RSNN Regulatory Science Network Netherlands

"REGULATORY READINESS LEVELS" AS A TOOL TO DRIVE REGULATORY INNOVATION

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RSNN EXPERT MEETING JUNE 2021

"REGULATORY READINESS LEVELS" AS A TOOL TO DRIVE REGULATORY INNOVATION

In June 2021 the RSNN organised an expert meeting on 'Regulatory Readiness Levels as a tool to drive regulatory innovation'

Eighteen experts affiliated to academia, industry, and national and European government bodies discussed this topic.

The invited experts introduced a broad spectrum of knowledge and contributed on personal title

The ‘Regulatory Readiness’-problem

- A significant delay exists between the high pace of regulatory innovations and their implementation in the regulatory framework.
- Regulatory authorities have the complex task to ensure protection of public health while facilitating access to the best possible healthcare interventions in a timely and affordable manner.
- This necessitates an adaptive regulatory framework that is ‘ready’ to incorporate innovations in medicinal product development as well as the regulatory science methods to assess these products.
- Although national and international collaborations (e.g. IMI, Horizon 2020) yield prominent results, there is a perception that the current regulatory innovation ecosystem still follows innovation rather slowly.
- Quotes from the RSNN-EMA 2020 workshop:
  - “This ‘regulatory readiness’-problem hinders recognition and implementation of new technologies”
  - “Achieving innovation is not enough; innovations should be implemented for the society and economy to benefit”
  - “It is understood – regulation follows science, and it can be reasonably anticipated that this time lag will always exist. But how do we make it as short as possible?”

Novel medicinal products, technologies and require novel regulatory science methodologies

- New regulatory methodologies (e.g. methods, tools, and approaches) need to be based on **convincing evidence**

- Each of the stakeholders (i.e regulators, industry, academia, patients, funding bodies…) have **different perspectives** regarding medicine regulation.
  - While this sometimes result in a certain **degree of misunderstanding** and attrition……
  - **…. diversity** is key to progress and contribute to the optimal focus of the development process.

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Examples of innovations that require novel regulatory methodologies

Remote patient monitoring, cell and gene therapy, artificial intelligence, patient-derived organoids, **use of registry data**…..

Within this range of these examples, common considerations, actions and steps could be identified to **achieve regulatory endorsement** of methodology, including:

- Societal demand for regulatory innovation.
- Conceptualisation.
- Explorative research.
- Technical and clinical validation.
- Defining the regulatory requirements to prove benefit under acceptable risk.
- Review by authorities against regulatory requirements

Bottlenecks and potential solutions

- The examples have common bottlenecks:
  - First, **regulatory authorities** have the fundamental responsibility to **deal with uncertainties,** associated with implementation of novel regulatory methodology.
  - Second, the magnitude of science required to reach a level of **convincing data** meeting the regulatory requirements goes beyond the capabilities of **academic** groups. Early involvement of **industry and regulators** as partners is fundamental to align expectations and requirements.

- **Increased multi-disciplinary interaction and open dialogue** may help to overcome both challenges aid regulators to define the regulatory requirements, while developers will gain knowledge concerning the evidence necessary to comply to the governing requirements.

The Technology Readiness Levels (TRL)-system

- Outside the regulatory field, tools have been designed to assess the maturity of projects to guide them from the phase of **explorative research up to the level of implementation** into practice.
- The so-called **Technology Readiness Levels (TRL**)-system was developed by NASA during the 1970's to mature projects (aircrafts) from innovation to proven for implementation (flight qualified).
- The TRL system is a **stage-gated concept of maturity progression** based on risk reduction
- Since 2014, the European Commission has adopted this system as a tool for innovations in project management, progress planning, and resource allocation in the Horizon 2020 program
- Would it be possible to design a similar tool that accelerates maturation of new regulatory methodologies?

Level	Definition	Phase	Evidence	Risk
1	Basic Principles Observed	RESEARCH		
2	Technology concept formulated			
3	Experimental Proof of Concept			
4	Technology validated in lab	DEVELOPMENT		
5	Technology Validated in relevant environment			
6	Technology demonstrated in relevant environment			
7	System prototype demonstration in operational environment	DEPLOYMENT		
8	System complete and qualified			
9	System proven in operational environment			

The concept of a "*Regulatory* Readiness Level" system

- To assess readiness of **regulatory methodology**
- To facilitate multi-disciplinary interaction to **accelerate implementation**.
- The focus is not the medicinal products themselves, but the **regulatory methodology** evaluating the quality, benefits, and risks of medicinal products.
- The RRL-tool could **facilitate dialogue and transparency** within the regulatory ecosystem
- The RRL-system may help to establish the effect on society of **early adoption of specific methodology with increased uncertainty** in comparison with late endorsement and decreased risk.
- **Risk aversion** by means of later endorsement of regulatory methodology **may not always be beneficial** (e.g in cases where alternative treatment is missing).
- **Academia plays a leading role during the initial research-phase** while mainly **industry directs the deployment phase.**

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The Regulatory Readiness Levels-system A pilot?

Level	Definition	Phase	Evidence	Risk
1	Basic principles Observed	RESEARCH		
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- A pilot assessing a novel regulatory methodology **using the RRL-system** could be performed to bring the concept of RRL-system further. Key considerations for a **successful pilot**:
  - First, since societal demand plays a crucial role in driving innovations, maturity of a methodology applied in a field with **clear unmet medical** need is required.
  - Second, risk minimization is an important limiting factor for regulatory endorsement. Piloted methodology should be accompanied with **a minimal amount of uncertainty**.
  - Third, methodology should be chosen in a **pre-competitive space**. The added benefit for society when adopting the methodology earlier with increased risk, should be baknced against later adoption and decreased risk. **Could lives have been saved if earlier adopted?**
- **Research questions:**

- Which regulatory methodology and disease domain is suited for this pilot?
- Which level of readiness can be identified for this specific regulatory methodology?
- Which activities need to be performed to achieve regulatory endorsement?
- What is the effect on society of early adoption: higher risk versus later adoption?

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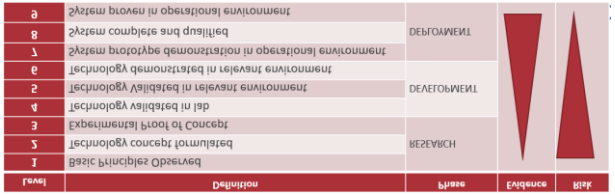
CONCLUSIONS



- The **high-speed developments** in the field of medicines are being pursued by **adaptations of the regulatory framework.**
- Bottlenecks that may delay the implementation of novel regulatory methodology include:
  - The challenging task of regulators to define regulatory requirements for **proven efficacy under acceptable risk for novel regulatory methodology**
  - **The magnitude of science** required to reach a level of convincing data meeting the regulatory requirements **necessitates a early collaborative effort of academia and industry.**
- The proposed RRL-system may facilitate **early multi-disciplinary interaction** and open dialogue may help to define the regulatory requirements and to communicate these to developers.

- **RSNN considers to propose to the participating experts to initiate a pilot assessing a novel regulatory methodology using the RRL-system to bring the concept of RRL-system further.**

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THANK YOU!

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