At these meetings, the 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 (104) 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 5mg and 10mg 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?"

b. Paper trail of FDA's decision-making process for individual drugs

The decision-making processes leading to regulatory approval of various drugs are available, at least in part, on the website of the FDA. The available documents include:

- Clinical Review,
- Pharmacology Review,
- Statistical Review,
- Approval Letter, and
- Package Insert.

These documents are available to the public at the following website.

http://www.accessdata.fda.gov/scripts/cder/drugsatfda/

c. Clinical review

The Clinical Review provides a background of the disease, tools for diagnosing the disease, as well as methods for assessing the stages of the disease. The document may also describe drugs already on the market.

The Clinical Review may identify all of the sponsor's clinical trials conducted to date, including specialized clinical trials, such as PK trials, and emergency-basis trials conducted on individual patients. The document may also list the sponsor's earlier submissions on the same drug, such as safety updates, responses to requests for information, and submissions of revised package inserts.

The Clinical Review may reiterate details of the study design for each of earlier and ongoing clinical trials, comment on methods of blinding, and identify personnel responsible for evaluating specific types of data.

[104] Grignolo A. *Meeting with the FDA in FDA Regulatory Affairs*. 2nd ed. In: Pisano DJ, Mantus DS, eds. New York, NY: Informa Healthcare, Inc.;109–123.