It's Starting to Register: FDA Draft Guidance Addresses Use of Registries to Support Regulatory Decision-Making for Drugs & Biological Products

Showing no signs of food coma, the FDA issued **draft guidance** on the Monday following the Thanksgiving holiday weekend that outlines considerations for sponsors proposing to design a registry or use an existing registry to support regulatory decision-making about a drug's effectiveness or safety. This draft guidance represents the Agency's latest response to the mandate in the 21st Century Cures Act to issue guidance on the use of real world evidence in regulatory decision-making, and expands on the **Framework for FDA's Real-World Evidence Program** from December 2018.

The draft guidance, ***Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products***, defines a registry as "an organized system that collects clinical and other data in a standardized format for a population defined by a particular disease, condition, or exposure," and identifies three general categories of registries: disease registries, health service registries, and product registries.

Given the range of registry types, FDA notes that registry data can have varying degrees of suitability for use in a regulatory context depending on several factors, including how the data are intended to be used for regulatory purposes, the patient population enrolled, the data collected, and how registry datasets are created, maintained, curated, and analyzed. FDA advises sponsors to be mindful of both the strengths and limitations of using registries as a source of data to support regulatory decision-making. In general, the draft guidance advises that (i) a registry that captures objective endpoints, such as death or hospitalization, is more likely to be suitable to support regulatory decision-making than a registry that collects subjective endpoints, such as pain; and (ii) a registry that is specifically designed to answer a particular research question is more likely to be useful to support regulatory decision-making than a registry that was designed for a different purpose.

At the same time, the Agency acknowledges that an existing registry can be used to collect data for purposes other than those originally intended, and that leveraging an existing registry's infrastructure to support multiple purposes can be efficient. Therefore, the draft guidance describes factors sponsors can use to assess the **relevance** and **reliability** of a registry's data to determine whether the registry data may be fit-for-use.

When determining **relevance** of registry data, the draft guidance advises sponsors to consider, among other things, whether the data elements captured by the registry are sufficient given the intended use or uses of the registry (e.g., external control arm vs. a tool to enroll participants in an

interventional study) and whether the methods involved in patient selection may have impacted the representativeness of the population in the registry.

When assessing the **reliability** of registry data, the draft guidance advises sponsors to assure the registry has appropriate governance measures in place to help ensure the registry can meet its objectives, such as processes and procedures governing the operation of the registry, adequate training of staff, and other recommended practices including:

- Defined processes and procedures for data collection, management and storage;
- A data dictionary and rules for validation of queries and edit checks of registry data;
- Conformance with **21 CFR part 11**, as applicable, including access controls and audit trails; and
- Adherence to applicable human subject protection requirements, including safeguarding the privacy of patient health information.

The draft guidance specifically recommends that sponsors interested in using a registry to support a regulatory decision should meet with the relevant FDA review division (e.g., through a Type C meeting), *before* conducting a study that will include registry data. Sponsors also should be prepared to submit protocols and statistical analysis plans for FDA feedback prior to conducting a study that includes data from registries.

Comments on the guidance should be submitted to the docket by February 28, 2022.