

Law Course/Section	LAW 6390/23164 in person	LAW 6390/23173 online
Engineering Course/Section	EGN 6933/21160/BIO1 in person	EGN 6933/29055/BIO2 online

BIOTECHNOLOGY & MEDICAL AI POLICY

Prof. Barbara Evans – Spring 2021

Tuesday, Thursday 10:30 – 11:55 am (3 semester hours)

Syllabus Version 1-3-2020

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Brief description. An accessible survey of regulatory, privacy, and ethical issues with advanced biotechnologies and AI medical software, which can revolutionize healthcare and reduce nagging disparities but raise unsolved ethical and policy dilemmas. The course covers safety regulation by FDA and the U.S. Coordinated Framework and protections for privacy and individual rights. **No prerequisites or special legal or scientific background required.** The course is suitable for law students and engineering and science graduate students. The course requires no prior legal experience or special science/engineering background. It is suitable for anyone who will need to navigate the major regulatory, privacy, and ethics frameworks affecting discovery, commercialization, clinical translation, and payment for innovative medical products and software.

Course Materials. This course uses:

- (i) Clayton M. Christenson, Jerome H. Grossman, and Jason Hwang, The Innovator’s Prescription: A Disruptive Solution for Health Care (available in paperback)
- (ii) National Academies of Science, Engineering & Medicine, Preparing for Future Products of Biotechnology (2017) **provided in electronic form on Canvas**
- (iii) Institute of Medicine, Medical Devices and the Public’s Health (2011) **provided on Canvas**
- (iv) Government Accountability Office/National Academy of Medicine, AI in Health Care (and Health Settings Outside the Hospital and Clinic) **provided on Canvas**
- (v) Other readings, slides, supplements provided in electronic form on Canvas
- (vi) Links within this Syllabus point to regulatory agency materials. Accessing regulatory agency materials on-line, using the URL links in this Syllabus, is the best way to read them, because many regulatory documents have embedded links that make it easy for you to refer to relevant background material by clicking on the links.

Grading. See further in the **Resources and Course Policies** section below. There is no final exam. Grading is based 60% on a 1.5-hour exam to be administered approx. 2/3 of the way through the course on a date to be determined in consultation with students to minimize conflicts,

and 40% on a final short paper or project report on a topic students each choose in consultation with Prof. Evans. With approval from Prof. Evans, pairs or small groups of students can collaborate on the final short paper/project report.

	Tuesday	Thursday
Start of classes for engineering graduate students only	Intro for engineering students only 0.1(Jan 12) Lawsuit risks: ways to get sued, and ways to avoid it	Intro for engineering students only 0.2(Jan 14) How FDA regulation affects liability for AI/ML medical software
Start of classes for law students	1(Jan 19) Social & ethical issues with AI software; intro to FDA and the U.S. Coordinated Framework	2(Jan. 21) Healthcare business models: traditional and emerging
	3(Jan 26) The role of disruptive technologies in modern healthcare	4(Jan 28) The challenge of DIY biotechnology, genomics, neurotech
	5(Feb 2) Technology impacts across health care subsectors (providers, payers, pharma, devices, ...)	6(Feb 4) The uniquely American approach to regulating safety risks vs. the rest of the world. Which is better?
	7(Feb 9) Intro to FDA: What does FDA regulate? When? How?	8(Feb 11) Ways innovators fall under FDA regulation (without meaning to)
	9(Feb 16) What can innovators say? free speech vs. regulated speech	10(Feb 18) Intro to the device industry and types of medical devices
	11(Feb 23) Basics of FDA medical device regulation	12(Feb 25) Basics, <i>cont'd</i> and challenges regulating diagnostic devices and software
The date for online midterm to be agreed in early March, with the online midterm to occur in early April. Date will be selected in consultation with students to minimize scheduling conflicts	13(Mar 2) Review of topics-to-date and discussion of new regulatory challenges FDA is facing.	14(Mar 4) How to get paid for an innovative medical product: navigating the U.S. reimbursement system
	15(Mar 9) Special reimbursement challenges for novel technologies	16(Mar 11) Intro to research ethics and data privacy
	17(Mar 16) Who owns people's health data? Is it OK to use people's data without their consent?	18(Mar 18) Major privacy frameworks affecting access to data for research and medical AI (HIPAA, GDPR, others)
Period for review and consolidation of topics through March 30 to prepare for online midterm	19(Mar 23) Problem-solving: How to navigate privacy laws to get lawful, ethical access data for research, public health, medical AI software	20(Mar 25) Re-identification risks, return of results, and rights of people whose data are used in research and medical AI datasets
Online midterm to take place in early April.	21(Mar 30) Practical privacy and ethics problem-solving + review of privacy and research ethics	22(Apr 1) Student brief presentations and discussion of their proposed final projects or paper topics; class feedback
	23(Apr 6) Student brief presentations and discussion of their proposed final projects or paper topics; class feedback	24(Apr 8) Data-informed duties of AI software developers. Ethical and social impacts of biased software
	25(Apr 13) Ethical & social impacts of DIY bio, the sharing economy, and AI medical software: Will regulation as we know it break down?	26(Apr 15) Emerging liability issues with AI software, genetic reinterpretation, and other emerging medical technologies
	26(Apr 20) Unresolved policy challenges in the regulation of biotechnology & medical AI software. How to shape policy	end of classes – Student short papers or project write-ups due during final exam period (date to be finalized in consultation with students)

Short Summary of Major Topics Covered and Objectives

This list summarizes the major topics this course covers. They are not necessarily covered in the order listed here. See syllabus below and the summary chart on page 2 for the order of topics.

Topic 1. Introduction - Business models for disruptive innovation in health care

Learning objectives. Inventing a great technology will not, by itself, bring about transformative change. Other required steps can include developing an innovative business model and creating a value network that lets the new technology be delivered safely and at a price that works for both the consumers and the developers. After this unit, you will be able to: (1) define and recognize three distinct business models that have long existed in the medical product manufacturing and health care industries; (2) evaluate how technological innovations are disrupting existing business models and spawning new models; and (3) understand how the choice of business model can affect which regulator(s) innovators will have to deal with.

Topic 2. Introduction to consumer safety regulation: FDA oversight of medical products and its role in the U.S. Coordinated Framework for Regulation of Biotechnology

Learning objectives: Most researchers understand that their publications and speeches can affect their ability to claim patent protection for new products. Less well understood is the fact that their communications also affect whether FDA will regulate their products and what the specific regulatory requirements will be. After this unit, you will be able to: (1) recognize and define various categories of products that FDA regulates (e.g., drug, device, biological product, combination product, food, food additive, dietary supplement, cosmetic, tobacco product, etc.); (2) apply the factors that FDA looks at when deciding whether an innovative product falls under FDA's regulations; (3) understand that things researchers and inventors say, write, and publish can affect whether and how FDA will regulate their discoveries; (4) manage communications to optimize the regulatory pathways available to you.

Topic 3. Guiding new medical technologies through the relevant regulatory pathways

Learning objectives. This unit provides practice-oriented instruction on how to navigate the FDA framework and other relevant regulations to bring new medical products to market. It also explores unresolved policy challenges as FDA works to modernize its frameworks. Specific topics to be covered will include

1. Overview of the U.S. Coordinated Framework for oversight of gene editing technologies (both as therapeutics and as production tools) – for example, FDA/USDA/EPA regulation of food, gene-edited plants and animals, “biopharming” in which gene-edited plants produce pharmaceuticals and other materials, with a focus on FDA's roles.
2. FDA's oversight of traditional medical devices (e.g., prosthetics, MRI machines, etc.), diagnostics (e.g., genomic tests), biological products (e.g., engineered tissues or gene-editing tools), and medical software (e.g., AI/ML clinical decision support software, patient decision support and non-regulated wellness and other

consumer-grade software, and predictive health analytics software used for population health, public health, and quality improvement)

3. FDA and CMS/CLIA oversight of clinical laboratories and genomic and other advanced *in vitro* diagnostics

Topic 4. The health care reimbursement challenge

Learning objectives. Many promising health technologies fail to achieve timely clinical translation because of difficulties with the murky process for Medicare/private payer insurance reimbursement approval. After this unit, you will understand: (1) Medicare/payer reimbursement approval is a separate step that follows FDA approval, but reimbursement strategy needs to be planned at the earliest stages of research and development to make sure needed data are collected; (2) How the Medicare reimbursement approval process works (and how it differs) for various types of medical products; (3) Why Medicare's decisions have a large influence on private insurance approvals; (4) How to choose between national and local coverage decisions for Medicare; (5) The difficult reimbursement pathway for genomic and advanced diagnostic tests; (6) the role of States in mandating appropriate coverage for advanced prosthetics and other superior emerging technologies.

Topic 5. The challenge of accessing high-quality data for biomedical discovery

Learning objectives. Access to high-quality, generalizable, longitudinal health data is the fuel for 21st-century biomedical discovery. It is challenging to assemble data sets because of privacy and ethical concerns and because of the fragmented U.S. system for health care delivery. After this unit, you will: (1) be able to explain how "data ownership" currently works; (2) explain the "civil rights" approach to data privacy that the U.S. and European Union adopted in lieu of "data ownership," (3) develop a data acquisition plan to obtain needed types of data in a lawful manner under the HIPAA Privacy Rule and major federal research ethics regulations (the Common Rule and FDA research regulations); (4) understand the role of state privacy laws, (5) participate knowledgeably in the ongoing policy debate about re-identifiability of deidentified data; and (6) acquire de-identified or identifiable data for use in research in a lawful manner, when your or your client's research requires it.

Topic 6. Novel policy issues and new lawsuit risks facing biotechnology and software product developers

Learning objectives. This unit briefly surveys the types of liability suits that traditionally affected the manufacture and clinical use of medical technologies (malpractice, general negligence, products liability, etc.). It explores how FDA's expanded role in regulating medical software threatens to confront software innovators, clinical and research laboratories, and academic medical centers with new lawsuit risks and discusses strategies to manage those risks.

Syllabus - Assigned Readings

CGH refers to the Christensen, Grossman, and Hwang *Innovator's Prescription* book.

NASEM Biotech refers to Preparing for Future Products of Biotechnology

IOM Devices refers to Institute of Medicine, Medical Devices and the Public's Health

All readings other than CGH available on Canvas or via URL links to web sites

Intro for Engineering Students Only (January 12 and 14)

The College of Engineering starts its semester one week before the Law School starts. There will be two sessions (January 12 and 14) exclusively for engineering students. These will cover tort liability, for which law students have had a course already but engineers typically have not.

Reading 0.1 (1/12/21) SLIDES, **A Quick Tour of Tort Law: What should you worry about if you are a researcher, product developer, or entrepreneur?**

There is no need to review this material before class. Just download or print the slides and have them available. We will work through this material in class.

Reading 0.2 (1/14/21) Evans & Pasquale, **Product Liability suits for FDA-regulated AI/ML Software.** Read this before class.

Combined law/engineering class starts on 1/19/2021

Class 1. Intro to social and ethical issues, intro to FDA and Coordinated Framework

b

Assignment. Before Class 1, read any 4 of the following 8 short articles and come to class prepared to discuss the ones you read.

1. **AI software could displace 47% of workers:** Pham et al, "The Impact of Robotics and Automation on Working Conditions and Employment," IEEE Robotics and Automation Magazine (June 2018)
2. **Lawyers and other skilled workers are not safe from AI-related job loss:** Kevin Finneran, "Overdetermined," Issues in Science & Technology (Vol. xxv, Fall 2018), at <https://issues.org/overdetermined/>
3. **Non-transparency of AI Software:** Cliff Kuang, Can AI be Taught to Explain Itself? New York Times (Nov. 21, 2017) available at: <https://www.nytimes.com/2017/11/21/magazine/can-ai-be-taught-to-explain-itself.html>
4. **Gene-edited and synthesized food falls into regulatory gaps:** Dan Charles, "Will Gene-Edited Food be Government Regulated?" NPR (May 10, 2019), at <https://www.npr.org/sections/thesalt/2019/05/10/717273970/will-gene-edited-food-be-government-regulated>

5. **Gene editing offers medical miracles for patients who can pay millions of dollars:** Carolyn Y. Johnson & Brady Dennis, “Gene Therapies offer dramatic promise but shocking costs,” The Washington Post (Nov. 14/15, 2015), or see https://www.washingtonpost.com/business/economy/gene-therapies-offer-dramatic-promise-but-shocking-costs/2015/11/11/01f11cf0-824b-11e5-9afb-0c971f713d0c_story.html
6. **Gene editing has unresolved safety risks:** Sharon Begley, “Potential DNA damage from CRISPR has been seriously underestimated, study finds,” StatNews (July 6, 2018), at <https://www.statnews.com/2018/07/16/crispr-potential-dna-damage-underestimated/>
7. **Human rights impacts of AI and big data:** Molly Galvin, “Human Rights in the Age of Social Media, Big Data, and AI,” National Academies of Science, Engineering, and Medicine News (Sept. 23, 2019), at <http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=9302019>
8. **Ultrapersonalized medicine:** Gina Kolata, “Scientists Designed a Drug for Just One Patient. Her name is Mila,” New York Times (Oct. 9, 2019), at <https://www.nytimes.com/2019/10/09/health/mila-makovec-drug.html?action=click&module=Editors%20Picks&pgtype=Homepage>

SLIDES Intro to FDA Part 1. Introduction to FDA’s jurisdiction, what the agency regulates, and where FDA fits into the broader U.S. Coordinated Framework for Regulation of Biotechnology)

Unit I. Introduction - Business Models for Disruptive Innovation (Topic 1 - Classes 2, 3, 4, 5)

Learning objectives. Inventing a great technology will not, by itself, bring about transformative change. Other required elements sometimes include developing an innovative business model and creating a value network that lets the new technology to be delivered safely and at a price that works for both the consumers and the developers. After this unit, you will be able to: (1) define and recognize three distinct business models: the solution shop, the value-added process business, and the facilitated network, and which pricing options work for each; (2) analyze how particular technological innovations can help shift existing businesses (such as healthcare or agriculture) from one business model to another one.

Class 2. Healthcare business models – traditional and emerging

Assignment. Read I.C (Topol reading) and come prepared to identify troubling practical, ethical, economic, or regulatory issues you spotted. Simply bring the handouts in I.A and I.B with you to class. You don’t need to look at them before class.

- I.A Basic definitions to get us started: Categories of products that FDA Regulates and 21st Century Cures Act provisions on FDA regulation of software
- I.A SUPPLEMENT FDA Guidance on CDS Software (September 2019)
- I.B U.S. Coordinated Framework agencies and major statutes
- I.C Eric Topol, “High Performance Medicine: The Convergence of Human and Artificial Intelligence,” Nature Medicine 25, 44-56 (2019)

Questions for discussion: How does AI medical software fit into the business model(s) of modern healthcare? What ethical concerns do you have about the types of software Topol describes?

Class 3. The role of disruptive technologies in modern healthcare

Assignment. Read I.D

I.D CGH, “The Role of Disruptive Technology and Business Model Innovation in Making Products and Services Accessible and Affordable,” pages 1 – 33.

SLIDES Intro to FDA Part 2. Bring to class if you like to have a copy to refer to.

In class. Volunteer reporters will sign up to give informal class reports on other chapters in CGH, to be reported during Class 5 (brief, 6-8 minute presentations).

- Ch.3 Disrupting hospitals
- Ch.4 Disrupting physicians
- Ch.5 Disrupting chronic disease
- Ch.6 Integrating
- Ch.7 Reimbursement
- Ch.8 Pharma
- Ch.9 Medical devices/diagnostics
- Ch.10 Medical education
- Ch.11 Regulatory reform

Questions for discussion: How do advanced diagnostics, medical software, gene therapy, and emerging neurotechnology devices enable disruption of healthcare? Try to identify some recently emerging technologies that have been in the news that you regard as potentially disruptive and be ready to discuss your examples in class.

Class 4. The challenge of DIY biotechnology, genomics, and neurotechnology

Assignment. Read I.E. Bring a copy of the slides in I.F to class if you would like to have it to help take notes. You don’t need to look at the slides before class.

I.E Daniel Grushkin, Todd Kuiken & Piers Millet, “Seven Myths and Realities about Do-it-Yourself Biology”

I.F **SLIDES Regulatory Challenges and Moral Limits of DIY Genomics**

Homework. Everybody should do a web search or look at the NASEM Biotech Book Supplement below and find at least one interesting news item, blog post, etc. describing do-it-yourself activities in genomics, neurotech, or another biotechnology and be ready to discuss it briefly in class.

Supplement NASEM Biotech Book (provided in electronic form) pages 27 – 40. I am not assigning this reading, but it gives an excellent discussion of technical drivers that are restructuring biotech manufacturing, leading to emergence for four new business models. These drivers include, for example, standard biological parts, contract laboratories and community laboratories; new software platforms; the changing scale of manufacturing activities, and changing sources of funding for R&D (including crowdsourced funding).

Questions for discussion: Where does DIY Bio fit into the spectrum of business models CGH discuss? What is its potential to bring about disruptive change? Is it dangerous? Does it need to be regulated? How?

Class 5. Technology impacts across healthcare subsectors

Assignment. Everybody should read I.G

I.G CGH, “The Technological Enablers of Disruption [in biomedicine]” pages 37 – 66.

Volunteer reporters will give informal 6-8 minute summaries on other chapters in CGH.

Unit II. Introduction to Consumer Safety Regulation (Topic 2 - Classes 6, 7, 8, 9)

Learning objectives: Most researchers understand that their publications and speeches can affect their ability to claim patent protection for new products. Less well understood is the fact that their communications also affect whether FDA will regulate their products and what the specific regulatory requirements will be. After this unit, you will be able to: (1) recognize and define various categories of products that FDA regulates (e.g., drug, device, biological product, combination product, food, food additive, dietary supplement, cosmetic, tobacco product, etc.); (2) apply the factors that FDA looks at when deciding whether an innovative product falls under FDA’s regulations; (3) understand that things researchers and inventors say, write, and publish can affect whether and how FDA will regulate their inventions; (4) manage communications to optimize regulatory pathways; and (5) understand how the choice of business model also may affect whether you (or your client) will be regulated by FDA.

Class 6. The uniquely American approach to safety regulation

Assignment. Before class, read II.A, II.B, II.C

II.A Daniel A. Farber, *Uncertainty*, 99 **GEORGETOWN LAW JOURNAL** 901 (2011) – excerpts

II.B Alliance for Bio Integrity v. Shalala, 116 F.Supp.2d 166 (2000) – excerpts

II.C Int’l Dairy Foods Ass’n v. Amestoy, 92 F.3d 67 (1996)

SLIDES Risk and Innovation Policy

Also bring the old Reading I.B. The U.S. Coordinated Framework agencies and statutes

Supplements. These are not assigned as readings but may be mentioned in class

II.D Deference to Federal Agencies - Chevron-Mead Supplement

II.E Paternalism and the Moral Basis of Consumer-safety Regulation

Questions. What are the distinctive features of the American model of biotech safety regulation? What principles does it rest on? What does it cost and does it even keep consumers safe? What sort of reforms, if any, would you suggest?

Class 7. What does FDA regulate?

Assignment. Read II.F, II.G before class:

- II.F Excerpts from cases: U.S. v Bacto-Unidisk 394 U.S. 784 (1969)
 Nutrilab, Inc. v. Schweiker, 713 F.2d 335 (7th. Cir 1983)
 National Nutritional Foods Ass'n v. Mathews, 557 F.2d. 325 (2d Cir. 1977)
- II.G Bradley Merrill Thompson, Strategies for Technology Companies Entering the Health Care Internet of Things, Bloomberg Health IT Law & Industry Report, Vol. 9, No. 4 (January 16, 2017).

SLIDES FDA Oversight of Clinical Decision Support Software

Questions. How does FDA get its power to regulate? What is the scope of that power? Does FDA have unlimited power to decide which product category a new technology falls into? Do people have any control over whether they fall under FDA's regulations?

Class 8. Be careful what you say! How FDA determines what your "intent" is when deciding whether to regulate you

Assignment. Read II.H (FDA's intent algorithm) and II.I (What are labels, labeling, and advertising?). Take a quick look at the three slides in II.J before class. They review the Commercial Speech Doctrine we saw earlier in the Amestoy dairy case in Unit 6.

- II.H 21 C.F.R. § 801.4: the regulatory "intent" algorithm
- FDA's failed attempt to shift to a "totality of circumstances" standard and the industry pushback: Excerpts from FDA, "Clarification of When Products Made or Derived From Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding "Intended Uses" 82 Fed. Reg. 2193 – 2217 (January 9, 2017)
 - U.S. v. Travia 180 F.Supp. 2d 115 (D.D.C. 2001) – *excerpts*
- II.I What constitutes a label, labeling, and advertising and why does it matter?
- FFDC §§ 201(k), 201(m): definitions of label and labeling
 - Kordel v. U.S., 335 U.S. 345 (1948) - *excerpts*
 - U.S. v. Urbuteit, 335 U.S. 355 (1948) - *excerpts*
 - U.S. v. 24 Bottles of "Sterling Vinegar & Honey", 338 F.2d 157 (2d. Cir. 1964) *excerpts*

II.J Basics of First Amendment Commercial Speech Doctrine.

Questions. When is a scientific publication or conference presentation just free speech, and when does it become "labeling" that affects how FDA will regulate you and your product? If FDA decides something you wrote amounts to "product labeling," what is the impact of that? Can you fall under FDA regulation even if you never intended for your invention to be used in clinical healthcare applications? How likely is that to happen? Can you help avoid it?

Class 9. Be careful what you say, cont'd.

Assignment. Read II.K and II.L

- II.K Nathan Cortez, *Can Speech by FDA-Regulated Firms Ever Be Noncommercial?*, 37 AM. J.L. & MED. 388, 397 (2011) – *excerpts*
- II.L When is speech "misleading" in a way that causes you to lose First Amendment protection under the Commercial Speech Doctrine?

Questions. Should people be able to have access to experimental or scientifically uncertain information (such as genomic test results about themselves or environmental data), even if they might misunderstand or misuse the information and make harmful decisions? Should FDA and other regulators “protect” people by blocking any communication of results the regulators consider to be of low quality or uncertain? How paternalistic should safety regulators be? Are there better options to protect people from uncertain or evolving scientific information, other than just blocking their access to the information altogether?

**Unit III. Basics of Medical Device Regulation:
(Topic 3 - Classes 10, 11, 12, 13)**

Learning objectives. After completing this unit, students will be able to: (1) describe the major features of FDA’s medical device regulatory process, including both premarket and postmarket controls; (2) develop plans for positioning a new product for the most favorable regulatory treatment and obtaining an FDA investigational device exemption, clearance and/or premarket approval and then complying with FDA’s postmarketing controls; (3) explain how FDA’s device regulations (and other major federal regulatory frameworks such as the Clinical Laboratory Improvement Amendments of 1988) affect genomic tests and other advanced diagnostics and software; (4) contribute to the debate about key policy issues that FDA has not yet been able to resolve, such as how to determine whether AI software is sufficiently “explainable” that physicians and other healthcare professionals can use it safely, and (5) explain how regulation of diagnostic tests (including genetic tests) works and which agenc(ies) and non-governmental organizations play key roles.

Class 10. Intro to the Medical Device Industry and Types of Medical Devices

- III.A **Intro to the Medical Device Industry.** Medicare Payment Advisory Commission – June 2017 Report to Congress, Ch. 7, “An Overview of the Medical Device Industry” Read 207 – 214 (stop before “Unique Device Identifier”)
- III.B **SLIDES: Overview of Medical Device Regulation, including Diagnostic Devices.** Covers: Basics of FDA device regulation; the shifting mix of premarket to postmarket evidence collection to establish safety and effectiveness; FDA’s new evidentiary paradigm after the Food and Drug Administration Amendments Act of 2007; and regulation of diagnostic devices (incl. genomic tests). (to be discussed in class in coming days; no need to look at them ahead of time).
- SUPPLEMENT. Background on CRISPR Gene Editing Technology** (not required reading)

Class 11. Intro to FDA’s Regulation of Medical Devices

We will spend a couple of days on Reading III.C. I recommend you read it through one time, and then re-read it for the second of the two classes (Class 11):

- III.C **Institute of Medicine, Medical Devices and the Public’s Health: The FDA 510(k) Clearance Process at 35 Years (2011): Read Chapter 3 pages 41-62 and 68-73**

Note: Only Chapter 3 is posted as Reading III.C, but an electronic copy of this entire book is provided on Canvas. The book is also available for free PDF download at http://nationalacademies.org/hmd/reports/2011/medical-devices-and-the-publics-health-the-fda-510k-clearance-process-at-35-years.aspx?_ga=2.39970402.1981029323.1512495203-886719148.1512334659

III.C.1 **SUPPLEMENT Reading Guide** to accompany Institute of Medicine III.C. Use this as you go through reading III.C and **try to answer all the questions.**

Class 12. FDA Medical Device Regulation, cont'd.

Assignment. Read III.D (LawSeq Task Force report) and look at the FDA resources at the links provided below. In class, we will continue discussing the IOM reading III.C and SLIDES III.B, especially the slides at the end that discuss special problems FDA faces in regulating diagnostic tests (including genomic tests).

III.D LawSeq Quality Task Force, “How Can Law and Policy Advance Quality in Genomic Analysis and Interpretation for Clinical Care?” (2020)

The following FDA resources are clear and useful. You should click the links and tour them. They really help!

FDA Device Advice – Comprehensive Regulatory Assistance

<https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm>

If you scroll down on the left side of that web page, there are useful links on: “Overview of Medical Device Regulation” and “How to Study and Market Your Device.”

Class 13. Emerging Regulatory Challenges with Medical Software

III.E Browse around in 2020 Report of the Government Accountability Office and National Academy of Medicine on AI software for clinical healthcare and for Health-related settings outside of Clinics and Hospitals. **Copy available in “Book” section on Canvas.**

Volunteers will provide brief summaries/class reports on topics of interest.

III.F Excerpts from: 2019 draft guidance titled [Clinical Decision Support Software](#) describing FDA’s regulatory approach to clinical decision support software functions (replacing the 2017 draft guidance entitled *Clinical and Patient Decision Support Software*).

SLIDES.1 FDA’s Oversight of Clinical Decision Support Software

SLIDES.2 FDA’s Proposed Regulation of Genomic Testing Software

In-class exercise: How to access, use, and file public comments in an FDA regulatory proceeding. This exercise will explore comments filed on the 2019 Clinical Decisions Support Draft Guidance, at www.regulations.gov under docket number FDA-2017-D-6569. The comment period closed Dec. 26, 2019.

Unassigned supplemental links related to FDA software regulation. These are not assigned readings, but links are provided in case they may be relevant to your chosen paper topics:

1. FDA, “Developing Software Precertification Program: A Working Model” (v0.2, June 2018), at <https://www.fda.gov/media/113802/download>.

2. Final guidance, [Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act](#). This guidance details the changes to existing guidance documents that relate to the regulation of the software functions.
 3. Updates to conform past guidances to the above documents:
 - [Policy for Device Software Functions and Mobile Medical Applications](#) (*originally titled Mobile Medical Applications*)
 - [General Wellness: Policy for Low Risk Devices](#)
 - [Off-The-Shelf Software Use in Medical Devices](#)
 - [Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices](#)
 4. FDA, Artificial Intelligence and Machine Learning in Software as a Medical Device (April 2019) at <https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-software-medical-device>
 5. FDA, “Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) - Discussion Paper and Request for Feedback” (April 2, 2019) at <https://www.fda.gov/media/122535/download>
 6. FDA’s long-term Digital Health Innovation Action Plan [DH Action Pl \(fda.gov\)](#)
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**Unit IV. Unaffordable Miracles: The Challenge of Making Innovative Biomedical Technologies Accessible to People Who Need Them
(Topic 4 - Class 14 – 15)**

Learning objectives. This unit introduces economic factors that can interfere with commercialization of innovative medical technologies, using examples from diagnostics, gene therapies, and rehabilitation devices. These themes are revisited throughout the course. The objective here is simply to emphasize that value network innovation is as crucial as (and sometimes more challenging than) technology innovation.

Classes 14 and 15. Reimbursement of Advanced Medical Technologies

IV.A **Everybody should read this for Class 14.** Medicare Payment Advisory Commission – June 2017 Report to Congress. **Read pages 219 – 231** (stop before “Ramifications of bundling...”)

Class reports for Classes 14 and 15. For the other readings, we will adopt a “divide and conquer” strategy, dividing into working groups to provide brief presentations/class reports of these materials during Classes 14 and 15. Everybody should glance at one of these additional readings, even if you are not a class reporter.

IV.B Gregory Daniel, Nick Leschley, Jeff Marrazzo & Mark McClellan, “Advancing Gene Therapies and Curative Health Care Through Value-Based Payment Reform,” Health Affairs Blog (Oct. 30, 2017)

- IV.C Institute for Clinical & Economic Review, “Gene Therapy: Understanding the Science, Assessing the Evidence, and Paying for Value” (March 2017) – selected excerpts.
- IV.D Cornelia Henschke & Rita F. Redberg, “Medical Device Price Differentials in the U.S. and Europe – Rethinking Price Regulation,” Health Affairs Blog (Dec. 7, 2018), available at <https://www.healthaffairs.org/doi/10.1377/hblog20181206.716970/full/>
- IV.E Brian Buntz, “Why Medical Technology Is So Expensive in the United States,” Medical Device & Diagnostic Industry (Aug 6, 2013), at <https://www.mddionline.com/why-medical-technology-so-expensive-united-states>
- IV.F Patricia A. Deverka and Jennifer C. Dreyfus, “Clinical Integration of Next Generation Sequencing – Coverage and Reimbursement Challenges” J. Law, Med. & Ethics Supp (Fall 2014) 22 – 38 – *selected excerpts*
- IV.G Michelle Mello and Rebecca E. Wolitz, Legal Strategies for Reigning in Unconscionable Prices of Prescription Drugs (Nw. U. L. Rev. 2020 forthcoming) – *selected excerpts*

In-class discussion. Basics of Medicare and private insurer coverage and reimbursement approvals – what innovators have to do to get a new technology to be covered.

Think about this exercise ahead of class and we will work it during Class 15.

- IV.H **Exercise/example to work in class.** The downside of bringing a device to market through one of FDA’s pathways that have lower requirements to prove safety and effectiveness (e.g., 510(k), or as a non-FDA-regulated LDT). If you provide less data to FDA, then you don’t have data that Medicare and private insurers expect, in order to grant a reimbursement approval.

**Unit V. Privacy and Ethics of Research with Large Data Sets:
Data Ownership and the U.S. Civil Rights Model of Medical Privacy
(Topic 5 - Classes 16 – 21)**

Basic concepts in human-subject protection

- V.A Gelsinger Case Summary
- V.B Traditional Common Rule (pre-2019) any why it still matters
- V.C Traditional and New Common Rules
- V.D Text Handout Human Subject Protections

The following articles are important because they reflect an emerging and still controversial view, which is at odds with the current Common Rule, that people may have a bounded duty to allow their data to be used in socially beneficial research and public health activities.

- V.E Articles on Learning Healthcare System

Problems to be worked in class:

- V.F Problems. QI vs. Research; Public Health Practice vs. Research
- V.G Notes on Public Health Practice vs. Research
- V.H Problem on Engagement in Research
- SUPP. OHRP Guidance Engagement in Research

SUPP. More OHRP Guidance on Nonengagement in Research
SUPP. Resolution of the V.H Problem (try to solve it before you look)

Materials on HIPAA. You need to understand these and be able to explain how HIPAA’s handling of jurisdiction, treatment/QI/public health, research waivers, and other categories of use differs from the Common Rule. Also understand the basic obligations covered entities have to obtain authorizations, protect information, etc.

V.I HIPAA Privacy Rule Excerpts

SUPPLEMENT. Office for Civil Rights HIPAA Covered Entity Decision Tool

V.J Ellen Clayton et al. Genetic Data Privacy

V.K EU/GDPR

V.L Pormeister: Did GDPR go too far?

V.M. Health Aff-2014-Cohen-1139-47.pdf

V.N Halamka Early Experiences Article

V.O PCAST Report (2014) Read Pages 33-45 Only

V.P Daniel Barth-Jones studies of re-identification risk

**Unit VI. Broader Social and Ethical Impacts of the Sharing Economy, DTC and DIY Technologies, Neurotechnology, and Knowledge Commons; Liability for Medical Software Developers and Users
(Topic 6 – Classes 22-26)**

Recent ethical quandaries

VI.A Andrea Wiggins & John Wilbanks. The Rise of Citizen Science in Health and Biomedical Research. Am. J. Bioethics (2019).

VI. B Lisa Ikemoto: DIY Bio: Hacking Life in Biotech’s Backyard, 51 UC Davis L. Rev. 539 (2017).

VI.C Kellen Zale, When Everything is Small: The Regulatory Challenge of Scale in the Sharing Economy, 53 San Diego L. Rev. 949, (2016).

VI.D Cook-Deegan et al., Trade Secret Protection of Data/Data Hoarding/Antitrust Issues.

VI.E Aas & Wasserman: Ethical Issues with Brain-Computer Interfaces.

VI.F Nathan Cortez, excerpts from “Regulating Disruptive Innovation,” 29 Berkeley Tech. L. J. 175 (2014)

VI.G Liability for AI/ML Medical Software

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Resources and Course Policies

Prof. Evans – Biotech & Medical AI Policy

Health and wellness. Graduate school can be a little daunting at times, and I am always happy to act as a sounding board on strategies to make it feel less stressful. If you or a friend is in distress, there are also other resources available on our campus:

U Matter, We Care: please contact umatter@ufl.edu or 352 392-1575 so a team member can reach out to the student.

Counseling and Wellness Center: <http://www.counseling.ufl.edu/cwc/Default.aspx> or 392-1575 or University Police Department 392-1111 or 9-1-1 for emergencies

Sexual Assault Recovery Services (SARS): Student Health Care Center 392-1161

University Police Department 392-1111 or 9-1-1 for emergencies

Other helpful resources. E-learning center technical support, 352-392-4357 (select option 2)

Academic honesty. Academic honesty and integrity are fundamental values of the University community. Students should be sure that they understand the UF Student Honor Code at <http://www.dso.ufl.edu/students.php>.

Grading information and grading scale.

For law students, the Levin College of Law's grading standards are posted on the College's website and this class adheres to that posted grading policy. The law school grading policy is available at <http://www.law.ufl.edu/student-affairs/current-students/academic-policies#9>. A student's grade can be adjusted by one "notch" (e.g., from an A minus to a B plus) for issues with class participation, preparation, or habitual lateness.

Grading for engineering graduate students taking this course will be in accordance with Department of Engineering graduate grading norms.

Basis for evaluation in this course. There is no final exam. Other than any adjustments for class preparation and participation (see below), the course grade will be based on an "in-class" midterm exam (1 hour, 20 minutes) offered during approximately 2/3 of the way through the course (on a date to be determined in consultation with class members to avoid conflicts with other activities), and it will count for 60% of your grade. Because of pandemic procedures, the midterm exam will be administered online.

The remainder of your grade will be based on a short paper/project report that you write on a chosen topic, to be determined in consultation with Prof. Evans. The paper will be due during the

final examination period. It is envisioned that these papers/reports can be shorter works (e.g., 3,000-6,000 words) in a style suitable for a medical/engineering journal, or they can be in a law format. With approval from Prof. Evans, students can submit collaborative final paper/project proposals in which a pair or small group of students collaborate to prepare a paper/project. The scope of collaborative works will be adjusted to ensure each contributing student does the equivalent amount of work expected with an individual project.

The midterm examination will consist primarily of essay questions (accounting for 50-60% of total points on the exam) but also will include some short answer and multiple choice problems (accounting for the remaining 40-50% of the exam). The short answer questions could include T/F, multiple choice, or “mini-essay” questions that ask you to provide a very brief answer (e.g., a couple of sentences) addressing a single point of law, ethics, or policy. The exam will be based on the assigned (required) readings and materials and topics discussed in class.

Law students’ grades can be adjusted one “notch” (e.g., from A to A minus) up or down based on class participation. Such adjustments are rare and the expectation is that your grade will be based on your midterm exam and final paper/project (see above). However, participation-related adjustments can be made for habitual lateness or lack of preparation and engagement in class discussions, or for exceptional performance in class participation or in-class presentations.

Accommodations. Students requesting accommodation for disabilities must first register with the Disability Resource Center (<http://www.dso.ufl.edu/drc/>). Once registered, students will receive an accommodation letter which must be presented to the Assistant Dean for Student Affairs when requesting accommodation. Students with disabilities should follow this procedure as early as possible in the semester.

Conduct of classes

Naming and pronouns. I go by “Professor Evans” or “Barbara” and I use she/her/hers as my pronouns, although it won’t upset me if you use something else. I care about making sure I use your preferred name and pronouns, too. Please feel free to reach out to me in person, by phone, via text message, or by e-mail to make sure I know your preferences. Thereafter, if I ever fail to get it right, please kindly attribute it to imperfections of memory, and never feel awkward about correcting me gently in front of other people if I make a mistake.

COVID-related policies. Many students will have face-to-face instructional sessions to accomplish the student learning objectives of this course. In response to COVID-19, the following policies and requirements are in place to maintain your learning environment and to enhance the safety of our in-classroom interactions. I may take noncompliance into account when grading students or determining if a student may remain in the course.

- You are required to wear approved face coverings at all times during class and within buildings. Following and enforcing these policies and requirements are all of our responsibility. Failure to do so will lead to a report to the Office of Student Conduct and Conflict Resolution. You also will no longer be permitted on the UF Law campus. Finally,

Dean Inman will also report your noncompliance to the relevant state board of bar examiners.

- This course has been assigned a physical classroom with enough capacity to maintain physical distancing (6 feet between individuals) requirements. Please utilize designated seats and maintain appropriate spacing between students. Please do not move desks or stations.
- Sanitizing supplies are available in the classroom if you wish to wipe down your desks prior to sitting down and at the end of the class.
- Be mindful of how to properly enter and exit the classroom. Practice physical distancing to the extent possible when entering and exiting the classroom.
- If you are experiencing COVID-19 symptoms (<https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>), please do not come to campus or, if you are already on campus, please immediately leave campus. Please use the UF Health screening system and follow the instructions about when you are able to return to campus. <https://coronavirus.ufhealth.org/screen-test-protect/covid-19-exposure-and-symptoms-who-do-i-call-if/>.
- Course materials will be provided to you with an excused absence, and you will be given a reasonable amount of time to make up work. <https://catalog.ufl.edu/UGRD/academic-regulations/attendance-policies/>.”

Course Requirements

Preparation: It is anticipated that you will spend approximately 3 hours out of class reading and/or preparing for in-class assignments such as your chosen presentation and paper topics for every 1 hour in class.

Class participation and attendance: Attendance is mandatory and you are expected to be on time. It is your responsibility to initial the electronic sign-in sheet for each class session. I will “call the roll” for the first couple of classes, while I learn your name. Thereafter, you are responsible for signing in according to the electronic procedures in use this semester because of the pandemic. It will be considered a violation of the course rules and the Honor Code to misrepresent that you were present in class, or to assist a classmate in such misrepresentation.

Students deemed absent for more than 20% of scheduled classes may not sit for the examination and cannot pass the course. There are no “excused” absences, although I am always interested if you wish to reach out to me to let me know if you are experiencing an illness or special circumstance. Punctuality shows respect for your colleagues and professors and is part of the professionalism expected of you in your future careers. Please arrive at school early enough to allow yourself enough time to be in your seat ready to begin. Any student not in class within the

first fifteen minutes of class (or leaving more than fifteen minutes early) is not permitted to sign the attendance sheet.

The best thing to do, if you know you are going to miss a class, is to ask a fellow student for notes. There will also be recordings of class available for quarantined students or students otherwise having bona fide reasons for missing a class. Student notes often are the best record of the give and take of questions and answers that actually took place during class. However, I also will be glad to discuss questions with you if you have been ill or otherwise unable to attend and need to go over any concepts that are still not clear.

Lateness: Notwithstanding the prior rules, I understand that lateness sometimes happens despite students' best efforts. Never feel embarrassed to join my class because you are slightly late. You've paid for the class, and I want you to get the benefit of any portion of it you are able to attend. However, you must be considerate of your fellow students, and follow social distancing requirements to protect their health, if you are arriving late. If arriving late, please don't slam the door when you come in and make sure the door is closed behind you.

What to do if circumstances require you to exit a class while it is in session: From time to time in life, we all have a sudden illness or other emergency that requires us to enter or leave a class while it is in session. If this should happen to you, simply enter or leave as quietly and unobtrusively as you can, observing all social distancing requirements to protect others. Obviously, it is understood that you will do this only when there is a pressing need to do so.

What good class participation means: One of the goals of this class is to teach you good professional communication skills. It is surprising but true that the most important communication skill is not talking and saying clever things, but listening and getting a sense of what other people think. If that other person is the opposing counsel, listening is the way you analyze the weakness in their arguments and thought processes. If that person is your client, listening is how you learn what the client's problem is and how the client feels about various approaches for solving it. If that person is a regulator or judge, you had better listen!

If you have previously asked to be recognized twice in a single class, I am unlikely to call on you again until all other persons in the class have had the opportunity to share their views. In that situation, do not continue to hold your hand up for a long time; it will just get tired. This is mainly done for your own learning. Whenever one is waiting to speak, one becomes completely absorbed with planning one's own remarks and loses the opportunity to hear what other people have to say. Beware of being absorbed in your own thoughts, when you could be listening to what other people have to say.

Also, it is not the case that talking a lot leads to a higher class participation credit or makes you look wiser. Sometimes, a few well-chosen, well-prepared words are the most impressive. I particularly like it when students listen to one another's remarks and respond to them, either to amplify or debate them in a tactful, well-reasoned manner.

Be aware of any positions of privilege that you occupy and regulate your participation in a way

that ensures everybody has an opportunity to express their views and receive respect for them.

Practice examinations. I typically do not give out old exams as practice exams, but we will work many class exercises and practice problems in class, so you will be well-prepared for the exam and it should not contain any surprises.

Cell phones, pagers, computers. Please make every effort to remember to disable the ringer on your cell phone and to silence any other device you have that makes noise. I understand why carrying these devices in class is necessary. Computers in class are to be used exclusively for taking notes or viewing documents directly relevant to what is then going on in the classroom, and not for otherwise distracting you or your classmates. Sanctions for violating these rules are at my complete discretion.

Policy on recording of classes. Please do not record class without my express permission. Recordings of class are being made by the law school for use by any students in this class who experience quarantine or other bona fide reasons for missing class. If you need the recordings, contact me and I can let you know whom to contact to request them.

Informal feedback for me. My goal is to help you learn this subject matter as thoroughly and enjoyably as possible. I welcome any comment or suggestion you may have regarding teaching style, topic coverage, class presentation, ways to make the class sessions more useful for you, or any other issue. I may not implement every suggestion that is offered, but I will certainly give it careful consideration, and I would never be offended by any good-faith suggestion on how to make this class more engaging and productive for you. If something isn't working for you, then let me know. Please feel free to provide me with any comments during the semester that you think will improve the overall learning experience.

Formal course evaluations. Students are expected to provide feedback on the quality of instruction in this course by completing online evaluations at <https://gatorevals.aa.ufl.edu/>. Evaluations are typically open during the last two or three weeks of the semester, but students will be given specific times when they are open. Summary results of these assessments are available to students at <https://gatorevals.aa.ufl.edu/>.

Expectations for participation in online synchronous digital education (SDE). To be counted "present" in an online class session, there are a number of requirements you must meet:

- (i) you must be connected to the internet videoconference when class starts;
- (ii) your computer must have a working video camera and quality audio capability; joining by audio only due to your lack of video capability will be treated as an absence (you may need an external mic or headset for sufficient audio quality);
- (iii) if your computer is a laptop, you must not be distracted by traveling or other activities when you join the internet videoconference;
- (iv) you may not join the class internet videoconference from a phone, unless in exceptional circumstances with prior approval from Prof. Evans;
- (v) you must listen closely and speak loud and clear, as hearing students speak in the classroom

- and classmates ability to hear the SDE student may not be optimal;
- (vi) you must identify yourself with your class roll name in the internet videoconferencing software;
 - (vii) you must present your face and upper body area professionally in the video stream; eating “on-camera” is not a professional presentation;
 - (viii) you must be able to fulfill your responsibilities if called on to discuss a case or course materials; and
 - (ix) you must manage the “mute button” when remote to keep a professional demeanor.