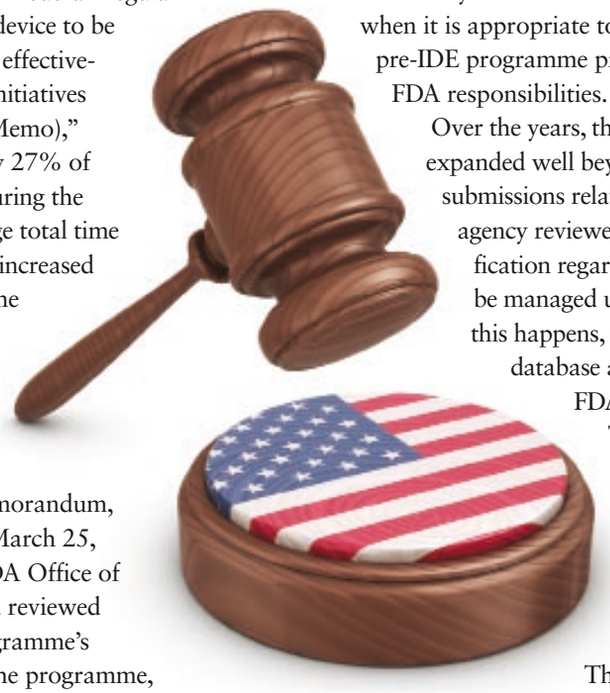
The Pre-IDE Programme Becomes the Pre-Submission Programme

Seventeen years ago, US FDA introduced the pre-IDE programme to help improve the medical device clinical study approval process. Over the years, the scope of the programme broadened significantly. This article discusses important new draft guidance that describes a new pre-submission programme and includes updated advice on procedures for meetings with agency staff.

Maria Donawa

When the pre-Investigational Device Exemption (pre-IDE) programme was introduced in 1995, it was intended to increase the approval rate of Investigational Device Exemption (IDE) applications and reduce approval times for original IDEs. An IDE, as specified in 21 Code of Federal Regulations (CFR) 812, allows an investigational device to be used in a clinical study to collect safety and effectiveness data. In a memorandum, "Goals and Initiatives for the IDE Program, #D95-1 (Blue Book Memo)," US FDA stated that in fiscal year 1994, only 27% of original IDE applications were approved during the initial review period. In addition, the average total time from receipt of the application to approval increased to 242 days; it had averaged 178 days for the previous 5 years. To address these problems, the agency introduced the pre-IDE programme, which included pre-IDE meetings, pre-IDE submissions and an interactive review process.



In 1999, US FDA published another memorandum, "Pre-IDE Program: Issues and Answers – March 25, 1999 (D99-1)," which reported that the FDA Office of Device Evaluation (ODE) had received and reviewed about 200 pre-IDEs per year since the programme's launch. In spite of the declared success of the programme, the agency explained that it had received complaints from industry that in some instances the programme was so burdensome and time consuming that future participation in it was jeopardised. Some sponsors complained that they felt "locked into" the pre-IDE programme and could not submit the formal IDE application until all of the issues raised by US FDA were resolved. In response to these and other complaints, the 1999 memorandum, which remains in effect until the pre-submission draft guidance becomes final, provided clarity on the intent of the pre-IDE programme; described when it is appropriate to use the programme; and explained pre-IDE programme procedures, including sponsor and US FDA responsibilities.

Over the years, the scope of the pre-IDE programme has expanded well beyond pre-IDE meetings and pre-IDE submissions related to IDE applications. For example, agency reviewers may decide that a request for clarification regarding a premarket submission should be managed under the pre-IDE programme. When this happens, the request is entered into the pre-IDE database and the requester is informed that US FDA will try to respond within 60 days. This timeframe is defined by US FDA policy and is not mandated by law or regulation.

Useful new draft guidance

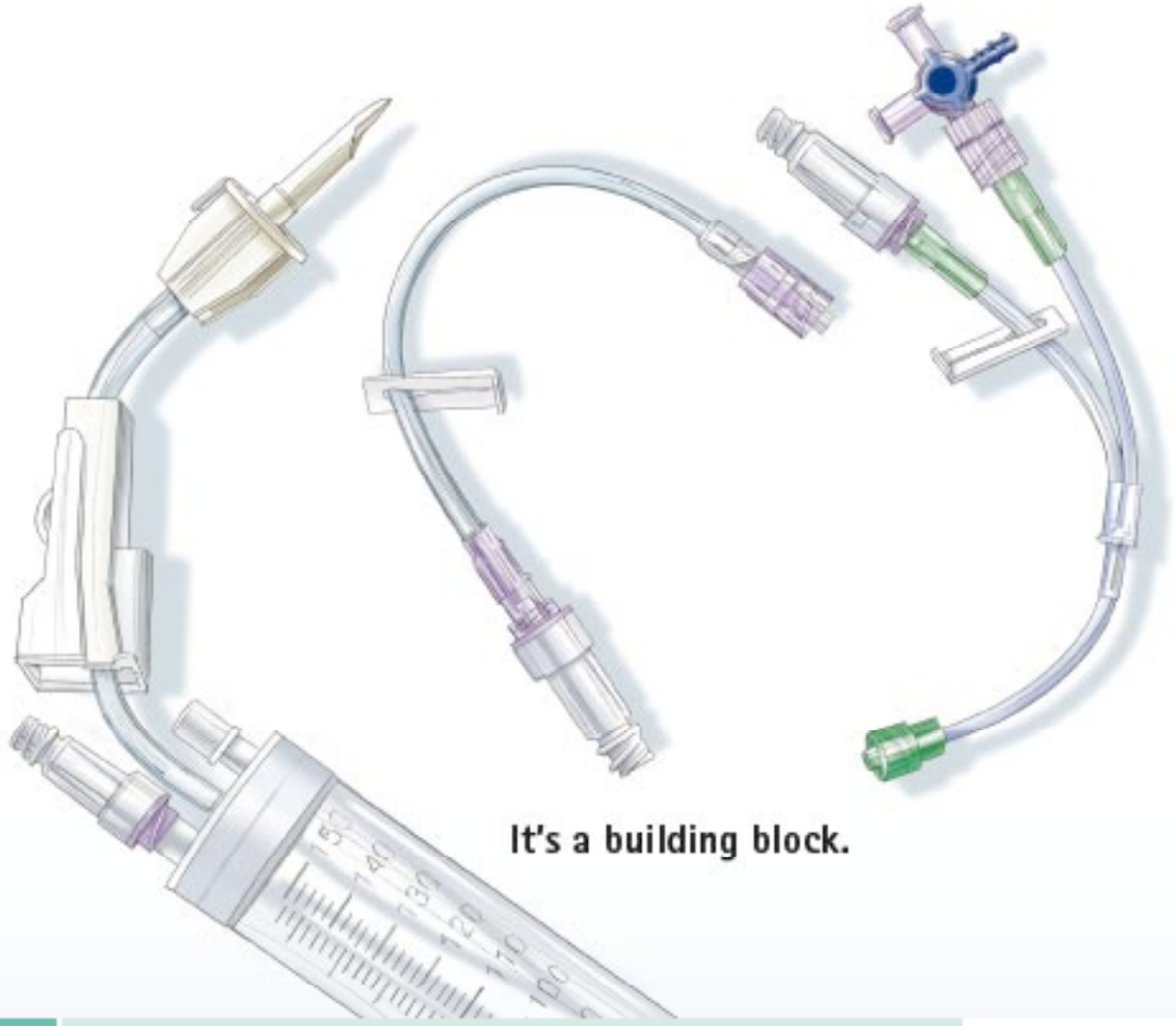
On 13 July 2012, FDA issued new draft guidance, "Medical Devices: The Pre-Submission Program and Meetings with FDA Staff," which can be found at www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm310375.htm. Readers should note that comments on the draft guidance can be submitted at any time.

Image: pagadesign/iStockphoto.com

Dr Maria E. Donawa

A physician, pathologist and pharmacist with nearly 30 years' regulatory experience, Maria E. Donawa worked with US FDA before becoming President of what is now Donawa Lifescience Consulting, a full service European CRO and international consultancy company that provides regulatory, quality and European Authorised Representative services to life science companies.

It's not just a device.



It's a building block.

Start with one of our components and build from there. B. Braun OEM Division manufactures hundreds of standard and custom fluid administration products ready to be integrated into your design. We have the extrusion capabilities to make devices of varying sizes and materials. As a full-service OEM supplier, we can help save you time and money with our engineering, packaging, sterilization and regulatory expertise. For details, visit www.bbraunoem.com or call +1-610-997-4685.

B. Braun Medical | OEM Division | USA

B|BRAUN
SHARING EXPERTISE

However, to ensure consideration of comments before work begins on the final version of the guidance, electronic or written comments should be submitted by 11 October 2012. Electronic comments can be submitted online at www.regulations.gov/#!submitComment;D=FDA-2012-D-0530-0001.

The purpose of the draft guidance is to update the pre-IDE programme, as it has evolved to include a mechanism to obtain US FDA feedback not only on future IDE applications before their submission, but also on Premarket Approval (PMA) applications, Humanitarian Device Exemption (HDE) applications, Premarket Notification (510(k)) submissions, and to address other regulatory questions regarding a specific device. It also broadens the scope of the programme to include devices regulated by the Center for Biologics Evaluation and Research (CBER). As a result, the draft guidance announces that the name is being changed from the pre-IDE programme to the pre-submission (Pre-Sub) programme. It is important to note, however, that the primary purpose of the Pre-Sub is the same as the pre-IDE programme—to provide applicants with an opportunity to obtain US FDA feedback before an IDE or premarket submission.

The draft guidance is a 35-page document that provides detailed information on general aspects of the programme, such as when to submit a Pre-Sub, the Pre-Sub process, what the Pre-Sub programme is not, and the various ways in which US FDA can provide feedback after receiving a Pre-Sub. The draft guidance provides specific examples of when a Pre-Sub would be particularly useful; in the case of a new device that involves novel technology, for instance, it may be advantageous to obtain early feedback on specific questions during the submission preparation and to familiarise the US FDA review team with the technology in advance of the submission. Another example is when the new device is an in vitro diagnostic (IVD) device that contains new technology, a new intended use, a new analyte, new clinical questions, complex data/statistical questions and/or where the predicate or the reference method is unclear or uncertain.

The draft guidance also describes the types of feedback that US FDA does not consider to be Pre-Sub, such as general information requests directed towards the Center for Devices and Radiological Health (CDRH) Division of Small Manufacturers, International and Consumer Assistance or the CBER Manufacturers' Assistance and Technical Training Branch. Other examples of feedback not meeting the definition of a Pre-Sub are general questions regarding US FDA policy or procedures and requests for clarification on technical guidance documents, especially when contact details are provided by the agency in the guidance document.

Other sections in the draft guidance document describe information that should be provided with all Pre-Sub packages, including a cover letter, table of contents, device description, proposed intended use/indications for use, summary of previous discussions or submissions, overview of product development, specific questions, mechanism for feedback (preferences on how feedback is provided, such as through an in-person meeting, teleconference or e-mail, for example), and other logistical information.

The appendix of the draft guidance includes recommendations for specific types of Pre-Subs including IDE applications; a non-significant risk, exempt, or outside the US clinical study; 510(k)s; PMAs; HDEs; and IVDs.

For example, the guidance on a Pre-Sub for an IVD suggests that, in general, it should include a cover letter, intended use statement, device description (including a description of the instruments, reagents and software), a development history and prior information, designs of proposed studies (including specimen information), analytical plan, clinical plan, statistical analysis plan, administrative information form, related literature and any specific questions that US FDA is asked to address.

Meetings with CDRH and CBER staff

The draft guidance addresses three types of meetings that can be requested of CDRH and CBER: Informational, Pre-Submission, and Submission issue meetings. The guidance does not cover agreement and determination or appeal meetings, nor does it cover the interactive review process. Readers interested in those types of meetings and processes should obtain information from the CDRH website: www.fda.gov/MedicalDevices/default.htm.

Informational meetings are for the purpose of sharing information with US FDA without expectation of feedback. The draft

guidance points out that these types of meetings may be useful when a company is planning multiple submissions within a six- to 12-month time period or when the company wishes to familiarise the US FDA review team about new devices with significant differences in technology from currently available devices.

The draft guidance specifies that Pre-Sub meetings may be conducted face to face or via teleconference. The intent of such a meeting is for US FDA staff to provide feedback on specific questions identified in the Pre-Sub. The draft guideline includes details on US FDA's current thinking on the timelines and procedures for requesting this type of meeting. Readers should review this section carefully and decide whether or not the timelines and procedures as described are reasonable and whether comments should be made suggesting alternative approaches. The draft guideline states that within 14 calendar days of receipt of a request for a meeting or teleconference, US FDA will determine if the request meets the definition of a Pre-Sub meeting. The agency states that it will aim to schedule a Pre-Sub meeting within 75 days, but no longer than 90 days, of receipt of the complete Pre-Sub. In rare cases where there is an urgent public health issue, US FDA will try to schedule the meeting within 21 days. At least three business days before the meeting, US FDA will provide initial feedback to the applicant by e-mail, which should include written responses to the applicant's questions; US FDA's suggestions for additional topics for the meeting or teleconference, if applicable; or a combination of both. Readers should refer to the draft guidance for additional details on this process.

Submission Issue meetings may be requested by a sponsor or applicant to discuss deficiencies identified during the premarket review of a 510(k), de novo, IDE, HDE or PMA application. These deficiencies may have been communicated in writing requesting additional information, indicating major deficiencies, or transmitting a "not approvable" letter, or by e-mail, telephone or fax. US FDA states that this type of meeting is intended to provide clarification of US FDA's questions or to discuss an approach to responding to complex issues and not to preview planned responses. The draft guidance states that US FDA will try to schedule Submission Issue meetings within 21 days of receipt of the meeting request.

Current pre-IDE submissions and meetings

The draft guidance document on the Pre-Sub programme and meetings with US FDA staff is not intended for immediate implementation. US FDA will receive comments on the document, consider the comments received, and decide whether or not modifications are needed. Nonetheless, readers may find that some of the guidance provided in this comprehensive document, with the exception of procedures that US FDA will not yet have implemented, may help them develop pre-IDE submissions or plan pre-IDE meetings or teleconferences more in line with US FDA's current thinking.

Maria E. Donawa
Donawa Lifescience Consulting, Piazza Albania 10, I-00153 Rome, Italy
tel. +39 06 578 2665 | medonawa@donawa.com | www.donawa.com