IMDRF International Medical Device Regulators Forum

Filling the Gap: Advances in Clinical Evidence

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Overview

- What is the “traditional” approach to clinical evidence?
- What are its limitations?
- When can a Real-World Evidence Approach help address these gaps?
- How can RWE support regulatory decision-making?
- Examples

Traditional Clinical Evidence

Mature Traditional Approach

- The traditional approach to clinical evidence is well-established and supported by comprehensive guidelines
- IMDRF provides terminology and frameworks for developing and analyzing clinical evidence effectively.

What Does the “Traditional Approach” Look Like?

Medical Device Clinical Evaluation Process

- Rooted in intended use
- Examination of available literature and clinical data -> clinical evidence
- Clinical investigation to address unmet needs within the clinical evidence
- Results integrated into the clinical evidence
- Forms part of evidentiary package supporting device authorization pathway

But…. This approach has its limitations

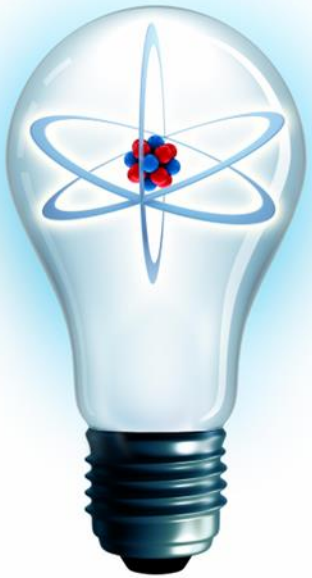
The traditional model can have limitations that may ultimately be useful to address, e.g.:

- Insufficient Data/Data Quality
- Limited Generalizability
- Unmet Needs and Rare Diseases
- Long-Term Outcomes/Safety
- Outcome Not Feasible for Trials
- Complex Treatment Scenarios
- Examining outcomes in routine care vs. ideal trial conditions

A Role for Real World Evidence

The use of Real World Evidence can help to address these limitations by providing broader, more representative, and often long-term view of technology performance in real-world settings

- Complementing focused information from traditional studies
- Supporting decision-making throughout the product's life cycle as a wider body of evidence becomes available



A Role for Real World Evidence

RWE is particularly useful for studying patient populations that are often under-represented or challenging to research in traditional Clinical Investigations

Heterogeneous and Diverse Patient Populations

Patients with Comorbidities

- Traditional clinical investigations often exclude patients with complex health profiles

Underrepresented Groups

- RWE can include patients from groups traditionally underrepresented in clinical investigations such as children, the elderly, pregnant women and minority groups

Heterogeneous and Diverse Patient Populations

Patients Not Participating in Traditional CIs

- RWE gathering can capture data from patients who are unwilling or unable to participate in traditional clinical investigations

Specific Subgroups of Interest

- RWE is useful for exploring particular patient subgroups where clinical benefit is likely to be the greatest, and supports hypothesis generation for subgroup effects

Hard-to-Study Populations

Patients with Rare / Low-Incidence Conditions

- When traditional studies are not feasible, unethical, or impossible to conduct due to the small number of patients, RWE can fill critical evidentiary gaps

Patients in Emergency Use Conditions

- RWD can be captured during emergency use conditions, and help with both ongoing monitoring and future regulatory decision-making

Examining Long-Term Effects

Patients Requiring Long-Term Follow-Up

Traditional Clinical Investigations often have relatively short follow-up periods

- RWE can provide information on a product's performance and safety over extended periods of time in a larger patient sample, particularly for long-term implantable devices

Post-Market Surveillance

- RWE is crucial for monitoring product safety after approval and identifying potential safety signals

Monitoring Clinical Practice

Following Device Use Patterns

- RWE reflects how products perform in routine clinical settings, where use is not necessarily dictated by rigid study protocols
- It helps in the understanding of patient management pathways and current standards of care
- Can capture real outcomes, such as complications, adverse events, disease progression, resource use, and quality of life
- Also helps to identify new use patterns

A Role for Real World Evidence

By leveraging Real World Data from sources such as electronic health records, claims data, patient registries, and patient-generated data, RWE enables a broader, more representative, and often longer-term understanding of patient experiences and outcomes

RWE Supports Regulatory Decisions

Data from all of these, and other, real-world sources can support regulatory activities and regulatory-decision making in multiple ways:

Pre-Market Submissions

- Can support or supplement traditional clinical investigation data for obtaining market approval, or even, in some cases where the device is well-established, can serve as pivotal clinical evidence

RWE Supports Regulatory Decisions

Post-Market Surveillance and Safety Monitoring

- RWE is routinely used for monitoring safety of products post-approval, including signal detection
- Can support post-approval study requirements

Expanding Indications and Labeling

- RWE can support the expansion of a device's labeling to include additional indications or updates to safety and effectiveness information

RWE Supports Regulatory Decisions

Optimization of Approved Therapies

- RWD can lead to revisions to therapeutic protocols in order to optimize outcomes

Analysis of and Transition from Emergency Use

- Collection of data during emergency use situations can be considered RWD and be used to support regulatory decision-making if appropriate

RWE Supports Regulatory Decisions

Support for Reclassification Decisions

- In jurisdictions that have mechanism for reclassification of devices, analysis of RWE can be used as a primary means of support for those decisions

RWE Also Supports Other Types of Policy Decisions

Local Economic Models

- Locally-derived RWD can help inform policy-making in specific contexts by providing local epidemiological estimates, cost data, and locally validating outcomes

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A Role for Real World Evidence

There are a variety of ways in which RWE can support both regulatory and non-regulatory decision-making

Consistent policies regarding its applicability and use can help broaden its adoption and general utility

Examples

Some examples to look at the ways RWE has already been used

Examples of Past RWE Use

Pediatrics - Premarket

- Product: Minimally Invasive Deformity Correction System for treatment of impending and actual pathology fractures of arm bones from metastatic bone disease
- Used RWD from commercial use in other jurisdictions combined with other clinical data to examine adverse events and probable benefit
- Led to US HDE

Examples of Past RWE Use

Cobalt and Cancer Risks

- Potential signal linking cobalt in medical device materials to increased risk of cancer
- Used RWD from range of devices to determine if there was a valid signal based on use of cobalt-containing devices and reported incidence of cancer in patients receiving them vs general patient population
- Determined that there was not a significantly greater risk associated with cobalt-containing devices

Examples of Past RWE Use

Indication Expansion

- Product: Drug-Eluting Peripheral Vascular Stent
- Used RWD from post-market surveillance and clinical practice as a supplemental source of clinical evidence
- Supported an indication expansion to allow treatment of longer total lesion lengths (also ultimately supported additional longer device lengths as well)

See also: https://www.fda.gov/media/146258/download

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Conclusion

The use of RWE can meaningfully add to the body of information available to support decisions around the approval and use of technologies.

A thoughtful, consistent approach to this source of data can ultimately enhance the safe, effective, and efficient use of technologies to drive positive patient outcomes.

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THANK YOU!

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