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HORIZON-HLTH-2022-TOOL-11-02 - New methods for the effective use of real-world data and/or synthetic data in regulatory decision-making and/or in health technology assessment

Expected Outcomes: *This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination 5 "Unlocking the full potential of new tools, technologies and digital solutions for a healthy society". To that end, proposals under this topic should aim for delivering results that are directed, tailored towards and contributing to all of the following expected outcomes:*

- Health regulatory bodies and/or *Health Technology Assessment (*HTA) bodies adopt optimised data-driven methodologies for the effective use of real-world data (including omics data)[1], and/or synthetic data derived from digital twins and advanced computational methods (such as modelling and simulation or approaches based on machine learning/AI), for the assessment of medicinal products and/or digital health innovations.
- Health regulatory authorities and bodies (e.g. medicines agencies, HTA bodies, notified bodies for medical devices) use optimised guidelines for the development and assessment of medicinal products and/or medical devices including digital health innovations.
- Health regulatory authorities and bodies across Europe are trained in data-driven decision making using emerging data types.

Scope: With the emerging use of real-world data (RWD), synthetic data by the pharmaceutical industry and medical devices industry, regulators and HTA bodies need to perform targeted validation of claims through independent analysis. The principal aim of this topic is to address the data needs of health regulatory bodies and HTA bodies across the EU, as outlined in the recently published "HMA-EMA Joint Big Data Taskforce Phase II report: 'Evolving Data-Driven Regulation'"[2] and its associated DARWIN (Data Analysis and Real World Interrogation Network) project[3].

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1 Real world data is an umbrella term for data regarding the effects of health interventions that are not collected in the context of highly-controlled RCTs. Instead, RWD can either be primary research data collected in a manner which reflects how interventions would be used in routine clinical practice or secondary research data derived from routinely collected data (https://www.ema.europa.eu/en/documents/presentation/presentation-session-1-use-real-world-data-pre-authorisation-what-can-it-answer-peter-mol_en.pdf)

2 https://www.ema.europa.eu/en/documents/other/hma-ema-joint-big-data-taskforce-phase-ii-report-evolving-data-driven-regulation_en.pdf

3 https://www.ema.europa.eu/en/documents/presentation/presentation-proposal-darwin-eu-data-analytics-real-world-interrogation-network-parlett-ema_en.pdf

To harness the potential of RWD and synthetic data from digital twins and advanced analytical models, and make them actionable for health regulatory decision-making and for health technology assessment, targeted research is needed on the evidentiary value of these data for a number of relevant use cases. In addition, methods need to be developed to increase the usability of such data by different stakeholder groups. Doing so will contribute to the European Health Data Space and maximise the positive impact of DARWIN in driving up the quality of evidence and decisions on the development and use of medicines and digital health innovations.

Access to and analysis of RWD and synthetic data can inform regulatory decision-making throughout the product lifecycle, namely: 1) support product development (e.g. scientific advice, PRIME[4]),); 2) support authorisation of new medicines and digital health innovations; and 3) monitor the performance of medicines and digital health innovations on the market (effectiveness and safety). Eventually, this will put in place methods and processes that will enable continuous learning from pre-authorisation procedures and authorisation applications on the use of RWD and/or synthetic data.

Proposals should address all of the following areas:

- Develop a set of evidentiary standards to be pre-specified and used in the analysis of real-word evidence and/or synthetic data applied to different types of regulatory advice and/or health technology assessment and decisions on the safety and efficacy/effectiveness of medicines and digital health innovations (e.g. in complement to clinical trial data in an authorisation application, or for extension of indications, post marketing surveillance, amendment of product information or regulatory actions on the marketing authorisation due to safety concerns). This includes validating the use of advanced analytical methods for regulatory decision-making and/or health technology assessment.

- Address aspects that would enable moving towards a standard data quality framework reproducible across different types of RWD and/or synthetic data sources for regulatory decision-making and/or health technology assessment, with a characterisation of the data collection, management and reporting and an empirical data quality validation. In this regard, it will be important that successful proposals liaise with and closely monitor the work carried out in the context of the European Health Data Space.

- Enhance the performance and efficiency of large randomised clinical trials and new models of clinical trials by developing standardised processes and methods to access RWD and/or synthetic data (e.g., facilitating the detection of various types of health outcomes during the treatment period of a double-blinded trial by linkage to appropriate electronic health care record databases, etc.), for regulatory decision-making and/or health technology assessment.

[4] https://www.ema.europa.eu/en/human-regulatory/research-development/prime-priority-medicines

- Define methodological standards for the regulatory acceptability of RWD, and/or synthetic data in the context of clinical trials augmented with RWD, and/or synthetic data, for regulatory decision making and/or health technology assessment.

- Test the ability of machine learning methods to help identify relevant RWD, and/or synthetic data to match with and to interpret clinical trials, for regulatory decision-making and/or health technology assessment.

- Assess and validate how machine learning methods can be systematically harnessed to screen a large amount of data, including unstructured data, in many electronic databases to identify factors affecting efficacy and safety of treatments and/or digital health innovations, for regulatory decision-making and/or health technology assessment. The cross-border interoperability dimension should be taken into account.

Proposals should involve researchers who are specialised in the use of real-world data and/or synthetic data to evaluate medicinal products and/or health care digital innovation products and services. Proposals should involve national competent authorities (national health care product regulatory bodies and/or medical device notified bodies) and could involve citizens and patients' representatives where relevant. Proposals should include capacity-building efforts to address inequalities of health regulatory processes across Europe. This should comprise education and training activities and sharing of best practices.

In addition to national competent authorities, proposals could consider the involvement of the European Medicines Agency (EMA) for an added value in order to provide an effective interface between the research activities and regulatory aspects and/or to translate the research results into validated test methods and strategies that would be fit for regulatory purposes.