

New Course Request

NOV 11 2008 Indiana University

Indianapolis Campus

Check Appropriate Boxes:

Undergraduate credit

Graduate credit

Professional credit 90

1. School/Division Science, Biostatistics 2. Academic Subject Code BIOS

3. Course Number 627 (must be cleared with University Enrollment Services) 4. Instructor variable

5. Course Title Statistics in Pharmaceutical Research

Recommended Abbreviation (Optional) Stat in Pharmaceutical Research
(Limited to 32 Characters including spaces)

6. First time this course is to be offered (Semester/Year): TBD

7. Credit Hours: Fixed at 3 or Variable from _____ to _____

8. Is this course to be graded S-F (only)? Yes _____ No X

9. Is variable title approval being requested? Yes _____ No X

10. Course description (not to exceed 50 words) for Bulletin publication: _____
P: STAT 512; BIOS 527, 546. An overview of the drug development process, including the various phases of development from pre-clinical to post-marketing. Topics: statistical issues in design, study monitoring, analysis and reporting. Additional topics may include regulatory and statistical aspects of population pharmacokinetics and real world applications.

11. Lecture Contact Hours: Fixed at 3 or Variable from _____ to _____

12. Non-Lecture Contact Hours: Fixed at _____ or Variable from _____ to _____

13. Estimated enrollment: 5-10 of which 100 percent are expected to be graduate students.

14. Frequency of scheduling: variable Will this course be required for majors? no

15. Justification for new course: Elective course in new biostatistics Ph.D. program

16. Are the necessary reading materials currently available in the appropriate library? n/a-see syllabus

17. Please append a complete outline of the proposed course, and indicate instructor (if known), textbooks, and other materials.

18. If this course overlaps with existing courses, please explain with which courses it overlaps and whether this overlap is necessary, desirable, or unimportant.

19. A copy of every new course proposal must be submitted to departments, schools, or divisions in which there may be overlap of the new course with existing courses or areas of strong concern, with instructions that they send comments directly to the originating Curriculum Committee. Please append a list of departments, schools, or divisions thus consulted.

Submitted by: Berk Boston Date 6/6/08
Department Chairman/Division Director

Date _____
Dean of Graduate School (when required)

Approved by: James M. Murphy Date 6/25/2008
Dean

Murray S. Quener Date 11/4/08
Chancellor/Vice-President

Date _____
University Enrollment Services

JULIE D'APRILE APPROVED OCT 01 2008
Curriculum Committee Date

After School/Division approval, forward the last copy (without attachments) to University Enrollment Services for initial processing, and the remaining four copies and attachments to the Campus Chancellor or Vice-President.

BIOS 627
Statistics in Pharmaceutical Research

Syllabus

BIOS 627 – Statistics in Pharmaceutical Research (3 cr.)

Instructors: Team of instructors from the IUPUI Department of Mathematical Sciences, IU Division of Biostatistics, and Eli Lilly & Company

A. Course Description:

This course is a collaborative effort between the IUPUI Department of Mathematical Sciences, the IU Division of Biostatistics, and Eli Lilly & Company. The goal of the series is to further strengthen the ties between industry and academia by introducing participants to the broad spectrum of issues surrounding the drug development process in the pharmaceutical industry. Practical examples will be discussed throughout the course and statistical software, e.g. SAS, will be utilized.

B. Prerequisites:

STAT 512, BIOS 527, BIOS 546

C. Textbooks

Required materials for the course will be distributed as needed by the instructors.

D. Description for Bulletin

P: STAT 512; BIOS 527, 546. An overview of the drug development process, including the various phases of development from pre-clinical to post-marketing. Topics: statistical issues in design, study monitoring, analysis and reporting. Additional topics may include regulatory and statistical aspects of population pharmacokinetics and real world applications.

E. Evaluation and Grading

The final grade will be determined by a combination of homework, midterm, and comprehensive final exam, as distributed below:

Homework – 20%

Mid-term exam – 30%

Final exam – 50%

The following grading scale will be used:

90 – 100	A's
80 – 89	B's
70 – 79	C's
60 – 69	D's
0 – 59	F

F. Course Outline

Note: This course outline reflects the course as delivered in the Fall 2007 semester (under STAT 598). Appropriate adjustments will be made in subsequent semesters to account for instructor availability, precise topics covered, pace of course, new discoveries, etc.

Week	Module	Description
1	Introduction	An overview of drug development from in-vitro, in-vivo and pre-clinical studies to clinical studies will be covered. The four phases of drug development will be described. The notion of risk/benefit analysis will be described and examples given. The critical path initiative will be discussed and the factors that affect the availability of innovative drugs including economics, regulatory hurdles and litigation. The "blockbuster" business model will be described and novel alternative business models such as "designer drugs" using technologies such as pharmacogenomics will be compared and contrasted. The influence of statistics on drug development under this alternative business model will be discussed.
2	Chemical Product R&D	Use of Experimental Design in developing / optimizing a chemical synthetic route for making the Active Pharmaceutical Ingredient (API), process capability and understanding error, linking to the measurement systems, Quality by Design initiative
4	Pharmaceutical Product R&D	Use of Experimental Design in developing / optimizing the formulation and process for making finished drug products (e.g. tablets, capsules), process capability, understanding error, linking to the API and measurement systems
4	Global Regulatory Landscape	Global guidelines, competing requirements, new FDA initiative for Quality by Design (QbD), use of multivariate statistics in conjunction with spectra data from PAT methods.
5	Drug Discovery	An introduction to discovery and some of the high throughput technologies including signal processing, normalization and data cleaning, smoothing and other denoising techniques pertaining to digital and analog signals. High dimensional problems, including visualization, the curse of dimensionality, projection, and multiple testing and high dimensional methods based on different penalties. This module will conclude with a discussion and approaches to build confidence in a prediction rule covering also ROC curves, and resampling techniques such as bootstrap and finally identifying candidates from a large collection of measurements.
6	Introductory PK/PD	What is PK, What is PD, Description on ADME, Definition and terminology, PK/PD in drug development. Types of PK analyses (non-compartmental, compartmental), Simple PD models. Give pharmacological interpretation of steady state, dose proportionality, bioequivalence. Discuss biomarkers and simple PD models.
7	Early Phase Clinical Trials	The general outline of SDSS/MDSS studies is introduced, which include: study planning, protocol drafting, operations, tox support, data management, data analysis, final study report. One case study will be employed to walk students through the processes to get a feel of what it is like to work on early phase drug development.
8	Early Phase Clinical Trials	Common statistical issues in early phase studies, which include: study design, sample size calculation, dose proportionality, dose response, biomarkers. Practical examples will be used for illustration.
9	Design issues in Phase III studies	Randomization methods, Determination of Sample Size, Stratification, Documentation of Design in Protocol. Multi-center trials, Multiplicity issues, Missing Data, Negotiation with Regulatory Authorities, Documentation of Analytical Methods in Protocol and SAP.
10	Interim Analyses	Charters and roles, Alpha spending functions, Conditional power, Adaptive dose finding designs, Adaptive sample size designs
11	Further Topics in Adaptive Designs	Group sequential and adaptive designs, Bayesian approaches to superiority, non-inferiority, safety, effect sizes, survival analysis Regulatory guidance, Motivate Bayesian adaptive designs, ASTIN study- Dose ranging, Bayesian Adaptive Non-Inferiority with Safety, Assessment and Bayesian Adaptive Dose Selection

12	Population PK	Population pharmacokinetics will be taught. Study designs and analyses and impact on the drug label will be covered.
13	Population PK	Statistical issues associated with non-linear models will be taught. Different computational methods will be described with an emphasis on methods for sparse sampling. NONMEM will be introduced.
14	Introduction to Biopharm packages	Objectives of biopharm packages and connections to the drug label, Types of biopharm studies with brief descriptions (BA/BE, DDI, Food effect, Mechanism of action, Renal impairment, Hepatic impairment, other special populations, QTc).
15	Bioequivalence study	FDA guidelines, Statistical hypotheses vs Confidence interval approach, Examples and Lab (nQuery and SAS) on Sample size estimation, Analysis of a BE study (or DDI)

G. Cheating and Plagiarism:

Academic misconduct will *not* be tolerated and all cases will be reported. Examine the IU Code of Student Rights, Responsibilities, and Conduct at <http://life.iupui.edu/help/code.asp> and in particular examine the rules regarding academic misconduct at http://life.iupui.edu/help/docs/Part_3all.html. Violations of these rules will result in a grade of "F" (or 0%) for the assignment in question, and may result in an "F" for the course or even expulsion from the university (see http://life.iupui.edu/help/docs/Part_4all.html#sanction).

H. Americans with Disabilities Act:

If you need any special accommodations due to a disability, please contact Adaptive Educational Services at (317)-274-3241. The office is located in CA 001E.