Real-World Evidence Usage in Regulatory Approvals from USFDA and EMA

Shaikh J[1], Samnaliev M[2]

[1]Axtria India Pvt. Ltd., India, [2]Axtria Inc., NJ, USA

INTRODUCTION

- Randomized controlled trials (RCTs) are considered the gold standard for evaluating drugs and medical devices' safety and efficacy. However, their restrictive inclusion/exclusion criteria, lack of diversity, and complexity can limit their generalizability to real-world patient populations.[1,2]
- Real-world evidence (RWE) studies can be used at all stages of the product lifecycle and can provide information that complements RCTs to support clinical, regulatory, and reimbursement decisions.[2,3]
- RWE can reveal how medications and devices are used in everyday clinical settings, which may differ from the controlled setting of RCTs, helping to fill gaps left by RCTs. RWE also offers an opportunity to comprehend rare diseases in smaller populations which are often not studied in clinical trials.[1,3,4]
- RWE is becoming a part of integrated evidence generation and creating continuity from premarket to iterative post-market approval decisions. The acceptance of RWE for regulatory approval differs across countries.[2]

OBJECTIVE

- This review identified and compared the inclusion of RWE as part of an evidence package to support approvals by the United States Food and Drug Administration (USFDA) & European Medicines Agency (EMA).

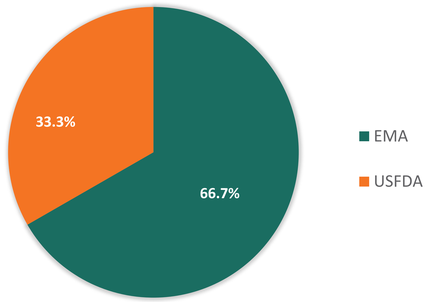
METHODS

- USFDA & EMA approvals between 2017 and 2022 were screened to identify the usage of RWE. Details of the name of the drug, disease area, approval year, & manufacturer were analysed and categorized using a pre-specified data extraction template.
- Data was mainly collected from drug's label, approval letter, and various types of review documents of USFDA submission and European public assessment reports of EMA submission. RWE was categorized into clinical evidence, supportive evidence, and future commitments based on their requirements during the regulatory assessment.

RESULTS

- A total of 1003 approvals were retrieved, with 669 approvals by EMA and 334 approvals by USFDA. RWE was used more frequently in EMA (66.7% of all approvals) than in USFDA (33.3% of all approvals) **(Figure 1)**.

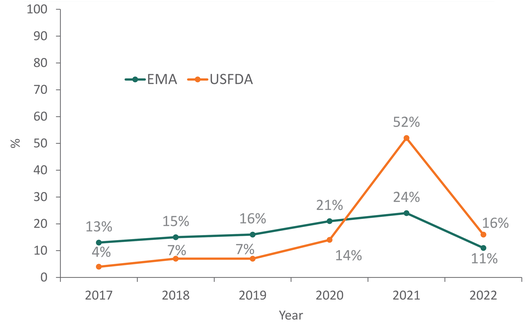
Figure 1. Percentage of RWE utilization in EMA and USFDA



RESULTS

- The number of approvals with RWE usage increased steadily from 2019 to 2021 in both EMA and USFDA but a decrease in approvals was observed in 2022 **(Figure 2)**.

Figure 2. Percentage of EMA and USFDA approvals that used RWE



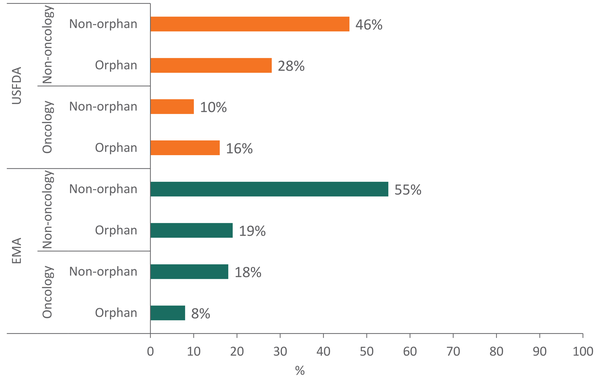
- The most common application of RWE in these approvals were as supportive evidence (EMA, 46.8%, USFDA, 55.4%), future commitments for post-approval studies (EMA, 44.4%; USFDA, 34.7%), and clinical evidence (EMA, 8.8%; USFDA, 9.9%) **(Table 1).**

Table 1. Application of RWE in EMA and USFDA approvals from 2017–2022

Type of evidence	Year	EMA approvals (%)	USFDA approvals (%)
Supportive evidence	2017	4.8	0.9
	2018	7.2	0.3
	2019	6.3	0.9
	2020	11.5	9.3
	2021	14.3	36.8
	2022	2.7	7.2
Future commitment	2017	5.7	2.4
	2018	6.9	5.1
	2019	9.3	3.6
	2020	9.0	2.7
	2021	7.5	13.1
	2022	6.1	7.8
Clinical evidence	2017	2.5	1.2
	2018	1.0	1.5
	2019	0.7	2.1
	2020	0.6	1.8
	2021	1.8	2.1
	2022	2.1	1.2

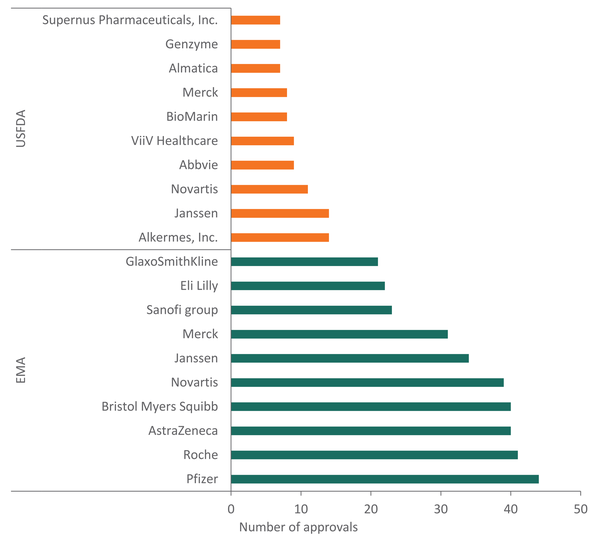
- RWE was used substantially in the approvals of oncology products (EMA, 26%; USFDA, 26%) and orphan drugs (EMA, 27%; USFDA, 44%) **(Figure 3)**.

Figure 3. Percentage of RWE approvals for orphan vs. non-orphan drugs



- Pfizer received the highest number of approvals (*n*=44) using RWE to EMA, followed by Roche (*n*=41). Whereas in USFDA, most approvals were made by Alkermes (*n*=14) and Janssen (*n*=14) **(Figure 4).**

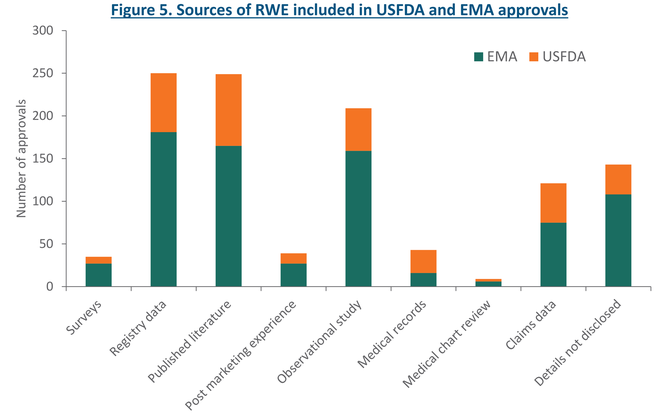
Figure 4. Companies with top RWE usage in approvals by EMA and USFDA



RESULTS

- Published literature (EMA, 21.5%; USFDA, 25.1%) and registry data (EMA, 23.6%; USFDA, 20.6%) were the most used sources of RWE, followed by observational studies (EMA, 20.8%; USFDA, 14.9%) and claims data (EMA, 9.8%; USFDA, 13.8%) **(Figure 5).**

Figure 5. Sources of RWE included in USFDA and EMA approvals



CONCLUSIONS

- There is increased use of RWE to support regulatory approvals of drugs in the US and EU. The use of RWE in USFDA approvals is quite limited compared to EMA but slowly gaining traction as new therapeutics modalities emerge.
- The increasing RWE usage from 2017 to 2021 indicates an accelerated acceptance of RWE data in regulatory approvals.
- RWE usage was prevalent in oncology and orphan drug products. Most used RWD sources across USFDA and EMA included published literature, registries, observational studies and claims data.
- In the US and EU, the development of RWE has entered a relatively mature stage with development of frameworks and regulations to promote practical applications of RWE. With changing policy framework around RWE, it is anticipated that RWE adoption will be accelerated in the coming years.
- RWE studies are becoming more commonly accepted when ethics, orphan diseases, or enrolment challenges limit the conduct of RCTs. Robust and appropriate RWE can accelerate patient access to new technologies in diseases with a high level of unmet need.

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