REGULATOR-PROOF YOUR STUDY

EARLY PHASE CLINICAL TRIAL MAXIM #2

Working closely with regulators is a key strategy for successful drug development, not a barrier to be sidestepped or overcome. Early and frequent consultation with regulators helps to avoid surprises during all phases of product development, particularly in the earlier phases.

Building regulatory advice into a trial program is an effective strategy to mitigate the regulatory risk inherent in product development and improve the likelihood of early product approval.

Regulators in both Europe and the United States have created tools to help developers to tailor research and development programs to meet regulatory needs: "the request for scientific advice".

Requesting scientific advice from the right regulatory body at the right time has become an essential tool to guide product development and to have answer on many aspects of the development program:

- Have I chosen the correct and most appropriate animal model? And if there is no pre-defined animal model, is my proposal appropriate?
- Is my FIH starting dose well calculated?
- Is the manufacturing process well defined and appropriate?
- Have I well classified my IMP? Chemical, biologic, vaccine, ATMP, herbal?
- Have I selected the appropriate comparator for my patient studies? Placebo/other treatment?
- Are my trials sufficiently statistically powered?
- Do I have sufficient data to start pediatric trials?
- Am I able to replace certain trials (TQT, Drug Drug interaction, …) by modeling and simulation?

Requests for advice – and responses – can be multidisciplinary and focus on a broad range of questions from product quality to acceptance of novel study designs, pharmacokinetic/pharmacodynamic modeling, biomarkers, hard versus surrogate endpoints or any other scientific question. Advice is also available on quality, nonclinical and clinical issues as well as pediatric issues in parallel with FDA, the World Health Organization (WHO), payers, patients and academic stakeholders.

The European Medicines Agency (EMA) provides financial incentives for small and medium-sized enterprises (SMEs) to seek scientific advice early and often. SMEs can expect fee reductions of up to 100%, as can larger companies seeking advice on products with orphan designation or products intended for pediatric-only use.

With regard the US Food and Drug Administration (FDA), the agency is committed to multiple iterative meetings with sponsors during the preclinical and clinical phases of development. The Prescription Drug User Fee Act (PDUFA) sets fees for scientific advice. PDUFA also incorporates fee waivers and reductions at the new drug application (NDA) and biological license application (BLA) stages for products with priority, fast track status, breakthrough designation, new molecular entities as well as products that face significant barriers to innovation.

CASE STUDY 1

The Importance of discussing non-clinical and manufacturing strategy before initiating a phase I trial
Scientific Advice for phase I trial for a diabetes product

A US Biotech company contacted SGS to advise them on their non-clinical and manufacturing plan, as well as their FIH study outline, and to assist them in a Scientific Advice meeting with a European National Authority, for their innovative diabetes product.

SGS reviewed the available in vitro and in vivo non-clinical data as well as the proposed GMP manufacturing plan. A number of questions for the agency were prepared and the briefing book developed. An innovative study design based on an approach usually used in oncology was also prepared.

During the Scientific Advice process the following was discussed:

- Validation of testing strategy and analysis steps in the manufacturing program, particularly the adventitious agent testing
- Approval for the GLP non-clinical program, in particular for the choice of animal model, as there was no 'standard' animal model available for this type of compound
- Design of phase I trial, where the 'oncology based' design was validated by the regulator
- Agreement by the regulator the FIH study can be performed in patients

The successful advice allowed the company to start its non-clinical program quickly and assured a smooth approval of the FIH trial.

CASE STUDY 2

Agreeing with regulators on 'late phase' regulatory strategy

European biotech company with a compound in phase IIa in women's health

SGS worked with a European biotech company with a women's health compound in phase II, to design the phase IIb/III regulatory strategy and to have it validated by both the FDA and the EMA. The regulatory strategy was designed and worked out together with the sponsor and their license partner.

- An agency meeting with both the FDA and EMA was organized to discuss:
- Set-up of the further clinical program
- Assessments to be conducted in the phase IIb study
- Further non-clinical testing, in particular carcinogenicity testing
- Development plan for specific sub-indication

The Agency meeting with both the FDA and the EMA gave a favorable result, as a clear outcome for phase IIb program was received and a more limited number of assessments for phase III was obtained.

The clear message from regulators in both Europe and the United States is that it is never too early to seek scientific advice. Whether the questions deal with broad issues of study design and appropriate indication/study population or more focused issues of chemistry, manufacturing and controls for a new product class, earlier agency consultation is better. Seeking and incorporating scientific advice into the product development program is an effective tool to reduce the regulatory risk inherent in product development and maximize the likelihood of product approval.

CONTACT INFORMATION

EUROPE

+32 15 27 32 45

clinicalresearch@sgs.com

WWW.SGS.COM/CRO

NORTH AMERICA

+ 1 877 677 2667

clinicalresearch@sgs.com

JOIN THE SCIENTIFIC COMMUNITY
CONNECT ON LINKEDIN

Discover and share current R&D market news and events including bioanalytical laboratory and clinical research drug development information.

www.sgs.com/Linkedin-Life