received. Following submission of the IND, receipt of the IND number, and initiation of the clinical trial, the Sponsor is required to provide FDA with other submissions, where applicable. These submissions include annual reports and amendments to the Clinical Study Protocol.

Further concerning FDA Form 1571, Holbein (92) reveals that "the serial number is 0000 with the initial application (section 10). Subsequent IND amendments increase the serial number by 1 in the order of submission."

The IND may or may not contain clinical data. According to Huff et al. (93), "[r]esults from a drug's CMC and nonclinical development programme are reported to the FDA in an IND application. This document is reviewed to see if clinical trials should be allowed to start." CMC means chemical manufacturing and controls (94). Title 21 CFR §312.23 also takes into account that a Sponsor may use one or more Contract Research Organizations (CRO) for conducting its laboratory research, clinical research, statistical analysis, drug manufacturing, and so on. Thus, with regard to the IND submission, the CFR states that what is required is a statement about the obligations transferred to the CRO. Referring to this statement, the CFR mandates that:

> [i]f a Sponsor has transferred any obligations for the conduct of any clinical study to a contract research organization, [what is required is] a statement containing the name and address of the contract research organization, identification of the clinical study, and a listing of the obligations transferred.

d. Submitting the New Drug Application or the Biological License Application

FDA defines the NDA and BLA, as follows (95). The New Drug Application (NDA) is the format for Sponsors to propose that a new drug be approved for sale and marketing in the United States. The Biologics License Application (BLA) is a request for permission to introduce a biologic product into interstate commerce. A BLA is submitted by the manufacturer and must contain data derived from nonclinical laboratory and clinical studies which demonstrate that the manufactured product meets prescribed requirements of safety, purity, and potency.

When *FDA Form 356h* is initially submitted, the space requesting the NDA number or BLA number is left blank (96). After submission of this form, FDA provides the NDA or BLA number, and the number is then used when the Sponsor subsequently submits supplemental information to the NDA or BLA.

The Investigator's Brochure is one of the components of the IND. The Investigator's Brochure finds a basis in 21 CFR §312.23 and 21 CFR §312.55. In short, the IND takes the form of a cover sheet (Form FDA-1571),

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

[93]Huff R, et al. The role of regulatory agencies in new drug development: a global perspective. J. Clin. Stud. 2014;6:20–22.

[94]U.S. Department of Health and Human Services. Food and Drug Administration Guidance for Industry. IND Meetings for Human Drugs and Biologics. Chemistry, Manufacturing, and Controls Information; May 2001 (15 pp.).

[95]U.S. Department of Health and Human Services. Food and Drug Administration SOPP 8401: administrative processing of Biologics License Application (BLA) and New Drug Application (NDA). Ver. no. 7; April 15, 2013 (35 pp.).

[96]Guidance kindly provided by Ms. Patricia Harley of FDA, in teleconference of February 11, 2015.