



Special Protocol Assessment Can Expedite Development Programs

Contributed by David Facklam, MS - Senior Director, Regulatory & Scientific Affairs

A strategic approach to expedite the development of a pharmaceutical product can include the Special Protocol Assessment (SPA) process offered by the FDA (The European Medicines Agency offers a similar program called Scientific Advice or Protocol Assistance Request).

The SPA was established with reauthorization of the Prescription Drug User Fee Act (PDUFA) in 1997 to evaluate the adequacy (design, conduct and analysis) of certain proposed studies for the development of human drug products. [In May 2002, the FDA issued a guidance that describes the procedure.](#)

There are three types of protocols that are eligible for SPA:

- Animal carcinogenicity protocols
- Final product stability protocols
- Clinical protocols for Phase 3 trials whose data will form the basis for an efficacy claim (in an original or supplemental NDA/BLA) under the following conditions:
 - If the study has been the subject of discussion at an End-of Phase 2/pre-Phase 3 meeting
 - Or, if the division agrees to such a review because the division is aware of the developmental context of the protocol and issues (typically used with supplemental NDAs)

How does the FDA SPA process work?

Phase 3 clinical trials are the most commonly requested type of SPA request, so this description will focus on those.

The SPA directs the FDA to meet with sponsors for the purpose of reaching agreement on the design and size of clinical trials.

The FDA will provide a written agreement if an agreement is reached. If FDA and sponsor fail to reach agreement, the FDA will issue a letter clearly stating the reasons. The FDA has 45 days to respond to an SPA request, and an SPA will not be provided after a study has started. Overall, the PDUFA goal of 45 days is met for 90% of requests.

An SPA request should be submitted at least 90 days prior to the start of the proposed study. A request should contain the complete protocol and focused questions concerning specific issues regarding the protocol. To facilitate discussions, it is highly recommended that additional detail be provided in a separate document to allow the Agency to make an adequate evaluation of the protocol. Examples include:

- Context of the role of the proposed study in the overall development of the product
- Information supporting the overall design, selection of the primary efficacy endpoints, sample size and choice of control
- Anticipated regulatory outcomes and proposed labelling that would be

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PANCREATIC CANCER ACTION NETWORK

The Pancreatic Cancer Action Network is a nationwide network of people dedicated to working together to advance research, support patients and create hope for those affected by pancreatic cancer.

Nominated by:
Brittany Donovan - Senior Study Coordinator

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supported by the study

There can be interactions between sponsor and FDA during the 45-day assessment period.

Per the guidance, SPAs are considered binding except in the following circumstances:

- Failure of a sponsor to follow a protocol that was agreed upon with the Agency
- Relevant data, assumptions, or information provided by the sponsor in a request for SPA change are found to be false statements or misstatements or are found to omit relevant facts
- FDA and the sponsor agree in writing to modify the protocol and such modification is intended to improve the study.
- The Director of the review division determines that a substantial scientific issue essential to determining the safety or efficacy of the drug has been identified after the testing has begun

The FDA's Office of Hematology and Oncology Products recently summarized a review of all SPAs submitted between 2003 and 2013 (Maher VE et al. *J Clin Oncol* 2014;32:suppl e17511). A total of 532 SPAs were submitted with 344 being original submissions. Of the 532 submissions, agreement was reached on 132 (25%). Of those 132 protocols, 30 were submitted to the Agency as part of an NDA/BLA.

CTI has extensive experience working with sponsors to prepare and navigate the SPA process

Partnering with an experienced regulatory group, such as CTI's regulatory team, is essential in determining when an SPA represents a strategic approach to expediting a development program versus when it poses the risk of lost time/resources due to a premature or inappropriate attempt to use this unique regulatory pathway.

Our experience indicates the following:

- The SPA process is widely used
- The review cycle is often longer, and at times, much longer than the 45-day review goal
- The greatest benefit is likely to be seen in therapeutic areas with significant uncertainties, such as a cutting-edge area of research or first-in-class compound
- Agreements are not necessarily binding and often change as a result of changing standards of care

For more information:
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Upcoming Meeting Spotlight

Outsourcing in Clinical Trials West Coast
San Mateo, CA
February 10-11, 2016



**Stop by and visit us at
Booth #20 throughout the meeting!**

[Click here](#) to schedule a meeting with us while we're at Outsourcing in Clinical Trials West Coast!

Upcoming Meetings We Will Be Attending

Phacilitate Cell and Gene Therapy World
Washington, DC
January 25 - 27

Alliance for Regenerative Medicine Rare Disease Clinical and Patient Education Roundtable
Washington, DC
January 27

Outsourcing in Clinical Trials West Coast
San Mateo, CA
February 10 - 11

To schedule a meeting with us at one of these, please [click here](#)

New Additions & Promotions at CTI

Rick Bohnke promoted to Assistant Director, Clinical Data Management

Lisa Campbell promoted to Assistant Study Manager

Jennifer Graham joins as Senior Administrative Assistant, Accounting

Flávia Gois joins as Clinical Trial Assistant, Latin America

Melissa Martz joins as Senior Clinical Safety Scientist

Dave McCollum promoted to Director, Biostatistics

Robert McRae promoted to Manager, Business Development & Client Management

Join our Team!!
We're looking for individuals to fill these positions:

Assistant Director, Global Safety & Pharmacovigilance (Cincinnati, OH or Raleigh, NC)

Associate Director, Health Outcomes Research (Cincinnati, OH; Philadelphia, PA; Raleigh, NC)

Clinical Research Associate (US, Germany, France, Spain, Australia, Brazil, Korea, Taiwan, Japan, Argentina)

Clinical Research Coordinator (Cincinnati, OH)

Information Technology Support Specialist (Cincinnati, OH)

Medical Director (Cincinnati, OH)

Regulatory Specialist (Cincinnati, OH)

Senior Analyst/Statistician, Health Outcomes Research (Cincinnati, OH; Philadelphia, PA; Raleigh, NC)

Study Coordinator (Cincinnati, OH)

Study Manager (Cincinnati, OH; Raleigh, NC; Philadelphia, PA; San Francisco, CA; Ulm, Germany; Paris, France; Madrid, Spain)

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