Appendix F: The industry perspective on the RWE journey

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Strategy

- Establish a cross-functional team to coordinate the development of yearly RWE strategic plans based on evidence gaps in healthcare as well as patient, medical, payer and regulatory needs

Planning

- Identify and prioritize relevant scientific questions and how they fit into a pre-defined publication plan to address most important internal and external needs. Bringing together interdisciplinary teams to define and sharpen the research questions that need to be unbiased, answerable, relevant, intriguing, pertinent, focused.

Execution

- Scientific function to execute study plans so as to ensure that both the study design and statistical analyses are scientifically sound. Create study synopsis which should include study design, data source (i.e. internal data vs. external research collaborations), methods and brief summary following the PICO(T) scheme. Study lead to establish study team with internal and external members. Ideally, to include external medical experts with a good understanding of RWE and observational studies. Follow internal and external transparency regulations, e.g. study registration to increase trust and acceptability while developing the protocol, statistical analysis plan and executing the study.

Communication

- Study lead to ensure study report and publication (based on publication plan) is in line with transparency regulations and uploaded in respective study registries. Scientific teams to support in creation of communication material by translating statistical results, ensure appropriate use and interpretation of results and limitations - (statistical challenges). Additionally, help to overcome non-statistical challenges (e.g. understanding the data source, legal and data privacy concerns, validity of data)

Archiving

- Recommendation to have proper content and knowledge management for the conducted RWE studies. It is very important that studies conducted in the past, and their corresponding results are findable and retrievable, so as to maximize the value derived from RWE research efforts. This creates a culture of content/knowledge capturing, sharing and seeking in RWE study planning and execution

Key stakeholder

- Material to be created around RWE can have various external customers, e.g. patient organizations, physicians, payers, regulators and HTA agencies but also internal customers, e.g. market access, medical affairs, commercial, corporate communication and IT which makes it necessary to have very individual channels around the use and communication of RWE

The industry perspective on RWE used in the product lifecycle

Preclinical Phase and onwards

- Disease Epidemiology, Patient numbers, sub-populations and phenotyping, unmet medical needs

Phase 1-3 studies and onwards

- Clinical trial protocol feasibility, modeling for feasibility (virtual trials), internal validity vs. generalizability
- Patient pathways and patient journey, from diagnosis to treatment, support labelling process
- Patient characteristics, treatment patterns, adherence and persistence of the population
- Burden of illness for patients and payers

Post launch and onwards

- Safety and effectiveness of the entire population as well as subgroups in the real world
- Signal detection, indication-seeking as well as label-expansion
- Payer segmentation for product
- Patient characteristics, treatment patterns, adherence/persistence,
- How will the medication be used

The industry perspective on RWE data sources

- Prospective data collection post launch (Pragmatic trials, phase IV studies, observational studies, non-interventional trials)
    - Self-sponsored, full access, data owned by industry
- Prospective data collection linked with available databases/registries (hybrid studies)
    - Academic partnerships, restricted access, data partially owned by industry
- Disease registries, clinical registries, national registries
    - Restricted access, data usually not owned by industry
- Administrative claims data, secondary data (database studies)
    - Direct access to licensable data sources or public RWD sources that have low or no cost associated, data not owned by industry
- Electronic health records, electronic medical records (database studies)
    - Direct access to licensable data sources, no access to others, data not owned by industry
- Patient-generated data
    - Direct access to aggregated data, data owned by patient
- Survey data (population survey), public and other licensable sources, data not owned by industry

Due to growth of RWD sources also metadata services, like B.R.I.D.G.E. TO DATA, is getting increasingly important due to the number and variability of data sources globally available. This variability makes it increasingly more challenging to gather information about existing data sources as well as have proper metadata for each.

The industry perspective on the near future of RWE

- New players will come to the market and existing players will grow in expertise
    - Google, IBM, Apple, raising startup-culture

- New capabilities will be generated, data scientists as a key contributor for technological progress on methods and new business models
    - Artificial intelligence solutions, deep learning methods
- New alliances/partnerships with full service data information to enhance evidence generation by e.g. developing industry-wide platforms for RWD and RWE sharing - considering that many of the companies are paying for the same datasets, the competitive advantage no longer lies chiefly in the access to the data sources, but rather in the RWE strategy and analytics capabilities, which make data sharing an important step towards increasing the efficiency and reducing R&D costs
- More and more mobile apps proliferation to capture outcomes
    - Important to have a validated standard and consistent approach to capture similar outcomes
- Use of automated rapid cycle analytics with existing data sources to increase efficiency of generating evidence
- New business models
    - Once data and methods are fit for purpose more and more new approaches, e.g. outcomes based pricing and pay-for-performance contracts will be seen
- New and much more as well as bigger datasets, including big data
    - Linked data sources such as administrative claims and E.H.R. producing richer source of RWD from patients health experience
    - Smart sensors, wearables, tracking tools, omics data, imaging, biobanks and social media will create a new dimension of data metrics
    - Next generation infrastructure to accommodate newer big data sources (e.g. image data, real time data capture)

All these points are influencing each other. Therefore collaborations are getting more and more important to ensure adequate, transparent and conscious use of data to generate valuable evidence.

The industry perspective on the vision for RWE

Raising the quality and interoperability of underlying data

- Increase quality of data by creating/enhancing incentives for “front line” of data capturing
- New models to create databases/datasets that are less burdensome and more useful for patients/providers/industry
- Use technological progress to generate new EHR systems and patient portals with standard outcome measures and standard capture of needed measures/biomarkers to generate outcomes
- Shift towards “outcomes focused” healthcare systems which allow RWD to improve efficiency and introduce new business models

Sustainable industry access to data

- New legal, ethical and governance frameworks to ensure responsible data access for industry
- New guidelines for “Big Data” – linkage from different sources
- National clinical research networks to facilitate clinical as well as RW research
- Adopt GCP to make pragmatic trials more feasible
- Business models encouraging alliances to access data via federated approaches

Promoting best practice in methods

- Multi-stakeholder approach to refine best practices for conducting and reporting RWE studies
- Take into consideration new methods and new players to analyze big data

Improving trust and acceptability of RWE

- Industry commitment for internal governance processes for working with RWD
- Industry commitment for full transparency and reproducibility of results of RWE studies submitted to regulators and HTA agencies
- Additional options for using RWE should be raised and dispassionately discussed during scientific consultation meetings
- Jointly develop guidelines (across regions and within EU) on acceptability of RWE in post launch activities, assessments of new indications, label updates and pro-active promotion

Critical questions for the industry

- Should RWE be established as a discipline of "medical affairs"?
    - The key to a successful implementation of a RWE landscape not related to where it is located in a company but rather the potential of a strong collaboration interface between a broad spectrum of key functions in the journey of RWE (e.g. Regulatory Affairs, Clinical Development, Medical Affairs, Epidemiology, Pharmacovigilance, HEOR, Market Access, Marketing Operations, Market Research, Therapeutic Areas, Statistics, IT). Important to ensure transparency and independence between scientific rigor (study execution) and strategic planning (Marketing).

- How does the industry make sure the scientific research question is in the focus?
    - Dedicated scientific RWE study teams will establish external research collaborations and will take care of high quality study execution. Disease experts should be involved to adequately design a study which answers the underlying question. This infrastructure should ideally be in place globally but also in regions and in local organizations

- Does more and broader data access for Big Pharma really help increasing trust in RWE?
    - Any research activity should ideally be conducted by the involvement of external experts, e.g. physicians, patient organizations, patients, academic institutes independent of whether data sources are either owned or not owned or licensed by the industry. A broader access to data sources will help in establishing best practices and enables methodological research in collaborations which again, yields into higher quality and transparency of RWE

- Is there a common understanding across the pharmaceutical industry on the terms "Real World Data", "Real World Evidence" and Big Data?
    - While there is a common understanding how RWD and RWE is defined, definitions, understanding and potential of Big Data vary broadly across the industry. It is also up

to collaborations like IMI to create a common understanding, not only within the industry

- Are there scientific questions the industry avoids to address?
    - While good planning on research and publication plans is essential for a trustful and transparent communication of RWE, there are still a lot of limitations around data sources, statistical methods and interpretation of results. These limitations are often the reason why specific questions cannot adequately be addressed.

References and further readings

ISPE-ISPOR Special Task Force on RWE in Healthcare Decision-making
https://www.ispor.org/RWEInHealthcareDecisions/JointISPEISPORSpecialTF

ISPE Guidelines for Good Pharmacoepidemiology Practices (GPP), 2015
https://www.pharmacoepi.org/resources/guidelines_08027.cfm

AHRQ: Agency for Healthcare Research and Quality, *Registries for Evaluating Patient Outcomes: A User's Guide*, April 2014. http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?productid=1897&pageaction=displayproductPASS guidance

AMS/ABPI: Real world evidence: Summary of a joint meeting held on 17 September 2015 by the Academy of Medical Sciences and the Association of the British Pharmaceutical Industry:
https://acmedsci.ac.uk/policy/policy-projects/real-world-data

COMET: http://www.comet-initiative.org

EMA Adaptive pathways pilots:
http://www.ema.europa.eu/docs/en_GB/document_library/Report/2016/08/WC500211526.pdf

EMA Big Data Taskforce:
http://www.ema.europa.eu/docs/en_GB/document_library/Other/2017/03/WC500224262.pdf

EMA / EUNetHTA cooperation

HTA bodies' reflection paper on collaboration with regulators:
https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20161110_co06_en.pdf

…and meeting minutes from their recent meeting which touches on registries and RWD and planning for RWE generation
http://www.ema.europa.eu/docs/en_GB/document_library/Minutes/2017/05/WC500227598.pdf

EMA and HTA Parallel Consultation:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001857.jsp&mid=WC0b01ac0580a11c96

EMA PAES guidance:
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2015/11/WC500196379.pdf

EMA Registries Initiative:
http://www.ema.europa.eu/docs/en_GB/document_library/Other/2017/05/WC500227793.pdf

EMA Scientific Consultation pilots:
http://www.ema.europa.eu/docs/en_GB/document_library/Report/2016/03/WC500203945.pdf

ENCePP: http://www.encepp.eu/index.shtml

EU Consultation on Health and Care in the Digital Single Market
http://europa.eu/rapid/press-release_IP-17-2085_en.htm

GRACE: https://www.graceprinciples.org/

GVP: Guideline on Good Pharmacovigilance Practices (GVP) Module VIII- Addendum I – Requirements and recommendations for the submission of information on non-interventional post-authorisation safety studies:
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/06/WC500129147.pdf

ICHOM: http://www.ichom.org

IEA guidelines: http://ieaweb.org/guidelines/

IMI: https://www.imi.europa.eu/

IMI BD4BO: http://www.lse.ac.uk/LSEHealthAndSocialCare/impacts/news/European-health-outcomes-research-initiative.aspx

IMI BIG DATA@HEART: http://blogs.ucl.ac.uk/ucl-global/tag/bigdataheart/

IMI DO->IT:

IMI HARMONY: https://www.imi.europa.eu/content/harmony

IMI RADAR: https://www.radar-cns.org/

IMI ROADMAP: http://roadmap-alzheimer.org/

IMI EMIF: http://www.emif.eu/

IMI GetReal: http://www.imi-getreal.eu

IMI GetReal Final Glossary
https://www.imi-getreal.eu/Portals/1/Documents/01%20deliverables/D1.3%20-%20Revised%20GetReal%20glossary%20-%20FINAL%20updated%20version_25Oct16_webversion.pdf

IMI GetReal insights on Acceptability e.g. report on PCTs
http://www.imi-

getreal.eu/Portals/1/Documents/01%20deliverables/Deliverable%201.6%20Report%20-pragmatic%20clinical%20trials_webversion.pdf

IQWIG criticism of adaptive pathways
https://www.iqwig.de/en/press/press-releases/press-releases/adaptive-pathways-ema-still-leaves-open-questions-unanswered.7492.html

STROBE https://www.strobe-statement.org/index.php?id=strobe-home