Making the Grade: Registries as Sources of Regulatory-Grade RWE

Dr Peter Wahl, MLA, MS, ScD, unpacks the diverse range of registry uses—from safety and effectiveness studies to regulatory decision-making—and offers expert guidance on selecting the right type of registry to meet specific needs.

Dr Peter Wahl, MLA, MS, ScD
VP, Global Head of Scientific Affairs
CorEvitas, part of the PPD clinical research business of Thermo Fisher Scientific

Registries are an invaluable resource for safety studies and comparative effectiveness studies, and can include multi-sponsor registries, bespoke registries, and nested studies. Dr Peter Wahl, MLA, MS, ScD, Global Head of Scientific Affairs at CorEvitas, part of the PPD clinical research business of Thermo Fisher Scientific, shared his thoughts with *Pharmaceutical Executive*, covering best practices for registry selection.

PHARM EXEC: What differentiates registries over other types of real-world healthcare data sources? Why choose a registry over other types of tools or data?
WAHL: At the risk of over-simplifying things, it really boils down to filling data gaps in a highly purpose-driven way. A properly designed and executed registry will collect clinical measures of disease activity and severity that are actively assessed by investigators, detailed treatment dosing, regimens, frequency, and changes for dosing or changes in medications, reasons for starting or stopping therapies, and patient reported outcomes (PROs). It will also include procedures for active safety surveillance and collection of any needed source documents. All of this is done under a carefully-designed protocol with scientific input from expert clinical thought leaders.

These factors differentiate well-designed and executed registries from other sources of real-world data and evidence (RWE) that lack that kind of detail. And this is not surprising to anyone. We know that treating physicians are usually focused, as they should be, on taking the best care of their patient. Thus, electronic medical records (EMR) and claims datasets exist to serve the administration or reimbursement of healthcare, rather than for research purposes, and don't have that type of data.

A protocol-driven registry leverages the clinical expertise of the physician who is enthused to participate as an investigator and to conduct active assessments of disease severity and activity. This ensures that key clinical measures are available under truly regulatory-grade data collection, particularly for treatment outcomes that may be the same as those collected in pivotal Phase III trial endpoints.

PHARM EXEC: What types of registries are available? What differentiates them?
WAHL: There are four major types of registries, and I'm not counting pure EMR datasets that have been "subsetted" through query code into specific disease groupings. I'm speaking of clinical registries that are driven by a well-designed protocol with a primary purpose of research.

Public health registries collect information on specific exposures like vaccines and may be maintained by a local or national government. Institutional or consortium-based registries may capture the experience of a single institution or a group of like-minded research institutions. Drug registries focus on a single exposure or drug. Finally, disease or patient registries capture data on many therapies for a particular disease or a group of related conditions. What really differentiates them is how the data are collected. Who is sponsoring the registry, and what data collected are mandatory per protocol versus voluntary, and what specific measures are collected under that protocol? This varies from registry to registry.

PHARM EXEC: How does someone know what kind of registry is best for their needs?
WAHL: We talked about different types of registries, but there is also a decision between single-sponsored versus independently-sponsored registries, and you have to consider a few key factors. What are my internal stakeholder needs? Do internal policies, politics, or intellectual property pressures dictate that I must own all the data or not? What level of credibility am I seeking for the evidence to be generated? What are the implications for my relationships with the clinical or patient communities if I can't maintain the registry or a network of specialty key opinion leaders (KOLs) and support those communities over the long term? How complete will the data be? Can I achieve scale of enrolled patients and follow up over a long period of time? What are regulators going to accept in terms of evidence needed for safety or label expansions? Finally, do I have a trusted partner that has established credibility with clinical and regulatory stakeholders that I can leverage? There are other factors as well, including budget, which is one of the main issues that may ultimately tip the balance in favor of one approach over another.

PHARM EXEC: What should someone look for when using a registry?
WAHL: I would say the top things to look for when evaluating registries or to fulfill your evidence needs are: What data are collected that satisfy those needs? What processes are in place to ensure the validity and complete capture of key clinical measures, PRO measures, or safety events that may impact credibility of evidence with stakeholders? Does the registry have flexibility to embed more granular studies or biospecimen collection when needs may dictate and budget allows? Can the registry add measures or safety events that may be critical to my needs if such emerge over time? You also need a true partner that is willing to adapt with you as your evidence needs evolve over the life cycle of your drug.

PHARM EXEC: How can registries help us fulfill regulatory requirements? What is CorEvitas seeing in terms of regulatory requirements as they relate to registries?
WAHL: First of all, CorEvitas and Thermo Fisher Scientific registries have supported regulatory studies for over 24 years. Our investigator sites conduct active assessments of clinical disease activity and severity, concomitant medications, comorbid conditions, and disease-specific dosing or treatment changes or regimens at and between each and every visit. All of that helps to contextualize safety and track clinical outcome measures that are often the same measures as pivotal Phase III trial endpoints. In terms of safety, our processes for investigator active screening of targeted adverse events, event source documentation, event verification by our pharmacovigilance and clinical team, and adjudication all meet regulatory definitions of full ascertainment and central verification. What we've seen is really twofold. First, these processes have been accepted by both the Food and Drug Administration (FDA) and European Medicines Agency (EMA) to fulfill post-marketing safety requirements. Second, we know from a practical perspective that the first instinct for a marketing authorization holder or regulator is to ask if off-the-shelf datasets like claims or EMR can address a safety concern with enough rigor. We're seeing that for certain therapeutic areas those datasets may actually be sufficient, but others—for example, where you need long term follow up, in-depth characterization or grading of a safety event, or where disease severity is a confounder of comparative safety—can only be properly assessed using a purpose-built, protocolized approach. Certain FDA therapeutic area divisions within the FDA and the EMA have required a registry-based approach to satisfy these more rigorous post-authorization safety study requirements. This is particularly true for pregnancy-related safety studies that are done in combination with database studies, but also for many disease areas in the broader population that are exposed to biologics and novel advanced therapies.

PHARM EXEC: Do you have examples of use cases for your registry data?
WAHL: For examples of where CorEvitas registries have been or are being used to fulfill FDA or EMA post-authorization safety requirements, you can generally find information on ClinicalTrials.gov. In the case of the EMA, the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) website can be used to search for CorEvitas—or as we were previously known, CORRONA. For external control or contextualization arms, we have done and are still doing these types of studies mostly to contextualize safety of a marketing authorization holder's Phase IIB, long-term extension study, or a Phase III study, or to look at effectiveness of other standard-of-care therapies. These data may be used to provide real-world context side-by-side with what is observed in the registrational trials.

You can also find a list of publications from our registries on our website that describe a wide range of real-world evidence studies that are derived from the unique clinical and patient reported data that we collect as part of our clinical registries.

PHARM EXEC: Do you have any final thoughts to share?
WAHL: Yes—properly designed prospective registries that are truly purpose built to ensure that the data collected are regulatory grade can be an incredibly robust source for RWE needs. Any investment in a registry, either through a partnership or done in house, should be viewed as a strategic investment; you can realize the maximum return on that investment by planning ahead, engaging with your relevant internal and external stakeholders early, and making sure that the design and the data can serve multiple and evolving evidence needs across the drug development cycle. Having spent my career working with all types of real-world data sources, a registry can be a great investment for RWE needs, if leveraged wisely.