

REG 6250 Manufacturing Novel Therapies & Imaging Agents

Fall 2024

Instructor Information

Course Director

Andrew Fesnak, MD, MHCI

Class Format & Time

Online

M 4:00 – 5:30 pm, ET

*syllabus is subject to change at professor's discretion

Course Description

Novel therapeutic and diagnostic agents (eg. CAR T cells, gene therapy for sickle cell disease, radionuclides etc.) have revolutionized modern clinical medicine. Historically, these agents were first developed in academia then transferred to industry for clinical scale manufacturing. Recently, however, some academic centers have developed clinical scale biomanufacturing facilities. Operation of these new facilities requires a unique blend of manufacturing, clinical, basic, regulatory and laboratory sciences. Examples of areas in which academic medical centers have developed in-house manufacturing include cell therapy, gene therapy and novel imaging agents. This course will cover manufacturing approaches, challenges, and controversies in each of these domains.

Each week includes a combination of synchronous and asynchronous work. Synchronous sessions will include instructor led discussions based on pre-recorded lectures or case-based discussions. Asynchronous material includes pre-recorded lectures and discussion board prompts to which students will respond throughout the week. One unique aspect to this course are the debates. These debates are meant to be a fun and interactive way for students to engage with controversial and evolving topics in the field.

By the end of the course, students will appreciate the academic perspective on core elements of therapeutic and diagnostic agent manufacturing.

Course Objectives

At the completion of this course students will be able to:

1. Describe the general approach to development, manufacturing, quality control and regulatory compliance in academic manufacturing facilities.
2. List critical steps in the manufacturing cycles of cell therapies, gene therapies and imaging agents.
3. Explain current challenges in development, manufacturing, and maintaining regulatory compliance in academic manufacturing.
4. Contrast key considerations and relative merits of different positions in the current controversies surround these agents.
5. Synthesize evidence from texts and expert testimony to develop arguments relating to controversies surrounding academic manufacturing.

Course Format

Each module consists of "lecture week(s)" and "debate week(s)".

During a lecture week, the student will watch 1-2 hours of pre-recorded asynchronous material, write a 1-2 paragraph post on the discussion board prompt to apply the knowledge, respond to peer posts, and attend a 1 hour synchronous session. These synchronous sessions during the lecture week may take different forms (eg. lecture, Q&A, facility tour, office hours etc.) depending on the needs of that specific week's content.

In the beginning of the semester, you will be assigned as a "debater" for at least one week in the second half of the semester. For your debate week, you will read the assigned materials and meet with a designated faculty advisor in advance of the debate. During the synchronous session that week, you will present and defend your assigned position on the topic. Details about the debate format will be discussed in the introduction to the course, however, in brief the debate will include prepared remarks, then interactive sessions between debaters and amongst the audience. All students, including those who are not assigned as "debaters" for a given week, will be provided with required pre-reading and pre-recorded lectures relevant to the debate topic. Students who are not assigned as debaters for that week will post questions to the discussion board ahead of the debate. The debaters will deliver a short introductory statement.

Assignments & Grading

There will be 4 deliverables. The grading for participation and these deliverable are outlined below

| Assignment | Percentage |
|---|------------|
| Participation (In class participation, mindmap activities) | 33% |
| Discussion Posts (5) and responses | 33% |
| Debate Participation (preparation/performance for your debate week, posting questions for your non debate week) | 33% |

A grade of C- is considered passing for this course. However, note that the MRA degree requires a grade of B- for credit toward matriculation.

Course Schedule

Asynchronous material including readings, pre-recorded lectures and discussion posts should be completed in advance of that week's synchronous session. Synchronous sessions will be held each Monday from 4-5:30 pm.

| Synchronous Session Day | Topic | Faculty |
|-----------------------------------|--|----------------|
| 1 Monday 9/9 | Introduction to course, peers and faculty | Fesnak |
| 2 Monday 9/16 | GMP mfg principles, processes, and facilities | Fesnak |
| 3 Monday 9/23 | Drug product development and quality control | Fesnak |
| 4 Monday 9/30 | Approach to manufacturing cell therapies | Fesnak |
| 5 Monday 10/7 | <i>Case studies:</i> Challenges in CT biomanufacturing | Fesnak |
| 6 Monday 10/14 | <i>Debate:</i> Allogeneic v. autologous v. (v. in situ manufacturing) CAR T | Hexner, Fesnak |
| 7 Monday 10/21 (no synch session) | <i>Pre recorded Debate:</i> Engineered T v. NK (v. Macrophages) cell therapies | Fesnak |
| 8 Monday 10/28 | Approach to manufacturing imaging agents | Lee |
| 9 Monday 11/4 | <i>Case studies:</i> challenges in imaging agent manufacturing | Lee |
| 10 Monday 11/11 | <i>Debate:</i> USP v GMP in phase I/II for novel imaging agents | Lee |
| 11 Monday 11/18 | Approach to manufacturing gene therapies | van der Loo |
| 12 Monday 11/25 | <i>Case studies:</i> Challenges in GT manufacturing | van der Loo |
| 13 Monday 12/2 | <i>Debate:</i> aav v. retrovirus | van der Loo |
| 14 Monday 12/9 | Hot topics in cell and gene therapy | TBD |
| | | |

Assignment Details

Discussion Posts

There will be 5 discussion posts over the course the term. While students are expected to post thoughtful, engaging, well-rounded responses to each prompt, it is expected that the length of a discussion post should be one to two paragraphs at most. If you do not post by the due date you will not receive the full points. Typically, discussion posts will be by the Thursday prior that week's synchronous session.

Discussion posts topics include:

1. Week 2: Good manufacturing practices
2. Week 3: Drug development and quality control
3. Week 4: Biomanufacturing cell therapies
4. Week 8: Biomanufacturing imaging agents
5. Week 11: Biomanufacturing gene therapies

Discussion Responses

Once you have posted to the discussion board you are also expected to respond to at least one peer. These responses should be insightful, thoughtful, and offer a unique perspective. It is expected that responses are brief (as little as one to two sentences, no more than one paragraph). You must respond to your peers by the due date, which will typically be the Sunday prior to that week's synchronous session. If you do not, then you will not receive the points.

Debate

The debate is worth 33% of your overall grade and requires you to dive into your selected topic. To obtain all points:

- Prior to the debate, you will meet (independently) with selected faculty to assist you in preparing for the debate.
- You will present your topic and address questions posted in advance of your presentation by peers.
- Address questions in real time during the debate.

The debate format will include

1. A five-minute introduction from each side
2. Followed by an interactive portion between positions and amongst the audience
3. The debate will close with a short closing statement by each position (no more than five minutes)

The goal of the debaters is to convince the audience to change their minds. Grading on your contributions to the debate will take into account effort in preparation and thoughtfulness in responding to questions as well as overall facility with the material.

Debate Questions

During each debate week, students who are **not** actively debating will be expected to post at least 1 question for the debaters during the week prior to the debate.

Academic Policies:

Participation Expectations

Participation in class is crucial to students' education in this program. Students are expected to attend and actively participate in all courses. Examples of active participation in a synchronous session may include asking or answering questions, posting comments in the chat, or collaborating with other students during group work. Examples of active participation in an asynchronous session may include asking or answering questions via Canvas or email, commenting on discussion boards, or interacting with other students outside of class.

This program is committed to providing a supportive and productive learning environment for all. Active participation requires professionalism and demonstration of respect for peers, course instructors, and guest lecturers.

Attendance Expectations

Students are allowed 1 excused absence. If you anticipate the need to be absent, please contact the course director prior to your absence. If you have other concerns about your ability to meet the attendance requirements, you must contact the course director prior to your absence.

Students are expected to be on time to all classes and stay for the duration of the class. If you anticipate being late to class or may need to leave early, please email the course coordinator and instructor in a timely manner to let them know of may be late or need to leave early. Any student who is more than 15 minutes late will be considered absent from that class. Additionally, any student who leaves early may be marked absent. Attendance also includes keeping video feed on during synchronous sessions.

Academic Integrity:

As a University of Pennsylvania student, you are required to uphold Penn's Code of Academic Integrity. Specifically, this means that materials that you submit either online or in person should be independent works created by you that uphold all tenets of academic integrity (i.e. do not cheat, fabricate, or plagiarize, amongst others). We encourage you to reach out to the course director or coordinator if you are not clear on what potential violations are.

Course Management: Canvas

All course materials and assignments will be managed on Canvas. Log in with Pennkey and password at <https://canvas.upenn.edu>.

Course Evaluations:

Course evaluations are completed in the BLUE system. These are a required part of course participation. An email from the BLUE team will be sent to students with a link and directions on how to complete the course evaluation(s).

Student Disabilities Services

The University of Pennsylvania provides reasonable accommodations to students with disabilities who have self-identified and been approved by the office of Student Disabilities Services (SDS). Please make an appointment to meet with me and the course coordinator as soon as possible in order to discuss your accommodations and your needs. If you have not yet contacted SDS, and would like to request accommodations or have questions, you can make an appointment by calling SDS at 215-573-9235 or accessing the [MyWeingartenCenter](#) portal. The office is located in the Weingarten Learning Resources Center at Hamilton Village, 220 S 40th St Suite 260. All services are confidential.