the NDA, for small-molecule drugs, and the BLA, for drugs that are biologicals. Before submitting the NDA or BLA, the Sponsor meets with FDA personnel in a pre-NDA meeting or a pre-BLA meeting. The subject matter of these meetings can include, for example, a review of the name for the drug, the planning of pediatric clinical trials, discussions of the risk management plan for use in the marketing phase, and the identification of manufacturing facilities (84).

Pre-NDA and pre-BLA meetings find a basis in 21 CFR §312.47b (2), which states that the main goal of these meetings is to uncover unresolved problems, to identify those studies that the Sponsor is relying on as adequate and well-controlled to establish the drug's effectiveness, to discuss methods for statistical analysis of the data, and to discuss the best approach to the presentation and formatting of data in the marketing application.

The purpose of the pre-NDA or pre-BLA meeting is to discuss filing and format issues. Topics of discussion include the adequacy of the data and information possessed by the Sponsor to warrant submission of the NDA or BLA, the need for an Advisory Committee, and the need for a Risk Evaluation and Mitigation Strategy (85). Also, discussions in these meetings concern the relationship between the manufacturing, formulation, and packaging of the drug product used in the phase 3 studies and the final drug product (as intended for marketing), and assurance that any comparability or bridging studies agreed upon at the end-of-phase 2 meeting have been completed, assuring that the NDA or BLA submission will contain adequate stability data in accordance with stability protocols agreed upon at the EOP2 meeting, and confirming that all facilities (eg, manufacturing, testing, packaging) will be ready for inspection by the time of the NDA or BLA submission (86).

The most important meetings with the FDA are the pre-IND meetings, end-of-phase II meetings, pre-NDA/BLA meetings, advisory committee meetings, and labeling meetings, as summarized below (87,88):

- *Pre-IND Meetings.* The sponsor presents nonclinical test data on efficacy and safety, data on the characterization and manufacturing of the drug, and the proposed Clinical Study Protocol. The goal is to acquire feedback from the FDA, in an effort to place the clinical trial on "active status," rather than on "hold."
- *End-of-Phase II Meetings.* After completing the phase II trial, the sponsor provides proof of concept for the drug or medical device, through data on efficacy from phase I and phase II trials, and from nonclinical data. Phase III trial designs are discussed,

[84]U.S. Department of Health and Human Services. Food and Drug Administration. Center for Drug Evaluation and Research (CDER) Good review practice: good review management principles and practices for effective IND development and review. Manual of Policies and Procedures (MAPP 6030.9); April 29, 2013 (42 pp.).

[85]Milstein J. FDA Meetings. Center for Drug Evaluation and Research (CDER). U.S. Food and Drug Administration. (slide presentation); June 20, 2013 (40 pp.).

[86]U.S. Department of Health and Human Services. Food and Drug Administration Guidance for Industry. IND meetings for human drugs and biologicals. Chemistry, manufacturing, and controls information; May 2001 (10 p).

[87]U.S. Department of Health and Human Services. Food and Drug Administration. Guidance for Industry. Formal meetings with sponsors and applicants for PDUFA products; February 2000 (13 pp.).

[88]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.