February 2012

FDA Issues Draft Guidance Regarding Safety Data Collection in Late-Stage Premarket and Postapproval Clinical Studies

On February 10, 2012, the U.S. Food and Drug Administration ("FDA" or "the Agency") announced the availability of a new draft guidance document entitled "Determining the Extent of Safety Data Collection Needed in Late Stage Premarket and Postapproval Clinical Investigations."[1] The draft guidance is intended to assist clinical trial sponsors in determining the amount and types of safety data to collect in late-stage premarket and postmarket clinical investigations for drugs or biological products, based on existing information about a product's safety profile.[2] FDA is seeking public comments on the draft guidance and recommends submission by April 10, 2012, to ensure that comments are considered in the development of the final guidance.

Background

A key component of a development program for drugs, including biological products, is clinical testing to gather information regarding the drug's risks. In the late stages of development or postmarketing period, the collection of certain safety data may no longer be useful because risks have been adequately evaluated and characterized in previous data collection. Further, the gathering of additional safety data may not only be unnecessary but may even have detrimental effects on research, such as deterring the conduct of clinical trials or discouraging clinical investigator participation. In such cases, a selective and targeted approach to safety data collection may be warranted and, among other things, may (1) improve the quality and utility of a drug's safety database, (2) reduce the burden on clinical trial investigators and subjects and (3) decrease costs.

The following summarizes FDA's recommendations regarding how and when to implement simplified safety data collection. As always, sponsors should first consult with the relevant FDA review division before implementing any such proposed plan.

Recommendations for Targeted Safety Data Collection

A variety of factors affect the amount and types of safety data that are collected during clinical trials and observational safety evaluations. These factors include but are not limited to the disease being treated, relevant patient population, preclinical findings, any prior experience with the drug and/or drug class, phase of drug development and study design. Types of safety data that may be collected include:

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[1] Draft Guidance for Industry on Determining the Extent of Safety Data Collection Needed in Late Stage Premarket and Postapproval Clinical Investigations; Availability; 77 Fed. Reg. 7166 (FDA, HHS Feb. 10, 2012).

[2] Guidance for Industry: Determining the Extent of Safety Data Collection Needed in Late Stage Premarket and Postapproval Clinical Investigations; Draft Guidance (FDA, HHS Feb. 2012), *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM291158.pdf.

- Serious adverse events (expected or unexpected);
- Adverse events that lead to treatment discontinuation or dose modification;
- Nonserious adverse events (expected or unexpected);
- Routine laboratory data (e.g., basic blood and urine analyses);
- Specialized laboratory data (e.g., radiographic tests, EKGs, pulmonary function tests, lipid fractions);
- Physical examination findings;
- New concomitant medications (post-enrollment); and
- Patient history (e.g., concomitant illnesses and medications at baseline, prior treatment and medical histories, cardiovascular risk factors).

The Agency advises that the first two types of data, as well as laboratory tests of particular interest for the study or population, should always be collected. As to the remaining types of data, it may be appropriate to forgo or limit their collection in the later phases of drug development or postmarketing studies.[3]

Circumstances In Which Targeted Data Collection May Be Appropriate

In considering a targeted approach to safety data collection, the draft guidance emphasizes the importance of preserving the ability to identify new safety problems and avoiding premature adoption of a selective approach. In general, selective or targeted safety data collection is appropriate under the following conditions:

- A sufficient number of patients has been exposed to the drug in prior studies to characterize the safety profile for all but rare events;
- Adverse events have been generally similar across multiple studies; or
- A reasonable basis exists for concluding that adverse events in the population to be studied will be similar to previously observed rates.

The draft guidance states that these criteria are most likely to exist in postmarket studies (specifically, studies of new indications, studies conducted to meet postmarketing requirements and large outcome trials) and late phase 3 studies.

Safety Data That May Be Appropriate For Abbreviated Collection Or Noncollection

When appropriate circumstances for selective or targeted safety data collection exist, the FDA has identified the following types of data as appropriate for modified collection:

- Nonserious adverse events not associated with drug discontinuation;
- Routine lab monitoring;
- Information on concomitant medications; and
- Patient history and physical exams.

[3] The draft guidance is not intended to affect adverse event postmarketing requirements established by 21 C.F.R. §§ 314.80 and 600.80.

Methods for Targeted or Selected Collection of Safety Data

Based on FDA's recommendations, any plan for targeted or selective safety data collection should be clearly described in the study protocol. Specifically, the protocol should identify the types of data that will not be collected, collection of safety data limited to a subset of the study population (including methods for targeting patient subsets) and any decrease in the frequency of data collection.

When Comprehensive Data Collection Is Generally Needed

The draft guidance explains that comprehensive safety data collection is generally expected in the following circumstances:

- Development programs for original applications;
- Postmarketing studies involving differences in patient population, dose or other conditions of use;
- Development programs for orphan indications; and
- Assessments of specific adverse events and baseline risk factors.

Types of Data That Should Typically Be Collected

Finally, although some types of data are appropriate for selective or targeted collection, the following types of safety data should almost always be collected:

- Data in special populations;
- Data on all serious adverse events, deaths, events that lead to dose modification or treatment discontinuation, and adverse events that are troubling due to their potential seriousness (e.g., suicidal ideation or thoughts);
- Data for all study subject withdrawals;
- Targeted adverse event data; and
- Data characterizing the time course of risk for long-term exposure to chronic usage treatments.

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