Public update on the In Silico World project

September 2023

"In Silico World: Lowering barriers to ubiquitous adoption of In Silico Trials" (hereinafter ISW) is a collaborative project funded by the European Commission (EC) in the frame of the Horizon 2020 programme. The In Silico World project aims at accelerating the uptake of modelling and simulation technologies used for the development and regulatory assessment of medicines and medical devices by lowering seven identified barriers: development, validation, accreditation, optimisation, exploitation, information, and training. The project started in January 2021, and in this time, we accumulated many individuals and institutions following our work with interest as they see its potential to impact the future of In Silico Trials. This brief note is for all of them to provide an update on the project and its more interesting achievements.

In ISW, we are further developing eleven in silico trial solutions for the development of drugs, medical devices, or Advanced Therapeutic Medicinal Products (ATMPs) targeting different medical specialities, such as orthopaedics, cardiology, neurology and oncology. This development activity will finish in December 2023, and we can already see that all solutions advanced significantly in their Technology Readiness Level during these three years of work. BBCT-Hip, UISS-TB, InSole and UISS-MS, the most mature solutions at the start of the project, are or will soon be available through commercial partners as pre-regulatory tools. For all the others, their developers are defining a clear regulatory and exploitation strategy that will be pursued after the project ends.

We are working to produce seven publicly available validation data collections. Three are already available on Zenodo: HipValid, StentValid and TBValid. We are running a bit late for the others, so the related work package will likely need an extension. However, we expect all planned collections to be ready before June 2024.

The project underwent an in-depth analysis of the ethical and legal aspects of in silico trials. In June 2023, we published a second report summarising the main legal challenges surrounding in silico EU trials. The report is available on Zenodo. There, we summarised how data protection barriers impact data sharing healthcare, the standardization shortcomings in the regulatory system for medical devices and medical technologies, and the future challenges that artificial intelligence regulation could entail for scientific research.

A considerable effort has been spent exploring the regulatory barriers and finding ways to lower them. We completed a first Qualification Advice with EMA for BBCT-Hip, and plan to complete the second for UISS-TB before the end of 2023. The "Towards Good Simulation Practice" consensus report has now been finalised, and we expect it to be published by Nature-Springer as an open-access book in early 2024. Thanks to our activities, the IEC-ISO has started a new workgroup to develop a technical standard on the credibility assessment of predictive models to develop medical products, consistent with the ASME VV-40:2018, but that will allow the harmonisation of the EU regulatory system for medical devices and medical technologies. The colleagues from the Avicenna Alliance will sit in this workgroup as representatives of our Community of Practice. But these are just a few highlights of the intense activity we have done in this area, as documented also by the numerous publications[1].

In the first half of 2024, we plan to produce a public report detailing and discussing this work so that any other practitioner can capitalise on our experience.

We aim to boost the outreach of In Silico World's outcomes and to conduct collective, anticipatory governance of in silico trial technologies, referred to as Responsible Research & Innovation (RRI). On the communication side, most of the work done has been dedicated to the creation of regular branded content for our website, blog, social media channels and newsletter, ensuring a smooth journey for our audience. We produced more than 180 communication activities including papers, conferences, scientific events, workshops, and press releases. Part of the effort consists of the production of tailored content for social media, where we published over 700 communication items (including various cross-dissemination activities with other EU-funded projects). The strategy adopted within the communication activities identifies those project outputs that are particularly

[1] https://doi.org/10.1002/psp4.12669; https://doi.org/10.1007/s10439-022-03078-w; https://doi.org/10.1109/jbhi.2022.3198145; https://doi.org/10.1109/jbhi.2021.3090469

suitable for the outreach towards key stakeholders as well as relevant external events and media that can be used to further enhance the project's dissemination. Those activities mainly targeted researchers and academics, the industry field, but also patients and the general public. All the project's outputs are listed in a dedicated section on the In Silico World website and made available on the ISW Zenodo repository. The communication teams organised the 2nd In Silico World General Assembly, a 2-day event that included an RRI Workshop and the Consortium Meeting. We conducted many internal activities to involve and engage other partners, such as interviews with WP leaders and researchers who are working on the project; these activities will allow the communication team to produce even more varied content.

As for the engagement with stakeholder communities, we organised 3 focus groups around Europe (Belgium, Italy, Hungary) to monitor the perception of in silico trials among senior management of medical industries, clinicians, and policy experts, and to promote citizens and patients' trust in i*n silico* technologies. We provided an analysis of the data collection during the focus groups and held an RRI Workshop among our experts on governance solutions for the barriers to in silico medicine. It saw the participation of consortium experts in technological research, clinical research, and industrial innovation in the field of in silico trials from six European countries, all cooperating to reach a common goal: accelerating the adoption of in silico trials. The main aim of the RRI workshop was to provide an opportunity for the consortium members to discuss the possible ethical, legal, and societal barriers throughout the innovation process and to reflect on existing and potential governance solutions. This workshop was also a good occasion to reflect on the connection between society and research, allowing the consortium members to better grasp the current understanding of different stakeholders. This aligns with the final objective of this workshop, the Policy Brief, which will be enriched by the broad range of perspectives gathered throughout the different research steps done so far.

We also started the Associate Partner Programme, open to universities, research hospitals, biomedical companies, software vendors, contract research organisations, notified bodies and regulatory agencies, etc. The goal is to maximise the impact of our work on the Community of Practice that is developing around in silico medicine. Associate partners will be informed in real-time of our latest achievements and will be able to request preferential access to specific project outputs.

An important task in the project is to educate the future workforce in this innovative domain. This refers to educating new graduate students and retraining employees who are already active in the field of innovation in clinical care, pharmaceutics, or medical devices. We have identified the learning needs of several stakeholder categories, such as engineering and medical students, or professionals active in relevant fields either with a medical, engineering or even legal background. Learning material is now being developed with a focus on offering it in an on-site way. Test material will be evaluated first in small groups of course takers, and then expanded to more elaborated courses towards the end of the project.

Specific activities have been dedicated to exploring exploitation opportunities for the computational results obtained within ISW, to defining viable business models (such as internal R&D tools, consultancy services, software-as-a-service, on-premises software…), and plan of the post-project commercialization through the marketplace InSilicoTrials.com. In the past two years, periodic monitoring was established for each solution, together with the developer partners, to track progress and collect valuable information regarding the product area of application, envisioned context-of-use, expected target users and market sector, and intellectual property management. This analysis produced a "List of viable business models" at the end of 2022 and will finally be collected in a detailed "Exploitation Plan" at the end of 2023. The circulation of these outputs is confidential, but associate partners could ask for preferential access to them.

Following market opportunities, a first exploitation contract between ISW partners was signed leading to the integration of UISS-MS solution as web-based software-as-a-service on https://insilicotrials.com/mstreatsim/. Similarly, a second contract has been signed that will lead to the integration of BBCT-Hip as a commercial cloud-based product by early 2024. All other ISW solutions are expected to be accessible, directly, or indirectly, from the InSilicoTrials.com marketplace by the end of 2024.