Part 1: Introductory Remarks

1.1 The significance of facilitating open access to research in Regulatory Science

Brian O'Neill, Director of Research and Enterprise, Dean of Graduate Research School, TU Dublin

It is a real pleasure to be associated with this monograph based on the TU Dublin seminar on 4 April 2019 *An Audience with Regulators, Academia and Industry* organised by the School of Chemical and Pharmaceutical Sciences, the Health Products Regulatory Authority and Regulatory Science Ireland. TU Dublin highly values its associations with the pharmaceutical sector in general and with the emerging field of Regulatory Science in particular. We are proud to be involved in the dialogue evident in this monograph among global thought-leaders, practitioners and researchers in this important field.

As you know, TU Dublin is a new nomenclature and a new legal entity as a university building on its long traditions of teaching and research in the city. We are now the largest higher education institution in the state with *circa* 29,000 students and continuing our collaborations with industry, the labour market and civic society.

In TU Dublin we take pride in the research and scholarship being undertaken by our staff and postgraduate students in the areas of Pharmaceutical Regulatory Science which is at the forefront of our mission as a forward-thinking, progressive new university on both national and global landscapes.

The topics in this monograph around innovations in regulation of health products manufacturing and the benefits of science to society could not be closer to what we as a university are committed to continue doing i.e. fostering and supporting dialogue, making research knowledge available, and actively dissemination knowledge to the wider society so that members of the public can become involved in decision-making that affects their lives.

Because the key economic sector in Ireland – pharmaceutical, financial services and ICTs – are vital to our future, our eyes are constantly on global industry and on the important decision-making that informs it. We as a university very much want to be part of facilitated discussions towards decision-making. This is very much my understanding of the context for the work that is presented in this monograph, the second in the series.

On my own behalf, and on behalf of President David FitzPatrick, I sincerely support and commend this worthy publication.

1.2 The importance of research into QRM and KM for patient safety

John Lynch, Director of Compliance, HPRA

This monograph contains important contributions to knowledge for the regulatory science sector, for regulators themselves, for industry, and for academia. Following on from the seminar in October 2018 and the first monograph published thereafter, we are delighted that a second monograph has resulted from the second seminar of April 2019. We are also delighted that TU Dublin has brought together some of the world's thought-leaders to discuss the real value that can be delivered by practicing effective quality risk management, not just as a compliance requirement, or as an aid to business, but most importantly as a means to reduce risk to patients, both human and animal, from the biopharmaceutical products the industry produces.

Regarding quality risk management, it is heavily used by regulators and industry alike. As a regulator, we use it in a wide range of areas: in our planning and conduct of GXP inspections, in marketing, and in assessment strategies around applications to place medicines on the market. We also use it in decision-making around quality defects and recalls, in the design of surveillance programmes, in pharmacovigilance work, and in a variety of other areas.

Now I will make a rare admission of fallibility: *we are still learning to apply QRM principles and tools really well!* QRM is now widely embedded in the GMPs of the EU and other regions and industry has certainly embraced it. Fifteen years ago we would rarely come across formal risk assessment on inspection. Some practices might not have been very good and may have had a pre-determined outcome from the risk assessment exercise, but not in all cases. Nowadays, risk assessments are very widely applied and are of far better quality. That said, there is still some way to go to ensure that our work is paying dividends for patients, both human and animal.

That brings me to the second theme of this monograph: knowledge management. I think it is reasonable to say that collectively we are not so advanced in the area of formal knowledge management. Hence it is an area in which we all have a keen interest.

Speaking about knowledge management and quality risk management, the integration of QRM and KM in management systems in an organisation is a key factor in enabling effective QRM in order that decision-makers have access to the right information when and where they need it. Indeed, it is a welcome sign that a large part of this monograph is about knowledge management.

So, this monograph righty focuses on the roles both QRM and KM can play in ensuring medicinal product safety for patients in the twenty-first century, which is in line with the vision of ICH Q10.

1.3 Introduction to Regulatory Science Ireland (RSI)

Frank Hallinan, Founder-Owner Quality Systems Support

Regulatory Science Ireland (RSI) is an initiative that Technological University Dublin (TU Dublin), University College Cork (UCC) and a number of state bodies have been involved in for a number of years now. We established RSI in 2012 to a large extent based on the initiative of the US Food and Drugs Agency (FDA) in this area. So, let me start by explaining a little about what Regulatory Science actually is. The US FDA was the first organisation to use this term. They defined it as "*the science of developing new tools, standards and approaches to assess the safety, quality and performance of drug products*." So, to us it is about taking the methodology for approving drug products and looking at it in an objective, data-driven way in terms of the way it is being done, as opposed to simply continuing to do it as it has been done in the past. The EMA came up with a reasonably similar definition and has developed a strategic plan in this area. So, this is a real, live topic in the field of regulation of medicines at this particular point in time. Therefore, when we set up RSI we felt it was important that we would have an initiative in this area in Ireland.

The reason for Regulatory Science as a concept at this point in time is perhaps because the FDA pointed out in 2011 that the challenges of product development and globalisation underscore the critical importance of modernising and advancing regulatory science to match the advances in basic and applied science and technology.

So, the sciences generally are moving forward very quickly, and therefore the sciences concerned with regulation need to move forward in parallel with that. The then FDA Commissioner, Dr Scott Gottlieb commented in 2017 on the occasion of FDA approval of the first gene therapy product Luxturna in the US that there were more than six-hundred INDs related to gene therapy products with the Agency at that particular time, and that it is estimated by experts in MIT that about forty of these proposed products might have won approval by 2022 from a current list of 932 pipeline candidates, with 45% of these products related to treatments for cancer.

Based on this level of activity it seems likely that the world of biopharmaceuticals is changing quite radically even as we speak at this symposium.

Consequently, we need to ensure that the regulatory paradigm and regulatory approach keep up to date with current and possible future changes. In that regard, the type of work and research contained in this monograph from TU Dublin is a very good example of the activities that need to be done both to up-skill people and to transfer knowledge into Ireland Inc. so that we continue to be at the forefront in this area.

Regulatory Science has evolved since the concept was first put forward in 2010 by the FDA for the purpose of advancing science for public health. The 2011 document from the FDA built on the original concept.

The EMA 2012 document and the Roadmap to Regulatory Science currently under discussion are pan-European examples of the concept.