It’s never too early to start crafting a global regulatory submissions strategy. Both the European Medicines Agency (EMA) and EU Member State National Competent Authorities (NCAs) offer scientific advice (SA) to drug sponsors from the early stages of the development process. The EMA’s SA often comes in written form, although the Scientific Advice Working Party (SAWP) may invite the sponsor to meet, if warranted. In contrast, many NCAs offer face to face meetings. Likewise, the FDA grants meetings in advance of an investigational new drug (IND) application filing, as well as End of Phase I or End of Phase II (EOPI or EOPII) meetings to those who request one.

But while early engagement with regulatory authorities sounds like an obviously good thing to do, there are some potential pitfalls.

By Bridget Heelan
Vice President, PAREXEL Consulting
BOOSTING REGULATORY SUCCESS RATES, SHORTENING CLINICAL DEVELOPMENT

EMA data suggest advice can boost success: between 2008 and 2012, 85% of marketing authorization applications (MAAs) that received and followed early SA were approved, as opposed to only 41% that did not (Hofer et al., 2015).

Early meetings can also shorten clinical development timelines. One recent study looked at 132 new product applications submitted to the FDA’s Center for Drug Evaluation and Research (CDER) between 2008 and 2012. It found that the 49 marketing applications which followed a pre-IND (PIND) meeting had a median clinical development time (CDT) of 6.4 years; whereas the 83 applications submitted without a PIND meeting had a median CDT of 8.3 years (Vu and Pariser, 2014).

MAXIMIZE BENEFITS AND MINIMIZE HAZARDS WHEN SEEKING SA FROM THE EMA

The EMA recommended 93 medicines for marketing authorization in 2015, including 39 novel drugs. According to the agency’s annual report, about half of all applicants who won a positive recommendation had requested and received SA at some point during development; that figure rose to 85% for medicines containing a new active substance (European Medicines Agency, 2016).

Advice provided by the SAWP or by an NCA is not binding, but it can certainly be useful. However, minutes from scientific advice sessions must be included in any future MAA, whether a sponsor is pursuing a centralized or decentralized approach. Sponsors who choose not to follow advice must explain and justify that decision.

Companies must, therefore, carefully consider the issues on which they would like advice, and reflect on the possible consequences beforehand. In PAREXEL’s experience, there are several benefits of obtaining SA, and some hazards to avoid.

Benefits of Seeking Scientific Advice

• Preparation of briefing documents can strengthen and refine the product value story (i.e., clear position statements, strong justification for planned approach) at an early stage.

• Seeking agreement on planned trial design and endpoints prior to initiating trials can help avoid regulatory delays.

• Early engagement can establish a constructive working relationship with regulators.
Hazards of Seeking Scientific Advice

• Poorly-prepared briefing documents can increase chance of unwanted outcome.
• Lack of agreement on development plan can lead to delays and increased costs.
• Obtaining and adhering to advice does not guarantee that HTAs will consider the clinical data sufficient.

GETTING THE MOST OUT OF PRE-IND AND OTHER EARLY-STAGE FDA MEETINGS

PIND meetings, by definition, can be conducted at any time before an IND submission, and may include discussions of clinical data developed outside the US. Early meetings can be especially helpful for new chemical entities, novel indications, orphan drug products, and biologics – in other words, for situations where there is no established regulatory roadmap regarding clinical efficacy endpoints or pharmacologic or toxicological signals of concern.

To reap the full benefits of meetings with the FDA, sponsors should:

• Request a meeting at the right time. That means at a point when you can incorporate FDA’s development guidance into your program. Schedule meetings to discuss specific issues—with focused, specific questions. Do not ask open ended or hypothetical questions.
• Take the lead. Don’t be passive. Summarize the discussion, outline agreements, list action items. Make sure all of concerns/questions have been addressed before you leave the meeting. Review the FDA’s official meeting minutes and notify the agency of any discrepancies. Ask for clarification
• Do their homework. Even in early development, you should provide a robust information package for the review team, including an analysis of the indication (disease, syndrome, or symptom to be treated), the medical need, and the expected benefits/risks of your product, along with the proposed clinical trial program.

In PAREXEL’s experience, the positives of early regulatory engagement outweigh the negatives. However, only for sponsors that are well-prepared.

REFERENCES
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