PURDUE
UNIVERSITY

DEPARTMENT OF AGRICULTURAL & BIOLOGICAL ENGINEERING

TO: The Faculty of the College of Engineering

FROM: Bernard A. Engel, Department Head Agricultural & Biological Engineering

DATE: November 21, 2018

RE: New Graduate Course, ABE 51200 – EFD 66-19

The faculty of the School of Agricultural & Biological Engineering has approved the following new course. This submission is recommended to the Engineering Faculty for approval.

ABE 51200 Good Regulatory Practices
Lecture, Cr. 3

Course Description
Includes a review of the FDA and ICH regulations on good manufacturing, good laboratory, good clinical practices. The meaning of these regulations, the globalization of practices and the roles and responsibilities of various professionals implementing these regulations will be addressed. Special emphasis will be detailed coverage of the process for the assembly and submission of an IND or NDA, and the function of the regulatory affairs department in a pharmaceutical company.

Justification
The purpose of this course is to provide graduate students education in the important aspects of Good Regulatory Practices as it relates to biotechnology innovation, regulatory affairs and quality control and quality assurance. Individuals completing this course will be able to describe information about biotechnology drug development and innovation and explain how this information relates to the regulation of biotechnology products and drugs.

Modern biotechnology companies must conduct drug discovery, development, and sales in a highly regulated environment with competition and pricing pressures increasing. Integrated management systems for biotechnology innovation, discovery, development, quality control, quality assurance, compliance, and business improvement are critical elements for success in this complex and evolving environment. The cost of poor quality and the penalties for non-

Department of Agricultural & Biological Engineering
225 S. University Drive ▪ West Lafayette, IN 47907-2093
(765) 494-1162 ▪ Fax: (765) 496-1115 ▪ http://www.purdue.edu/abe

compliance are unacceptable in today's drug development business. Knowledge of effective manufacturing principles and practices is a critical part of getting things "right the first time".

This course is a core course for both the Biotechnology Quality and Regulatory Compliance graduate certificate and the Area of Specialization in Biotechnology Innovation and Regulatory Science.

TLI 52200 Good Regulatory Practices (3 credits)

COURSE DESCRIPTION:

Includes a review of the FDA and ICH regulations on good manufacturing, good laboratory, good clinical practices. The meaning of these regulations, the globalization of practices and the roles and responsibilities of various professionals implementing these regulations will be addressed. Special emphasis will be detailed coverage of the process for the assembly and submission of an IND or NDA, and the function of the regulatory affairs department in a pharmaceutical company.

Course Rationale

The purpose of this course is to provide graduate students education in the important aspects of Good Regulatory Practices as it relates to biotechnology innovation, regulatory affairs and quality control and quality assurance. Individuals completing this course will be able to describe information about biotechnology drug development and innovation and explain how this information relates to the regulation of biotechnology products and drugs.

Modern biotechnology companies must conduct drug discovery, development, and sales in a highly regulated environment with competition and pricing pressures increasing. Integrated management systems for biotechnology innovation, discovery, development, quality control, quality assurance, compliance, and business improvement are critical elements for success in this complex and evolving environment. The cost of poor quality and the penalties for non-compliance are unacceptable in today's drug development business. Knowledge of effective manufacturing principles and practices is a critical part of getting things "right the first time".

This course is a core course for both the Biotechnology Quality and Regulatory Compliance graduate certificate and the Area of Specialization in Biotechnology Innovation and Regulatory Science.

LEARNING OUTCOMES

The overall learning outcomes for the program include:

Comprehension: The student shall comprehend strategies used for biotechnology innovation: regulatory and quality documents and materials in the areas of drug development and discovery.

Integrative competence: The student shall be able to meld theory and practice

Critical thinking and decision making abilities: The student shall examine issues rationally, logically, and coherently; and shall acquire, evaluate, and synthesize information and knowledge relevant to an identified problem; and shall make sound decisions in both familiar and unfamiliar contexts.

Communication abilities: The student shall read, write, speak, listen, and use data, media and computers to send and respond effectively to communications for varied audiences and purposes.

Responsible use of values and ethical principles: The student shall demonstrate sensitivity to and facility with personal values and ethical principles in professional and social contexts.

COURSE LEARNING OUTCOMES

Students will learn about major regulatory areas that must be met for filing in support of new drugs, devices and combination products with health authorities.

Learning Outcome 1: Students will learn cGMP regulations, and relationship to maintaining control of the chemical and ultimately the drug product with a focus on Phase 3, product introduction, and post marketing

- Students will learn about the regulatory history of the FDA and the GxP framework
- Students will learn about NDA and BLA applications, product control including specifications, quality outcomes, critical quality attributes, and ICH framework.
- Students will learn about the regulations governing the manufacture of drug products, including the methods used to prove this, validation of those methods, validation of the manufacture, quality by design, comparability protocols, and continuous improvement
- Students will learn about compliance to GMP and warning letters
- Students will learn about Good Distribution Practices (GDP) and the integration of supply chain controls into the Quality Management System

Learning Outcome 2: Students will learn GCP, clinical regulations, and relationship to ensuring the drug or device is safe and efficacious

- Students will learn basic clinical trial design and how to write the investigator's brochure that informs patients (through the informed consent document that they sign) of clinical information
- Students will learn the rigid control that governs the clinical protocols and processes such as compliance oversight procedures, the role of clinical auditors and the process of auditing a clinical trial to ensure that it is done right
- Students will learn about the impact of technology and patient involvement in clinical trials through online resources, such as clinicaltrials.gov, youtube instruction videos including videos describing GCP for devices.

- Students will learn about the impact of recent adverse clinical trial events with innovative applications such as in biologics (Tegerno) and gene therapy (Gelsinger).
- Students will also learn about the role of approved Risk Evaluation and Mitigation Strategies (REMS), pharmacovigilance programs and adverse drug event reporting.

Learning Outcome 3: Students will learn GLP and regulations that ensure a drug product is safe.

- Students will learn about GLP protocols, toxicology testing, including animal and human safety, and indicators for safety (irregular heartbeats in animals, etc.)
- Students will learn the ethical considerations of testing, including impact of falsifying safety testing
- Students will learn about how GLP regulations are implemented during development and testing of devices.

Learning Outcome 4: Students will learn how technology and innovation impact the regulatory process

- Students will learn about data integrity and compliance with cGMP
- Students will learn about the role of computer systems and computer systems validation
- Students will learn about the emerging area of predictive toxicology and the potential for testing without animals
- Students will learn about innovation in safety and adaptive clinical trials
- Students will learn about innovation in CMC including quality by design and predicting the quality of manufacturing on the large scale with small scale experiments, including analytics modeling

Learning Outcome 5: Students will learn how the global environment impacts the regulatory process

- Students will learn special considerations of implementing a generic system in the developing and third world country
- Students will learn about global regulatory authorities and WHO PQ process.

Learning Outcome 6: Students will learn about special considerations of the regulatory process as applied to devices, diagnostics and generics

- Students will learn the importance of design to a device, attributes that lead to the specifications and raw materials for diagnostics and the importance of product equivalence for generics and special considerations for biologics

Textbooks and Resource Materials:

Two textbooks are required:

- *New Drug Development: A Regulatory Overview* by Mark Mathieu (http://www.amazon.com/New-Drug-Development-Regulatory-Overview/dp/1882615859) ISBN-13: 978-1882615858)
- **12 Golden GCP Rules for Investigators** by David Hutchinson, Canary Publications (September 1, 2010) ISBN: 978-1903712702

These will be used to provide a foundational background. Purdue students can access primary literature and databases online through the Purdue Libraries: https://www.lib.purdue.edu/ and extensive use is made of documents available online from regulatory agencies such as FDA (www.FDA.gov).

Pedagogy

A blended pedagogical approach for course delivery will be used. Class time will focus on interactive and engaging sessions, to learn and practice the application of course material. Guest lectures will be provided from professional experts from industry, focused on current topic lectures and discussions. Additional resources and fundamental core content is provided online using the Blackboard Learn course management system.

Student evaluation is based upon case studies, quizzes, reflections and a final project with application to drug development. Students also work in groups and practice professional communication through presentations and discussions surrounding the course topics, case studies and final project.

Assessment

Assigned Readings.
Readings will be assigned to provide more information and background on the course concepts. There will be oral discussions in class over the readings, quizzes and case studies.

Case Studies:
Case studies will be assigned to give you practice using the concepts learned in class. Therefore, it is particularly important that you personally do the work. Working with other individuals is fine as long as you actively participate; learning is virtually eliminated when simply copying another person's work. Due dates for case studies will be posted on Blackboard Learn.

Final Project:
A final project will be used to evaluate your understanding of course material and provide you with an additional opportunity to apply knowledge from the lectures and case studies to a project that is relevant to the current field of drug development.

Grading:

The final grades for the course will be determined by a total accumulation of points from all activities and assignments. Individual progress toward course learning outcomes and final grades will be computed based on the following weights:

Assignments	**Percentage**
Reflections	10
Final Project	50
Case Studies	40
Total	100

Grading Scale:

Grade	**GPA Value**	**% Range**
A	4.0	93-100
A-	3.7	90.0-92.9
B+	3.3	87.0-89.9
B	3.0	83.0-86.9
B-	2.7	80.0-82.9
C+	2.3	77.0-79.9
C	2.0	73.0-76.9
C-	1.7	70.0-72.9
D+	1.3	67.0-69.9
D	1.0	63.0-66.9
D-	0.7	60.0-62.9

F	0.0	<60.0

Academic Dishonesty
Purdue prohibits "dishonesty in connection with any University activity. Cheating, plagiarism, or knowingly furnishing false information to the University are examples of dishonesty." [Part 5, Section III-B-2-a, Student Regulations] Furthermore, the University Senate has stipulated that "the commitment of acts of cheating, lying, and deceit in any of their diverse forms (such as the use of substitutes for taking examinations, the use of illegal cribs, plagiarism, and copying during examinations) is dishonest and must not be tolerated. Moreover, knowingly to aid and abet, directly or indirectly, other parties in committing dishonest acts is in itself dishonest." [University Senate Document 72-18, December 15, 1972]

Please refer to Purdue's student guide for academic integrity for additional information: https://www.purdue.edu/odos/academic-integrity/

Use of Copyrighted Materials

Students are expected, within the context of the Regulations Governing Student Conduct and other applicable University policies, to act responsibly and ethically by applying the appropriate exception under the Copyright Act to the use of copyrighted works in their activities and studies. The University does not assume legal responsibility for violations of copyright law by students who are not employees of the University.

A Copyrightable Work created by any person subject to this policy primarily to express and preserve scholarship as evidence of academic advancement or academic accomplishment. Such works may include, but are not limited to, scholarly publications, journal articles, research bulletins, monographs, books, plays, poems, musical compositions and other works of artistic imagination, and works of students created in the course of their education, such as exams, projects, theses or dissertations, papers and articles.

Please refer to the University Regulations on policies:
http://www.purdue.edu/policies/academic-research-affairs/ia3.html

Attendance
Purdue University policy states that all students are expected to be present for every meeting of the classes in which they are enrolled. Only the instructor can excuse a student from a course requirement or responsibility. When conflicts or absences can be anticipated, such as for many University sponsored activities and religious observations, the student should inform the instructor of the situation as far in advance as possible…For unanticipated or emergency absences when advance notification to an instructor is not possible, the student should contact

the instructor as soon as possible by email, or by contacting the main office that offers the course. When the student is unable to make direct contact with the instructor and is unable to leave word with the instructor's department because of circumstances beyond the student's control, and in cases of bereavement, the student or the student's representative should contact the Office of the Dean of Students.

The link to the complete policy and implications can be found at:
http://www.purdue.edu/studentregulations/regulations_procedures/classes.html

Missed or Late Work
Assignments must be turned in at the beginning of class or submitted via Blackboard Learn. Assignments will not be accepted via email unless special arrangements have been made in advance.

Late assignments will not be accepted unless special arrangements have been made with the instructor, preferably in advance. If prior arrangements have not been made, missed or late assignments will not receive credit. See policy above regarding arriving late/leaving early. Assignments can be accepted early.

Grief Absence Policy for Students
Purdue University recognizes that a time of bereavement is very difficult for a student. The University therefore provides the following rights to students facing the loss of a family member through the Grief Absence Policy for Students (GAPS). GAPS Policy: Students will be excused for funeral leave and given the opportunity to earn equivalent credit and to demonstrate evidence of meeting the learning outcomes for misses assignments or assessments in the event of the death of a member of the student's family.

See the University's website for additional information:
http://www.purdue.edu/studentregulations/regulations_procedures/classes.html

Violent Behavior Policy
Purdue University is committed to providing a safe and secure campus environment for members of the university community. Purdue strives to create an educational environment for students and a work environment for employees that promote educational and career goals. Violent Behavior impedes such goals. Therefore, Violent Behavior is prohibited in or on any University Facility or while participating in any university activity.

See the University's website for additional information:
http://www.purdue.edu/policies/facilities-safety/iva3.html

Emergencies
In the event of a major campus emergency, course requirements, deadlines and grading percentages are subject to changes that may be necessitated by a revised semester calendar or other circumstances beyond the instructor's control. Relevant changes to this course will be

posted onto the course website or can be obtained by contacting the instructors or TAs via email or phone. You are expected to read your @purdue.edu email on a frequent basis.

See the University's website for additional information:
https://www.purdue.edu/ehps/emergency_preparedness/

Accessibility and Accommodations
Purdue University strives to make learning experiences as accessible as possible. If you anticipate or experience physical or academic barriers based on disability, you are welcome to let me know so that we can discuss options. You are also encouraged to contact the Disability Resource Center at: drc@purdue.edu or by phone: 765-494-1247.

Nondiscrimination
Purdue University is committed to maintaining a community which recognizes and values the inherent worth and dignity of every person; fosters tolerance, sensitivity, understanding, and mutual respect among its members; and encourages each individual to strive to reach his or her own potential. In pursuit of its goal of academic excellence, the University seeks to develop and nurture diversity. The University believes that diversity among its many members strengthens the institution, stimulates creativity, promotes the exchange of ideas, and enriches campus life.

Purdue University prohibits discrimination against any member of the University community on the basis of race, religion, color, sex, age, national origin or ancestry, genetic information, marital status, parental status, sexual orientation, gender identity and expression, disability, or status as a veteran. The University will conduct its programs, services and activities consistent with applicable federal, state and local laws, regulations and orders and in conformance with the procedures and limitations as set forth in Executive Memorandum No. D-1, which provides specific contractual rights and remedies. Any student who believes they have been discriminated against may visit www.purdue.edu/report-hate to submit a complaint to the Office of Institutional Equity. Information may be reported anonymously.

Please refer students to Purdue's nondiscrimination statement:
http://www.purdue.edu/purdue/ea_eou_statement.html

Course Schedule and Lecture Topics

Core Lecture Topics:

- History of FDA and Modern Regulations; Framework for GxP – Drugs/Devices/Combinations (Learning Outcome 1)
- Structure of the FDA – Overview of how an application is reviewed; How does FDA communicate with industry (Learning Outcome 1)

- Quality Systems Approach for Pharmaceuticals: QbD, CAPA, QRM, Change Control, Self audits (Learning Outcome 1 & 4)
- Process Validation – Documentation, Master Validation Protocols, Specifications, How to manage post approval changes – pharmaceuticals (Learning Outcome 1 & 6)
- Part 11- Electronic Records; Computer Systems Validation, Data Integrity (Learning Outcome 4)
- Medical Device Regulations; Combination Product Regulations, Part 820: QS regulations (Learning Outcome 6)
- Approval process for devices, device labeling and post approval commitments: medical device reporting (Learning Outcome 6)
- Overview of GLP regulations as applied to drugs and devices – how implemented and application of controls (Learning Outcome 3)
- Overview of GCP, ISO 14155 (Learning Outcome 2)
- Basic clinical trial design, Writing Investigator's Brochure (Learning Outcome 2)
- Clinical Quality Management: Drugs and Devices (Learning Outcome 2)
- Inspections and Audits – FDA perspective (Learning Outcome 2)
- REMS, Basics of Pharmacovigilance, Post Marketing Commitments, FAERS (Learning Outcome 2)

Additional Lecture Topics with selections from the following:

- Review of Food and Drug Law
- Globalization the Regulations: the ICH process and the outcomes
- Key elements of GXPs: GMPs/GCPs/GLPs/"GRPs"
- Philosophies and principles of Quality Management
- Operating in Compliance: Roles and Responsibilities of various parties
- Regulatory Agencies – what they do
- INDs/NDAs
- GMP Module
    - Why GMP (Statistics, Inspection Results, Wrecks)
    - Details of GMP's (guidances, specifications, ICH, BACPAC, Site specific stability)
    - Roles and responsibilities in the manufacturing of a drug
    - Compliance oversight: QC, QA (quality assurance) and regulatory inspections
- GLP Module
    - Why GLP (Statistics, Inspection Results)
    - Details of GLP's (protocols, accountability, review)
    - Roles and responsibilities in toxicology and non-clinical pharmacology
    - Compliance/Oversight QC, QA, and regulatory agency inspections
- GCP Module

    - Why GCPs (Statistics, Inspection Results)
    - Details of GCP's (protocols, accountability, review)
    - Adverse drug event reporting
    - Roles and responsibilities in clinical research
    - Compliance oversight
- The "Submission"…the NDA…the Dossier…the "big Event"!
- Post-Approval Research, Advertising and Promotion: Regulations and Compliance
- CROs
- Scientific Misconduct and Fraud: Prevalence and Prevention