European Federation of Pharmaceutical Industries and Associations

Pharmaceutical industry's experience and challenges with RWE submission in marketing authorisation applications






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Experience of RWE submissions in marketing authorisations - A Journey

- Generally, the use of real-world data/real-world evidence (RWD/RWE) is still an emerging field with limited systematic evaluation of experiences.
  - It contributes to medicines development (including the pre-approval phase), learning and regulatory decisions in virtually all phases and across different therapeutic areas and product characteristics.[2]
    - Approaches range from applying data analytics and predictive algorithms to convert RWD to RWE with simple descriptive and advanced techniques[3].
  - There is widespread use of RWD/RWE to support evaluation of marketing authorisation applications, extension of indications and adding new populations.[1-3]
    - For many such applications its use is complementary to clinical trials.
    - It particularly supports conditional marketing authorisations and approval of orphan medicines.[2]
  - It is also used widely, post authorisation, to address safety and effectiveness questions although it remains uncertain as to how and to what extent.[2, 3]

1. Flynn, R., Plueschke, K., Quinten, C., Strassmann, V., Duijnhoven, R.G., Gordillo-Marañon, M., Rueckbeil, M., Cohet, C. and Kurz, X. (2021), Marketing Authorization Applications Made to the European Medicines Agency in 2018–2019: What was the Contribution of Real-World Evidence?. Clin Pharmacol Ther. https://doi.org/10.1002/cpt.2461
2. Eskola, S.M., Leufkens, H.G.M., Bate, A., De Bruin, M.L. and Gardarsdottir, H. (2021), Use of Real-World Data and Evidence in Drug Development of Medicinal Products Centrally Authorized in Europe in 2018–2019. Clin Pharmacol Ther. https://doi.org/10.1002/cpt.2462
3. Varnai P, Davé A, Farla K, Nooijen A, Petrosova L. The Evidence REVEAL Study: Exploring the Use of Real-World Evidence and Complex Clinical Trial Design by the European Pharmaceutical Industry. Clin Pharmacol Ther. 2021 Nov;110(5):1180-1189. doi: 10.1002/cpt.2103. Epub 2020 Dec 17. PMID: 33216976.

Experience of RWE submissions in medicines development - A Journey

- Specifically for COVID,
  - In addition to RCTs, **RWE** is helping to provide important insights about **comparative effectiveness of COVID-19 vaccines and treatments.**
  - RWE can also advance our understanding of **COVID-19 high risk groups, temporal trends and effectiveness of vaccines against emerging variants.**
  - **Availability of high-quality data** from fully integrated data sources is critical to fully characterise real world safety and effectiveness and validate RWD used to assess safety and effectiveness.
  - **Data generation and collection are multidimensional and distributed across database owners** - it is critical that research designs, data, underlying data collection and processing platforms as well as review processes and methodologies are validated and robust.
  - **Collaboration is key** to ensuring compliant and secure access to datasets for the purposes of evaluation.

Challenges of RWE in medicines development

Advice procedures

- Potential delays in development decisions due to lack of integration of advice procedures

Guidelines

- Lack of predictability due to absence of a suite of RWE guidelines, standards and framework for submissions
- Lack of clarity relating to GDPR/privacy

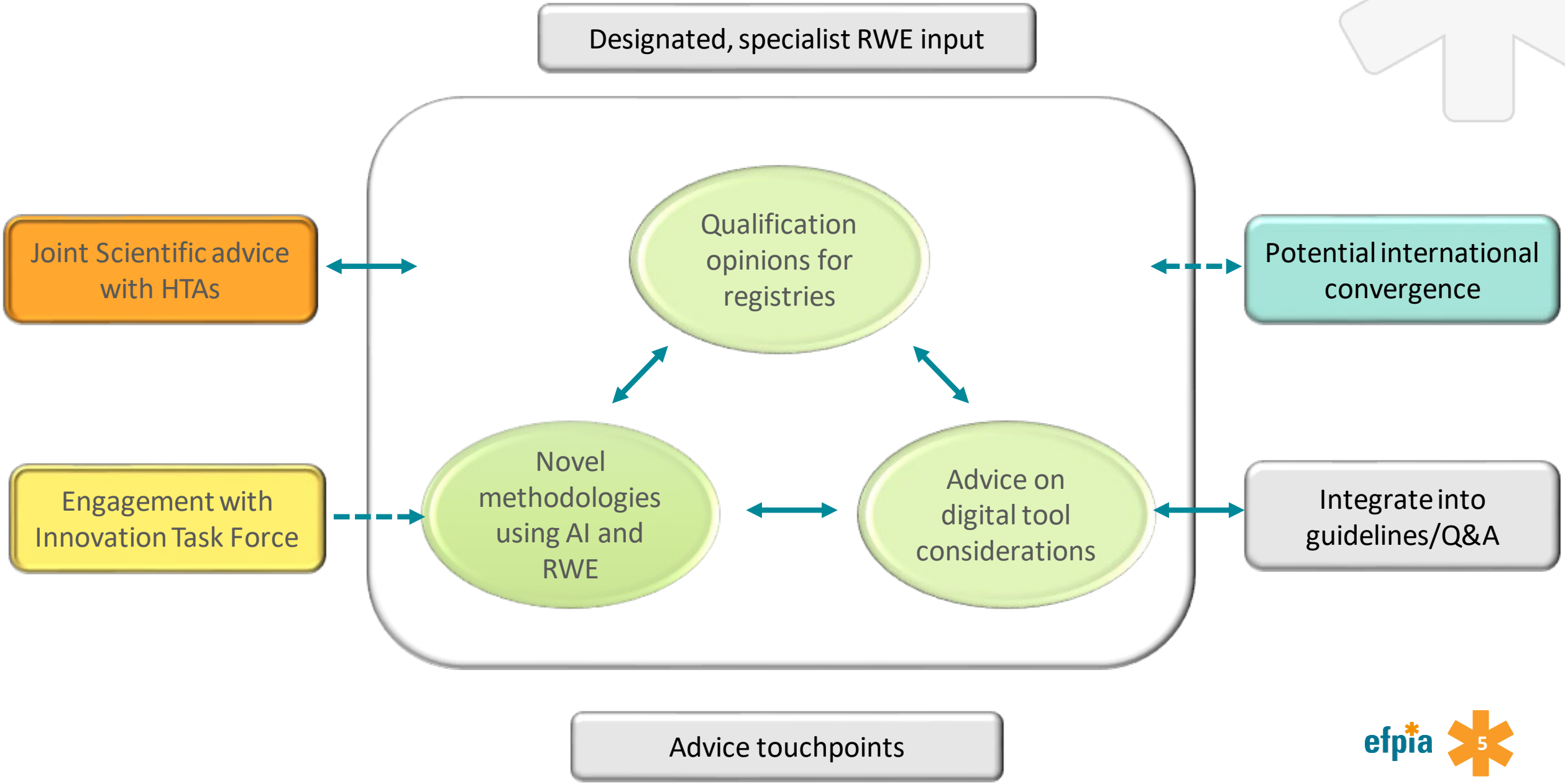
New technologies

- Clarity on regulatory framework for evaluating new technologies in clinical development

Transparency

- Limited transparency of RWE assessment within EPARS
- Potential lack of transparency regarding decisions based on evidence from DARWIN EU

An agile framework for advice procedures will promote delivery



General principles can be applied to the development of guidelines

Provide more predictability for submission elements and submission outcomes

Flexibility to allow for technological advances and complement existing guidelines

Focus on less well established use cases

Internal procedures reflect stakeholder perspective

GDPR/privacy clarity will ensure consistency for secondary research

ICH harmonisation for better health

Priorities for industry: Guidelines on data, analysis and submissions

- Data quality framework
- Guidance on submission of patient level data
  - Data standards: Format for submission of patient level data to regulatory authorities
  - Procedures for submission/validation of data, etc.
- Guidance on submissions that include RWE (design, choice of data source, etc)
- Principles/best practices associated with analytical methodology
- Optimised qualification procedure for registries

Priorities for industry: Transparency and new technologies

- Clarity on the required regulatory framework for evaluating new technologies in clinical development such as artificial intelligence

- Structured approach and greater transparency to addressing RWE in EPARs
- Procedural guidance associated with the use of DARWIN EU findings

The journey continues ...

- The delivery of an integrated approach for advice procedures, together with a range of guidelines and procedural transparency, will provide greater predictaibility to the outcome of RWE submissions.
- Optimising how RWE can be used, to support a wide range of regulatory decisions, requires the ongoing collboration of all those who are impacted by those decisions.
- The Industry welcomes continued collaboration and interactive learning opportunies with all stakeholders involved.