RSNN annual workshop 2023 report: Highway to innovation

On 6 June 2023 the Regulatory Science Network Netherlands (RSNN) organised its Annual Workshop on the topic of “Pharmaceutical regulation - Highway to innovation”. As one of the speakers of the workshop Tony Humphreys (European Medicines Agency, EMA) mentioned: the revision of the pharmaceutical legislation is “a once in a generation legislation revision”. And with the revision just being published on 26 April 2023 RSNN brought together various stakeholder groups to discuss their views on the role of innovation in the legislative revision.

The workshop was introduced by the chair of the day Marjon Pasmooij (Dutch Medicines Evaluation Board, co-chair RSNN) who introduced the legislative revision in terms of its key goals and the legislative process. Key goals were summarized in terms of triple A: *access, availability and affordability*, and later *agility* was added during the panel discussion led by Sjaak Bot (Janssen, co-chair RSNN) in regard to fast responsiveness and expedited pathways. Tony Humphreys also explained the triple C: *competitive regulatory framework, compliance with environmental sustainability and combat AMR*.

After the introduction, Jarno Hoekman (Utrecht University) introduced three ways to better understand the role of innovation in various provisions of the legislative revision. He argued that most attention has been given so far to proposed changes to the *regulation of therapeutic innovation,* such as the incentives for therapeutic innovation provided through data exclusivity as well as changes to marketing authorisation requirements to make sure that therapeutic innovations that reach the market are safe, effective, of high quality and sustainable. However, the legislative revision also proposes changes to *regulation through innovation*, for instance by fostering the development and implementation of novel regulatory sciences, such as the use of new approach methodologies for pre-clinical safety assessment, real-world data in the context of clinical development and digital innovations such as the electronic product information. Moreover, the legislative revision focuses on *regulatory innovation* defined as novel functions, structures, organizational processes in regulatory systems that change the performance of the system, with the introduction of sandbox approaches being a prime example.

In his presentation, Jarno Hoekman argued that adopting a broad view on the role of innovation in regulation makes clear that all stakeholders in the regulatory system have a role to play in innovation processes. Moreover, he firmly positions the legislative revision in the broader regulatory and innovation ecosystem raising questions about dependencies, complexities and implementation capacities. This view was echoed during the day for instance when Paul Korte (Janssen) discussed the important role of financing and business models in relation to the goals of the legislative revision to create a competitive Dutch and European innovation ecosystem; during discussions that emphasized the critical dependencies between the revised pharmaceutical legislation and the Health Technology Assessment (HTA) regulation. Aimad Torqui (Dutch Medicines Evaluation Board) also discussed the capacities of regulatory agencies and other stakeholders in the system to implement legislative provisions.

What followed were several presentations from the perspective of stakeholders on the revised legislation. The overall tone of these presentations was that regulation can be a powerful stimulus to innovation and that regulation matters at all stages of the innovation process. There was a general impression that the legislative revision is ambitious in this regard, with Tony Humphreys mentioning that about 60-70% of the text of the existing EU regulation has been revised. Proposed changes reflect this, for example with changing provisions on market exclusivity, extended scientific advice, marketing authorisation times and methods, antimicrobial resistance (AMR) voucher, and the regulatory sandbox development support. Given the myriad of changes and uncertainties about their effects it was not surprising to see that every stakeholder had specific expectations about the implementation of the regulation in line with their interests and perspectives. During the presentations, these expectations and interests were shared which resulted in lively discussions, particularly at the end of the workshop. Three topics that stood out in this regard were discussions on regulatory pathways and marketing authorisation decisions, the definition of unmet medical need (UMN) and standards for drug repurposing. These are discussed below.

REGULATORY PATHWAYS AND DECISION-MAKING

Considerable attention was given to the introduction of new pathways in the legislative revision (e.g. priority medicines (PRIME) scheme is included in the proposed legislation, pathways for drug-device and drug-diagnostic combinations) as well as provisions to reconsider the EMA committee structure and reduce marketing authorisation assessment timelines. Sini Eskola (EFPIA) mentioned that many of these changes are welcomed by industry but also provided a number of caveats including the definition for PRIME eligibility and scientific advice for in-vitro diagnostics. In relation to these changes, Aimad Torqui

argued that we can not only look at laws and regulations but also have to look at the implementation of regulations including the capacity available to shorten for instance regulatory timelines. The importance of creating capacity in the broader system was also acknowledged. Elizabeth Macintyre (EHA) emphasized that medical specialists realise that regulatory affairs at European level impact their daily practice and the wellbeing of their patients. However, she also acknowledged that regulatory science is still relatively poorly understood by the medical community, creating a need for training. Regarding the restructuring of committees, patient representatives questioned whether this really helps to increase the patient voice to be heard, since there will be less representation of patients than in the current structure.

DEFINITION OF UNMET MEDICAL NEED

A second important point of discussion was the extent to which the definition of UMN in the legislative revision is clear and specific enough and what constitutes high unmet medical need. From an industry perspective, the definition of UMN is relatively narrow and the ultimate goal is that all medicines brought to market address unmet medical needs. Vivianna Giannuzzi (Fondazione per la Ricerca Farmacologica Gianni Benzi Onlus; APS Bottega del Sorriso patients association) argued that UMN is not defined well enough. There was an expectation among participants that in the process the definition will be further discussed and operationalized, as pointed out by Aimad Torqui. There was also a consensus that the patient community needs to become involved in these discussions including further impact assessment and definitions of endpoints.

PROVISIONS FOR DRUG REPURPOSING

Another point of considerable attention was the provisions that increase the possibility for not-for-profit entities to add an indication to the product label. The provision raises expectations for drug repurposing to cover UMN and was welcomed by patient organisations and other parties. Sini Eskola mentioned that it is important in this context to consider that standards for evidentiary requirements should be equal for market authorisation holders and other parties such as academic or non-profit developers. Sibren van den Berg (Medicijn voor de Maatschappij) discussed that for older products with a small market used for specific rare diseases, an obligation for marketing autorisation holders of the repurposed drug can give so much extra costs that the medicine will be withdrawn, reaching the opposite of what we want. He also added that the proposed 4 years of data exclusivity for repurposed drugs will likely not make the business case positive because generics would still be used for the repurposed indication. Both points underline that more

than just the regulatory framework needs to change in order for drug repurposing to be successful.

Throughout the discussions it became clear that it is important to note that the regulatory system has its limits in achieving policy objectives and should not be looked at in isolation. There are various complexities and interdependencies that should be considered besides laws and regulations. One is how effectively they will be implemented and enforced There is a financial system and an investment climate that drive innovation which have to be taken into account. There is also a reimbursement system that can either be supportive or create a hurdle for innovation depending on the stakeholder's perspective. So in the effects of regulation we have to consider synergies and trade-offs between legislative reforms and the broader regulatory, innovation and investment systems in which these changes are embedded. The workshop was concluded by Marjon Pasmooij who emphasized the importance of trying to actively deal with the uncertainties we are all presented with, whether through a lens of triple (or quadruple) A (*access*, *availability*, *affordability* or *agility*), triple C (*competitive regulatory framework*, *compliance with environmental sustainability* and *combat AMR*) or triple P that drive investments (*potential*, *protection*, *predictability*).