Course Materials. See list of assigned readings starting on Page 5. 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 for about $12.00)
(ii) Materials provided at no cost through the UH electronic blackboard
(iii) Links within this Syllabus 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.
(iv) Supplements delivered via e-mail. This course presumes you monitor your e-mail address regularly.

Course Summary. This course brings law students and engineering graduate students together in an interdisciplinary classroom setting to explore solutions to defining challenges that surround big data systems, AI software, and advanced biotechnologies designed for use in healthcare and many other industrial and agricultural settings.

These challenges are many and perplexing. Recent California legislation aims to protect workers in the gig economy (e.g., Uber and Lyft) but ironically amps up pressure to replace them with artificially intelligent (AI) robots. Skilled workers may also be in the AI job-destruction firing line: Will law professors soon be replaced by AI “Socratobots” that can pepper students with incisive questions at a fraction of today’s tuition rates? AI software enhances business productivity—such as by evaluating who is a bad credit risk—but its methods are non-transparent and threaten to place a new high-tech gloss on invidious discrimination, while evading current civil rights protections. Under current regulations and healthcare business models, gene editing promises to restore sight to the blind, provided the blind—who experience above-average rates of poverty, unemployment, and non-insurance--
can pay a $1 Million+ per eye of uninsured costs for the therapy. Simultaneously, the U.S. Coordinated Framework for regulating biotechnology products has wide gaps where whole classes of future products escape even the most rudimentary consumer-safety oversight. The United States has no plan to support or retrain the millions of workers set to be replaced by AI systems and genetically modified yeast foundries that will synthesize many of the foods, industrial chemicals, and products currently manufactured by humans. What would modern industrial economies look like with unemployment rates of 40, 50, or 60%?

This course surveys the regulatory frameworks now in place for overseeing innovative software and biotechnology products. Students taking this course will receive practice-oriented instruction to help lawyers and technology innovators navigate:

1. business model innovation, such as DIY biotechnology, contractual bioinformatics and lab service providers, and the use of crowdfunding rather than traditional public and corporate funding sources for R&D

2. U.S. and E.U. privacy laws and ethical standards that protect consumer privacy and constrain access to data by software developers

3. biotechnology economic frameworks: e.g., antitrust issues in data access, safety nets for displaced workers, and Medicare/insurance reimbursement and value networks that affect consumer access to new technologies

4. the non-drug FDA frameworks for regulating innovative medical devices, software, and advanced diagnostics including genomic tests; genetically modified foods and dietary supplements; combination products; and novel biological products such as gene therapies, gene-editing tools, and cellular and tissue-based products. Transformative change in healthcare is expected to come primarily from innovation in these product categories. The opioid epidemic and alarming rates of antibiotic resistance teach us, yet again, that pharmaceuticals are an ancient technology that benefits a few random patients while injuring, killing, addicting, bankrupting, or just failing to help countless others. The future of healthcare lies with advanced diagnostic devices that enable personalized medicine by predicting whether a drug is likely to injure you or help you, before you take it; neuromodulation devices that electromagnetically override your pain and bust up Alzheimer’s plaques; robotic exoskeletons that help the paralyzed walk; gene therapies that cure chronic conditions once and for all instead of treating people with high-cost drugs forever; mobile software tools to help people manage their own future health; and clinical decision support software that can leverage an overstretched physician workforce to make better care more accessible to all.

5. oversight of industrial and agricultural technologies by EPA, USDA, and law enforcement for open-release technologies that pose wider environmental, agricultural, or bioterror risks
Prerequisites. No prerequisites or special legal or scientific background are required. This course does not duplicate Biotech & Law, the U.S. Biotechnology Regulatory Framework, or FDA Law. Students who have enrolled in those courses may take this course. This course is suitable as an elective or as a course for law students expecting to serve clients in the health care, consumer products, and technology industries, and for engineers and other technology innovators faced with navigating regulations in order to commercialize their discoveries.

Evaluation Methods and Participation Requirements. There is no final exam. Students’ grades will be based on two 75-minute in-class quizzes (each counting 40% of the grade) and a short project paper or “thought piece” (3,000 – 6,000 words) on a topic that students will choose in consultation with Professor Evans (counting 20%).

(i) The two in-class quizzes will be scheduled in coordination with students to minimize scheduling conflicts, with make-ups available for students with bona fide conflicts on the chosen test dates. Make-ups need to be completed no later than 1 week after the regular test date. The short papers will be due during the finals period.

(ii) The in-class quizzes include one given near the middle of the semester that covers the first half of the course, and one given during the last week of classes that covers only the second half of the course.

Students also are expected to have read assigned materials prior to class and to participate actively in class discussions. In addition, students (or teams of students) are expected to lead one short (10 – 15 minute) presentation during the semester, on a topic similar to the examples shown in Appendix A, or on a relevant topic of students’ own choosing. Failure to attend class or to participate actively can result in lowering a student’s grade by one “notch” – e.g., from A to A minus.

(i) JD Law students (including JD/LLM students who have not yet completed 90 semester hours of credit) are subject to the usual Law Center class average grading practices for 2L and 3L classes.

(ii) LLM students are subject to the customary Law Center LLM grading practices.

(iii) Engineering graduate students are graded on a separate scale consistent with engineering departmental norms.

Message from the University: Counseling and Psychological Services (CAPS) can help students who are having difficulties managing stress, adjusting to the demands of a professional program, or feeling sad and hopeless. You can reach CAPS (www.uh.edu/caps) by calling 713-743-5454 during and after business hours for routine appointments or if you or someone you know is in crisis. No appointment is necessary for the “Let's Talk” program, a drop-in consultation service at convenient locations and hours around campus. http://www.uh.edu/caps/outreach/lets_talk.html.

Naming and pronoun preferences. I go by Professor Evans or Barbara and I use she/her, hers/theirs, you/y'all as my pronouns. Please reach out to me in person, by e-mail, or by phone if you have preferred pronouns you would like for me to use or if you prefer “Dr.” or “Mx.” to “Mr.” or “Ms.” I’ll try my best to honor your preferences. Please attribute any lapses to failings of memory and do not feel embarrassed to correct me if I make any mistakes.
**Synchronous Digital Education.** Students pursuing an LL.M. degree at the Law Center are permitted to participate in this course through synchronous distance education, as are engineering students and professionals at non-UH sites. For any student using the classroom’s internet videoconferencing capability for synchronous distance education, 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;
(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.
(x) testing procedures for SDE students will be separately announced.

**Class Recording.** The Law Center will record class sessions with audio and video for the sole and limited educational purpose of allowing students to stream the recorded sessions for review or to enable students who missed a class to hear the class presentation. Students may not listen to recorded class sessions to avoid an absence. Any recordings created will be deleted and destroyed shortly after the final exam for the class. There is a chance that your contributions to class discussion, whether voluntary or while on call, may be included in the recording. Your continued registration in this class indicates your acquiescence to any such incidental recording for the purposes described above.

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**Continue to Reading List on Page 5**
List of Assigned Readings

“CGH” refers to the Christensen, Grossman, and Hwang *Innovator’s Prescription* book in the reading list below

Other readings available on the Electronic Blackboard or via links to regulatory agency web sites

**First Day’s Assignment**

Before class, read any four of the following short articles and come to class prepared to discuss them.


Unit I. Introduction - Business Models for Disruptive Innovation

**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 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.

**Readings ahead of class:**


**In class exercises** (to be presented and discussed in class—you don’t need to read these beforehand)

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

**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?


**Questions for discussion:** How does AI medical software fit into the business model(s) of modern healthcare?
I.E  Introduction to the categories of products the U.S. federal government regulates. Principal federal agencies and statutes in the U.S. Coordinated Framework for Regulation of Biotechnology (FDA, EPA, USDA, and others)

**Questions for discussion:** How do advanced diagnostics, medical software, gene therapy, and emerging neurotechnology devices enable disruption of healthcare?

**Unit II. Unaffordable Miracles:**
**The Challenge of Making Innovative Biomedical Technologies Accessible to People Who Need Them**

**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.


II.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

II.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.
Unit III. What Causes a New Technology to Fall under FDA Regulation?

**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.

III.A National Academies of Science, Engineering, and Medicine, Preparing for Future Products of Biotechnology (2017), App. D (Categories of Regulated Technology Products)

III.B Software regulation under Section 3060 of the 21st Century Cures Act, Public Law 114-255 (December 13, 2016)


III.D Be careful what you say! This reading unit compiles excerpts from key regulations and court decisions on FDA’s power to determine what category of regulation applies to a new technology and whether the technology developer or manufacturer has the “intent” that triggers FDA regulation of a new product.

**D.1** FDA’s wide (but not unlimited) power to decide which product category a new technology falls into:

- U.S. v Bacto-Unidisk 394 U.S. 784 (1969)- excerpts
- Nutrilab, Inc. v. Schweiker, 713 F.2d 335 (7th. Cir 1983) - excerpts
- **Example for class discussion:** CRISPR gene-editing – is it a drug, or a device, or a biological product? Could it be any of the above? What did FDA decide?

**D.2** FDA’s algorithm for deciding whether researchers, product developers, manufacturers, and distributors have the “intent” that allows FDA to regulate them.

- 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)

D.3 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?

- Brief summary of the First Amendment framework for protecting speech and the commercial speech doctrine
- FFDCA §§ 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.22 157 (2d. Cir. 1964)- excerpts

III.E How the choice of business model can affect regulatory jurisdiction

E.1 National Academies of Science, Engineering, and Medicine, Preparing for Future Products of Biotechnology (2017), pages 27 - 40. Excerpts discussing 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).


IV. Basics of Medical Device Regulation:

General framework of FDA’s device oversight; regulation of genomic testing and diagnostics as devices and under the Clinical Laboratory Improvement Amendments; regulation of software under FDA’s device framework

**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.

IV.A The shifting mix of premarket to postmarket evidence collection to establish safety and effectiveness.

A.1 FDA’s new evidentiary paradigm after the Food and Drug Administration Amendments Act of 2007
A.2 FDA, “Developing Software Precertification Program: A Working Model” (v0.2, June 2018), at https://www.fda.gov/media/113802/download


**Supplemental resource**

IV.C How FDA and other federal regulators oversee genomic testing and other advanced diagnostics.


C.2 When is an Investigational Device Exemption (IDE) required in research involving genome sequencing and genomic testing?

C.3 Supplement - 21 C.F.R. Part 812 -- FDA’s IDE Regulation

IV.D Understanding FDA’s new software-related guidance documents (published on September 26, 2019)

*Class members will form teams to report on these various new developments*

D.1 FDA’s long-term Digital Health Innovation Action Plan

D.2 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*).

D.3 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.

D.4 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*


D.6 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](https://www.fda.gov/media/122535/download)

**In-class exercise:** How to access, use, and file public comments in an FDA regulatory proceeding. This exercise will explore comments filed on the new Clinical Decisions Support Draft Guidance, at [www.regulations.gov](http://www.regulations.gov) under docket number FDA-2017-D-6569. The comment period will close on Dec. 27, 2019.

V. Combination Products, Biological Products, and Biotech Cosmetics:
(Advanced Cellular, Tissue, and Tissue-Based Products; Gene Therapy Products; and Advanced Biotech Cosmetics and Enhancement Products)

**Objectives:** Biological drugs (e.g., penicillin) date back decades and FDA has a longstanding paradigm for regulating them under the Public Health Service Act and the Food, Drug, and Cosmetic Act. Today’s challenging regulatory issues relate to novel biotech products that are difficult to fit into that old paradigm. Examples include human gene editing tools; engineered tissues such as genetically synthesized knee cartilage or transplant organs; biotech cosmetics such as synthetic scalp tissue able to grow hair and eliminate baldness; biologically-based and biocompatible computing equipment to enhance human performance. After this unit, students will understand key safety challenges and be able to participate in the policy debate to resolve unsettled problems in how to regulate these products.
VI. Beyond Biomedicine: Agricultural Technologies; Genetically Modified and Synthesized Food; Animal Gene Editing

Learning Objectives. This unit acquaints students with the interplay of regulatory oversight among FDA, the Centers for Disease Control, the U.S. Department of Agriculture, and the Environmental Protection Agency. We use the examples of genetically modified plants and animals, genetically modified food and synthesized food, and open-release products that might have unintended environmental impacts.


VI.E Open-release research and production of genetically modified agricultural products: Selected excerpts from case law.

VI.F Ethical and human safety problems with genetic modification of animals: Can FDA, CDC, USDA, and EPA effectively regulate DIY and professional biotechnology that aims to modify animals—for example, to produce ultra-beautiful showcats, glowing fish, ultra-aggressive animals for dog-fighting, or de-extincted Wooly Mammoths?

VII. Beyond Biomedicine: Industrial Biotechnologies, The Sharing Economy, DTC and DIY Technologies, and Knowledge Commons


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


VII.D Governing Medical Knowledge Commons (Strandburg, Frischmann & Madison, eds., 2017) – excerpts

VII.E Excerpts from National Academies of Science, Engineering, and Medicine, “Preparing for Future Products of Biotechnology” – non-medical biotechnologies.

VIII. Data Science, Genomics, and Neurotechnology: The Privacy, Human Rights, and Ethical Impacts

VIII.A Ellen Clayton et al. Genetic Data Privacy

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

VIII.C Text Summary: The Traditional vs. New Common Rules

VIII.D Text Summary: The Common Rule vs. FDA Human Subject Protections

VIII.E Supplement: HIPAA Privacy Rule Excerpts

VIII.F The EU General Data Protection Regulation

VIII.G Accessing Data for Research: Practical Problem-Solving Exercises
VIII.H Aas & Wasserman: Ethical Issues with Brain-Computer Interfaces

VIII.I Frank Pasquale, excerpts from “The Black Box Society” – how AI and big data systems enable new methods of discrimination and privacy violations that fall through cracks in existing civil rights and federal privacy laws.

VIII.J Dorothy Roberts, excerpts from “The Fatal Invention” – how genomics threatens to provide a scientific paradigm to undergird new forms of invidious discrimination.

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Appendix A. Examples of Possible Case Study and Presentation Topics

Collaborations among students and team presentations are welcome. Please talk to Prof. Evans for approval of topics and scope of work for team projects.

**Topic 1. What is regulatory science?**

**Sources to explore.** FDA, Advancing Regulatory Science, at
Follow the links to FDA’s 2011 Strategic Plan for Regulatory Science
https://www.fda.gov/ ScienceResearch/SpecialTopics/RegulatoryScience/ucm267719.htm and 2013 amendments
https://www.fda.gov/ScienceResearch/SpecialTopics/RegulatoryScience/ucm452830.htm

**Key questions.** What problems are regulators trying to solve? How can academic researchers help them? What is the role of science in the regulatory processes of agencies like FDA, EPA, and USDA? How do regulatory agencies use scientific information and are they using the right stuff? Who should pay to develop scientific evidence: the government, companies that want to bring new products to market, or consumers (through fees tacked on to the price of new products?), or new funding sources like crowdfunding? What sources of grant funding for regulatory science projects are available now? What will it take to move regulatory science forward and transform the regulatory enterprise?

**Topic 2. What is Real-World Evidence (RWE) and what role should it play in regulators’ decisions about the safety and effectiveness of new products?**

**Sources to explore.** FDA, Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices: Guidance for Industry and Food and Drug Administration Staff (August 31, 2017)
**Key questions.** How would RWE differ from the sources of evidence regulators traditionally relied on? What are the advantages (e.g., generalizability to real populations) and disadvantages (e.g., selection bias) with RWE? Who is it that wants regulators to look at RWE? (See Prof. Evans; there have been some patient advocacy groups that went to Congress claiming their real-world experiences were being ignored.) Why do people care about RWE? Did Congress listen to those people? How are regulators trying to incorporate RWE into their day-to-day decisions?

**Topic 3. Disrupting the 20th-century Hospital Business Model**

**Sources to explore.** Christensen, Grossman & Hwang, Ch. 3, pp. 73 – 105, sources cited in that chapter, and recent news items searchable on Google.

**Key questions.** How did hospitals transform themselves from charitable institutions where poor people went to die in the late 1900s into the profit-seeking businesses they became by the end of the 20th century? Should they continue to exist in their current form, or have they outlived their usefulness in an era when technology can empower people to stay well? What should society do with all the capital that has already been sunk into hospital facilities? For example, could hospitals be converted into low-cost housing for demented Baby-Boomers who need supervision to keep them from tormenting their kids? What is the future of the American hospital? Or will hospitals always exist, because even if technology manages to extend the human lifespan to 150 years, people will still want to spend massive amounts of Medicare money to try to stay alive a few more days when they are 149 years and 350 days old? Is there something in the American psyche that makes people want to spend their final few days in an ICU ward with tubes stuck up their noses because they think they should live forever?

**Topic 4. Disrupting the Business Model of the Physician’s Practice.**

**Key sources.** Christensen, Grossman & Hwang, Ch. 4, pp. 111-143 and sources cited in that chapter. Works of Eric Topol on technologies that enable people to monitor and manage their own health (Prof Evans can lend you copies of Dr. Topol’s books and he has made numerous videos available on YouTube). Other sources include FDA’s recent guidances on Clinical Decision Support software and Patient Decision Support software.

**Key questions.** Is today’s physician workforce able to wield the clinical and patient decision support tools that engineers and software developers are making available? Do we need a new generation of physicians dually trained in technology and medicine? Three respected medical schools are already responding to this need, but should they all be doing so? Will patients, enabled by emerging software tools, be able to do a better job than physicians have traditionally done at managing their health? Can software and device solutions extend basic healthcare to populations that presently lack access? Are medical schools training physicians who have “the
right stuff” to keep patients healthy at an affordable cost? What are the technological alternatives?

These are just examples. Students can work with Professor Evans to select a different topic.