including information on indications, doses, safety, and manufacturing, suitable for the NDA or BLA.

- *Pre-NDA/BLA Meetings.* The sponsor and the FDA discuss how the application (NDA or BLA) will be organized.
- *Advisory Committee Meetings.* These meetings take place after submitting an NDA or BLA, and are conducted when the FDA needs advice from external experts and thought-leaders about the approvability of an application. Advisory Committee Meetings are open to the public. Advisory Committee members discuss the benefits and risks of the drug, and vote on whether to recommend it for FDA approval. The FDA is not required to follow the recommendations of its Advisory Committees, but it usually does. An Advisory Committee is used for about one third of new drugs (89).
- *Labeling Meetings.* Labeling meetings are held after an NDA or BLA is submitted and prior to the FDA approval of a drug. These meetings occur at the end of the NDA review process, when the FDA and the sponsor meet to agree on writing that informs physicians of the indications the product has been approved for, the dosages, and adverse drug reactions.

At these meetings, FDA expects the discussions to be driven by the data, with an emphasis on science and medicine, and that discussions focus on issues directly related to the product and to FDA regulations.

According to Grignolo (90), the Sponsor should not direct open-ended questions to the FDA, such as, the following: "The phase II trials demonstrated that several different doses were effective. Which dose do you recommend for our phase III trial?" Or, "How many subjects should be included in our phase III trial?" Or, "Our drug is effective against several diseases. Which should we select for further development?" Instead, at meetings with the FDA, the Sponsor's questions should take the form of reasoned proposals, such as the following. "Several different doses were tried, and the 5 mg and 10 mg doses were the most promising for our phase III trial. Do you agree?" Or, "Our statistical calculation shows that a phase III study with 1000 subjects will provide statistically significant results. Do you agree that 1000 subjects will be sufficient?"

c. Submitting the IND

The IND is submitted by way of *FDA Form 1571*. Form 1571 includes check boxes, indicating whether the IND is for a phase 1, phase 2, or phase 3 clinical trial. Form 1571 also has check boxes, indicating whether the IND submission includes, for example, a Clinical Study Protocol, an Investigator's Brochure, or a Pharmacology and Toxicology section.

After receipt of FDA Form 1571 and accompanying documents, the IND is routed to the appropriate division for review. FDA sends a letter of acknowledgment to the Sponsor, where the letter provides an IND number, date received, and name and telephone number of the FDA project manager (91). The Sponsor is permitted to begin the clinical trial at the time point of 30 days after the data are

[89]Lurie P. Financial conflicts of interest are related to voting patterns at FDA Advisory Committee meetings. MedGenMed. 2006;8:22 (1 p).

[90]Grignolo A. Meeting with the FDA in FDA regulatory affairs. 2nd ed. In: Pisano DJ, Mantus DS, editors. New York (NY): Informa Healthcare, Inc. p. 109–123.

[91]Holbein ME. Understanding FDA regulatory requirements for investigational new drug applications for sponsor-investigators. J. Invest. Med. 2009;57:689–93.