

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 51100 Drug Development – EFD 65-19

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 51100 Drug Development
Lecture, Cr. 3

Course Description

A review of drug discovery and drug development, with emphasis on the regulatory aspects of these activities. Animal preclinical research and human clinical research are discussed in detail. In addition, the process for the assembly of an IND and NDA is discussed along with the Phases (I,II,III) of human clinical trials. The CMC (chemistry manufacturing and control) aspects of drug development are presented along with ICH documents and manufacturing process analytical technologies. The course concludes with a brief review of international regulatory issues and patents.

Justification

The purpose of this course is to provide graduate students education in the important aspects of Drug Development 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 discovery and registration of 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.



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TLI 52100: Drug Development (3 credits)

COURSE DESCRIPTION:

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Course Rationale

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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

Learning Outcome 1: Students will learn the overall process of drug development, including the major steps such as discovery, toxicology and formulation.

- Students will learn the overall drug development and approval process.
- Students will learn the major components of clinical trial design within drug development
- Students will learn functional role of discovery chemistry, discovery biology, ADME, toxicology, CMC and how the functions contribute to drug development in a team environment.
- Students will learn how to develop a TPP
- Students will learn how to file an IND and the factors involved in making a product decision during the drug development process, including the factors involved in moving a compound to an IND and subsequently moving a compound to phase II

Learning Outcome 2: Students will learn the role of a quality system in the process of drug development and how the process of drug development is regulated.

- Students will learn about phase appropriate development, specific CMC deliverables at each stage of development including elements of process validation and understand ICH guidelines for drug development.
- Students will learn about Quality by Design principles
- Students will learn about the design of clinical trials, clinical trial endpoints and the organization and administration of clinical trial research.
- Students will learn how a quality system operates by learning the process for FDA review of documents during drug development

Learning Outcome 3: Students will learn the ethical considerations of drug development,

including the critical analysis and evaluation of ethical situations

Learning Outcome 4: Students will learn how the drug development process has been adapted for devices, diagnostics and biologics, including specific examples for each

- Students will learn about the design control process as it relates to the development of a device
- Students will learn about development of biologics and biosimilars
- Students will learn about development of vaccines: bench to market

Learning Outcome 5: Students will learn how the drug development process has been adapted for global applications, including WHO, EMEA, ICH

Learning Outcome 6: Students will learn how innovation is applied to the drug development process

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)
- *Translating Molecules into Medicines: Cross-Functional Integration at the Drug Discovery-Development Interface*, Editors Shobha N. Bhattachar, John Morrison, Daniel R. Mudra, and David M. Bender <http://www.springer.com/us/book/9783319500409> ISBN 978-3319500409.

The textbooks will be used to provide a foundational background. Additional supplemental readings from the primary literature will be used in addition to online databases. Purdue students can access primary literature and databases online through the Purdue Libraries: <https://www.lib.purdue.edu/>.

Online lectures, quizzes, case studies, and the major project as well as other current reading material and resources will be provided through the Purdue course management system, Blackboard Learn (BBL) <http://www.itap.purdue.edu/learning/tools/blackboard/>

Supplementary Resources:

- Al-Achi, A., *Integrated pharmaceuticals applied preformulation, product design, and regulatory science*. Hoboken, N.J., John Wiley & Sons: Hoboken, N.J., 2013.
- Amato, S., *Regulatory Affairs for Biomaterials and Medical Devices*. : Burlington: Elsevier Science: Burlington, 2014.

- Boname, M. L., *Advancing the Discipline of Regulatory Science for Medical Product Development: an Update on Progress and a Forward-Looking Agenda: workshop summary*. Washington, DC: The National Academies Press: 2016.
- Foote, M., *Targeted Regulatory Writing Techniques Clinical Documents for Drugs and Biologics*. Basel: Birkhäuser Basel: 2008.
- Goodsaid, F., *The Path from Biomarker Discovery to Regulatory Qualification*. Burlington: Elsevier Science: Burlington, 2013.
- Institute of Medicine. Forum on Drug Discovery, D.; Translation, *Building a national framework for the establishment of regulatory science for drug development: workshop summary*. Washington, D.C.: National Academies Press: Washington, D.C., 2011.
- Raybould, A.; Kurtz, R.; Zeph, L., *Regulatory science, research science and innovation in agricultural biotechnology*. 2014; p 317-333.
- Sakamoto, Yu & Otsubo, Yasuto & Ishiguro, Akihiro & Uyama, Yoshiaki. (2014). *PGx/Biomarker Utilization for Regulatory Decision Making*. Handbook of Pharmacogenomics and Stratified Medicine. p 951-967.
- Suckow, M. A., *Research Regulatory Compliance*. Burlington: Elsevier Science: Burlington, 2015.
- Welty, G., *Quality Assurance Problem Solving and Training Strategies for Success in the Pharmaceutical and Life Science Industries*. Burlington: Elsevier Science: Burlington, 2013.
- Yu, L. X., *FDA Bioequivalence Standards*. New York: Springer New York: New York, 2014.
- Ziegler, O., *EU Regulatory Decision Making and the Role of the United States Transatlantic Regulatory Cooperation as a Gateway for U. S. Economic Interests?* Wiesbaden: Springer Fachmedien Wiesbaden: Imprint: Springer VS: 2012.

Resources from Regulatory Agency for Semester Project including:

- **Guidance Documents**

<https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredeveloped>

[dandapproved/approvalapplications/investigationalnewdrugindapplication/default.htm](http://www.fda.gov/oc/ohrt/dandapproved/approvalapplications/investigationalnewdrugindapplication/default.htm))

Per the FDA website: *“Guidance documents represent the Agency's current thinking on a particular subject. These documents provide FDA review staff and applicants/sponsors with guidelines to the processing, content, and evaluation/approval of applications and also to the design, production, manufacturing, and testing of regulated products. They also establish policies intended to achieve consistency in the Agency's regulatory approach and establish inspection and enforcement procedures.*

Because guidances are not regulations or laws, they are not enforceable, either through administrative actions or through the courts. An alternative approach may be used if it satisfies the requirements of the applicable statute, regulations, or both. For information on a specific guidance document, please contact the originating office.”

- **Guidance for Industry:**

- Content and Format of Investigational New Drug Applications (INDs) for Phase I Studies of Drugs, Including Well-Characterized, Therapeutic, Biotechnology-derived Products
- Estimating the Maximum Safe Starting Dose in Initial Clinical Trials for Therapeutics in Adult Healthy Volunteers
- Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products (draft guidance)
- Immunotoxicology Evaluation of Investigational New Drugs
- IND Meetings for Human Drugs and Biologics: Chemistry, Manufacturing, and Controls Information
- M3 (R2) Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals
- Nonclinical Studies for the Safety Evaluation of Pharmaceutical Excipients
- Safety Testing of Drug Metabolites

- **Regulatory Agency Review Guidelines**

- Center for Drug Evaluation and Research: Manual of Policies and Procedures: Office of Clinical Pharmacology: Good Review Practices: Clinical Pharmacology Review of New Molecular Entity (NME) New Drug Applications (NDAs) and Original Biologics License Applications (BLAs)
- Center for Drug Evaluation and Research (CDER); Center for Biologics Evaluation and Research (CBER): Guidance for Review Staff and Industry Good Review Management Principles and Practices for PDUFA Products
- CDER Draft Guidance for Industry and Review Staff: Target Product Profile---A Strategic Development Process Tool
- **International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use**
 - ICH E8: General Considerations for Clinical Trials
 - ICH Topic E15: Definitions for genomic biomarkers, pharmacogenomics, pharmacogenetics, genomic data and sample coding categories
 - European Medicines Agency Note for Guidance on Definitions for genomic biomarkers, pharmacogenomics, pharmacogenetics, genomic data and sample coding categories
 - ICH E16: E16 Biomarkers Related to Drug or Biotechnology Product Development: Context, Structure, and Format of Qualification Submissions
 - ICH Q3A: Impurities in New Drug Substances
 - ICH M3 (R2): Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals
 - ICH Q1A (R2): Stability Testing of New Drug Substances and Products
 - ICH Q2A: Text on Validation of Analytical Procedures
 - ICH Q3B (R2): Impurities in New Drug Products
 - ICH Q6B: Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products

- European Medicines Agency Note for Guidance on Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products
- ICH S2B Genotoxicity: A Standard Battery for Genotoxicity Testing of Pharmaceuticals
- ICH S6 Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals
- ICH S7A Safety Pharmacology Studies for Human Pharmaceuticals
- ICH Q6A: Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances

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.

General Course Policies

Use of Technology: Computers and other technologies are welcome in class when related to the current topic and course discussions but please be professional and keep cell phone or other uses of technology, i.e. texting, social media, to a minimum as it may be distracting to both your fellow classmates and instructors.

Class Participation: You should attend all classes. Please see a more detailed description of Purdue's attendance policy below. You are expected to be both punctual and prepared for group activities and discussion. In addition, you are expected to stay for the entire class period. It is simply a matter of courtesy to your fellow students and the instructors. Class discussions enhance and clarify your understanding of course material. Students who are absent are still responsible for knowing course material and getting assignments and announcements regardless of attendance. Past experience shows that successful students were those who attended class, participated in discussions, and completed all assignments and quizzes.

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.

Briefing Document Project:

A mock application 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. The briefing document requires a team effort to develop and the team will develop a project management plan with timeline and individual deliverables to achieve expected project outcomes. A successful, cohesive briefing document will also require consistent communication among all team members to ensure that each piece is well integrated. Individuals will be graded based on the submission of the functional piece assigned to them within the team.

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
Briefing Document Project	60
Case Studies	30
Attendance and Class Participation	10
Total	100

Grading Scale:

Grade	GPA Value	% Range
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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/ehrs/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:

- Drug Development Overview
- Overview of Briefing Document Project (Learning Outcome 1)
- Discovery Chemistry and Early Phase Process Scale up (Learning Outcome 1 & 6)
- Discovery Biology: Roles and Responsibilities for Drug Candidate Searching and Screening (Learning Outcome 1 & 6)
- Toxicology for Drug Candidate Selection (Learning Outcome 1)
- ADME (Absorption, Distribution, Metabolism, Elimination) of Drugs (Learning Outcome 1)
- Phase appropriate CMC development program (Learning Outcome 2 & 5)
- Integrated Pharmaceutical Quality Systems (Learning Outcome 2)
- Design of clinical trials, Role of Translational Science in successful clinical development (Learning Outcome 2)
- Organization and administration of clinical trials (Learning Outcome 2 & 3)
- Specifications for Drug Substance and Drug Products (Learning Outcome 1)
- Development of biologics and biosimilars (Learning Outcome 4)
- Development of vaccines: Bench to market (Learning Outcome 4)
- Development of generic drug products (Learning Outcome 4)
- Development of devices and diagnostics : Application of design control principles, Global adaptations for registration of devices (Learning Outcome 4)

Additional Lecture Topics with selections from the following:

- Therapeutic Drug Use in America
- Review of Food and Drug Law
- Overview of steps in drug development
- ICH process related to Drug Development

- Drug Discovery Module---The theory and practice of drug discovery
- The regulations and standards applying to drug discovery research
- The IND/NDA discovery sections and the need for good research practices
- Candidate selection and other infrastructure battles
- Early Chemistry& Formulations, Scale-up
- Early Toxicology and safety pharmacology
- ADME & analytical chemistry
- Toxicology for worldwide submission
- The ethics of human research, informed consent, IRB's
- The phases of clinical research and drug evaluation: – Phase I, II and the IND
- Phases of clinical research and drug evaluation: Product decision and the Phase III “product registration” trials for an NDA
- Research standards to protect human subjects
- Oversight of clinical trials: Monitoring, QA, auditing, Regulatory affairs, pharmacovigilance, and regulatory agency inspections
- Regulatory affairs and drug labeling
- Submitting an NDA
- NDA review process in the US and worldwide
- Phase IV Research, Regulation of promotion activities
- Regulatory Reform
- Advisory committee meetings, regulatory compliance
- Chemical synthesis
 - ICH Quality Documents
 - ICH Q1, Q2
 - ICH Q3, Q4, Q5
 - ICH Q6 – Specifications
- Stability & USP
- BACPAC, manufacturing, controls, in-process controls
- Process Analytical Technologies (PAT)
- Quality control & quality assurance
- Pre-approval inspections
- Global Dossiers
- International Regulatory
- ANDA's
- Patents