HARNESSING THE POWER OF REAL-WORLD EVIDENCE IN CLINICAL RESEARCH

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Foreword

The pharmaceutical industry has experienced significant growth in the past decade due to advances in technology and globalization. The digital push and increasing focus on patient centricity along the way has enabled access to huge amounts of real-world data (RWD) from disparate systems, thus influencing pharma companies to rethink their clinical research strategy. This data, if used collectively, can generate real-world evidence (RWE) or valuable insights that could potentially drive impactful decisions around the development of precision medicines or in redesigning business processes for faster production of drugs.

The white paper highlights how life sciences organizations can better utilize the capabilities of RWE through RWD generated from disparate systems along the pharma value chain to accelerate their shift from a product-focused to patient-focused organization.

Impact of COVID-19 on the Healthcare Industry

COVID-19 has significantly impacted pharma operations in the clinical research and commercial space, creating an inflection point for digital transformation. With 88% of global pharmaceutical companies already investing in remote trial monitoring solutions and Healthcare professionals engagement strategies, the adoption of RWE is seen as the next imperative. The RWE solutions market is projected to reach $3.13 Bn by 2027 at a CAGR of 16.5% [3].

Researchers from the US Food and Drug Administration (FDA) define RWE as: “Healthcare information derived from multiple sources outside of typical clinical research settings, including electronic medical records (EMRs), claims and billing data, product and disease registries, and data gathered by personal devices and health applications.”

RWE holds an important aspect in supporting the entire life cycle of a drug and in complementing the traditional Randomized Clinical Trial (RCT) outcomes, thereby reducing the overall trial timeline. In a recent survey conducted by Deloitte with Pharma C-suite executives, 94 percent of respondents believed that using RWE in R&D will become important to their organizations by 2022 [1]. Similarly, an RWE benchmarking study shows 70 percent of respondents’ biopharma companies indicating increased RWE budgets [2]. To encourage further adoption of RWE by sponsors and applicants, the US FDA issued draft guidance on the use of RWE and RWD in May 2019. This is seen as an important milestone in the exploratory process.

Embrace RWE to drive clinical research

The pharmaceutical industry needs to find new ways of improving the efficiency of drug development processes and measuring clinical outcomes in order to thrive in the current competitive landscape and cater to the rapidly changing demands of consumers. Typically, observations captured in traditional randomized clinical trials are limited to data that is part of regular care (e.g. broad eligibility criteria, preliminary assessment of benefits and common harms) and may not provide a holistic view of the patient's journey through the continuum of care (e.g. assessing the "real-world" treatment effects of healthcare). RWE generated from data collected outside of RCT (e.g. data from sales, medical affairs, pharmacovigilance, patient surveys, etc.) augments the traditional trials and real-world studies, with external validity across the care continuum by providing important evidence when we want to assess the harms of uncommon events, answer questions on adverse events that involve interactions between multiple interventions or generate hypotheses for further testing.

By incorporating real-world features in the study design with an integrated clinical trials approach, pharma companies can provide persuasive evidence to healthcare bodies and regulatory authorities for expanding the approved uses of a drug for new types of patients and diseases or in expediting approvals, thus gaining a competitive advantage with reduction in R&D cost and time to market.

Table 1: RCTs versus RWE [4]

Variables	RCTs (Randomized Clinical Trial)	RWE (Real-World Evidence)
Purpose	Efficacy	Effectiveness
Setting	Experimental Setting	Real-world setting
Follow up	Designed	In actual practice
Treatment	Fixed Pattern	Variable pattern
Study Group	Homogenous	Heterogenous
Attending Physician	Investigator	Many Practitioners
Comparator	Placebo/selective alternative interventions	Multiple alternative interventions
Patient Monitoring	Continuous as per protocol	Changeable

Sample uses of RWE include support for identification of unmet medical needs, design of registered clinical trials, post-approval drug safety assessment, pharmacovigilance, payment and coverage decisions, healthcare quality improvement, new indications of medical products, assessment of healthcare technologies and clinical practice guideline development.

Several drug manufacturers have already established a way to take advantage of RWE. In 2016, Celgene pharmaceutical collaborated with M2gen and the Oncology Research Information Exchange Network (ORIEN) to generate massive amounts of clinical data on patients which helped in accelerating the recruitment of eligible patients for biomarker-driven clinical trials and matching them with therapies tailored to their specific cancer type [5].

Similarly, in 2019 - US FDA approved IBRANCE (palbociclib) for treatment of male breast cancer. The approval was backed by data from electronic health records and post-marketing reports of real-world use of IBRANCE in male patients from three databases: IQVIA Insurance database, Flatiron Health Breast Cancer database and the Pfizer global safety database [6].

Studies indicate that several cases on New Drug Application (sNDA)/label expansion through indications supported by (RWE) data are being approved by the European Medical Agency (EMA) and FDA [7].

Impediments to Real-World Evidence model

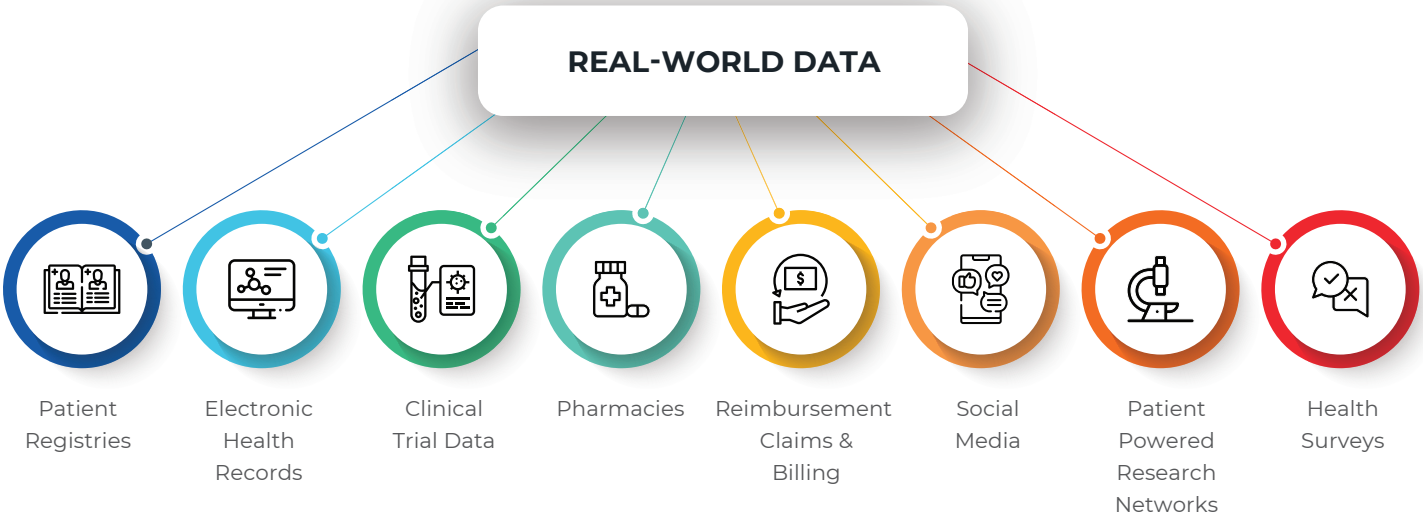
Although building robust RWE capabilities could serve as a potential key differentiator for pharma companies, there are several barriers that one needs to overcome in order to gain a better understanding of RWE and explore the use of RWD to its full potential.

Limited access to real-world data

Huge amounts of data is being generated every day, but the access to it is restricted due to multiple constraints – one major reason being data privacy. Healthcare organizations are not willing to share data with peers due to competitiveness while patients withhold sharing of relevant information due to lack of awareness on data usage or privacy concerns.

Unstructured data sources

The value of RWE can be understood only from real-world data derived from a range of sources such as social media posts, observational studies, ongoing safety surveillance, administrative claims, EHRs or personal devices. In addition to data acquisition, curation of this raw data from unstructured, semi-structured and structured data sources, to generate RWE is a massive task involving significant efforts.



Understanding gaps in sourced data

In most cases, growing amounts of datasets are directly flowing into data warehouse, making data cleansing (i.e. identifying missing data/irregularity in data sets which can impact the analysis) and data mining an extremely cumbersome process. Therefore, data profiling and data integration coupled with an in depth understanding of data flow from disparate systems is seen as a prerequisite for developing valuable insights and outcomes.

Accurate data analysis

We are all aware that data powers strategic decision-making, unearths new revenue streams and reveals hidden waste generators eating into the bottom line. That said, data alone cannot do any of those things. Organizations need to assemble a tech stack that connects all relevant data sources, select the right analytics tools and platform to uncover hidden insights from RWE. Nailing down the right solution for the organization's data is not easy.

Governance issues

As the real-world data could be a mix of different types of data at a global level, including de-identified, anonymized and limited data sets, the life sciences organization may need to come up with their own governance framework to adhere to the local authorities' regulations and comply with data privacy concerns.

Way forward in creating a next-generation RWE engine

Unlocking the value from real-world data is the only way forward for the life sciences industry to achieve accelerated clinical trials and support regulatory decisions such as approval of new indications or label expansions for existing drugs. Pharmaceutical companies will need to adapt a pragmatic and collaborative approach with end-to-end (E2E) evidence management strategies by breaking down the traditional evidence silos with platforms and processes to access data and knowledge assets across the organization for supporting data-driven decision making.

Creating and implementing such strategies, however, will likely require companies to assess and re-align their current infrastructure, governance, operating model, people, and processes.

We propose the following steps for life sciences organizations to implement new RWE capabilities or enhance their existing capabilities.

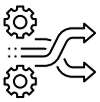
Strategic steps for implementing next-gen RWE

Plan & Acquire

- Idenfity RWE needs
- Conduct fit gap analysis on available vs required RWE
- Develop an RWE prioritization plan
- Review product and business portfolio objectives for building disease registries/research repositories in specific therapeutic areas
- Identify relevant data sources
- Collaborate or partner with data providers to acquire high quality data

Build & Analyze

- Adapt clinical data standards to aid convergence of real world data from multiple sources
- Build a centralized data hub/scalable enterprise platform
- Strengthen the data analytics team for intensive data analysis
- Optimize the use of analytics with a cloud based advanced analytics platform



Transform

- Leverage automation to manage big data or to handle complex RWE data science workflows and innovate at the pace of business
- Implement AI/ML solutions to generate quick meaningful insights
- Measure outcomes for continuous improvement

Building data lakes

One of the key steps towards building a robust RWE engine is establishing a cloud-based centralized data repository. We suggest that organizations replace their on-premises siloed data repositories with cloud-based data lakes to create a centralized repository or data hub, allowing storage of structured and unstructured data sets. This would enable the organization to cultivate an integrated data environment housing diverse data sources from disparate systems and in varying formats that could potentially support advanced analytic methodologies and tools for creating meaningful insights to business users. As datasets will continue to grow in volume and complexity, it is important that organizations select a scalable and low-cost solution to build the centralized data hub.

Secondly, implementing a secure and advanced analytics platform, enabling data scientists to query, extract and visualize meaningful data from the underlying data lake 'at ease' is critical in driving an effective RWE strategy. This platform should also have the ability to act as a "self-service" portal for business users to be able to generate meaningful reports through the different phases of clinical trials and in pharma commercial during pre-launch, go-to-market and post launch to drive innovation and value.

Strengthening the data analytics team with the right skill set

The data analytics team comprising of data engineers, clinical data analysts, data scientists or BI specialists working in a clinical research setting are primarily responsible for managing and monitoring data collection, and reporting findings to the clinical trial staff and administrations. For an organization implementing RWE, it is important to ensure that this team has the right mix of skills with strong domain and technical expertise to compile data from varied real-world data sources, identify inaccuracies in data sets, build highly accurate machine learning algorithms and present key findings through customized state-of-the-art dashboards that translate data into actionable insights for trial clinicians, administrators and senior executives across the organization in managing RWE strategies. Developing the scare skillsets for delivering innovative RWE analytics can take years. Building long-term partnerships with data and analytics service organizations to insource the right talent would be fruitful in building a data-driven culture and improving the clinical research operational performance.

Leveraging artificial intelligence (AI) & machine learning (ML) to turn big data into smart data

AI algorithms, combined with big data, can help analyze data at scale with the potential to solve major challenges in clinical research. It can generate insights by analyzing complex patterns that directly influence various aspects of clinical research ranging from drug discovery (e.g. support for identification of unmet medical needs) to reducing the clinical development timeline with evidence based (e.g. via exploration of clinical research questions on disease burdens, prognoses, and clinical predictions). The adoption of AI is therefore becoming a critical business imperative across the pharma ecosystem.

Similarly, ML tools learn from the historical actions of business users and have the ability to automate complex workflows. It can capture and apply data modelling knowledge from repeated onboarding of RWD sources, understand previously developed schema-mappings and automatically map new RWD to common data model, saving significant time and effort. ML also helps in automatically correcting small schema discrepancies in the new ingested RWD. AI combined with ML can generate quick meaningful insights within seconds.

Overall, with a focused strategy in place, life sciences organizations can leverage the power of real-world evidence to identify new targets for drugs, accelerate time-to-market, improve the formulary position and payer negotiations and generate stronger evidence of differentiation and benefit/risk balance for in-market, potentially improving patient outcomes (e.g. getting the right drug to the right patient at the right time). Companies that lack this vision could struggle to compete with others that are able to base their decision on richer insights generated at a fraction of the usual time and cost.

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Learn more about Hexaware at **www.hexaware.com**

NA Headquarters
Metro 101, Suite 600,101
Wood Avenue South, Iselin,
New Jersey - 08830
Tel: +001-609-409-6950
Fax: +001-609-409-6910

India Headquarters
152, Sector – 3
Millennium Business Park
'A' Block, TTC Industrial Area
Mahape, Navi Mumbai – 400 710
Tel : +91-22-67919595
Fax : +91-22-67919500

EU Headquarters
Level 19, 40 Bank Street,
Canary Wharf,
London - E14 5NR
Tel: +44-020-77154100
Fax: +44-020-77154101

APAC Headquarters
#09-01, One Finlayson
Green, 1 Finlayson Green,
Singapore - 049246
Tel : +65-63253020
Fax : +65-6222728

Australia Headquarters
Level 3, 80 Mount St
North Sydney NSW 2060
Australia
Tel : +61 2 9089 8959
Fax : +61 2 9089 8989