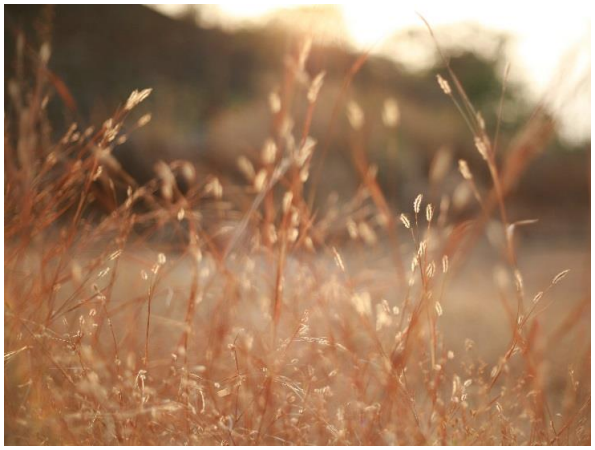
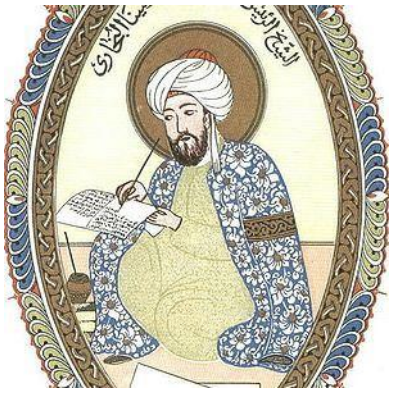
An Interview with Marco Viceconti – Director of INSIGNEO



How do you find a needle in a haystack? A tiny target buried in a jumbled mass. Luck? Persistence? One approach would be to work systematically through the pile. Start at one end and analyse every blade of dried grass. Check its colour, feel, texture, to see whether its appearance and characteristics match the object for which you are searching. It would take a while, but eventually you would find what you were looking for.

Now imagine you are being charged for this process. The more time spent looking, the more thorough your search, the greater the cost incurred. Imagine now that upon finding the needle, you discover it is broken. Or blunt. Or the eye is too narrow to be of any use. Your search has not only been timely and costly, but ultimately wasted.

In silico clinical trials (ISCTs) are a new way of approaching the clinical trial process. They allow the researcher to disrupt the systematic process – a process which has remain unchanged since the time of Avicenna – with *in silico* technologies, to target more quickly and cheaply the best option. Instead of starting at phase one and working through, potentially to find that the trial fails three quarters of the way into the process, ISCTs allows users to immediately explore multiple assumptions and funnel down to the most likely scenario. A quicker, cheaper and more effective way to target what they were looking for.



Picture of Avicenna
Courtesy of Wellcome Library, London

Avicenna (Abū ʻAlī al-Ḥusayn ibn ʻAbd Allāh ibn Sīnā') was a Persian physician and philosopher (980-1037), who first gave a formal structure to the process of evaluating the effect of a treatment on a disease in his most famous work, the Canon of Medicine (al-Qānūn fī al-Ṭibb). He introduced systemic experimentation and quantification of the study of physiology and the introduction of experimental medicine, clinical trials, randomised controlled trials and efficacy tests. The fundamental nature of clinical trials has changed surprisingly little since Avicenna's time. The beginning of the 21st century, however, saw the birth of *in silico* medicine, a completely new way to investigate living organisms and the diagnosis, treatment, or prevention of a disease through modelling, simulation and visualisation of biological and medical processes using computers simulations. It is based on the use of Virtual Physiological Human (VPH) models, which aim to integrate physiological processes across different length and time scales (multi-scale modelling) to provide improved predictive and individualised healthcare.

We asked Professor Marco Viceconti – the Director of the INSIGNEO Institute for in silico *medicine to tell us more about ISCTs and their benefits.*

Currently, clinical trials, the studies that are routinely conducted to establish the safety and efficacy of new medical interventions , medical treatments, drugs and devices takes place *in vitro* – in a test system, and/or *in vivo* – in living organisms, either animal models or patients; both methods are costly. The former is often quite distanced from reality, and the latter puts both animals and humans at risk. The term *in silico* medicine indicates the use of computer modelling and simulation in the design of new biomedical products, and in the assessment of their safety, accuracy and efficacy. ISCTs will reduce the costs of development and assessment; reduce the time to market; reduce, refine and partially replace animal experimentation; in the case of trial failure, ISCTs will provide explanatory evidence that can be used to correct the product and bring it to market.

Can you give us an example of a successful use of ISCTs?

In 2007, *in silico* studies done by Entelos, a leader in predictive biosimulation for pharmaceutical R&D, predicted that Rituximab would be superior to anti-TNF in preventing bone erosion in patients with severe disease. This recommendation was later confirmed by clinical research. In 2010 NICE issued guidelines recommending that rituximab, adalimumab, etanercept, infliximab and (in certain circumstances) abatacept, be used as possible treatments for rheumatoid arthritis after treatment with a tumour necrosis factor (TNF) inhibitor has failed. Rituximab (MabThera) in combination with methotrexate, was also recommended as an option for the treatment of adults with severe active rheumatoid arthritis that has responded inadequately to other disease-modifying anti-rheumatic drugs (DMARDs), including treatment with at least one TNF inhibitor, or those who are intolerant of other DMARDs.

The 2007 *in silico* modelling predated the NICE guidelines by three years. The Entelos biosimulations showed that rituximab induces sustained benefits in joint structure, even after joint inflammation returns. The success of Entelos' *in silico* predictions suggests broad application in more efficient drug development and wide implications for the future of clinical trials.

What is the background to the Avicenna Support Action?

The European Commission (EC) is broadening its investment in *in silico* medicine by funding the development of a 'roadmap' describing the route by which *in silico* techniques of computer simulation will be introduced into clinical trials. This roadmap initiative Avicenna: A strategy for *in silico* Clinical Trials, began in October 2013 and will run till September 2015. Avicenna is designed to cultivate consensus amongst a broad range of stakeholders who will come together to agree a research and technological development strategy.

Why is it important to bring stakeholders together through Avicenna process?

Avicenna has two goals. The first is the compilation of a research roadmap, which hopefully will inform future calls for proposals in European H2020 framework, but also national funding for research. We need industrial stakeholders on board to ensure that such research roadmap is driven the real industrial needs. The second goal is the formation of a Community of Practice that involves all stakeholders that collaborate pre-competitively to ensure that a correct perception of computer modelling and simulation among corporate managers, regulators, etc.

Who can benefit from being involved in the Avicenna process?

The different stakeholders have diverse viewpoints and motivations, but they all have crucial contributions to make to the Avicenna process and roadmap:

Biomedical industry experts will be able to get what they need to improve the rate of innovation, the time to market, and cost to market. They can influence the research and technological development agenda at the European level toward the needs of a vital industrial sector.

Biomedical researchers can complement their wet-bench methods; manage the complexity and reduce and refine animal experimentation.

Clinical trials experts will be able to obtain better estimates of safety and efficacy from pre-clinical assessment; obtain outcome indicators earlier and more cheaply and reduce risk profile for patients.

Regulatory experts will be able to support a better rate of innovation with lower risk; ensure regulatory aspects are central in the development of *in silico* clinical trials methods and technologies.

Patient representatives can find better and faster innovation, more personalised products, better treatments for rare diseases and lower risk in clinical trials.

Healthcare providers can develop more products, better products and cheaper products and have better evidence of efficacy and safety.

Virtual Product Development experts will be able to find a new, fast-growth, high-return market for VPD products and services.

Avicenna is calling out to all these stakeholders and representatives from MedTech industries. By collaborating in the discussion, we can ensure that ISCTs are driven by real industrial needs, reducing the time to market and cost of development, making the lengthy trial process that little bit more straightforward.

Our next Event

Avicenna's fifth and final event is to be held in Barcelona, Spain on the 4th and 5th June 2015. If you are interested in attending this or other events, please contact Martina Contin: manager@vph-institute.org

For further information on Avicenna, please go to http://www.avicenna-isct.org/ or to join our alliance please contact Martina Contin: manager@vph-institute.org