Each participant was given a yellow and a green star to place next to the challenge they felt would have the greatest impact and could be implemented at the earliest time.

	Devices Research Challenges	Yellow = Greatest Impact Green = Earliest Delivery
1	Develop, as part of pre-competitive industrial collaborations, an *in silico* assessment framework for each family of devices, which investigates all relevant failure modes for that device. Allow for research groups to extend the framework with refined/alternative predictors for the various failure modes.	
2	Retrospective assessment: to build confidence in the methods, a well-defined *in silico* assessment framework for each family of devices, which investigates all relevant failure modes for that device, should be tested retrospectively on a number of designs for which the clinical outcome is well known. These should include both successful and unsuccessful devices; no device-specific tuning should be allowed.	
3	Create digital marketplaces for the accumulation and usage of large-scale repositories for anatomical and/or organ & tissue physical property information relevant to the design of selected medical devices. Focus on the exploration of business models that favour the participation and the long-term sustainability after the termination of public funding.	
4	Develop "anatomical fitting" tools fully integrated with widely used industrial design tools (such as 3D CAD software) that automate the process of fitting a new design into hundreds or thousands of digital anatomies, and automatically analyse the anatomical fitting, highlighting cases where the design poses some anatomical fitting issues.	
5	Statistical atlases can be used to generate artificial digital patients, when data relative to real patients are not available for whatever reason. It is necessary to demonstrate for selected anatomies, and for specific features relevant for classes of devices, if and when such artificial digital patients can be used as replacement of real digital patients, generated from the data of an existing individual.	
6	Develop *in silico* analysis frameworks that model a new medical device, its deployment, simulate the implantation over large collections of digital patients, and provide an *in silico* risk assessment for various failure modes relevant for that device.	
7	Develop an audit trail process where for a set of new devices submitted for Pre-Marketing Authorisation, both the *in silico* and the experimental evaluation are conducted in parallel, so as to confirm (using double blind design) that the conclusions based on *in silico* predictions are the same as those based on experimental data.	
8	Develop "replay" technologies that allow to the designer to fully automatically re-run, whole *in silico* assessment workflows once minor modifications are made to the device design.	
9	Provide information visualisation technologies that allow a rapid comparison of the expected clinical performance for each design variation, and support the decision and the reporting. Use additional information available that only *in silico* models can provide to refine your design decision.	
10	Develop specific interactive visualisation technologies that facilitate communication with non-technical members of the design team, such as clinical specialists, or regulators.	
11	Develop *in silico* models to falsify mechanistic theories that would explain clinically observed failure modes, with the underlying engineering failure modes.	

12	Collect data and develop *in silico* models to account for the "physiological envelope", the range of life-style and environmental conditions relevant for a class of medical devices, under which such medical devices must operate when implanted in a given population.	
13	Design validation studies to confirm that the procedural variability observed using surgical simulators is comparable, for the same device type, to that achieved in reality by comparably trained surgeons.	
14	Develop *in silico* outcome models capable of predicting the long-term outcomes that a device-related adverse effect may cause over selected populations.	
15	Development and validation of *in silico* models to improve outcomes reproducibility in clinical trials, or simplify the trials by surrogate outcomes which are with less challenging to obtain.	
16	Development and validation of *in silico* models to provide patient-specific surrogate metrics for late outcomes, so as to reduce the duration of clinical trials. This should include investigating the implication in terms of statistical power of adverse rare clinical events and of relevant inclusion/exclusion criteria.	
17	Replication of clinical trials of new medical devices with *in silico* clinical trials, so as to demonstrate that each patient and the *in silico* digital version individualised on the data of that patient present comparable outcomes/complications.	
18	*In silico* clinical trials of new medical devices capable of predicting functional or other complex outcomes from proxy measurements on the patient.	

	Pharma Research Challenges	
1	What makes in silico simulation findings trustable and their consequence/interpretation capable for helping a new medicine to be put on the market? Define and agree a minimum set of standards and criteria to build confidence in models reliability and work more closely with FDA.	
2	Create a framework to share knowledge, collection, curation, assessment of strength of evidence and library of models.	
3	Define models that scales and extrapolates in vivo and in vitro data to clinical findings.	
4	Based on the successful show case of type1 diabetes model, generalize the model to type2 diabetes or other multi-factorial diseases. This requires: - multilevel and multi-organ mechanistic models (we have some but we need more) - multi-scale in terms of time (i.e. For diabetes: both response to a meal and disease progression) - prediction of clinical outcome	
5	Develop multi-level models to merge image based data with intracellular data, blood samples, other biomarkers that are used in the clinic for individualized therapy	
6	Using the model to inform decision making in the value chain (Conceptual/ experimental /mathematical)	
7	Knowing who to work with. Identify the stakeholders (actors, regulators, patients) we wish to involve and how to cross-fertilize between different industries and sectors for having the most comprehensive case studies.	
8	M&S driven/directed R&D compared with standard approach/paediatric-rare disease-focus	
9	Confirmation of clinical outcome from retrospective studies using M&S – Could M&S have given you the answer?	
10	How to create an entity that can represent the community (CaSym, Avicenna, System Pharmacology)?	

Socio-Economic Research Challenges

1	The definition of a validation and certification framework for *in silico* models and providers is a precompetitive requirement.	
2	Research into study of IPR legislative framework on the nature of modelling and biomedical research industries.	
3	Call for study on regulatory issues which could prompt a transformation/regeneration of the biomedical industries to implement/promote *in silico*. Eg by making *in silico* models acceptable in place of animal models.	
4	Policy & governance framework for access to the data, storage, processing and infrastructure needed for *in silico* modelling & simulation.	
5	What are the societal consequences of a patient using an *in silico* simulation to make informed decisions about their treatment and lifestyle?	
6	Can *in silico* be a significant opportunity for CRO 2.0s? And could such CROs be a driver for changing the biomedical sector?	
7	European pre-competitive high performance and grid/cloud computing infrastructure for data storage, modelling and simulation for *in silico* – making "*in silico* as a Service" open to all.	
8	Patent durations could be shortened to act as a driver to use cheaper clinical trial systems (leading to greater use of *in silico* simulation).	
9	In what measure can *in silico* derived stratification of patients reduce short term and long term as well as direct and indirect welfare costs?	
10	What is the economic potential of sharing in silico knowledge for defining different healthcare systems.	
11	How can we make the type of testing used in development and testing of a biomedical product be made transparent? «in silico as a socially responsible brand.