AC 2008-1276: A CASE-STUDY BASED COURSE ON "DEVICE EVALUATION AND FDA APPROVAL"

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Abstract

Preclinical evaluation of new devices and therapies is an integral part of research and development in the medical device industry, and the regulatory process for FDA approval is a major driving force behind much that goes on in a company setting. A large number of graduating biomedical engineers enter this medical device industry or a related environment upon graduation from our institution. Although these engineers are equipped to address many of the technical challenges that will arise, there is currently limited formal training in or exposure to the regulatory process that is required to bring new devices to market. Knowledge of the typical progression through preclinical testing, as well as an understanding of clinical trial guidelines and the FDA regulatory process would allow students to work more effectively and productively in industry or other medically-related positions. Therefore, a course has been designed entitled "Device Evaluation and FDA Approval" as an upper division elective at our institution. The goal of this course is to expose students to the overall process of FDA approval, including aspects of both preclinical and clinical testing, in order to prepare them to succeed in a regulatory-based environment.

This is a case-study based course, where cases range from small in-class examples that facilitate active student engagement in the material, to large cases that span multiple lessons and incorporate out of class assignments and projects. Cases are selected and presented such that students gain insights into the progression and complexities of "real-life" devices, while learning *in vitro* and *in vivo* preclinical evaluation techniques, clinical trial guidelines, FDA processes and requirements, and overall regulatory constraints.

Introduction

FDA regulations are a large part of many facets of life in the medical device industry. In roles ranging from business and management positions to manufacturing and process engineers, and from marketing to research and development scientists or engineers, many medical device career paths will incorporate some interaction with FDA regulation. Currently, our institution graduates a large number of engineers that enter this medical device arena, and previously no formal instruction was offered in the area of FDA approval processes. Although several institutions have implemented entire degree programs focused on regulatory affairs[1], the goal at our institution was to design a single course as an upper division elective that would expose students to the overall process of device evaluation and FDA approval. The purpose of this paper is to outline and describe the format, activities, and implementation of this new course at our institution.

Format and Content of the Course

This is a quarter-long course that is designed to meet for two 2-hour classroom sessions each week. The course is geared towards senior level undergraduate or master's level students in

Biomedical Engineering or other engineering disciplines, however no prerequisites or requirements exist that would preclude students in other majors from enrolling in the course. The overall course goals are as follows:

1. *To promote student ability to recognize and understand the steps necessary for preclinical and clinical evaluation of new medical devices.*
2. *To expose students to the FDA regulatory process.*
3. *To prepare students to enter the medical device industry or related field by providing an overview of the steps involved in getting a device to market.*

Learning objectives for the course state that at the end of the quarter, students will be able to:

1. *Outline the three classes of medical devices and summarize the corresponding oversight and regulatory paths to market.*
2. *Compare and contrast different in vitro and animal models used for device evaluation and discuss the issues and regulations related to animal testing.*
3. *Describe in detail the progression of a specific device through preclinical evaluation and clinical studies.*
4. *Recognize and interpret regulatory guidelines and requirements as they pertain to the development of new devices.*

Content is covered as outlined in Figure 1, with topics progressing from underlying FDA processes as a driving force and framework, to *in vitro* safety studies, preclinical animal models, clinical trials, and finally back to FDA procedures and regulation. Two lessons are entirely devoted to case study activities, and in addition topics of reimbursement, combination products, and approval outside the United States are briefly discussed. Case study activities and student presentations will be discussed in more detail in subsequent sections of this paper.

WEEK	TOPIC
1	Overview of course and Introduction to the FDA
	FDA submissions and requirements for approval
2	Medical device classification and testing
	GMP for medical devices: Quality systems regulations
3	Safety testing: Bench models and in vitro systems
	Animal models for preclinical studies: Part I
4	Animal models for preclinical studies: Part II
	Good Laboratory Practices in preclinical studies
5	Case study: Progression through preclinical testing
	MIDTERM
6	Pilot and pivotal clinical studies
	Clinical studies: a physician's perspective
7	FDA approval: timelines, panels, and communication
	FDA enforcement and post-approval procedures
8	Case study: Progression through clinical studies and FDA approval
	Device approval in non-US markets
9	Student Presentations
	Student Presentations
10	It's never that simple: Reimbursement, combination products, and other issues
	Course review and wrap-up

Figure 1: Outline of course topics covered on a weekly basis, with two class meetings per week.

The goal of this course is not to develop student expertise in any given area, as that primarily comes with more extensive experience, but rather to expose students to terminology, procedures, and the broad progression such that they have a framework to build upon in their future career.

Student Opinions Entering the Course

At the beginning of the first offering of this course, students were given an anonymous survey in order to broadly assess opinions regarding perceived knowledge and abilities, as well as the usefulness of the course topic. These questions were intended to provide feedback to the instructor to inform subsequent class session structure and to confirm- for both students and the instructor- an awareness of applicability and relevance of the topic. The mean values of responses for each of four questions are provided below. Responses were given on a scale from 1 to 5, with 1 representing little or no knowledge/usefulness and 5 representing expertise or highest level of usefulness. A total of 45 enrolled students provided responses.

> QUESTION 1: How much experience have you had adhering to or interpreting regulations for medical device development? *(Mean score = 2.0)*
>
> QUESTION 2: How would you rank your knowledge and abilities in the area of FDA regulatory pathways and requirements for medical devices? *(Mean score = 2.1)*
>
> QUESTION 3: How likely is it that your job will require knowledge of the regulatory process? *(Mean score = 3.9)*
>
> QUESTION 4: How valuable do you think this course will be for enhancing your abilities and productivity in your current/future job? *(Mean score = 4.1)*

Responses indicate that on average, students do not feel that they have significant experience or knowledge in the topic area, but that most students foresee themselves entering a career in which this topic is important. As an elective course, it is not surprising that the students enrolled are those that recognize a need or perceived usefulness for education in this area. If this course were to be required, it is likely that the incoming knowledge and experience would remain very low, but that perceived usefulness may also decrease. For purposes of course design and implementation, these preliminary survey questions suggest that the student participants will be motivated to learn and to expand their knowledge.

Use of Case Studies

Although a significant amount of background information, guidelines, definitions, and procedural content is required for the topics chosen in this course, the goal is to frame the course around “real-life” case studies and examples in order to give students a specific, and interesting, context for a large amount of new information. These case studies range from small, in-class examples to larger, more comprehensive cases that span multiple lessons. For example, discussion of FDA submissions begins with definitions and outlines of potential pathways, including the 510(k) premarket notification, premarket approval (PMA), and humanitarian device exemption (HDE) approaches. A specific example of each is then introduced and

students are asked to consider and discuss the submission pathway that was chosen for each device, including the financial and time implications. A subsequent out-of-class homework activity is assigned that includes further student investigation into predicate devices of the 510(k) example and research into the voluntary withdrawal of the HDE device (the example had been specifically selected due to its withdrawal from the market in 2006).

On a larger scale, the PMA device provides the foundation for a continued case study throughout the quarter, as topics of bench testing, animal studies, clinical trials, and post-market procedures are addressed. Lessons in each specific content area focus on defining and understanding methods and approaches as well as the relevant regulatory oversights and requirements, while the two devoted "case study" sessions are utilized for tying key concepts and approaches together in a specific context. For example, mechanical testing, cell culture techniques, selection of animal models, Good Laboratory Practices, and other key topics can be defined and discussed prior to the devoted case study sessions, such that the foundational knowledge exists for students to understand and explore a device progression through specific models. Learning objectives based on the multi-lesson case study are as follows. Students will be able to:

1. *Outline a progression of steps that a class III device would undergo to demonstrate safety and efficacy and receive FDA approval.*
2. *Identify and describe in detail at least 3 methods of in vitro safety testing that would be utilized to evaluate a cardiovascular (or other field of choice) device.*
3. *Select and describe 2 specific animal models that could be chosen for preclinical testing and discuss limitations of these models.*
4. *Compare and contrast pilot and pivotal clinical trials.*

Specifically in regards to the case study class sessions, students are provided with introductory case study material regarding the disease, the device, and the intended use. Students are asked to answer questions that will prepare them to fully understand the device prior to attending class. In class, students get in groups and discuss their responses, followed by a group activity to outline and determine specific aspects of the path through safety and efficacy studies. Following additional class sharing, a detailed progression of the specific device is outlined and discussed.

Device case studies can be based upon an instructor or student-selected area of interest. Devices can be found and information gathered by utilizing the FDA website to access the Center for Devices and Radiological Health databases[2]. This information is available to the public.

A Case-Study Based Student Project

As a culminating course activity, an additional case-study based approach is taken in the form of a student project. Students form groups of 3-4 and must select a class II or III device of interest. The project deliverables are a 4 page written outline and an 8 minute PowerPoint presentation that describe key aspects of the chosen device path to market. Students are to include the device classification and submission pathway, specific *in vitro* and bench testing performed to evaluate device safety, animal models utilized and clinical trial results (if applicable), and current market

status. If devices did not go through traditional bench and *in vivo* testing, then students must provide detailed information on the performance standards or other special controls that apply.

This project provides two key opportunities for students. First, it allows students to apply concepts discussed throughout the class to a culminating, real-world example of their choice. It also requires students to use the FDA website and to navigate through guidance documents and other useful information that is publicly accessible. Second, the two days devoted to student presentations at the end of the quarter expose all students to a variety of devices and examples. This serves as an excellent course review, as well as an excellent opportunity for students to learn from one another.

Conclusions

Overall, this course provides an introduction to a range of topics that are important in the medical device industry. The goal is that an overview of key topics coupled with specific examples and case studies will provide students with a foundation of knowledge with which they can successfully enter the medical device industry. Post-graduation feedback from students who take this course will be necessary to truly assess its usefulness and impact.

Bibliography

1. Robinson R. "Is it time for academic preparation of future regulatory affairs professionals?" *Journal of Medical Device Regulation*; May 2006.
2. FDA website: www.fda.gov