SCIENTIFIC AND REGULATORY CONSIDERATIONS IN MEDICAL PRODUCT DEVELOPMENT

CERSI IMMERSION PROGRAM

UCSF-STANFORD CENTER OF EXCELLENCE
IN REGULATORY SCIENCE AND INNOVATION

Spring Quarter
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Stanford University
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INTENDED AUDIENCE: Graduate students, postdocs, academic researchers, life science and regulatory professionals

FORMAT: Face-to-face lectures, online activities, and group work

ASSESSMENT: In-class case studies

CORE COMPETENCIES
1. Discuss current regulatory system and structure relevant to drug development
2. Describe the drug development process and its current challenges
3. Describe two key FDA submissions: the IND and the NDA
4. Explain the principles of FIH studies and determining a starting dose
5. Contrast Phase 1, Phase 2 and Phase 3 clinical studies
6. Describe regulatory considerations for clinical trials
7. List oncology considerations for the design of clinical trials
8. Discuss different ways of interacting with the FDA
9. Explain the use of biomarkers in clinical drug development
10. Describe the regulatory requirements around biomarker qualification and assay validation.
11. Discuss the pathways for incorporating biomarkers into drug labels as companion or complementary diagnostics
1. INTRODUCTION TO US FDA

LECTURE 1: OVERVIEW OF U.S. LEGAL SYSTEM
LECTURE 2: FDA OVERVIEW
LECTURE 3: FDA REGULATORY AUTHORITY
LECTURE 4: FDA MEDICAL PRODUCT JURISDICTION

Lecturer: Natalia Khuri, MBA, PhD

Learning Outcomes
1. Discuss the historical events that led to enactment of the Food, Drug and Cosmetic Act of 1938, which forms the basis of current food and drug regulatory framework, and notable amendments.
2. Describe the current FDA organization and structure, with a focus on new drug review.
   - describe how medical products are defined and name FDA Centers responsible for the review of safety and effectiveness of these products
   - discuss the mission and regulatory remit of the U.S. Food and Drug Administration
   - describe and contrast laws, regulations and guidances used by the FDA to regulate medical products
   - describe the organizational structure of the agency
Lecture 1: Introduction to US Drug Regulation

Lecture 2: Drug Development Process

Lecturer: Robert Harris, PhD and Parnian Zia-Amirhosseini, PhD

Learning Outcomes

We review the history and evolution of the laws that give regulatory authority to US Food and Drug Administration. Laws, regulations, and guidances are discussed, with an emphasis on the manner in which they may be used to inform drug development. We also present the current principles, processes and stages of drug development in the pharmaceutical industry. Students participate in a case study that illustrates strategic factors to be considered when generating a drug development plan. Upon completion of this mini-course, students will be able to:

- describe current regulatory system and structure relevant to drug development
- describe the drug development process and its current challenges
- discuss two key FDA submissions: the IND and the NDA
LEcTure 1: Medical Devices and FDA Regulatory Pathways

Lecture 2: Regulatory Pathways and Medical Device Life Cycle

Lecturer: Michael Quinn, PhD

Learning Outcomes
You will learn the basics of U.S. regulation of medical devices in the context of the medical device development cycle. FDA’s regulations, guidance documents, and on-line informational resources will be highlighted and used throughout the course. Upon completion of this mini-course, students will be able to:

- describe how medical devices are defined
- name required features and characteristics of medical devices
- describe the steps needed to obtain approval to market a medical device
- describe how medical devices are assigned to regulatory classes
- use FDA’s web site to classify a device and determine its regulatory history
- explain the impact of regulatory pathways on medical device development
- describe the major phases of the Medical Device Life Cycle
Learning Outcomes
We will introduce key concepts in therapeutic drug discovery, focusing on large molecule discovery. The first lecture provides an overview of therapeutic target considerations, including what makes a large vs. small molecule target. The role of human genetic evidence as well as in vitro and in vivo biology studies in target validation will be discussed. The second lecture addresses large molecule therapeutic development. We will discuss manufacturing considerations for large molecules, including common manufacturing platforms utilized in the biopharma industry. Regulatory considerations for marketing large molecules will be presented. The case study will present an actual pre-clinical therapeutic antibody discovery and development program, and discuss decision points and potential pitfalls along the pathway to developing a therapeutic. Upon completion of this mini-course, students will be able to:

- Describe differences between target classes and tractability for either large or small molecule development
- Describe the types of tool molecules required for target validation
- List the types of information and data required to pursue a potential therapeutic target
- Describe different large molecule modalities and when they are used
- Describe properties of antibodies that enable therapeutic development
- Explain why manufacturability matters to the overall drug development process
- Discuss what makes a good target product profile
- List some common concerns regarding large molecule production
5. BIOMARKERS AND COMPANION DIAGNOSTICS

LECTURE 1: THE SCIENCE AND THE ART
LECTURE 2: PRECISION MEDICINE AND IVD COMPANION DIAGNOSTICS

Lecturer: Donna Flesher, PhD and Ning F. Go, MD.

Learning Outcomes
You will learn definitions and examples of biomarkers; discuss how they are qualified and validated, and how they are used in drug development both as pharmacodynamic endpoints and as tools for patient selection and “precision medicine” approaches to therapy. We will discuss issues and challenges inherent in bioassays and the measurement of biomarkers in the lab and in the clinic, including the setting of cut-off values and the interpretation of assay data. Finally, we will discuss in vitro diagnostics and their regulation - including the co-development of drugs and associated companion and complementary diagnostics. Using case studies and examples, attendees will be exposed to the myriad ways that biomarkers are used in modern drug development, regulatory science and clinical practice. Upon completion of this class, students will be able to:

- describe how biomarkers are used in clinical drug development to assess drug target coverage and toxicities, inform dose selection and select appropriate patients.
- explain the many considerations around the assessment of physiologic, metabolic and genetic biomarkers including sensitivity, specificity, and precision that influence how biomarker assays are made “fit for purpose.”
- discuss the regulatory requirements around biomarker qualification and assay validation,
- and the pathways for incorporating biomarkers into drug labels as companion or complementary diagnostics.
- describe the scientific, logistical and regulatory challenges and opportunities associated with drug/diagnostic co-development from laboratory, clinical trial and clinical practice/commercialization perspectives.
6. REGULATORY FRAMEWORK FOR MOBILE MEDICAL DEVICES

LECTURE 1: MOBILE HEALTH INDUSTRY LANDSCAPE
LECTURE 2: RELEVANT HEALTH CARE MACROECONOMICS, POLICY TRENDS
LECTURE 3: U.S. REGULATORY AGENCIES WITH MOBILE MEDICAL HEALTH OVERSIGHT
LECTURE 4: FDA’S OVERSIGHT APPROACH
LECTURE 5: MEDICAL DEVICE DATA SYSTEMS (MDDS) GUIDANCE AND FDASIA IT REPORT
LECTURE 6: GENERAL WELLNESS GUIDANCE
LECTURE 7: MEDICAL DEVICE ACCESSORIES GUIDANCE
LECTURE 8: REGULATORY TRENDS IN HEALTH IT
LECTURE 9: SOFTWARE AS A MEDICAL DEVICE AND CLINICAL DECISION SUPPORT SOFTWARE PART I
LECTURE 10: SOFTWARE AS A MEDICAL DEVICE AND CLINICAL DECISION SUPPORT SOFTWARE PART II
LECTURE 11: CDRH REGULATORY SCIENCE PRIORITIES PART I
LECTURE 12: CDRH REGULATORY SCIENCE PRIORITIES PART II
LECTURE 13: PRIVACY, CONFIDENTIALITY AND DATA SECURITY
LECTURE 14: GOVERNANCE OF HEALTH DATA

Lecturer        Martha Zanchi, PhD

Learning Outcomes
We expect that, upon completion of this course, you will be able to:

- discuss the regulatory approach, priorities and relevant guidances that the Food and Drug Administration has developed to clarify the scope of its regulations and to further promote development of mobile health products.
7. EARLY CLINICAL DRUG DEVELOPMENT

LECTURE 1: PRINCIPLES AND PRACTICE
LECTURE 2: INNOVATIVE APPROACHES & CLINICAL PHARMACOLOGY

Lecturer       Maurice (Maury) Emery, PharmD, PhD and Graham Jang, PhD, MBA

Learning Outcomes
You will learn about the overall components of an IND and pertinent regulatory guidances. The nature and types of nonclinical information that must be obtained and interpreted before dosing can occur in humans will be presented. We will discuss the regulatory guidance relevant to the design of an FIH trial and how nonclinical data are used to assess and reduce safety risks for patients and healthy volunteers and learn how Sponsors incorporate this information and the predicted pharmacology in humans to design FIH studies that enable decision-making in drug development. A high-level overview of the scope of Clinical Pharmacology-related guidance that impacts drug development will also be presented. Upon completion of this course, students will be able to:

- describe early development/First-in-Human (FIH) Studies
- discuss FDA guidances for Phase 1 studies
- describe traditional vs. innovative approaches to drug development
- discuss the impact of clinical pharmacology on drug development.
8. NON-CLINICAL SAFETY ASSESSMENT

LECTURE 1: INTRODUCTION TO NONCLINICAL SAFETY ASSESSMENT

Lecturer  Herve Lebrec, PharmD, PhD

Learning Outcomes
You will learn about generic workflow of studies performed during drug development, including target liability assessments, material requirements, types of studies. ICH guidances and non-clinical components of an IND submission will be discussed. We will emphasize predictability and present several failed drugs due to toxicity issues. Upon completion of this course, students will be able to:

- explain how target liability can be assessed
- name and describe requirements for material purity, stability and formulation
- name and describe non-clinical studies in drug development
- analyze ICH guidances for non-clinical studies
10. POST MARKETING CONSIDERATIONS FOR DRUGS

LECTURE 1: PHARMACOVIGILANCE
LECTURE 2: PRODUCT COMMUNICATION

Lecturer
Bruce Donzanti, PhD and Julie Kang Sallam, PharmD

Learning Outcomes
We will focus on two topics for postmarketing regulation of drugs: pharmacovigilance and communications. We will discuss the concepts and approaches used to identify an adverse event (AE), FDA AE reporting requirements, and potential post-marketing requirements (PMR)/commitments (PMC). We will provide an overview of regulations and industry practices related to product-specific Communications. Students will work in groups on a case-study. Upon completion of this class, students will be able to:

- describe historical perspective, regulatory concepts, and current practices for
- pharmacovigilance
- describe historical context for advertising and promotional regulations