

Avicenna Alliance & VPHi - FP9 Recommendations: Making medicine modern

I. Introduction

FP9 is set to launch in 2021. Its ambition should be worthy of the digital era. Today we cling to 20th century concepts of healthcare while 21st century *in silico* solutions stand ready to be deployed for the benefit of patients, clinicians, industries and regulators.

As a member of the Avicenna Alliance and a supporter of the uptake of the *in silico* approach, the Virtual Physiological Human Institute has presented ground-breaking research in the past years. Researchers have completed numerous EU-supported studies on societal issues showing the many benefits of personalised medicine.

The Avicenna Alliance believes that as we enter 2021 with a new framework programme set to end in 2030 we should do nothing short of fundamentally dismantle the traditional way in which healthcare operates and make the EU the centre of *in silico* fuelled change.

The Avicenna Alliance aims to help create a world where there is a fundamental reduction in uncertainty regarding patient response and the outcome of treatment using personalised predictions. The uptake of advanced simulations will fundamentally redefine what it means for a health technology or drug to be considered “safe”.

The Alliance wants to map out a future where reimbursement authorities look back on the waste of taxpayer money on treatments that did not perform adequately and are weeded out by *in silico* approaches that give value to only the most effective treatment solutions.

With *in silico* modelling and simulation technologies offering an understanding of complexity on a scale never before known in human history, the concept of *the right treatment for the right patient at the right time* no longer becomes an aspiration, it becomes standard practice.

Members of the Avicenna Alliance ecosystem have the know-how to build this futuristic bridge from big data to personalised medicine. FP9 can provide the means.

II. Making *in silico* approaches the rule not the exception

The Commission has expressed its ambitions for a Digital Europe and has set high ambitions for what that should mean. No matter which direction we wish to advance in, no matter what goals we set – they will all depend on the key tenet of the digital era – that we have the technology to make a quantum leap in understanding and integrating data.

Demanding more from applicants to FP9 and expecting them to embrace complexity in a way that only *in silico* approaches can allow will raise the standard of applications. Doing so can give rise to entirely new subdivisions of technological pursuits.

Computer modelling and simulation (CM&S *in silico* approaches) should be viewed as an enabling technology that can support not just existing sciences but has the capacity to create entirely new sciences.

- *It is the recommendation of the Avicenna Alliance that the European Commission raise its expectations and demands on applicants, by calling for in silico approaches to form an integral part of proposals throughout FP9 proposals.*

III. Reviewing the reviewers

Not just the way in which we look at medicine should change, our approach to research should do so as well. The European Commission has repeatedly stressed the need for multidisciplinary approaches. This request however, has not come with the corresponding provision of multidisciplinary committees to support the review of such proposals.

Research is constantly reinvented and committees reviewing research proposals should evolve as well. Selection committees have done important work in the past years and to be able to continue selecting research proposals with the greatest value for society, review committees should embrace a multidisciplinary mix. Multidisciplinary committees and more expertise in assessing a broader range of applications are necessary to ensure that important research opportunities are not missed. At the same time, the composition of committees should be regularly reviewed to ensure that they continue to match developments within the research field.

In order to ensure the core Commission tenet of excellence in science remaining a theme in Horizon Europe, an evaluation of reviewers should also be developed. This would ensure accuracy in the execution of reviews and formulation of the judgements, as well as discourage accepting review assignments without having appropriate qualifications. In this scheme, a team of highly experienced evaluators would review randomly a small percentage of project evaluations. This procedure would not necessarily affect the outcome, unless there are really macroscopic issues that might justify a redress action under Article 263, but might be a mechanism for excluding, at least temporarily, insufficiently accurate evaluators from being asked again to do this job for the EC. We believe that even a very small percentage (2%) of second level evaluations could already substantially enhance the quality and accuracy of a large number of evaluations.

- *Avicenna recommends that committees that review FP9 proposals embrace multidisciplinary to effectively assess a broader range of proposals and suggests to develop a mechanism for reviewer evaluation.*

IV. Providing the tools to effectively implement recent legislation and policies;

The medical devices regulation will come into effect in 2020. An often overlooked section of this is Article 4.5.4. “Pre-clinical evaluation assessment” which provides:

“The notified body shall examine, validate and verify that the manufacturer's procedures and documentation adequately address... the planning, conduct, assessment, reporting and, where appropriate, updating of the pre-clinical evaluation, in particular of... the pre-clinical testing, for example laboratory testing, **simulated use testing, computer modelling**, the use of animal models...”

This is the first instance in which computer modelling and simulated testing has formed part of the regulatory framework in medical devices legislation.

In order to reach the point where computer modelling and simulation can be relied on by regulators however, standards need to be created and a body of evidence collected to support them.

- *Avicenna recommends that calls for proposals be developed that encourage the development of CM&S solutions specifically geared towards the clinical evidence expectations of regulators in both medical devices and medicinal products.*

V. Enabling Personalised Medicine – not just talking about it

The Commission, Parliament and Council have all supported personalised medicine approaches and have declared their desire to capitalise on the potential of Big Data. Computer modelling and simulation is the bridge between these two political goals, turning raw data into actionable information that is usable by patients, doctors, industries and researchers.

Personalised medicine will not be possible without understanding complexity on a scale that only computer modelling can provide. Big data will remain an untapped resource without the processing tools needed to make sense of it and implement this promising technique. There is a need for an integrative strategy promoting the development of a range of digital technologies including machine learning. We need to stop talking about what personalised medicine can do and start talking about how we are going to do it.

- *Avicenna recommends that specific calls be dedicated to the creation of models that can help create tailored treatments and adapt existing treatments towards individual patients.*

VI. New solutions to an old issue

Our ageing society has been on the top of the political priority list for some time. While eHealth solutions for outpatient care show great promise and should be pursued, few solutions have even been put forward to address the issue of multimorbidities.

The interaction of multiple drugs prescribed for multiple conditions in the same body is a level of complexity not properly accounted for in current healthcare models. The link between ageing animal models, the benchmark of ageing studies, and actual ageing people can be improved. As current models are no longer fit for purpose, the Commission should call upon the *in silico* community to develop new ones.

- *in silico tools for our ageing society should form a stand-alone FET programme*