Syllabus
US Food and Drug Administration, Drug Development, Science and Health Policy (PH 298.015)
UC Berkeley, School of Public Health
Thursday 6:30 – 8:20 PM

Course Description: This course is an in depth review of the history, authorizing statute and regulatory authority of US FDA and the influence and impact of FDA on science and health policy. Drug development, especially in the area of HIV/AIDS, is used throughout this course to demonstrate the interdisciplinary nature of the agency's mandate (basic sciences, statistics, clinical, toxicology, pharmacology, policy, law, political science, economic, foreign policy) and its impact on public health policy. HIV/AIDS examples are used as case studies to illustrate both the ability of public entities to affect FDA policy and FDA's impact on health and scientific policy.

Instructor:	Veronica Miller, PhD Jur Strobos, MD, JD, FACEP Forum for Collaborative HIV Research School of Public Health veronicam@berkeley.edu; jur@berkeley.edu Office hours: by appointment
GSI:	N/A
Attendance:	Students are expected to attend 14 classes each of one hour and fifty minutes duration. Class time will be divided between lectures and case study discussions. Students will participate in case study discussions based on materials assigned in the syllabus.
Grading:	Final exam (1/3); group-work based written assignment related to an HIV/AIDS regulatory and scientific policy; drug development issue; or, a hypothetical drug development plan (1/3); participation in socratic dialogue based on assigned reading materials (1/3). Questions for the final exam will require short essays; law students will have alternative questions based on the Food, Drug and Cosmetics Act (FDCA), Code of Federal Regulations Title 21 (21 CFR) and related regulatory guidance. The grading will follow the University of California at Berkeley policies (http://berkeley.edu/catalog/policies/grades.html). Cheating or plagiarism on exams is against the University regulations.
Textbooks:	A textbook is not required for this course. Course materials will be distributed electronically and will include selected excerpts from a variety of books and published articles; policy and regulatory documents of the US Food and Drug Administration; reports from the Forum for Collaborative HIV Research (www.hivforum.org) over its 15 year history as a public private partnership facilitating and enhancing drug research for HIV/AIDS; and excerpts from other publications, such as judicial opinions and FDA slide presentations (each sessions reading materials are provided in the syllabus). Reading assignments are listed in the course outline.

Course Objectives:

This course will provide an in depth consideration of the major issues in drug development focusing on the US Food and Drug Administration laws, regulations and guidance and using HIV/AIDS as exemplary. Drug products represent approximately 9% of the US economy. The regulation of drug

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products in the US and worldwide is the most comprehensive regulation of any scientific activity and serves as a model for the intersection of science, policy and regulation. The course includes an understanding of the history and development of the statutory framework, the scope of regulatory authority, and the process of completing a drug marketing application dossier. The history of current and historical HIV/AIDS drug development is covered from the impact on accelerated approval, on international pharmacovigilance and on international drug regulation and drug distribution (PEPFAR). The course has been designed with an interdisciplinary audience in mind. In discussions and assignments, students will be able to emphasize their own area of interest and/or expertise (*e.g.*, basic sciences, statistics, clinical medicine, toxicology, pharmacology, health policy, law, political science, etc). The course has been designed to benefit, and be critical to the education of, graduate students in medicine and those in public health, law, or business who envision a possible career in government or federally-regulated industry.

Course Learning Objectives

1) Describe and discuss the historical and public policies underlying current drug regulation and the impact on areas of international science outside drug development such as clinical trial design and statistics, manufacturing, drug safety and toxicology, medical ethics, basic sciences, and foreign policy, with a focus on HIV/AIDS.
2) Describe and discuss the major issues in first-in-man exposure to a new drug product including accelerated access, parallel track/treatment IND, ethical standards for medical research and their enforcement mechanisms.
3) Understand the role of the private sector including public private partnerships, industry, community activists, and academic medicine in the evolving development of federal health policy and research with a focus on HIV/AIDS.
4) Understand the process for developing a drug, the economic and financial impact; be able to prepare a draft drug development plan and prepare for employment in the pharmaceutical or related industries.
5) Critically read and discuss drug regulatory literature.

Course outline:

Session #	Topic
1/2 (Jan 19)	INTRODUCTION TO FDA Introduction, History and Structure of FDA, New Drug Application Content, Definitions of Terms (Drug, Device, Food, Intended Use, Indication/Labeling); Forum as a Model for Academic, Community and Industry Involvement in Development of FDA Policy and Regulations Background and/or Assigned Reading Materials: Excerpts from definitional sections of the Food Drug and Cosmetics Act; FDA Form 356h; *Kordel* and *Nutrilab*; excerpts of 21 CFR § 201.128; Industry Supported Continuing Medical Education; Keystone National Policy Dialogue on Establishment of Studies to Optimize Medical Management of HIV Infection. Ann Forum Collab HIV Res 1997; Hamburg MAA and Sharfstein JM. The FDA as a public health agency. NEJM 2009; 360:2493; Miller V. The Forum for Collaborative HIV Research: A model for an integrated and inclusive approach to clinical research and drug development. Clinical Pharmacology & Therapeutics 2009; 86:332; Miller V, Mani N, Williams D, Strobos J, Bartlett JG. A Forum for Collaboration: A successful public-private model for regulatory and scientific policy advancement.

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3/4 (Jan 26) CHEMISTRY AND MANUFACTURING CONTROLS
Statutory, regulatory and agency guidance on manufacturing process validation and controls; fresh orange juice manufacture; effect of formulation changes.

Background and/or Assigned Reading Materials:
Statutory Adulteration and Misbranding Sections; Excerpts from 21 CFR Part 211 & Part 610; CPG 490.100; Juice HACCP Hazards; Karim et al., Tenofovir Gel, *Science*.

5/6 (Feb 2) HIV/AIDS – HISTORICAL PERSPECTIVES ON THE EPIDEMIC
Origins, pathogenesis, physiology, drug therapy, epidemiology
HIV/AIDS biology; drugs, mechanisms of action; combination therapy
HIV/AIDS as driver of changing FDA policies: blood bank

Background and/or Assigned Reading Materials:
FDA Guidance on Antiretroviral Products; Review Article on HIV Biology and Therapy

7/8 (Feb 9) REGULATORY AND SCIENTIFIC STANDARDS OF EFFECTIVENESS
Statutory, regulatory and clinical guidance criteria; origin of randomized clinical trials; approval path for generic drugs; other modifications in traditional approval (fast track, accelerated approval, treatment INDs); early history of AIDS drug development (AZT, ddI, ddC).

Background and/or Assigned Reading Materials:
FDA Guidance on Demonstration of Clinical Effectiveness, 21 CFR § 314.126, Excerpts from Fisher's Design of Experiments, ICH Guidance on Good Clinical Practices, excerpts from FDCA § 505(j) (generic drugs); 21 CFR § 312.35 (treatment IND), Part 312 SubPart E, Part 314 SubPart H (accelerated approval); Zechman, Cheng, Miller. Rethinking the approach to expanded access programs. Ann Forum Collab HIV Research 2007; Vol 9

9/10 (Feb 16) PHARMACOLOGY AND TOXICOLOGY; FIRST-IN-MAN
Setting scientific standards for pharmacokinetics and pharmacodynamics
Good Laboratory Practices; Content and Criteria for Opening on IND

Background and/or Assigned Reading Materials:
21 CFR Part 58; Summary of ICH Criteria for Nonclinical Studies (Index of Safety Studies); FDA Slide Show on GLP (Industrial Biotest); Northwick Park.

11/12 (Feb 23) SAFETY
Pharmacovigilance, risk evaluation and mitigation strategies (REMS), serious adverse events and reporting regulations, data sources for post-marketing safety evaluation, safety hurdles of biomedical interventions to prevent HIV acquisition, global antiretroviral pharmacovigilance

Assigned Reading Materials:

Forum report on PrEP REMS; Forum paper on pharmacovigilance; excerpted statutory sections on REMS REMS; 21 CFR § 314.80; Bisson, Gross, Miller, Weller, Walker Monitoring of long-term toxicities of HIV treatments: an

international perspective. AIDS 2003; 17:2407; Triant, V et al CID 2011 (in press)

13/14 (Mar 1) PROOF OF CONCEPT AND DRUG RESISTANCE
In vitro and/or in vivo proof-of-concept requirements; HCV drug development requirements; HIV drug resistance; algorithm based resistance testing and approval process

Background and/or Assigned Reading Materials:
Clinical Guidance on Development of Directly-Acting Antivirals; Forum papers on criteria for HIV drug approvals

15/16 (Mar 8) INDs, IRBs, INFORMED CONSENT & ETHICS
US Tuskegee Syphilis Experiments, Helsinki Accord, Common Rule; Regulation of Human Pharmaceutical Clinical Studies.

Background and/or Assigned Reading Materials:
The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research; Helsinki Accords, Common Rule; 21 CFR Parts 50 and 52.

23/24 (Mar 15) DRUG DEVELOPMENT PLAN
Costs and time to development, sample drug development plan, enhancing predictability, market dynamics, return on investment, mechanisms for financing, regulation and control of launch and marketing plans and interaction with approved label

Background and/or Assigned Reading Materials:
Guidance on Directly-Acting Antivirals; sample drug development plan

17/18 (Mar 22) PUBLIC IMPACT ON FEDERAL POLICY AND FDA REGULATIONS
Handling of evolving public health needs, role of community, academic and industry, special populations, interactions with other federal agencies (NIH, CDC), federal advisory committees

Background and/or Assigned Reading Materials:
21 CFR § 312.47 (public meetings); excerpts of FDA Advisory Cmte Hearing; Snyder, Cheng, Miller. Regulatory considerations for the treatment of lipodystrophy. Ann Forum Collab HIV Research 2005; Vol 7

19/20 (Apr 5) FOREIGN POLICY
International investigations, interactions with international regulatory bodies, PEPFAR, TRIPS (Agreement on Trade-Related Aspects of Intellectual Property Rights), Doha Amendments to GATT, UN Conference on Non-Infectious Disease Amendments to TRIPS authority.
FDA, EMA and other agencies

Assigned Reading Materials:
WHO Report on Doha; PEPFAR report to Congress

21/22 (Apr 12) HIV/AIDS AND INNOVATIONS IN DRUG DEVELOPMENT
Mechanisms of action, evolution of standards for clinical review and approval,

recent developments, Recent Hamburg “Vision” - - future development of the FDA.

Background and/or Assigned Reading Materials:
Chemokine antagonist report; Series of HIV clinical trial design papers; HCV drug development – special populations; Sebelius, Health Affairs 2011

25/26 (Apr 19)	STUDENT ASSIGNMENTS Presentation of group projects
27/28 (Apr 28)	STUDENT ASSIGNMENTS Presentations of group projects
29/30 (May 3)	REVIEW Policy impact of FDA and review for final examination