Management, and Guidance of Hypertrophic Cardiomyopathy Patients using Hybrid Digital Twin Solutions**

## D1.2 – Quality Assurance Plan

Revision: 1.0



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| CO | Confidential, restricted under conditions set out in Model Grant Agreement | |
| CI | Classified, information as referred to in Commission Decision 2001/844/EC | |

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# Revision History, Status, Abstract, Keywords, Statement of Originality

**Revision History**

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| Abstract (for dissemination) | This document presents the Quality Assurance Plan (QAP) for the project "Stratification, Management, and Guidance of Hypertrophic Cardiomyopathy Patients using Hybrid Digital Twin Solutions – SMASH-HCM". It outlines the procedures and protocols established to ensure that SMASH-HCM adheres to the highest standards of quality throughout its implementation. |
|---|---|
| Keywords | Quality Assurance |

**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This deliverable contains original unpublished work except where clearly indicated otherwise.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.

## Table of Content



## List of abbreviations

| | |
|---|---|
| D | Deliverable |
| DPO | Data Protection Officers |
| M | Milestone |
| PEB | Project Executive Board |
| QAP | Quality Assurance Plan |
| WP | Work package |

## Executive Summary

This document presents the Quality Assurance Plan (QAP) for the project “Stratification, Management, and Guidance of Hypertrophic Cardiomyopathy Patients using Hybrid Digital Twin Solutions – SMASH-HCM”. The QAP describes the procedures to be used throughout the project to coordinate the timely delivery of high-quality deliverables, scientific publications, and project results.

This plan will serve as a roadmap for project leadership to ensure the assurance of quality before the submission of deliverables and/or other publications. Moreover, it will provide clarity to all project partners regarding their roles in maintaining the quality of project processes, deliverables, and outcomes. The plan outlines the procedures for quality assurance, facilitating the identification of crucial tasks by responsible partners to ensure high-quality outputs and effective communication among relevant stakeholders. It aids in monitoring the project's progress and anticipating potential obstacles that could lead to delays, while also specifying measures to be taken in such scenarios.

# 1 Quality management in SMASH-HCM

## 1.1 Management bodies

Every partner participating in the SMASH-HCM project is responsible for ensuring a high-quality and timely delivery regarding the project's results, outputs, and processes that lead to reaching the project objectives. SMASH-HCM includes the following management bodies and roles:

**Key management bodies:**

1. Project Coordinator
2. Project Partners
3. Project Executive Board (PEB)
4. Project Management Support Team
5. General Assembly
6. External Ethics and AI Data Governance Advisory Board
7. SMASH-HCM Advisory Board

The composition of the key management bodies (1-7) has been detailed in D1.1 – Governance report.

**Further management bodies that safeguard the quality of the SMASH-HCM project:**

8. Work Package (WP) Leaders
9. Data Protection Officers (DPOs)

The composition of the further management bodies is as follows:

8. WP Leaders: WP Leaders from the nine SMASH-HCM WPs (Table 1) are encouraged to join the PEB. The PEB, as a more formal decision-making body, is a larger group than only WP Leaders as it consists of the Coordinator and representatives of the SMASH-HCM partners.

9. DPOs: Each partner undertaking such research in the project that it requires data protection, has a data protection officer or equivalent expert within the organisation, who monitors the processing of personal data and provides advice on compliance with data protection regulations.

Table 1. SMASH-HCM work packages and lead beneficiaries

| **WP#** | **Work Package name** | **Lead Beneficiary** |
|---|---|---|
| WP1 | SMASH-HCM management and coordination | TAU |
| WP2 | Data curation and management | UCD |
| WP3 | In-vitro HCM and patient models | UNIFI |
| WP4 | Validated in-silico cardiac models | UOXF |
| WP5 | Integrated multiscale vascular and multi-organ modeling | UNIVREN |
| WP6 | Data-based modeling and integration | POLIMI |
| WP7 | Digital Twin-based Decision Support Solution for HCM management | TAU |
| WP8 | Clinical, patient, and societal uptake of the Digital Twin system | TAU |
| WP9 | Exploitation, Dissemination and Communication | EMP |

## 1.2 Roles and responsibilities

Tampere University (TAU) is the Coordinator of SMASH-HCM project which involves 12 partners. The Project Executive Board (PEB) acts as the supervisory body for the execution of the project. It will report to and be accountable to the General Assembly, which is the ultimate decision-making body of the SMASH-HCM consortium. The Project Management Support Team supports the Coordinator in the management and communication. The External Ethics AI Data Governance Advisory Board will advise on ethical concerns and data protection compliance for sharing patient imaging, clinical and genetic data. SMASH Advisory Board, including representation from several patient organisations, provides independent advice and specialised insights to SMASH-HCM and helps to organise dissemination and patient awareness events involving patients. The WP leaders oversee and manage the project WPs. The DPOs support compliance with data protection rules and highlight any deficiencies.

The roles and responsibilities, including decision-making processes and meeting procedures of the key management bodies (1-7) have been detailed in D1.1 – Governance report.

## 1.3 How the roles support SMASH-HCM quality assurance

These roles and processes have been designed in a way that they contribute to the quality assurance of SMASH-HCM in various ways:

Project Coordinator:

- Ensures that project activities are aligned with the defined objectives and work plan.
- Monitors the progress of the project and identifies any deviations from the planned schedule or budget that may risk quality.
- Coordinates communication and collaboration among project partners to ensure effective teamwork enhancing quality.
- Implements quality control measures to ensure that project outputs meet the required standards.
- Acts as the main point of contact for the European Commission and other stakeholders, addressing any concerns related to project quality.

Project Partners:

- Contribute their expertise and resources to achieve the SMASH-HCM objectives.
- Adhere to project timelines and deliverables outlined in the work plan.
- Implement quality control measures within their respective work packages or tasks.
- Regularly report progress and any challenges that may compromise quality to the Project Coordinator and other relevant bodies.
- Participate in project meetings and discussions to provide input on quality assurance processes.

Project Executive Board (PEB):

- Provides oversight and strategic direction to ensure the high-quality implementation of the project.
- Reviews project progress reports and performance indicators to assess quality and identify areas for improvement.
- Offers guidance and support to project partners to address quality-related issues.

Project Management Support Team:

- Provides administrative and logistical support to project activities.
- Develops and maintains project documentation, including meeting minutes that can be used as checkpoints to quality.
- Assists in the implementation of quality management systems and procedures.
- Facilitates communication and information sharing among project stakeholders to ensure transparency and accountability and to enhance their understanding of quality assurance requirements.

General Assembly:

- Represents all project partners and ensures their interests are considered in project decision-making processes.
- Monitors overall project progress and evaluates its impact on achieving the desired outcomes.
- Provides feedback and recommendations to improve project quality and effectiveness.
- Ensures alignment between project activities and the broader strategic objectives of the consortium.

External Ethics and AI Data Governance Advisory Board:

- Provides independent oversight and guidance on ethical considerations and data governance practices related to the project.
- Reviews project protocols, policies, and procedures to ensure compliance with ethical standards and regulatory requirements.
- Advises on the responsible use of AI technologies and data management practices to mitigate potential risks and ensure accountability.

SMASH-HCM Advisory Board:

- Offers specialised expertise and guidance related to the specific focus area of the advisory board, thus increasing quality.
- Offers insights on societal implications arising from project activities.
- Provides input on best practices and emerging trends to enhance the quality and effectiveness of project outcomes form the patients' perspectives.
- Facilitates connections and collaborations with stakeholders in the SMASH-HCM field to maximize project impact and quality dissemination of results.

WP Leaders

- The WP Leaders must ensure that their teams implementing the WP work know what the objectives of the work are, are aware of the project plan (Annex 1 of the Grant Agreement), and are implementing it. The WP leaders' task is to arrange work package meetings when needed to ensure the planning and implementation are ongoing and to capitalise on the collective intelligence of the partners for the benefit of this work.
- By actively managing the key aspects regarding WP objects, planning, resources, WP leadership, communication, risk identification, problem solving and reporting, the WP leader contributes significantly to project quality assurance, ensuring that deliverables are completed successfully and meet the expectations of stakeholders.

DPOs

- The DPOs can provide guidance on how to handle personal data in accordance with legal requirements, thus minimizing the risk of non-compliance issues that could impact project quality.

# 2 Quality Assurance for Project Milestones

The WP Leader responsible for the milestone must ensure the milestone is met by the due date (Table 2). If the milestone requires active input from other partners, the WP Leader must actively contact the relevant partners to ensure timely progress.

Should the responsible WP Leader foresee a chance of delay for completing a milestone, they must notify the Coordinator without delay. If needed, the Coordinator will take action to mitigate the issue (e.g., request for more time from the Project Officer or other action).

The responsible WP Leader must notify the Coordinator of the status of the milestone one month before its due date. The WP Leader must also write a short description (5–10 sentences) of the achievements associable with the milestone. Please refer to the 'means of verification' of the milestone in Table 2 while writing the description.

Once the milestone is met, the Coordinator shall mark it as 'achieved' in the EU Funding and Tenders Portal and submit the short description. It is the WP Leader's duty to ensure the milestone's output is made available, when it is completed, to the partners that will be needing it to perform their own work.

Table 2. The List of Milestones (M). *Due date is expressed on project months.

| M# | Milestone name | WP# | Lead Partner | Means of Verification | Due* |
|---|---|---|---|---|---|
| 1 | Governance established | WP1 | TAU | D1.1 delivered | 2 |
| 2 | Data Management concepts established | WP1 | TAU | D1.4 and D2.1 delivered | 6 |
| 3 | Data transfer agreements (DTA) | WP2 | UCD | Each partner signs DTA | 6 |
| 4 | Sharing of patient data with WP3-6 | WP2 | UCD | D2.4 delivered | 15 |
| 5 | iPSC lines sharing | WP3 | UNIFI | iPSC lines shared | 12 |
| 6 | Two novel iPSC lines | WP3 | UNIFI | Lines generated | 24 |
| 7 | Initial populations for deep-phenotyping and data augmentation. | WP4 | UOXF | Initial calibrated populations available | 18 |
| 8 | Integrated calibrated populations for deep-phenotyping and data augmentation | WP4 | UOXF | D4.3 and D4.4 delivered | 30 |
| 9 | Predictions and retrospective validation of therapy response | WP4 | UOXF | Predictions shared | 42 |
| 10 | Population of smooth muscle cell models | WP5 | TAU | Delivery of D5.1 | 26 |
| 11 | Integrated personalized multi-organ models | WP5 | UNIVREN | Delivery of D5.2, D5.3 | 40 |
| 12 | Prognostics of personalized optimal therapy choices | WP5 | UNIVREN | Delivery of D5.4 | 48 |
| 13 | Results of validation of HCM risk stratification | WP6 | POLIMI | Delivery of D6.6 | 31 |
| 14 | API for HCM stratification algorithms available | WP7 | TAU | Delivery of D7.4 | 16 |
| 15 | Decision Support Solution ready for clinical pilot | WP7 | TAU | Delivery of D7.8 | 32 |
| 16 | Regulatory, validation, and adoption strategy | WP7 | TAU | Delivery of D8.4 | 32 |
| 17 | Stakeholder network for regulation and validation | WP7 | TAU | D8.2, D8.8, D8.9 | 38 |
| 18 | Socio-economic impact assessment framework | WP9 | EMP | Delivery of D9.3 | 24 |

# 3 Quality Assurance for Project Deliverables

A ready-made template with the EU logo and funding details has been made available for project deliverables. All deliverables must use the SMASH-HCM template for deliverables. The template is available for download on the project's SharePoint.

The coordinator shall submit all deliverables through the EU Funding and Tenders Portal. The partner responsible for the deliverable must ensure the deliverable can be submitted by the due date (Table 3).

For any deliverables requiring input from the other partners, it is the responsible partner's obligation to coordinate and collect this input and ensure it can be received timely. All partners must follow the Deliverable review-acceptance protocol (Figure 1), as agreed in the first Consortium meeting, and documented below.

The WP leader submits the deliverable to the Coordinator for quality review one month before its due date, unless otherwise agreed in advance. Coordinator reviews the deliverable and sends it for project's internal review (i.e., to partner other than the original author). Reviewer within the project reviews the deliverable and returns it with comments to the WP Leader. The WP Leader must submit the final revised version to the Coordinator two working days before the due date at the latest.

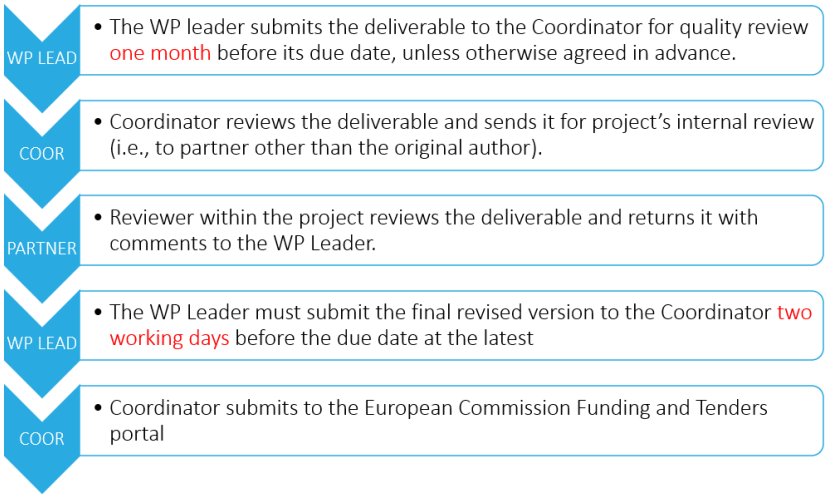


**Figure 1. Protocol for SMASH-HCM Deliverables**

Should the responsible WP Leader foresee a chance of delay for completing the deliverable, they must notify the Coordinator at earliest convenience. If needed, the Coordinator will take action to mitigate the issues (e.g., request for more time from the Project Officer).

Table 3. The List of Deliverables (D). *Due date is expressed on months.

| D# | Deliverable name | Lead | Type | Due* |
|---|---|---|---|---|
| D1.1 | Governance report | TAU | PU | 2 |
| D1.2 | Quality assurance plan | TAU | PU | 3 |
| D1.3 | Project Data Management Plan (P-DMP) | TAU | PU | 3 |
| D1.4 | Risk assessment reports | TAU | PU | 18 |
| D1.5 | Project Data Management Plan Update | TAU | PU | 22 |
| D2.1 | Research-Data Management Plan (R-DMP) | UCD | PU | 6 |
| D2.2 | VASC Submission package | TAU | PU | 9 |
| D2.3 | Curated datasets | UCD | SEN | 9 |
| D2.4 | Annotated CMR data | UCD | SEN | 12 |
| D2.5 | VASC Mid-term recruitment report | TAU | SEN | 21 |

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| D2.6 | VASC Report on the status of the posting of results to the registry | TAU | PU | 31 |
| D3.1 | Delivery of existing single iPSC cardiomyocyte measurement data | UNIFI | SEN | 6 |
| D3.2 | Generated and shared cardiomyocytes | UNIFI | PU | 24 |
| D3.3 | Novel platform for rapid pharmacological evaluations | UNIFI | PU | 24 |
| D4.1 | Libraries of HCM populations of cellular electromechanical models | TAU | PU | 18 |
| D4.2 | Technologies for optimal therapy choice | UNIBO | PU | 24 |
| D4.3 | Integration of biophysical modelling technologies | TAU | PU | 30 |
| D4.4 | Pipeline personalization of human heart electromechanical models | UOXF | PU | 30 |
| D4.5 | Technologies for personalized optimal therapy choice | UOXF | PU | 48 |
| D5.1 | HCM populations of smooth muscle cell models | TAU | PU | 26 |
| D5.2 | Integration of vascular biophysical multiorgan modeling technologies | UNIVREN | PU | 35 |
| D5.3 | Personalization of multiorgan models | UNIVREN | PU | 40 |
| D5.4 | Technologies for prognostics of personalized optimal therapy choices | UNIVREN | PU | 48 |
| D6.1 | Requirements SMASH-HCM predictive/clustering tool | POLIMI | PU | 4 |
| D6.2 | Initial Evidence-based models and biomarkers | PHARM | PU | 18 |
| D6.3 | Interpretable referral models for clinical use | PHARM | PU | 24 |
| D6.4 | Initial Data-driven models | POLIMI | PU | 21 |
| D6.5 | Predictive/stratification tools in HCM and related conditions | TAU | SEN | 30 |
| D6.6 | Validation results of HCM risk stratification models | POLIMI | PU | 42 |
| D7.1 | Requirements SMASH-HCM solution in clinical practice – initial | EMP | PU | 7 |
| D7.2 | Requirements for disease patients' self-management | EMP | PU | 7 |
| D7.3 | Design specifications of an API for DSS algorithms | TAU | PU | 9 |
| D7.4 | API for DSS algorithms | TAU | PU | 16 |
| D7.5 | Integrated DSS for HCM stratification and disease management – initial | TAU | SEN | 19 |
| D7.6 | SMASH-HCM solution as research tool requirements | EMP | PU | 21 |
| D7.7 | SMASH-HCM requirements in clinical practice - final | EMP | PU | 24 |
| D7.8 | Integrated DSS for HCM stratification and disease management - final | TAU | SEN | 31 |
| D7.9 | DSS software package for continued research | TAU | PU | 48 |
| D8.1 | Ethical approval of the whole SMASH-HCM study | UNIFI | PU | 9 |
| D8.2 | Patient organizations discussions and feedback | TAU | SEN | 12 |
| D8.3 | Clinical data use contracts: hospitals and universities | TAU | SEN | 15 |
| D8.4 | Contact with regulatory agencies FIMEA, DEKRA | TAU | PU | 18 |
| D8.5 | PILOT Submission package | TAU | PU | 18 |
| D8.6 | EU Clinical Trials Register | TAU | PU | 18 |
| D8.7 | Ethical approval for the pilot study | UNIFI | SEN | 24 |
| D8.8 | Discussion with ESC HCM subgroup | UNIFI | PU | 24 |
| D8.9 | Collaboration agreement pharmaceutical and technological industry | TAU | SEN | 24 |

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| D8.10 | PILOT Mid-term recruitment report | TAU | SEN | 36 |
| D8.11 | Requirements and guidelines for health technology assessment and health economics | TAU | PU | 40 |
| D8.12 | PILOT Report on the status of the posting of results to the registry | TAU | PU | 48 |
| D9.1 | Dissemination, communication and exploitation plan | EMP | PU | 6 |
| D9.2 | Project Website | EMP | PU | 6 |
| D9.3 | Socio-economic impact assessment framework | EMP | PU | 24 |
| D9.4 | Updated dissemination, communication and exploitation plan | EMP | PU | 28 |
| D9.5 | Exploitation & business plan | EMP | SEN | 36 |
| D9.6 | Final business model planning | EMP | SEN | 48 |
| D9.7 | Dissemination and communication report | EMP | PU | 48 |

# 4 Quality Assurance for Scientific Publications

## 4.1 Preparation

The themes or topics of scientific publications have not been specified in the Grant Agreement, so they are subject to more flexibility than other project deliverables. Deliverables are of importance but being able to transfer these also (at least partly) to publications will enhance the project impact. All partners participating in the scientific work, but university partners in particular, are responsible for identifying findings that can potentially be disseminated as scientific publications. The WP leaders should actively facilitate the identification of potential publications in their WPs.

A partner that intends to disseminate its results must give at least 30 days advance notice to the other partners (unless agreed otherwise), together with sufficient information on the results it will disseminate.

Any other partner may object within (unless agreed otherwise) 20 days of receiving notification, if it can show that its legitimate interests in relation to the results or background would be significantly harmed. In such cases, the results may not be disseminated unless appropriate steps are taken to safeguard those interests (Reference: Consortium Agreement, Article 8.4.2.1).

The partner(s) authoring the scientific publication must ensure that Responsible Conduct of Research[1] is followed. They must also agree on authorship: who is listed as an author and in which order are the authors' names listed following accepted guidelines on research integrity and responsible conduct of research (e.g., https://www.tenk.fi/sites/tenk.fi/files/TENK_suositus_tekijyys_EN.pdf). Moreover, they must ensure that no commercial exploitation interests are jeopardized because of the publication.

In case of conflicts in the aforementioned issues, the WP Leader in question, with Coordinator, will act as a mediator and must promote consensus building among the partners.

## 4.2 Open science

The partners must ensure open access to peer-reviewed scientific publications relating to their results. In particular, they must ensure that:

- at the latest at the time of publication, a machine-readable electronic copy of the published version or the final peer-reviewed manuscript accepted for publication, is deposited in a trusted repository for scientific publications,
- immediate open access is provided to the deposited publication via the repository, under the latest available version of the Creative Commons Attribution International Public Licence (CC BY) or a licence with equivalent rights; for monographs and other long-text formats, the licence may exclude commercial uses and derivative works (e.g. CC BY-NC, CC BY-ND) and
- information is given via the repository about any research output or any other tools and instruments needed to validate the conclusions of the scientific publication.

Partners (or authors) must retain sufficient intellectual property rights to comply with the open access requirements.

[1] Please see e.g. https://tenk.fi/en/research-misconduct/responsible-conduct-research-rcr

Metadata of deposited publications must be open under a Creative Common Public Domain Dedication (CC 0) or equivalent, in line with the FAIR (Findable, Accessible, Interoperable and Reusable) principles (in particular machine-actionable) and provide information at least about the following: publication (author(s), title, date of publication, publication venue); Horizon Europe or Euratom funding; grant project name, acronym and number; licensing terms; persistent identifiers for the publication, the authors involved in the action and, if possible, for their organisations and the grant. Where applicable, the metadata must include persistent identifiers for any research output or any other tools and instruments needed to validate the conclusions of the publication. Only publication fees in full open access venues for peer-reviewed scientific publications are eligible for reimbursement. (Reference: Grant Agreement, Article 17)

## 4.3 Dissemination

The partners must disseminate their results as soon as feasible, in a publicly available format, subject to any restrictions due to the protection of intellectual property, security rules or legitimate interests.

## 4.4 Acknowledgement & Disclaimer

All scientific publication must acknowledge EU support and display the European flag (emblem) and funding statement (translated into local languages, where appropriate):


The emblem must remain distinct and separate and cannot be modified by adding other visual marks, brands or text. Apart from the emblem, no other visual identity or logo may be used to highlight the EU support.

The emblem is available at: https://europa.eu/european-union/about-eu/symbols/flag_en

Any communication or dissemination activity related to the action must use factually accurate information. Moreover, it must indicate the following disclaimer (translated into local languages where appropriate):

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Reference: Grant Agreement, Article 17.2, 17.3.

Examples of acknowledgement of contributions: "Beyond the authors who contributed to this paper, we would sincerely like to thank to the whole SMASH-HCM Team / the contributing authors of project deliverables x-x; from Partner1: name…”.

# 5 Conclusion

In conclusion, the Quality Assurance Plan (QAP) outlined herein is not merely a static document but rather a dynamic roadmap guiding the project “Stratification, Management, and Guidance of Hypertrophic Cardiomyopathy Patients using Hybrid Digital Twin Solutions – SMASH-HCM” towards its objectives with the highest standards of quality. By adhering to the procedures delineated within this plan, project leadership can ensure the consistent delivery of superior deliverables and publications. Furthermore, this plan fosters transparency and accountability among project partners, clarifying their roles in upholding the project's quality standards. As the project progresses, the QAP will remain instrumental in identifying and addressing potential challenges, thereby safeguarding the project's success and ultimate impact. Through rigorous adherence to this plan, the project team is poised to achieve excellence in every facet of its endeavours, leaving a legacy of quality and innovation.