UNIVERSITY OF WYOMING

PHCY 5249

CLINICAL RESEARCH REGULATION, 2 Credit Hours

Asynchronous Online Delivery, Through WyoCourses

This Course Meets Daily on the Discussion Board in WyoCourses

Instructor Contact Information:

Professor David Brushwood, R.Ph., J.D., Phone: 307 766-6120, Email: dbrushwo@uwyo.edu, Office: HS 292. Your professor does not maintain an office in Laramie. Electronic communication through telephone or email (preferred) will always be welcomed.

Office Hours:

Sunday afternoons online, or at other times by appointment either by telephone or teleconference (Zoom meeting). Please post general questions about the course to the orientation module discussion board. Personal matters should be addressed directly to the instructor through email or telephone.

Course Prerequisites, Co-requisites, and Enrollment restrictions:

This course is open to professional students, and graduate students, with no prerequisites.

Course Description: The record of atrocities in human experimentation is reviewed. Federal and state legal requirements for the conduct of human experimentation are examined, with a focus on the Belmont Report and the Common Rule. Legal case studies are utilized as the basis for regulatory compliance strategies.

Student Learning Objectives:

Knowledge-Based Learning Objectives

- Describe exploitive practices through history that have led to legal restrictions on experimentation with human subjects.
- Consider the vulnerability of people who are likely to become subjects of human experimentation, and the potential eligibility of such vulnerable people for participation in clinical trials.
- Explain the process through which new drugs are developed and tested to determine whether they meet safety and efficacy requirement for FDA approval.
- Describe the quality and quantity of scientific evidence that is required to meet the "substantial evidence" standard for new drug approval under the federal Food, Drug & Cosmetic Act.
- Explain how pharmacy protocols are used in patient care, as distinct from research protocols that are used in clinical trials.
- Describe the activities of an institutional Pharmacy & Therapeutics Committee and the Medication Utilization Evaluation studies that are conducted to improve the quality of drug therapy within an institution.

- Explain the steps that are taken during the process of providing research subjects with informed consent.
- Discuss the factors necessary to conclude that a potential research subject has the capacity to consent to participation in research.
- Describe the legal requirements for research protocol design.
- Explain the primary elements of "Good Clinical Practice."
- Discuss the practices and procedures of the institutional review board.
- Describe how an investigator is accountable to the institutional review board and how the institutional review board is accountable to an investigator.
- Explain the process through which a research monitor engages in oversight of experimentation.
- Discuss the steps required for progress reporting that is compliant with applicable laws.
- Explain the standards that the FDA applies to pharmaceutical product labeling.
- Describe the regulatory requirements related to innovative uses of technologies that are not consistent with approved product labeling.
- Explain the procedure through which patients may use investigational drugs through the federal "Right to Try" law.
- Explain the procedure through which patients may receive access to investigational drugs through the FDA expanded access program.

Application-Based Learning Objectives:

- Develop policies and procedures for the handling of investigational drugs.
- Counsel patients on their right of access to investigational drugs that are not yet approved by the FDA.
- Determine whether an innovative use of an approved drug meets the criteria for an investigational drug study.
- Create and manage records necessary for the receipt, storage, and distribution of investigational drugs.

Practice-Based Learning Objectives:

- Conduct the informed consent of a patient who is considering enrollment as a subject in a clinical trial,
- Monitor a clinical research study to assure compliance with IRB protocols and requirements.
- Participate in meetings of an institutional review board.

Required texts, readings, and special tools or materials:

There is no textbook. However, there are background readings that must be downloaded from the internet (these readings are subject to change when they are updated or replaced by more current readings from the same source or from an alternative source). Selections from these documents will be assigned as required reading prior to each of the pre-recorded lectures.

- United States Department of Health and Human Services. The Belmont Report (1979). https://www.hhs.gov/ohrp/sites/default/files/the-belmont-report-508c_FINAL.pdf
- United States Department of Health and Human Services. Subpart A of 45 CFR Part 46 (The Common Rule): Basic HHS Policy for Protection of Human Subjects (2018).

https://www.hhs.gov/ohrp/sites/default/files/revised-common-rule-reg-text-unofficial-2018-requirements.pdf

- United States Department of Health and Human Services. Institutional Review Board (IRB) Written Procedures: Guidance for Institutions and IRBs https://www.fda.gov/media/99271/download
- United States Food and Drug Administration. Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products Draft Guidance for Industry (2019). https://www.fda.gov/media/133660/download
- United States Food and Drug Administration. General Considerations for Clinical Studies (2019). https://www.fda.gov/media/129527/download
- United States Food and Drug Administration. A Risk-Based Approach to Monitoring of Clinical Investigations Questions and Answers Draft Guidance for Industry (2019). https://www.fda.gov/media/121479/download
- United States Food and Drug Administration. Termination of the Food and Drug Administration's Unapproved Drugs Initiative; Request for Information Regarding Drugs Potentially Generally Recognized as Safe and Effective; Withdrawal (2021). https://www.govinfo.gov/content/pkg/FR-2021-05-27/pdf/2021-11257.pdf
- United States Food and Drug Administration. Right to Try Fact Sheet (2020). https://www.fda.gov/media/133864/download
- United States Food and Drug Administration. Expanded Access to Investigational Drugs for Treatment Use - Questions and Answers Guidance for Industry (2016). https://www.fda.gov/media/85675/download
- United States Food and Drug Administration. Draft Informed Consent Information Sheet: Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors; Availability (2014). https://www.govinfo.gov/content/pkg/FR-2014-07-15/pdf/2014-16492.pdf

There are 20 Pre-Recorded lectures that must be viewed, studied, and discussed on the discussion board:

- The Tuskegee Syphilis Study
- Vulnerability and Eligibility in Research with Human Subjects
- The "New Drug" Classification
- The "Substantial Evidence" Standard
- The NDA Submission
- Safety v. Efficacy; and Risk v. Benefit
- The Pharmacy Protocol
- Pharmacy & Therapeutics Committee Oversight
- The Process of Consent
- Capacity to Consent
- Placebos and Control Groups
- Good Clinical Practice
- IRB Procedures
- Accountability to the IRB and Accountability of the IRB
- The Research Monitor's Role

- Progress Reporting
- FDA Drug Labeling Standards
- Evolving Technologies and New Opportunities
- Right to Try Laws
- Expanded Access to Investigational Drugs

There are 10 journal articles that must be read, studied, and evaluated on the discussion board:

- Finder, Vulnerability in Human Subject Research: Existential State, not Category Designation, Am J Bioethics (2014)
- Shaffer, When the Alpha is the Omega: P-Values, "Substantial Evidence," and the 0.05 Standard at FDA, Food & Drug L J (2017)
- Holbein, Understanding FDA Regulatory Requirements for Investigational New Drug Applications for Sponsor-Investigators, J Investig Med (2019)
- Shulkin, Reinventing the Pharmacy and Therapeutics Committee, P&T (2012)
- Biros, Capacity, Vulnerability, and Informed Consent for Research, J Law Med Ethics (2018)
- Grimes et al., The Good Clinical Practice Guideline: A Bronze Standard for Clinical Research, The Lancet (2005)
- Lynch, Opening Closed Doors: Promoting IRB Transparency, J Law Med Ethics (2018)
- Cocchetto et al., Development of an Orientation Program for New Clinical Trial Monitors, Clin Res Practices and Drug Reg Affairs (2008)
- Kalil, Treating COVID-19—Off-Label Drug Use, Compassionate Use, and Randomized Clinical Trials During Pandemics, JAMA (2020)
- Fernandez, et al., Promoting Patient Interests in Implementing the Federal Right to Try Act, JAMA (2018)

General requirements and expectations for the course:

Each module of this course requires viewing of an online pre-recorded lecture, reading a posted journal article, participation in the discussion board to include assessment of a posted legal case study, and a module exam.

Upon completion of all modules, students must take a proctored comprehensive exam.

Final Examination or Final Project Date:

There is no final exam. However, there is a proctored comprehensive exam that must be taken once the course modules have been completed.

Grading Scale and Grading Policies: Attendance and Absence policies.

The final grade in this course will be comprised of:

Ten Unit Exams	40%
Comprehensive Exam	30%
Class Participation	30%

Grading:

A: 90-100
B: 80-89
C: 70-79
D: 60-69
F: <60

Students who miss exams or class participation may request an excused absence, which will be granted by the course instructor if warranted. Students who develop conflicts that prohibit their completion of 25% or more of course material should withdraw from the course. Students who satisfactorily complete 75% or more of the course material, and who cannot complete the balance within the confines of the course schedule, may be granted an incomplete, and missing coursework must be completed by the end of the following term.

Satisfactory participation in this course requires active posting on the course discussion board for each module (minimum of two posts per module), completion of the module exams, and completion of the proctored cumulative exam.

Classroom Behavior Policy

At all times, treat your presence in the classroom (discussion board) and your enrollment in this course as you would a job. Act professionally, pay attention to instructions and to your student colleagues, complete your work in a timely and professional manner, and treat all deadlines seriously. You will be respectful towards you classmates and instructor. Spirited debate and disagreement are to be expected in any classroom and all views will be heard fully, but at all times we will behave civilly and with respect towards one another. Personal attacks, offensive language, name-calling, and dismissive gestures are not warranted in a learning atmosphere. As the instructor, I have the right to dismiss you from the classroom, study sessions, electronic forums, and other areas where disruptive behavior occurs.

Classroom Statement on Diversity:

The University of Wyoming values an educational environment that is diverse, equitable, and inclusive. The diversity that students and faculty bring to class, including age, country of origin, culture, disability, economic class, ethnicity, gender identity, immigration status, linguistic, political affiliation, race, religion, sexual orientation, veteran status, worldview, and other social and cultural diversity is valued, respected, and considered a resource for learning.

Disability Support:

The University of Wyoming is committed to providing equitable access to learning opportunities for all students. If you have a disability, including but not limited to physical, learning, sensory or psychological disabilities, and would like to request accommodations in this course due to your disability, , please register with and provide documentation of your disability as soon as possible to Disability Support Services (DSS), Room 128 Knight Hall. You may also contact DSS at (307) 766-3073 or udss@uwyo.edu. It is in the student's best interest to request accommodations within the first week of classes, understanding that accommodations are not retroactive. Visit the DSS website for more information at: www.uwyo.edu/udss

Academic Dishonesty Policies:

Academic dishonesty will not be tolerated in this class. Cases of academic dishonesty will be treated in accordance with UW Regulation 2-114. The penalties for academic dishonesty can include, at my discretion, an "F" on an exam, an "F" on the class component exercise, and/or an "F" in the entire course. Academic dishonesty means anything that represents someone else's ideas as your own without attribution. It is intellectual theft – stealing - and includes (but is not limited to) unapproved assistance on examinations, plagiarism (use of any amount of another person's writings, blog posts, publications, and other materials without attributing that material to that person with citations), or fabrication of referenced information. Facilitation of another person's academic dishonesty is also considered academic dishonesty and will be treated identically.

Duty to Report: Statement referring to your duty to report status as instructional personnel under Title IX.

UW faculty are committed to supporting students and upholding the University's non-discrimination policy. Under Title IX, discrimination based upon sex and gender is prohibited. If you experience an incident of sex- or gender-based discrimination, we encourage you to report it. While you may talk to a faculty member, understand that as a "Responsible Employee" of the University, the faculty member MUST report information you share about the incident to the university's Title IX Coordinator (you may choose whether you or anyone involved is identified by name). If you would like to speak with someone who may be able to afford you privacy or confidentiality, there are people who can meet with you. Faculty can help direct you or you may find info about UW policy and resources at http://www.uwyo.edu/reportit

You do not have to go through the experience alone. Assistance and resources are available, and you are not required to make a formal complaint or participate in an investigation to access them.

Substantive changes to syllabus:

Note: This syllabus is a guide. Circumstances may alter the reading and/or test schedules. You are required to check WyoCourses and your email at least once a week.

Student Resources:

DISABILITY SUPPORT SERVICES: udss@uwyo.edu, 766-3073, 128 Knight Hall, www.uwyo.edu/udss
COUNSELING CENTER: uccstaff@uwyo.edu, 766-2187, 766-8989 (After hours), 341 Knight Hall, www.uwyo.edu/ucc
ACADEMIC AFFAIRS: 766-4286, 312 Old Main, www.uwyo.edu/acadaffairs
DEAN OF STUDENTS OFFICE: dos@uwyo.edu, 766-3296, 128 Knight Hall, www.uwyo.edu/dos
UW POLICE DEPARTMENT: uwpd@uwyo.edu, 766-5179, 1426 E Flint St, www.uwyo.edu/uwpd
STUDENT CODE OF CONDUCT WEBSITE: www.uwyo.edu/dos/conduct

Schedule of topics, activities, and assessment methods:

Module	Topic	Recorded Lectures	Assigned Articles	Assessment
I	The Historical Record of Human Experimentation	-The Tuskeegee Syphilis Study -Vulnerability and Eligibility in Research with Humans	Finder, Vulnerability in Human Subject Research: Existential State, not Category Designation, Am J Bioethics (2014)	Discussion Bd Case Study Module Exam
II	New Drug Discovery and Testing	-The "New Drug" Classification -The "Substantial Evidence" Standard	Shaffer, When the Alpha is the Omega: P-Values, "Substantial Evidence," and the 0.05 Standard at FDA, Food & Drug L J (2017)	Discussion Bd Case Study Module Exam
III	Criteria for New Drug Approval	-The NDA Submission -Safety v. Efficacy; and Risk v. Benefit	Holbein, Understanding FDA Regulatory Requirements for Investigational New Drug Applications for Sponsor-Investigators, J Investig Med (2019)	Discussion Bd Case Study Module Exam
IV	The Fine Line Between Research and Innovative Care	-The Pharmacy Protocol -Pharmacy & Therapeutics Committee Oversight	Shulkin, Reinventing the Pharmacy and Therapeutics Committee, P&T (2012)	Discussion Bd Case Study Module Exam
V	Legal Requirements for Informed Consent to Research	-The Process of Consent -Capacity to Consent	Biros, Capacity, Vulnerability, and Informed Consent for Research, J Law Med Ethics (2018)	Discussion Bd Case Study Module Exam
VI	Legal Requirements for Research Protocol & Design	-Placebos and Control Groups -Good Clinical Practice	Grimes et al., The Good Clinical Practice Guideline: A Bronze Standard for Clinical Research, The Lancet (2005)	Discussion Bd Case Study Module Exam
VII	The Institutional Review Board	-IRB Procedures -Accountability to the IRB and Accountability of the IRB	Lynch, Opening Closed Doors: Promoting IRB Transparency, J Law Med Ethics (2018)	Discussion Bd Case Study Module Exam
VIII	Monitoring Research for Regulatory Compliance	-The Research Monitor's Role -Progress Reporting	Cocchetto et al., Development of an Orientation Program for New Clinical Trial Monitors, Clin Res Practices and Drug Reg Affairs (2008)	Discussion Bd Case Study Module Exam
IX	The Legality of Off-Label Drug Use	-FDA Labeling Standards -Evolving Technologies and New Opportunities	Kalil, Treating COVID-19—Off-Label Drug Use, Compassionate Use, and Randomized Clinical Trials During Pandemics, JAMA (2020)	Discussion Bd Case Study Module Exam
X	Access to Unapproved Drugs	-Right to Try Laws -Expanded Access to Investigational Drugs	Fernandez, et al., Promoting Patient Interests in Implementing the Federal Right to Try Act, JAMA (2018)	Discussion Bd Case Study Module Exam
Comp Exam				Proctored Comp Exam

Discussion Board (Class) Preparation/Participation Grading Rubric (30% of Grade)

	Excellent (A)	Good (B)	Inadequate (C)
Contributions	Consistently initiates useful and relevant ideas when participating in the discussion board. A definite leader who contributes major effort and who makes class discussions better.	Usually provides useful ideas when participating in classroom discussion board. A strong student who tries hard but is more of a follower than a leader in discussions.	Inconsistent in providing relevant comments on discussion board. Fails to initiate new threads that stimulate participation by other students.
Attitude	Always respectful of others; has a positive attitude, and does not rudely criticize anyone else's ideas or work. Other students feel safe responding to this student's posts.	Occasionally becomes impatient with ideas or work of others. Usually has a positive attitude toward discussions. Usually treats others and self with respect.	On more than one occasion becomes disrespectful of ideas expressed by others, using insults rather than evidence to express contrary views.
Preparedness & Focus	Consistently stays focused on subject matter assigned for discussion board and achieves identified outcomes. Self-directed and highly motivated. Postings help with understanding of assigned materials.	Usually posts comments that are related to course materials, but occasionally rambles about subjects that are not relevant to the course.	Postings to discussion board are based on general knowledge and common sense, rather than on materials assigned for course.
Quality of Work	Provides work of the highest insight that motivates other students to achieve at a high level.	Provides quality work that is interesting but not consistently insightful.	Does work that reflects little understanding of the course material.