XII. TIMELINE OF FDA APPROVAL

a. Introduction

The timeline of FDA approval is activated when a Sponsor takes on the responsibility for product development and initiates a clinical investigation. The term "Sponsor" can refer to a person, organization, or pharmaceutical company. Submitting an IND is the first major step in the timeline. FDA assigns an IND number and reviews the application within 30 days. If no deficiencies are found, the IND becomes active and the study may proceed. In this textbook, the terms applicant and sponsor are generally used to mean the same thing. This textbook preferably uses Sponsor because the Sponsor is the party with the greater burden for complying with the rules in Title 21 of the Code of Federal Regulation.

But if deficiencies are found, FDA can impose a Clinical Hold. The Sponsor may request guidance for drafting the IND, prior to submitting the IND. This guidance can take the form of meetings with the FDA, and here, the Sponsor needs to submit information prior to the meeting. The Sponsor may also share new data during the meeting itself. Meetings prior to submitting an IND include informal discussions, mainly for reviewing preclinical data and their relevance to supporting entry of the drug in a clinical trial (72).

Legal aspects of an IND are described. By filing an IND, and by receiving FDA's approval of the IND, the Sponsor acquires an exception to laws that forbid the transport of drugs across state lines (73). In acquiring this exemption, the Sponsor is then free to conduct a typical clinical trial in human subjects, that is, a trial that involves transport of the study drug across state lines.

Prior to approving the initiation and conduct of any clinical trial on human subjects, FDA reviews the IND. The IND is reviewed by the Office of Pharmaceutical Science to provide feedback on drug quality, the Office of Clinical Pharmacology to evaluate data on pharmacokinetics (PK) and pharmacodynamics (PD), and the Office of Biostatistics to evaluate statistical plans (74).

After completing phase I, II, and III clinical trials, the Sponsor submits a NDA or a BLA. FDA has 180 days to review the NDA. If it finds deficiencies, such as missing information, the clock stops until the manufacturer submits the additional information. If and when the manufacturer is able to provide the information, the clock resumes and the FDA continues the review. When the FDA makes a final determination, it sends the Sponsor a "complete response letter" (75).

b. Formal Meetings with FDA

Formal meetings with the FDA include the pre-IND meeting (21 CFR §312.82), end-of-phase I meeting (21 CFR §312.82), end-of-phase 2 and prephase 3 meeting (21 CFR §312.47), and pre-NDA and pre-BLA meeting (21 CFR

[72]Feigal EG, et al. Perspective: communications with the Food and Drug Administration on the development pathway for a cell-based therapy: why, what, when, and how? Stem Cells Transl. Med. 2012;1:825–32.

[73]Feinsod M, Chambers WA. Trials and tribulations a primer on successfully navigating the waters of the Food and Drug Administration. Opthalmology 2004;111:1801–6.

[74]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.).

[75]Thaul S. How FDA approves drugs and regulates their safety and effectiveness. Congressional Research Service; June 25, 2012 (19 pp.).