SIMCor

In-Silico testing and validation of Cardiovascular IMplantable devices

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Self-assessment plan

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10/06/2021	1.0	Mirko De Maldè (LYN)	First draft by LYN (templates of self-assessment, document general structure)
22/06/2021	2.0	Mirko De Maldè (LYN	First complete draft with all self-assessments for each WP
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30/06/2021	Final	Jan Brüning (CHA)	Submission by PC

Executive summary

This document presents the self-assessment plan of the project. The document contains KPIs and procedures for completing the self-assessment for each WP. The document was completed with the contribution and direct involvement of each WP leader.

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Introduction

The aim of the self-assessment plan is to identify a clear set of criteria to evaluate the progress of the project activities and relevant outcome, allowing to compare the actual results with the expected results at different project time-points. Each WP leader was asked to define, for each task, quantitative and qualitative KPIs, associate to them target values (for acceptable and optimal results), and the relevant means of verification and schedule for the self-assessment activities. Following this approach, the Consortium have a clear tool for understanding the current implementation level of the project, making it possible to acknowledge the existence of delays or issues, ultimately allowing the timely implementation of appropriate mitigation strategies. At the same time, the self-assessment plan constitutes an objective tool for evaluation and understanding of the project status for the external reviewers.

The procedure: WPs performance indicators and self-assessment plans

The procedure followed consisted of two key steps:

1. Based on the existing WPs tasks, the first step has been the request to each WP Leader to define, for each of these tasks, a relevant and possibly quantitative measurement processes/unit, useful to assess the progress of a specific task.
2. Based on the measurement process/unit defined in the first step, a subsequent series of correlated indicators have been defined. These indicators are numerical values which represent the expected outcome in specific time-points of the project: two values have been provided, one for the minimum acceptable result, and one for the optimal result.
3. For each KPI, relevant means of assessment were indicated to clearly define the assessment procedure specific for each indicator.
4. Ultimately, the schedule for the self-assessment procedure is also provided.

As a result, it will be possible to compare the actual results at a certain time-point of the project with the forecast results defined in the self-assessment, thus having a clear and immediate understanding of the progress of the project compared with the initial plan.

Both the measurement process/unit and the indicators are provided in the dedicated tables in the following pages of the present document. Both qualitative and quantitative indicators have been used, depending on the nature of the specific task.

Project WPs

As a guidance to the document, it is useful to refer to the work breakdown structure.

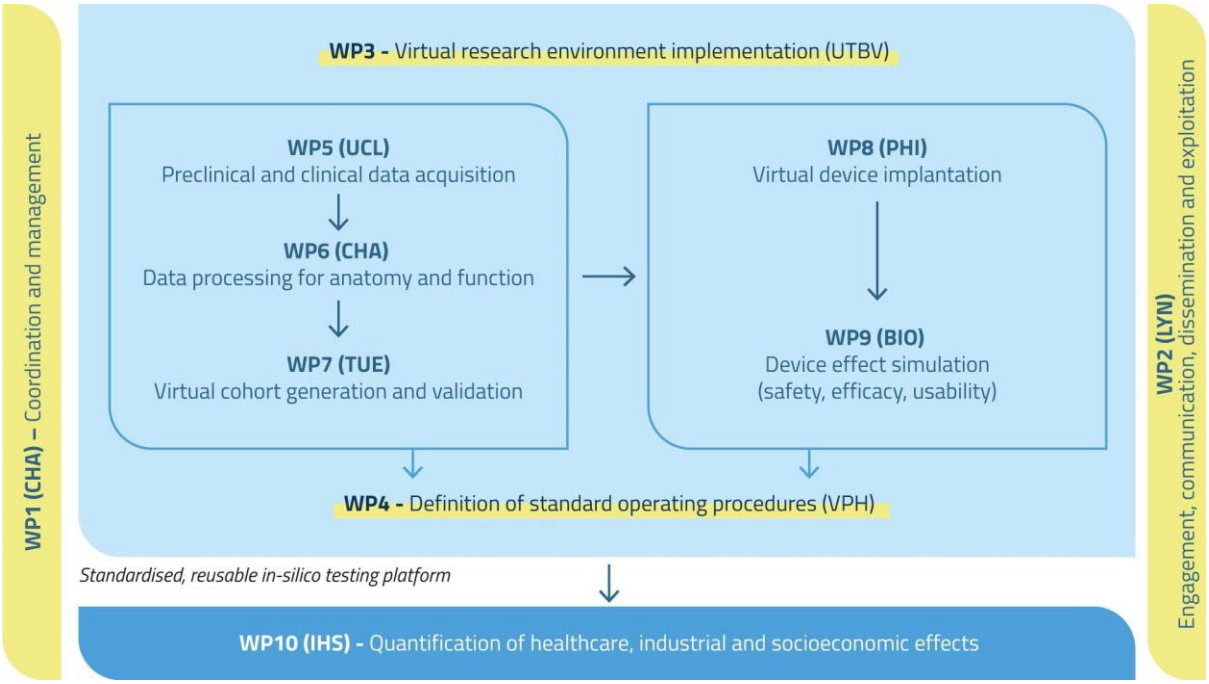

Figure 1: SIMCor implementation workplan and relevant work packages (WPs).

Self-assessment plans per WPs

WP1: Coordination and management

WP Leader: CHA

Tasks:

T1.1: Research strategy and project steering. Leader: CHA. Contributors: ALL. Duration: M1-M36.
T1.2: Operational management. Leader: LYN. Contributors: ALL. Duration: M1-M36.
T1.3: Project reporting. Leader: LYN. Contributors: ALL. Duration: M1-M36.
T1.4: Risk management and mitigation. Leader: LYN. Contributors: ALL. Duration: M1-M36.
T1.5: Financial, administrative and contractual coordination. Leader: CHA. Contributors: ALL. Duration: M1-M36.
T1.6: Ethical and legal clearance and monitoring. Leader: LYN. Contributors: ALL. Duration: M1-M36.

Key performance indicators (KPIs)

Please indicate for each task one or more KPIs:

TASK	KPI (quantitative and qualitative indicators can be included - quantitative KPIs are preferable)
T1.1	Definition of the strategy completed
T1.2	Project Meetings organised on a regular basis
T1.3	Project reports and deliverables provided in time
T1.4	Risk assessment performed on a regular basis
T1.5	Financial resources distributed in a timely fashion
T1.6	Ethical and legal assessment performed on a regular basis

Targets

Please associate to each KPI relevant (measurable) targets (acceptable and optimal - with acceptable indicating the threshold under which the activity cannot be considered properly completed):

KPI	Target
T1.1	Acceptable: Strategy available Optimal: N/A
T1.2	Acceptable: 1 meeting per month Optimal: 4 meetings per months
T1.3	Acceptable: Reports delivered in due time Optimal N/A
T1.4	Acceptable: Risk assessment performed every 6 months Optimal: Risk assessment performed every 3 months

T1.5	Acceptable: All financial and administrative issues sorted in due time Optimal: NA
T1.6	Acceptable: deliverables on ethical and legal issues available in due time Optimal: NA

Means of assessment

Please include here the specific means for performing the self-assessment, per task and KPI:

Task	KPI	Means of verification
T1.1	1.1	Deliverable 1.1 submitted in due time
T1.2	1.2	Count of the number of meetings
T1.3	1.3	Check of submission date against due data
T1.4	1.4	Availability of risk assessment and relevant timing
T1.5	1.5	Financial and administrative issues sorted
T1.6	1.6	Check of delivery date of the relevant deliverables

Schedule of the self-assessment

Task	Self-assessment schedule
T1.1	Every 6 months
T1.2	Every 6 months
T1.3	Every 6 months
T1.4	Every 6 months
T1.5	Every 6 months
T1.6	Every 6 months

WP2: Engagement, communication, dissemination and exploitation

WP Leader: LYN

Tasks:
T2.1: Communication and dissemination strategy, branding and tools (LYN/ALL, M1-M36)
T2.2: Dissemination events (LYN/ALL, M1-M36)
T2.3: Liaison with regulatory authorities (VPH/ALL, M1-M36)
T2.4: Exploitation planning (LYN/ALL, M19-M36)
T2.5: IPR management, open research and sustainability (LYN/ALL, M19-M36)

Key performance indicators (KPIs)

Please indicate for each task one or more KPIs:

TASK	KPI (quantitative and qualitative indicators can be included - quantitative KPIs are preferable)
T2.1: Communication and dissemination strategy, branding and tools (LYN/ALL, M1-M36)	• % of completion of the branding and communication materials • N° of newsletters • N° of press releases • N° of unique visitors on the website • N° of accesses on the website • N° of Tweets • N° of Twitter followers
T2.2: Dissemination events (LYN/ALL, M1-M36)	• N° of attended conferences (with presentation of results through presentations, posters or abstracts) • N° of organised workshops within healthcare ICT events • N° of industrial workshops • N° of webinars • N° of clinical focus groups
T2.3: Liaison with regulatory authorities (VPH/ALL, M1-M36)	• N° of iterations with relevant regulatory authorities
T2.4: Exploitation planning (LYN/ALL, M19-M36)	• Number of meeting for the planning of the exploitation strategy organised
T2.5: IPR management, open research and sustainability (LYN/ALL, M19-M36)	• Number of assessments of the conformity of the developed devices supervising also accordance with national regulations • N° of patents

Targets

Please associate to each KPI relevant (measurable) targets (acceptable and optimal - with acceptable indicating the threshold under which the activity cannot be considered properly completed):

KPI	Target

% of completion of the branding and communication materials	Acceptable: 70% Optimal: 100%
N° of newsletters	Acceptable: 2 (M18, M36) Optimal: 3 (M12, M18, M36)
N° of press releases	Acceptable: 2 (kick-off, platform launch) Optimal: 5 (kick-off, platform launch, publications and other milestones)
N° of unique visitors on the website	Acceptable: 3,000 by M36 (1,000 per year) Optimal: 6,000 by M36 (2,000 per year)
N° of accesses on the website	Acceptable: 6,000 by M36 (2,000 per year) Optimal: 12,000 by M36 (3,000 per year)
N° of Tweets	Acceptable: 150 by M36 (50 per year, about 1 per week) Optimal: 450 by M36 (150 per year, about 3 per week)
N° of Twitter followers	Acceptable: 300 by M36 (100 per year) Optimal: 900 by M36 (300 per year)
N° of attended conferences (with presentation of results through presentations, posters or abstracts)	Acceptable: 6 by M36 (2 per year) Optimal: 18 by M36 (6 per year)
N° of organised workshops within healthcare ICT events	Acceptable: 1 by M36 Optimal: 2 by M36
N° of industrial workshops	Acceptable: 2 by M36 Optimal: 5 by M36
N° of webinars	Acceptable: 2 by M36 Optimal: 5 by M36
N° of clinical focus groups	Acceptable: 1 by M36 Optimal: 3 by M36
N° of iterations with relevant regulatory authorities	Acceptable: 1 by M36 Optimal: 3 by M36
Number of meeting for the planning of the exploitation strategy organised	Acceptable: 2 by M36 Optimal: 6 by M36

Number of assessments of the conformity of the developed devices supervising also accordance with national regulations	Acceptable: 1 per device by M36 Optimal: 2 per device by M36
N° of patents	Acceptable: 2 by M36 Optimal: 6 by M36

Means of assessment

Please include here the specific means for performing the self-assessment, per task and KPI

Task	KPI	Means of verification
T2.1: Communication and dissemination strategy, branding and tools (LYN/ALL, M1-M36)	% of completion of the branding and communication materials	Check from branding and communication materials list
	N° of newsletters	Published Mailchimp newsletters
	N° of press releases	Press releases circulated by CHA press office
	N° of unique visitors on the website	Google Analytics
	N° of accesses on the website	Google Analytics
	N° of Tweets	Twitter Analytics
	N° of Twitter followers	Twitter Analytics
T2.2: Dissemination events (LYN/ALL, M1-M36)	N° of attended conferences (with presentation of results through presentations, posters or abstracts)	Project reporting, publications
	N° of organised workshops within healthcare ICT events	Project reporting
	N° of industrial workshops	Project reporting
	N° of webinars	Project reporting
	N° of clinical focus groups	Project reporting
T2.3: Liaison with regulatory authorities (VPH/ALL, M1-M36)	N° of iterations with relevant regulatory authorities	Deliverables, project reporting

T2.4: Exploitation planning (LYN/ALL, M19-M36)	Number of meeting for the planning of the exploitation strategy organised	Project reporting
	Number of assessments of the conformity of the developed devices supervising also accordance with national regulations	Project reporting
	N° of patents	Project reporting

Schedule of the self-assessment

Task	Self-assessment schedule
T2.1: Communication and dissemination strategy, branding and tools (LYN/ALL, M1-M36)	M6, M12, M18, M24, M30, M36
T2.2: Dissemination events (LYN/ALL, M1-M36)	M6, M12, M18, M24, M30, M36
T2.3: Liaison with regulatory authorities (VPH/ALL, M1-M36)	M18, M24, M30, M36
T2.4: Exploitation planning (LYN/ALL, M19-M36)	M24, M30, M36
T2.5: IPR management, open research and sustainability (LYN/ALL, M19-M36)	M24, M30, M36

WP3: Virtual research environment implementation

WP Leader: UTBV

Tasks:

T3.1: Computational platform requirements for infrastructure adaptation and extension

T3.2: Implementation of extensions to data repository

T3.3: Cloud facilities integration

T3.4: Web-based interface and user profiles

Key performance indicators (KPIs)

Please indicate for each task one or more KPIs:

TASK	KPI (quantitative and qualitative indicators can be included - quantitative KPIs are preferable)
T3.1: Computational platform requirements for infrastructure adaptation and extension	KPI1: number of use cases defined KPI2: available functional and non-functional requirements
T3.2: Implementation of extensions to data repository	KPI3: available secure repository for clinical and imaging data KPI4: available secure repository for storing model input data describing the virtual patient population
T3.3: Cloud facilities integration	KPI5: number of simulation workflows integrated in the VRE KPI6: number of simulation instances run in parallel
T3.4: Web-based interface and user profiles	KPI7: number of user profiles KPI8: available visualization of clinical and virtual patient data and medical images

Targets

Please associate to each KPI relevant (measurable) targets (acceptable and optimal - with acceptable indicating the threshold under which the activity cannot be considered properly completed):

KPI	Target
KPI1	Acceptable: 4 Optimal: 8
KPI2	Acceptable: functional and non-functional requirements defined Optimal: functional and non-functional requirements detailed
KPI3	Acceptable: secure repository for clinical and imaging data available at M18 Optimal: secure repository for clinical and imaging data

	available at M18
KPI4	Acceptable: secure repository for storing model input data describing the virtual patient population available at M18 Optimal: secure repository for storing model input data describing the virtual patient population available at M18
KPI5	Acceptable: 2 Optimal: 4
KPI6	Acceptable: 3 Optimal: 6
KPI7	Acceptable: 2 Optimal: 3
KPI8	Acceptable: visualization of clinical and virtual patient data and medical images available Optimal: visualization of clinical and virtual patient data and medical images available

Means of assessment

Please include here the specific means for performing the self-assessment, per task and KPI:

Task	KPI	Means of verification
T3.1	**KPI1**	Check number of use cases defined and included in D3.1.
	KPI2	Check number of functional and non-functional requirements defined and included in D3.1.
T3.2	**KPI3**	Test the implemented repository against the following key requirements / features that constitute the essential elements to consider the repository as secure: authorization, data encryption at-rest and in transit
	KPI4	
T3.3	**KPI5**	Run and count simulation workflows integrated in the VRE

	KPI6	Perform multiple test runs with increasing number of instances run in parallel
T3.4	**KPI7**	Count number of user profiles available in the VRE
	KPI8	Test whether all clinical and virtual patient data can be visualized on the VRE

Schedule of the self-assessment

Task	Self-assessment schedule
T3.1: Computational platform requirements for infrastructure adaptation and extension	M4: initial assessment M6: final assessment
T3.2: Implementation of extensions to data repository	M12: initial assessment M18: final assessment
T3.3: Cloud facilities integration	M24: final assessment
T3.4: Web-based interface and user profiles	M30: Initial assessment M36: final assessment

WP4: Definition of standard operating procedures

WP Leader: VPH

Tasks:

T4.1 Elaboration of the SOPs for the preclinical and clinical data acquisition for in-silico models

T4.2 Elaboration of SOPs for the processing of preclinical and clinical data

T4.3 Elaboration of SOPs for virtual cohort generation and validation.

T4.4 Elaboration of guidelines for documentation of in-silico models and simulation results for approval process.

T4.5: Elaboration of SOPs for the in-silico model development, verification and validation

T4.6: Elaboration of SOPs for validation of the in-silico model predictions

Key performance indicators (KPIs)

Please indicate for each task one or more KPIs:

TASK	KPI (quantitative and qualitative indicators can be included - quantitative KPIs are preferable)
T4.1	• N° of written SOPs. • N° of publicly accessible SOPs • Level of reproducibility of the steps • Compliance of SOPs with official guidelines and standards.
T4.2	• N° of written SOPs. • N° of publicly accessible SOPs • Level of reproducibility of the steps • Compliance of SOPs with official guidelines and standards.
T4.3	• N° of written SOPs. • N° of publicly accessible SOPs • Level of reproducibility of the steps • Compliance of SOPs with official guidelines and standards.
T4.4	• N° of publicly accessible guidelines • N° of meetings with regulatory advisory board for feedback • Compliance of guidelines with official recommendations and standards
T4.5	• N° of written SOPs. • N° of publicly accessible SOPs • Level of reproducibility of the steps • Compliance of SOPs with official guidelines and standards.
T4.6	• N° of written SOPs. • N° of publicly accessible SOPs • Level of reproducibility of the steps • Compliance of SOPs with official guidelines and standards.

Targets

Please associate to each KPI relevant (measurable) targets (acceptable and optimal - with acceptable indicating the threshold under which the activity cannot be considered properly completed):

KPI	Target
N° of written SOPs.	**Acceptable**: 1 **Optimal:** 3+ for T4.2 (number depends on tasks) NOTE: Most deliverables will be a set of SOPs, number to be defined within each task.
N° of SOPs publicly accessible	**Acceptable**: 1 **Optimal**: all SOPs written for the task (e.g., 3+ for T4.2)
Level of reproducibility of the described steps an procedures	**Acceptable**: at least 'quite well reproducible' (qualitative scale), based on SIMCor reviewer's feedback. NOTE 1: Example of scale: Not at all reproducible – not really – mostly reproducible – quite well reproducible – completely reproducible. NOTE 2: Reproducibility is to be intended provided that specified skills and resources are available. **Optimal**: Completely reproducible (qualitative scale), based on SIMCor reviewer's feedback.
Compliance of SOPs with official guidelines and standards.	**Acceptable**: Compliance discussed with regulatory advisory board members (= experts from AoB + recruited externals (e.g., TeamNB, etc.)). **Optimal**: Compliance discussed with regulatory advisory board members + positive informal feedback from external experts (ISW CoP, AA, etc.)
N° of open access guidelines	**Acceptable**: 1 **Optimal**: 1+
N° of iterations with regulatory advisory board for feedback	**Acceptable:** 1 **Optimal**: 1+ (iterative process)
Level of compliance of guidelines with official recommendations and standards	**Acceptable**: Compliance discussed with regulatory advisory board members. **Optimal**: Compliance discussed with regulatory advisory board members + positive informal feedback from external experts (ISW CoP, AA, etc.)

Means of assessment

Please include here the specific means for performing the self-assessment, per task and KPI:

Task	KPI	Means of verification
T4.1, T4.2, T4.3, T4.5, T4.6	N° of written SOPs.	EU WP4 deliverables
T4.1, T4.2, T4.3, T4.5, T4.6	N° of publicly accessible SOPs	SIMCor website, Zenodo
T4.1, T4.2, T4.3, T4.5, T4.6	Level of reproducibility of the described steps and procedures	Written feedback and answers from internal reviewers.
T4.1, T4.2, T4.3, T4.5, T4.6	Compliance of SOPs with official guidelines and standards.	Minutes and regulatory feedback reports from meetings with regulatory advisory board (D2.5, D2.5).
T4.4	N° of open access documents	SIMCor's website and Zenodo
T4.4	N° of meetings with regulatory advisory board for feedback	Announcements in SIMCor's website. Release minutes and feedback report from meetings with regulatory advisory board
T4.4	Level of compliance of guidelines with official recommendations and standards	Minutes and regulatory feedback reports from meeting with regulatory advisory board (D2.5, D2.5).

Schedule of the self-assessment

Task	Self-assessment schedule
T4.1	**M18**, M18-M19, M30-M31
T4.2	**M12,** M18-M19, M30-M31
T4.3	**M36,** M18-M19, M30-M31
T4.4	**M12**, M18-M19, M30-M31
T4.5	**M24,** M18-M19, M30-M31
T4.6	**M36,** M30-M31, M36

SIMCor self-assessment plan

WP5: Preclinical and clinical data acquisition	**WP Leader: UCL**
Tasks: **T5.1 Protocol definition for data collection tasks (retrospective, prospective; preclinical, clinical, synthetic).** **T5.2 Collection of retrospective and acquisition of prospective preclinical data from pig study.** **T5.3 Collection and organization of retrospective clinical data.** **T5.4 Creation of synthetic data**	

Key performance indicators (KPIs)

Please indicate for each task one or more KPIs:

TASK	KPI (quantitative and qualitative indicators can be included - quantitative KPIs are preferable)
T5.1	KPI5.1 Establishment of a protocol for collection of clinical and preclinical data
T5.2	KPI5.2 10 datasets collected for PAPS animal studies
T5.3	KPI5.3.1 250 datasets retrospectively collected for TAVI patients (125 from UCL; 125 from CHA)
T5.3	KPI5.3.2 125 datasets retrospectively collected for PAPS patients (CHA)
T5.4	KPI5.4.1 creation of 1,000 synthetic records for aortic stenosis (AS) population for TAVI study.
T5.4	KPI5.4.2 Creation of 1,000 synthetic records for heart failure (HF) population for PAPS study.

Targets

Please associate to each KPI relevant (measurable) targets (acceptable and optimal - with acceptable indicating the threshold under which the activity cannot be considered properly completed):

KPI	Target

KPI5.1	Acceptable: Submission of protocols for clinical and preclinical studies Optimal: Approval of protocols for clinical and preclinical studies
KPI5.2	Acceptable:75% of animal dataset collected Optimal: 100% of animal dataset collected
KPI5.3.1	Acceptable:80% of retrospective TAVI dataset collected Optimal: 100% of retrospective TAVI dataset collected
KPI5.3.2	Acceptable:80% of retrospective PAPS dataset collected Optimal: 100% of retrospective PAPS dataset collected
KPI5.4.1	Acceptable:80% of AS dataset created Optimal: 100% of AS dataset created
KPI5.4.2	Acceptable:80% of HF dataset collected Optimal: 100% of HF dataset collected

Means of assessment

Please include here the specific means for performing the self-assessment, per task and KPI

Task	KPI	Means of verification
5.1	**KPI5.1**	**Verification of protocols submission and approval**
5.2	**KPI5.2**	**Quantification**
5.3	**KPI5.3.1**	**Quantification**
5.3	**KPI5.3.2**	**Quantification**
5.4	**KPI5.4.1**	**Quantification**
5.4	**KPI5.4.2**	**Quantification**

Schedule of the self-assessment

Task	Self-assessment schedule
5.1	M7
5.2	M16
5.3	M16
5.4	M18

WP6: Data processing for anatomy and function

WP Leader: CHA

Tasks:

T6.1: Processing pipeline and database concept for TAVI and PAPS

T6.2: Anatomical and functional information from image data (heart, heart valves, large vessels)

T6.3: Boundary conditions for subject-specific simulations (4D and local properties)

T6.4: Boundary conditions for virtual cohorts simulations.

Key Performance Indicators (KPIs)

Please indicate for each task one or more KPIs:

TASK	KPI (quantitative and qualitative indicators can be included - quantitative KPIs are preferable)
Task 6.1	• Definition of standard data formats for anatomical and biomechanical properties • Definition of data interfaces for all image data processing steps • Database design
Task 6.2	Anatomical information for TAVI from human CT: • N° segmented aortas • N° segmented aortic valves • N° coronary ostia landmarks • N° annulus contours • N° segmented LV • N° segmented LVOT • N° centerlines Anatomical information for PAPS from human CT: • N° segmented PAs Functional information for TAVI and PAPS from human CT: • Development of tools for automatic calculation of functional information
Task 6.3	TAVI • left ventricular pressure information for all anatomies • aortic pressure information for all anatomies • volume flow rate for all anatomies PAPS • volume flow rate in main pulmonary artery for all anatomies • volume flow split in left and right pulmonary artery for all anatomies

	• vessel displacement from systole to diastole for all anatomies
Task 6.4	Synthetic anatomical shapes and functional parameters (e.g. flow rates, pressures, compliance) for PAPS cohorts generated: • N° PA of pigs (real cohort) • N° PA of pigs (augmented cohort) • N° PA of humans (real cohort) • N° PA of humans (augmented cohort) • N° PA of humans (paediatric cohort) Synthetic anatomical shapes and functional parameters (e.g. flow rates, pressures, compliance) for TAVI cohorts generated: • N° AV of humans (real CHA cohort) • N° AV of humans (real UCL cohort) • N° AV of humans (augmented CHA cohort) • N° AV of humans (augmented UCL cohort) General Quality Aspects • Requirement for remeshing, • quality of numerical meshes • % of synthetic data sets to be removed due to non-physiologic anatomy and/or function

Targets

Please associate to each KPI relevant (measurable) targets (acceptable and optimal - with acceptable indicating the threshold under which the activity cannot be considered properly completed):

KPI	Target
6.1	
Standard formats	Acceptable: Definition of standard data formats for anatomical and biomechanical properties Optimal: n/a
Data interface	Acceptable: Definition of data interfaces for all image data processing steps Optimal: n/a
Database	Acceptable: Database design completed and validated Optimal: n/a
6.2	Optimal: Development of tools for automatic segmentation, landmark detection and deduction of anatomical and functional parameters

N° segmented aortas	Acceptable: 100 Optimal: 2000
N° segmented aortic valves	Acceptable: 100 Optimal: 2000 with each leaflet being segmented individually
N° coronary ostia landmarks	Acceptable: 50 Optimal: 2000
N° annulus contours	Acceptable: 100 Optimal: 2000
N° segmented LV	Acceptable: 50 Optimal: 2000
N° segmented LVOT	Acceptable: 50 Optimal: 2000
N° centerlines	Acceptable: 100 Optimal: 2000
N° segmented PAs	Acceptable: 50 Optimal: 2000
Development of tools for automatic calculation of functional information	Acceptable: Semi-automatic extraction of at least the following parameters in 50 cases: • Left ventricular volume • Valve opening area • Different diameters for aorta, AV and PA • Strain • Wall thickness for aorta and PA • Calcifications around the AV • Ejection fraction • regurgitation Optimal: Automatic extraction of above parameters

6.3	
left ventricular pressure information for all anatomies	Acceptable: only peak-systolic and peak-diastolic pressure information available Optimal: transient pressure wave form for the whole cardiac cycle is available
aortic pressure information for all anatomies	Acceptable: only peak-systolic and peak-diastolic pressure information available Optimal: transient pressure wave form for the whole cardiac cycle is available
volume flow rate for all anatomies	Acceptable: only peak-systolic volume flow rate is available Optimal: transient volume flow rate over the whole cardiac cycle is available
volume flow rate in main pulmonary artery for all anatomies	Acceptable: only peak-systolic volume flow rate is available Optimal: transient volume flow rate over the whole cardiac cycle is available
volume flow split in left and right pulmonary artery for all anatomies	Acceptable: only the flow split in percent during peak-systole is available Optimal: transient information on the flow split for the whole cardiac cycle is available
vessel displacement from systole to diastole for all anatomies	Acceptable: only averaged information on the displacement in the main, left and right pulmonary artery are available Optimal: a spatially resolved displacement field for the whole pulmonary artery is available.
6.4	
• N° PA of pigs (real cohort)	Acceptable: 30 Optimal: 40
• N° PA of pigs (augmented cohort)	Acceptable: >100 Optimal: 1000

• N° PA of humans (real cohort)	Acceptable: 150 Optimal: 250
• N° PA of humans (augmented cohort)	Acceptable: >500 Optimal: 2000
• N° PA of humans (paediatric cohort)	Acceptable: >50 Optimal: 100
• N° AV of humans (real CHA cohort)	Acceptable: >50 Optimal: 100
• N° AV of humans (real UCL cohort)	Acceptable: >150 Optimal: 250
• N° AV of humans (augmented CHA cohort)	Acceptable: 700 Optimal: 1000
• N° AV of humans (augmented UCL cohort)	Acceptable: 700 Optimal: 1000
• Requirement for remeshing, quality of numerical meshes	Acceptable: manifold meshes, that require remeshing for high and low fidelity device (effect) models Optimal: manifold meshes that can be used for high and low fidelity device (effect) models without remeshing
• % of synthetic data sets to be removed due to non-physiologic anatomy and/or function	Acceptable: 15 % Optimal: 5 %

Means of assessment

Please include here the specific means for performing the self-assessment, per task and KPI

Task	KPI	Means of verification
Task 6.1		
Task 6.2	All N°	Count of data uploaded to the VRE
	Tool development	Applicable tool for generation of desired parameters with an error rate below 10%

Task6.3	All	Qualitative evaluation whether spatially or temporally resolved modelling is feasible or only values for relevant regions and cycle phases can be provided.
Task 6.4	All N°	Count of data uploaded to the VRE
	Mesh quality	Mesh analysis reports by respective solvers
	Non-physiologic exclusion	Counting exclusion throughout the synthetic generation procedure

Schedule of the self-assessment

Task	Self-assessment schedule
Task 6.1	M4
Task 6.2	M6; M9; M12
Task 6.3	M12; M24
Task 6.4	M24; M30

WP7: Virtual cohort generation and validation	WP Leader:
Tasks: T7.1: Definition of model output T7.2: Selection of model templates T7.3: Selection of data templates T7.4: Generation of virtual patient population T7.5: Three-level validation of virtual patient population T7.6: Use of the virtual cohorts for prediction of clinical trial related parameters	TUE

Key performance indicators (KPIs)

TASK	KPI (quantitative and qualitative indicators can be included - quantitative KPIs are preferable)
T7.1: Definition of model output	1. Minimum and maximum values for outputs that will be used for virtual patient selection are defined on **high-level model simulations** (e.g. WSS). 2. Minimum and maximum values for all geometrical and functional outputs that will be used for virtual patient selection are defined based on **clinical data**. This is done in WP5 and 6, which means that data sharing is of key importance. 3. Minimum and maximum values for all geometrical and functional outputs that will be used for virtual patient selection are defined based on **literature**. 4. Patient-groups and their corresponding outputs are stratified based on **demographic data.** This is done in WP5 and 6, which means that data sharing is of key importance. 5. Correlations and/or dependencies of outputs that are hidden in the clinical data but not (yet) captured by our physiology-based models, are defined. This is done in WP5 and 6, which means that data sharing is of key importance.
T7.2: Selection of model templates	1. An overview of available models within the consortium is composed. 2. Different surrogate modelling approaches are evaluated for our cohort generator, for example Kriging, Vectorial Kernelized Orthogonal Greedy Algorithms, Genetic-aggregate models, reduced-order models, reduced-basis models and/or physics-informed neural networks. 3. The optimal surrogate model for virtual cohort generation is determined. 4. The optimal surrogate model is developed in close collaboration with WP8 and WP9.
T7.3: Selection of data templates	1. Sensitivity analyses are conducted on high- and low-fidelity models to assess the most relevant model outputs. 2. How uncertainties in the inputs will affect the uncertainty in

	model calculations is quantified. 3. Minimum and maximum values of relevant model inputs based on **clinical data**, either directly or via inverse analysis, are derived. This is done in WP5 and 6, which means that data sharing is of key importance. 4. The minimum and maximum values for model inputs based on **literature** are derived in WP5 and WP6. 5. Stratification of patient-groups based on **demographic data** has been done. This is done in WP5 and 6, which means that data sharing is of key importance. 6. Possible correlations and/or dependencies between inputs that are hidden in the clinical data but not (yet) captured by our physiology-based models, are defined. This is done in WP5 and 6, which means that data sharing is of key importance.
T7.4: Generation of virtual patient population	1. A virtual cohort generator is developed that is based on an arbitrary model but that already includes the key steps: 1. Input sampling, 2. Model simulations, 3. Virtual patient selection and 4. Quantitative statistical description of the virtual cohort generated. 2. A virtual cohort generator for aortic valve stenosis (AVS) patients is developed and used to generate virtual patients that are like real patients in a sense that they have comparable statistical, demographic, geometrical and physiological behaviour. 3. A virtual cohort generator for heart failure (HF) patients is developed and used to generate virtual patients that are like real patients in a sense that they have comparable statistical, demographic, geometrical and physiological behaviour.
T7.5: Three-level validation of virtual patient population	1. A high-fidelity model that is validated on patient-specific level. 2. A surrogate model that approximates the high-fidelity model, and is validated on patient-level, is developed. 3. Virtual cohorts of AVS and HF patients are validated on the patient cohorts they were based on. 4. Virtual cohorts of AVS and HF patients are validated on independent and different patient cohorts with similar patient characteristics as the original one (e.g., the same patient group).
T7.6: Use of the virtual cohorts for prediction of clinical trial related parameters	1. The virtual cohorts are used to derive clinical trial-related parameters such as sample size, outcome criteria, inclusion, and exclusion criteria for the real patient population. 2. A vast collaboration is established between at least ECRIN and TUE for the mapping of engineering metrics to clinical outcomes such as morbidities etc.

Targets

A = Acceptable, O = Optimal

KPI	Target
KPI1-1	A = High-fidelity simulations for at least 10 patients/subgroup O = High-fidelity simulations for all patients/subgroup
KPI1-2	A: Data is based on at least 80% of the clinical data/subgroup and the ranges are shared with TUE
KPI1-3	O: Based on all data/subgroup and the ranges are shared with TUE
KPI1-4	A: Literature data only used to complement sparse data O: See acceptable
KPI1-5	A: The amount of data is insufficient to allow for stratification within AS or HF groups and we only distinguish between HF and AS patients. O: Stratification is done within groups based on for example age, gender, co-morbidities etc. A: No statistical correlations are found O: As much as possible
KPI2-1	A: Overview constraint to TAVI and PAPS CFD models O: Overview also includes FSI models
KPI2-2	A: One surrogate model already fulfilled the requirements which makes further evaluation less important O: At least 4 possible approach are benchmarked against each other
KPI2-3	A: The surrogate model only works for scalar outputs O: The surrogate model can deal with both scaler and velocity fields.
KPI2-4	A: The surrogate model is based on pre-interventional simulations O: The surrogate model is based on both pre- and post-interventional simulations
KP3-1	A: SA on high-fidelity models is limited to less accurate but computationally cheaper approaches O: SA is done by state-of-the art and highly accurate methods
KPI3-2	A: UQ on high-fidelity models is limited to less accurate but computationally cheaper approaches O: UQ is done by state-of-the art and highly accurate methods
KPI3-3	A: We use the a priori input space provided and shared by CHA and UCL (WP5 and 6) O: The input space is re-defined more accurately by using the results of the SA and UQ analyses.
KPI3-4	A: The amount of data is insufficient to allow for stratification within AVS or HF groups and we only distinguish between HF and AVS patients. A: Literature data only used to complement sparse data O: See acceptable

KPI3-5 KPI3-6	A: Stratification of patient-groups based on demographic data has been done. O: Stratification is done within groups based on for example age, gender, co-morbidities etc. A: No statistical correlations are found O: As much as possible
KPI4-1 KPI4-2 KPI4-3	A: A simplistic "dummy" model is implemented in the VRE to demonstrate the different step O: A first order approximation model for at least one of our application is implemented in the VRE A: The virtual cohort generator for AS patients only runs locally and has not yet been implemented in VRE O: The virtual cohort generator for AS patients works and is implemented in the VRE A: The virtual cohort generator for PAPS only runs locally and has not yet been implemented in VRE O: The virtual cohort generator for PAPS works and is implemented in the VRE
KPI5-1 KPI5-2 KPI5-3 KPI5-4	A: This is done for a limited number of patients (e.g. 5 patients/subgroup) O: This is done for all patients/subgroup A: This is done for a limited number of patients (e.g. 5 patients/subgroup) O: This is done for all patients/subgroup A: This is done for at least one of the resulting input space distributions of the virtual cohort O: This is done for the complete input distribution that results from the virtual cohort generator A: This is done for at least one of the resulting input distributions of the virtual cohort O: This is done for all input distribution that results from the virtual cohort generator
KPI6-1 KPI6-2	A: This is done without an accurate mapping of engineering metrics to clinical outcomes O: This is done after defining the mapping between engineering metrics and clinical outcomes A: Interactive discussions are limited to mail contact and WG meetings O: Additional meetings are setup

Means of assessment

Task	KPI	Means of verification
T7.1: Definition of	KPI1-1	WG Meeting WP7 – D7.1 – Use in VCG

model output	KPI1-2 KPI1-3 KPI1-4 KPI1-5	WG Meeting WP7 – D7.1 – Use in VCG WG Meeting WP7 – D7.1 – Use in VCG WG Meeting WP7 – D7.1 – Use in VCG WG Meeting WP7 – Use in VCG
T7.2: Selection of model templates	KPI2-1 KPI2-2 KPI2-3 KPI2-4	WG Meeting WP7 – D7.2 WG Meeting WP7 – D7.2 WG Meeting WP7 – SA – UQ Patient-level validation – Peer-reviewed scientific publication
T7.3: Selection of data templates	KP3-1 KPI3-2 KPI3-3 KPI3-4 KPI3-5 KPI3-6	WG Meeting WP7 – D7.3 – Peer-reviewed scientific publication WG Meeting WP7 – D7.4/D7.5 Done in WP5+6 – Updated after SA Done in WP5+6– Updated after SA Done in WP5+6– Updated after SA Done in WP5+6– Updated after SA
T7.4: Generation of virtual patient population	KPI4-1 KPI4-2 KPI4-3	WP Meeting WP7 – Embedding in VRE WP Meeting WP7 – Compare statistics WP Meeting WP7 – Compare statistics
T7.5: Three-level validation of virtual patient population	KPI5-1 KPI5-2 KPI5-3 KPI5-4	Patient-level validation + Peer-reviewed scientific publication Patient-level validation + Peer-reviewed scientific publication Comparison of cohorts' statistics + Peer-reviewed scientific publication Comparison of cohorts' statistics + Peer-reviewed scientific publication
T7.6: Use of the virtual cohorts for prediction of clinical trial related parameters	KPI6-1 KPI6-2	WG Meeting WP7 + Peer-reviewed scientific publication WG Meeting WP7 + Repeated discussion sections

Schedule of the self-assessment

Task	Self-assessment schedule
T7.1: Definition of model output	M6 – M24 – M36
T7.2: Selection of model templates	M12 – M24 – M36
T7.3: Selection of data templates	M15 – M18 – M24 -M36

T7.4: Generation of virtual patient population	M24 – M36
T7.5: Three-level validation of virtual patient population	M24 – M36
T7.6: Use of the virtual cohorts for prediction of clinical trial related parameters	M36

WP8: Virtual Device Implantation

WP Leader: PHI

Tasks:

T8.1 : Device model enhancement. Leader: BIO. Contributors.: IIB

T8.2: Simplified vessel model design. Leader: TUG. Contributors: BIO, IIB, PHI

T8.3: Validation of simplified vessel models. Leader: TUG. Contrib.: BIO, IIB, PHI

T8.4: Fast device deployment modelling. Leader: CHA. Contributors.: BIO, PHI, TUE

T8.5: 3D FE implant simulation. Leader: PHI. Contributors: CHA, BIO, IIB, TUG

T8.6: Model order reduction. Leader: PHI. Contributors: CHA, TUE, TUG

T8.7 : Isogeometric analysis. Leader: TUE. Contributors: PHI

Key performance indicators (KPIs)

Please indicate for each task one or more KPIs:

TASK	KPI (quantitative and qualitative indicators can be included - quantitative KPIs are preferable)
T8.1	Model ready
T8.2	Constitutive tissue model developed
T8.3	Validation performed
T8.4	Device deployment as good as FEM results
T8.5	Simulation performed
T8.6	Reduced order model able to capture the device behaviour
T8.7	Isogeometric model defined and used to compute device deployment

Targets

Please associate to each KPI relevant (measurable) targets (acceptable and optimal - with acceptable indicating the threshold under which the activity cannot be considered properly completed):

KPI	Target
Model ready	Acceptable: constitutive model parameters defined and qualitative validation against experimental test performed Optimal: constitutive model parameters defined and quantitative validation against experimental test performed
Constitutive tissue model developed	Acceptable: constitutive model parameters defined based on literature

	Optimal: constitutive model parameters defined and quantitative validation against experimental test performed
Validation performed	Acceptable: validation with 80% accuracy Optimal: validation with 95% accuracy
Device deployment as good as FEM results	Acceptable: qualitative behaviour captured Optimal: quantitative behaviour captured
Simulation performed	Acceptable: qualitative behaviour pre-post implant captured Optimal: quantitative behaviour pre-post implant captured
Reduced order model able to capture the device behaviour	Acceptable: simple algorithm able to describe the outcome of device implantation Optimal: simple and fast algorithm able to describe the outcome of device implantation
Isogeometric model defined and used to compute device deployment	Acceptable: qualitative behaviour pre-post implant captured Optimal: quantitative behaviour pre-post implant captured

Means of assessment

Please include here the specific means for performing the self-assessment, per task and KPI:

Task	KPI	Means of verification
T8.1	Model ready	Comparison with experimental data
T8.2	Constitutive tissue model developed	Comparison with literature data
T8.3	Validation performed	Comparison with experimental data
T8.4	Device deployment as good as FEM results	Comparison with FEM results
T8.5	Simulation performed	Comparison with segmentation results and hemodynamic data
T8.6	Reduced order model able to capture the device behaviour	Comparison with FEM results
T8.7	Isogeometric model defined and used to compute device deployment	Comparison with FEM results and with segmentation results and hemodynamic data

Schedule of the self-assessment

Task	Self-assessment schedule
T8.1	M18-M36
T8.2	M18-M36
T8.3	M18-M36
T8.4	M18-M36
T8.5	M18-M36
T8.6	M18-M36
T8.7	M18-M36

WP9: Device effect simulation

WP Leader: BIO

Tasks:

T9.1: Enhanced constitutive vessel model

T9.2: Device-specific effect models

T9.3: Low-fidelity validation of modelling tools

T9.4: Device effect simulation for assessing mechanisms of device failure and design optimization

T9.5: High-fidelity validation of device simulations

T9.6: Formulation of best practices for device approval

Key performance indicators (KPIs)

Please indicate for each task one or more KPIs:

TASK	KPI (quantitative and qualitative indicators can be included - quantitative KPIs are preferable)
T9.1: Enhanced constitutive vessel model	Availability of a constitutive vessel model ready for use within ANSYS **toolchain**
T9.2: Device-specific effect models	Model for TAVI to simulate the clinical endpoints Model for PAPS to simulate the clinical endpoints
T9.3: Low-fidelity validation of modelling tools	Bench tests performed and models validated (PAPS and TAVI) For PAPS acute animal tests performed and models validated
T9.4: Device effect simulation for assessing mechanisms of device failure and design optimization	Simulation regarding clinical endpoints performed with generic and patient specific vessels and virtual cohorts
T9.5: High-fidelity validation of device simulations	Chronic animal experiment performed, and high-fidelity validation done for PAPS Retrospective clinical trials data analysed and high-fidelity validation done for TAVI
T9.6: Formulation of best practices for device approval	White paper available for best practices for device approval for PAPS and TAVI

Targets

Please associate to each KPI relevant (measurable) targets (acceptable and optimal - with acceptable indicating the threshold under which the activity cannot be considered properly completed):

KPI	Target
Availability of a constitutive vessel model ready for use within ANSYS	Acceptable: Integrated constitutive model parameterised for humans of Aorta and PA

toolchain	Optimal: Integrated constitutive model parameterised for humans, ovine and porcine models with time-dependent reaction to implant
Model for TAVI to simulate the clinical endpoints	Acceptable: SM & CFD use case implemented in commercial SW package for simulation of thrombosis, paravalvular leakage and durability. Optimal: SM, CFD and FSI use case implemented in commercial SW package for simulation of thrombosis, paravalvular leakage and durability.
Model for PAPS to simulate the clinical endpoints	Acceptable: SM & CFD Model implemented in commercial SW package for simulation of thrombosis, device migration and vessel perforation. Optimal: SM, CFD Model implemented in commercial SW package for simulation of thrombosis, device migration and vessel perforation, deployment and endothelialisation
Bench tests performed and models validated (PAPS and TAVI)	Acceptable: models for all 3 endpoints successfully validated by at least one bench test per endpoint. Deviation between simulation and experiment below 50%. Optimal: models for all 3 endpoints successfully validated by more than one bench test per endpoint. Deviation between simulation and experiment below 20%.
For PAPS acute animal tests performed and models validated	Acceptable: models for all 3 endpoints successfully validated by at least one preclinical experiment / indicator per endpoint. Deviation between simulation and experiment below 50%. Optimal: models for all 3 endpoints successfully validated by more than one preclinical experiment / indicator per endpoint. Deviation between simulation and experiment below 20%.
Simulation regarding clinical endpoints performed with generic and patient specific vessels and virtual cohorts (PAPS)	Acceptable: Simulations for all 3 endpoints performed with 3 different generic, 10 different patient specific vessels and 20 samples from synthetic data each for 3 different species. Optimal: Simulations for all 3 endpoints performed with 5 different generic, 20 different patient specific vessels and 50 samples from synthetic data each for 3 different species.
Simulation regarding clinical endpoints performed with generic and patient specific vessels and virtual cohorts (TAVI)	Acceptable: Simulations for all 3 endpoints performed with standardized geometry and 5 different generic vessels geometry. Optimal: Simulations for all 3 endpoints performed with 5 patient specific vessels.
Chronic animal experiment performed and high fidelity validation done for PAPS	Acceptable: Model prediction of clinical endpoints does not deviate from experimental data by more than 20% Optimal: No statistical difference between model prediction

	and experimental data for each clinical endpoint
Retrospective clinical trials data analysed and high-fidelity validation done for TAVI	Acceptable: Model prediction of clinical endpoints reflects the trend of clinical studies Optimal: No statistical difference between model prediction and experimental data for each clinical endpoint
White paper available for best practices for device approval for PPS and TAVI	Acceptable: Main steps for device approval are described Optimal: All steps for device approval are described

Means of assessment

Please include here the specific means for performing the self-assessment, per task and KPI

Task	KPI	Means of verification
T9.1: Enhanced constitutive vessel model	Availability of a constitutive vessel model ready for use within ANSYS toolchain	Model is implemented and usable
T9.2: Device-specific effect models	Model for TAVI to simulate the clinical endpoints. Model for PAPS to simulate the clinical endpoints.	Models implemented and ready to simulate device behaviour regarding clinical endpoints
T9.3: Low-fidelity validation of modelling tools	Bench tests performed and models validated (PAPS and TAVI). For PAPS acute animal tests performed and models validated.	Match between models and experiments demonstrated.
T9.4: Device effect simulation for assessing mechanisms of device failure and design optimization	Simulation regarding clinical endpoints performed with generic and patient specific vessels and virtual cohorts	Simulation results are available and can be used for low- and high-fidelity validation.
T9.5: High-fidelity validation of device simulations	Chronic animal experiment performed, and high-fidelity validation done for PAPS. Retrospective clinical trials data analysed, and high-fidelity validation done for TAVI.	Statistical data analysis available.

T9.6: Formulation of best practices for device approval	White paper available for best practices for device approval for PPS and TAVI	White paper can be used as input for T4.6

Schedule of the self-assessment

Task	Self-assessment schedule
T9.1: Enhanced constitutive vessel model	M12, M18
T9.2: Device-specific effect models	M18, M24
T9.3: Low-fidelity validation of modelling tools	M18, M24
T9.4: Device effect simulation for assessing mechanisms of device failure and design optimization	M30, M36
T9.5: High-fidelity validation of device simulations	M30, M36
T9.6: Formulation of best practices for device approval	M30, M36

WP10: Quantification of healthcare, industry and socioeconomic effects

WP Leader: IHS

Tasks:

T10.1: In-silico trial impact assessment framework development

T10.2: Application of the in-silico trial impact assessment framework

T10.3: Development of a conceptual framework for the analysis of socio-economic effects

T10.4: Assessing impact on the biomedical device industry and the market

T10.5: Assessing the socio-economic impact

Key performance indicators (KPIs)

Please indicate for each task one or more KPIs:

TASK	KPI (quantitative and qualitative indicators can be included - quantitative KPIs are preferable)
T10.1: In-silico trial impact assessment framework development (ECRIN, M13-M24)	Development of a conceptual framework to model effects of computer simulation for medical device testing on clinical trial planning
T10.2: Application of the in-silico trial impact assessment framework (ECRIN, M24-M30)	Assessment of the clinical impact of in-silico trials and estimate benefits allowed by in-silico device testing technologies along several outcome dimensions
T10.3: Development of a conceptual framework for the analysis of socio-economic effects (IHS, M1-M20)	Development of a conceptual framework for the quantitative assessment of socioeconomic effects
T10.4: Assessing impact on the biomedical device industry and the market (IHS, M25-M36)	Assessment of the impact of in-silico technologies on the healthcare system, the medical device industry and the market
T10.5: Assessing the socio-economic impact (IHS, M15-M36)	

Targets

Please associate to each KPI relevant (measurable) targets (acceptable and optimal - with acceptable indicating the threshold under which the activity cannot be considered properly completed):

KPI	Target
T10.1	Acceptable: Framework available and validated Optimal: n/a
10.2	Acceptable: Assessment performed and benefits identified

	Optimal: n/a
10.3	Acceptable: Framework developed and validated Optimal: n/a
T10.4	Acceptable: Assessment completed
T10.5	Optimal: n/a

Means of assessment

Please include here the specific means for performing the self-assessment, per task and KPI

Task	KPI	Means of verification
T10.1	T10.1	Partners consensus / consortium validation / validation by external stakeholders if available
10.2	10.2	Partners consensus / consortium validation / validation by external stakeholders if available
10.3	10.3	Partners consensus / consortium validation / validation by external stakeholders if available
T10.4	T10.4	Partners consensus / consortium validation / validation by external stakeholders if available
T10.5	T10.5	Partners consensus / consortium validation / validation by external stakeholders if available

Schedule of the self-assessment

Task	Self-assessment schedule
T10.1	M12
T10.2	M36
T10.3	M20
T10.4	M36
T10.5	M36