



The Power of Real-World
Data to Detect Adverse
Events and Expedite FDA
Postmarketing Safety
Commitments

IN COLLABORATION WITH

Ocular
Therapeutix™



The relative speed with which pharmaceutical companies developed, tested and released vaccines in response to the COVID-19 global pandemic belies how time-consuming drug research has become. Clinical trials are often inefficient and costly, and results may not be sufficient for regulatory submission nor representative of diverse patient populations.

To overcome the limitations inherent in traditional clinical trials, researchers increasingly are turning to real-world data (RWD) to provide a picture of a drug's efficacy and safety. RWD can come from multiple sources, including electronic health records (EHRs), claims, disease registries, and patient-generated data from mobile and other personal devices that track health- and activity-related data.

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The authors of a recent U.S. National Library of Medicine publication write, "Data from real-world studies can provide evidence that informs payers, clinicians, and patients on how an intervention performs outside the narrow confines of the research setting, providing essential information on the long-term safety and effectiveness of a drug in large populations, its economic performance in a naturalistic setting, and for assessment of comparative effectiveness with other treatments."¹

One of the major challenges of prospective clinical trials is detecting rare safety outcomes. With the cost of just one patient in a clinical trial exceeding \$40,000, running a clinical trial that includes sufficient participants to measure rare events may be too costly and time-consuming to be feasible.² Researchers and biopharmaceutical companies need a way to obtain reliable safety data at-scale.

Why point-of-care EHR data is a game changer

EHR-derived data offer rich inputs for analyzing rare clinical outcomes such as certain adverse events. In aggregate—stemming from dozens of different EHR systems—these data often reside in qualified clinical data registries (registries), many of which were originally set up by medical societies to help with quality improvement and scientific research and discovery. Many also help practicing physicians comply with quality reporting requirements from the Centers for Medicare and Medicaid Services (CMS). Now, however, registries also offer the unique potential to inform real-world evidence.

¹ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6223979/>

² <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2702287>

When curated and analyzed with expertise, the unfiltered data residing in registries have several advantages:

- The ability to identify qualifying patients for a trial from a much larger population than a traditional clinical trial.
- The ability to capture a diverse patient population reflective of the “real-world” that includes greater racial, age, and socioeconomic diversity.
- The ability to capture clinical outcomes among patients with co-morbidities or pre-existing conditions that may have otherwise precluded trial inclusion. Measuring drug effectiveness and safety among these vulnerable “real-world” populations is critically important.

January 2022

The IRIS Registry includes data from more than

18,000

Contributing clinicians

400M

De-identified patient encounters

70M

De-identified unique patients

62

EHR Systems

9 Year

Longitudinal database

Verana Health offers de-identified*, real-world EHR data for multiple disorders in the therapeutic areas of ophthalmology, neurology, and urology. These data comprise nearly a half-billion raw, point-of-care health encounters which are ingested by and reside in Verana Health’s population health data engine, VeraQ™. VeraQ links the de-identified EHR data with other meaningful data sources, such as medical claims, pharmacy claims, and images, and then curates the data with physician oversight and natural language processing (NLP). This results in clinically true Qdata™, fit-for-purpose data modules, to enable research into patients’ care trajectories, longitudinal clinical outcomes, and health resource utilization.

Verana Health’s Qdata modules are derived from physician EHRs through exclusive partnerships with medical societies. Qdata offers researchers large sample sizes as well as safety signals that might not be detected in clinical trials with a relatively small number of participants. This outpatient EHR data draws from a wide variety of physician types and includes a large number of enrolled medical practices.

Verana Health’s partnership with the American Academy of Ophthalmology enables the ingestion, curation, and analysis of data from the American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight), the nation’s first comprehensive eye disease clinical registry and the largest specialty clinical database in medicine.³ The IRIS Registry includes data from more than 18,000 contributing clinicians, 400 million de-identified patient encounters, 70 million de-identified unique patients, 62 EHR systems, and a nine-year longitudinal database.

³ <https://www.aao.org/iris-registry/about>

*The research and analysis was conducted on anonymized data in accordance with the de-identification standard promulgated under 45 CFR § 164.514. No research was conducted on human subjects. FDA regulated research requires IRB review or IRB exemption.



While clinical trial demographics are skewed toward white, urban, educated and more affluent participants⁴, the IRIS Registry includes data from a broader range of patient types than normally would participate in a clinical trial. This matters because patients receiving a drug therapy in the real world may have other comorbidities or conditions that could be underrepresented in a clinical trial.

Study sponsors can collaborate with Verana Health to leverage de-identified IRIS Registry data powered by VeraQ to satisfy regulatory safety requirements and conduct analyses that would be very difficult in a prospective study. The breadth and depth of Verana Health's Qdata makes them particularly useful for studying rare outcomes. One recent example is Verana Health's work with Ocular Therapeutix, in which Qdata was leveraged to detect the incidence of rare endophthalmitis events following cataract surgery.

The ReSure Sealant Study



The Ocular Therapeutix use case is a compelling and illustrative example of how real-world registry data can be used to detect rare outcomes and fulfill an FDA requirement for postmarketing safety data. Specifically, the FDA requested Ocular Therapeutix to collect post-approval data relative to the incidence of endophthalmitis (within 30 days) for cataract surgery patients treated with its ReSure® Sealant, a hydro gel sealant that prevents wound leakage following cataract surgery.⁵

Endophthalmitis is a rare infection that can occur after cataract surgery. The American Academy of Ophthalmology estimates that endophthalmitis occurs at a rate of 0.04%, or 40 in 100,000 cataract surgeries.⁶ "It is vitally important to study rare outcomes because they can have a significant impact on patients," said Dr. Robert Chang, an associate professor of ophthalmology at Stanford Health Care and a Verana Health consultant. "In the case of endophthalmitis, that impact could be as serious as a loss of vision."

"Endophthalmitis is difficult to study because of its very low incidence, and the potential costs of a large-scale, prospective study are prohibitive as well as potentially limited in generalizability," the Academy writes.⁶ Indeed, if Ocular Therapeutix opted to fulfill the FDA mandate with a traditional trial, the biotechnology company would have needed to enroll nearly 5,000 subjects to detect a clinically significant difference in the rare safety outcome. Multiple discussions occurred between Ocular Therapeutix and the FDA to determine the best way to fulfill this post approval commitment. Despite a good faith effort, it was not possible for Ocular Therapeutix to complete this trial for several reasons including the ability to track use of ReSure utilization and the size of the study.

⁴<https://acrpnet.org/2021/04/20/diversity-in-clinical-trials-going-beyond-why-to-how/>

⁵<https://www.ocutx.com/products/resure-sealant/>

⁶[https://www.aaojournal.org/article/S0161-6420\(19\)31957-8/fulltext](https://www.aaojournal.org/article/S0161-6420(19)31957-8/fulltext)



In partnering with Verana Health for its postmarketing safety study, Ocular Therapeutix leveraged the IRIS Registry to study the results of 6 million cataract surgeries and perform the same type of safety analysis that would have otherwise required a lengthy 18 month trial⁷

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Ocular Therapeutix studied two cohorts—3.5 million eyes treated at practices that had access to ReSure Sealant and 3 million eyes that were treated at practices that did not—to determine the difference in the incidence of endophthalmitis within 30 days of cataract surgery for both groups. Ultimately, there was no clinically meaningful or statistically significant difference in the incidence rate of endophthalmitis between eyes treated at practices with and without access to ReSure Sealant. Sites with access to ReSure had an incidence rate of 0.609 per 1,000 surgeries and sites without access to ReSure had an incidence rate of 0.660 per 1,000 surgeries. When stratifying by routine and complex cataract procedures, there was also no statistically significant difference in the incidence of endophthalmitis between eyes treated at practices with and without access to ReSure.⁸

In May 2021, Ocular Therapeutix received notification from the U.S. Food and Drug Administration (FDA) confirming it has fulfilled all post-approval study requirements for ReSure[®] Sealant.

“As a biotechnology company, Ocular Therapeutix would not be able to run a postmarketing trial evaluating endophthalmitis after cataract surgery due to the size and costs involved,” said Dr. Michael Goldstein, chief medical officer and president of ophthalmology for Ocular Therapeutix. “Life Sciences needs access to RWD when conducting studies of rare outcomes when required by the FDA and to protect as many patients as possible.”

In the ReSure study, Verana Health was able to look at adverse events across 2,000 practices. This gave researchers the ability to detect both broader safety signals and safety signals in a more comprehensive population that reflect outcomes in the real world. Qdata also provided a potentially wider geographic scope because the source of the data, the IRIS Registry, contained more than 50 million patients as of 2019 and has collected data from more than 90% of U.S. ophthalmologists.⁹

⁷<https://www.fda.gov/drugs/surveillance/postmarket-drug-and-biologic-safety-evaluations>

⁸Incidence of Endophthalmitis Following Cataract Surgery and Risk Factors: Retrospective Study Using the IRIS Registry,” presented at ARVO 2021 by Michael H. Goldstein, MD, MBA

⁹<https://www.cdc.gov/visionhealth/vehss/data/ehr-registries/iris.html>



FDA embraces real-world data

Verana Health offers a robust and reliable method to inform clinical research, helping life science partners satisfy postmarketing safety commitments. The value of point-of-care EHR data for use in postmarketing studies is only growing as the FDA continues to promote the use of RWD. Under the 21st Century Cures Act, we expect to see the industry continuing to invest in generating real-world evidence (RWE) to assess product effectiveness, support approval for new indications, and satisfy post-approval study requirements.

In December 2018, the FDA released a framework for evaluating RWD/RWE for use in regulatory decisions.¹⁰ The framework calls for consideration of whether:

- The RWD are fit for use
- The trial or study design used to generate RWE can provide adequate scientific evidence to answer or help answer the regulatory question
- The study conduct meets FDA regulatory requirements (e.g., for study monitoring and data collection)

Verana Health has invested best-in-class engineering, data quality, and quantitative science practices to ensure that RWD is leveraged in an appropriate and effective manner through its population health data engine VeraQ. The team is committed to continuous improvements in data integrity, analysis, and application to advance the use of RWE in regulatory and clinical decision-making. Going forward, Qdata curated by Verana Health will be accessible for designing and implementing postmarketing surveillance studies to inform regulatory decision making.

¹⁰ <https://www.fda.gov/media/120060/download>



Conclusion

This Ocular Therapeutix case study demonstrates that researchers can satisfy adverse event FDA requirements using registry data without performing a traditional clinical study.

There is growing demand for high-quality real-world data to satisfy regulatory reporting. Enabling sponsors to leverage Verana Health's Qdata to satisfy certain postmarketing commitments fosters new opportunities for innovation in drug research and commercialization. Powered by VeraQ, Verana Health's RWD and analysis can help to satisfy postmarketing safety surveillance and offer a valuable perspective that cannot otherwise be gleaned from a clinical trial. Beyond safety requirements, Verana Health's broad datasets can also be valuable for studying rare diseases and outcomes that can otherwise be challenging to monitor. Ongoing projects include studies involving patients with rare inherited retinal disorders and autoimmune conditions with ocular manifestations.

This Ocular Therapeutix case study demonstrates that researchers can satisfy adverse event FDA requirements using registry data without performing a traditional clinical study. This opens up many potential possibilities for life science companies in the future.

About Verana Health

Verana Health is a digital health data company that delivers insights from unfiltered healthcare data with integrity to connect the dots between patient care and clinical research. Verana Health is exclusively entrusted by key specialty medical societies to manage data from real-world healthcare settings across more than 20,000 healthcare providers and 70 electronic health record systems. Its healthcare data ecosystem is powered by VeraQ™, a clinician-directed and AI-enhanced population health data engine that securely powers a data integrity feedback loop of nearly a half-billion raw, point-of-care health encounters. By applying advanced analytics to proprietary, curated datasets, Qdata™, Verana Health helps life sciences partners enhance evidence generation and speed clinical research that promote physicians' quality of care and patients' quality of life.

For more information, visit www.veranahealth.com.