Nanyang Technological University
Division of Chemistry and Biological Chemistry

Academic Year	AY20/21	**Semester**	2
Course Coordinator	Loh Zhi Heng		
Course Code	CM9201		
Course Title	Regulation in the Pharmaceutical, Biotechnology, and Medical Device Industries		
Pre-requisites	NIL		
Mutually Exclusive	NIL		
No of AUs	3		
Contact Hours	Lectures: 39 hours		
Proposal Date	06 July 2020		

Course Aims

This introductory course aims to provide an overview of regulatory affairs in relation to three key areas of development: Drugs, Biologics, and Medical Devices. Regulatory affairs comprise of the rules and regulations that govern product development as well as post-approval marketing. We will examine the laws and regulations that apply to development, testing, production and marketing. You will explore the responsibilities of a regulatory affairs specialist in the regulatory setting. Throughout the course, you will learn the practical issues facing regulatory specialist as they work with local and international regulatory bodies to secure and keep product approval.

Intended Learning Outcomes (ILO)

By the end of this course, you should be able to:

1. Explain the history and rationale behind policy, law and regulation pertaining to food and drug laws around the world as well as the creation of the US Food and Drug Administration (FDA), its current organization and responsibilities
2. Describe aspects of specific laws and regulations that are applicable to drugs, biologics and devices
3. Explain market clearance requirements and processes, including product classification, clinical studies, Good Laboratory Practices (GLPs), Good Manufacturing Practices (GMPs), Good Clinical Practices (GCPs), Investigational New Drug (IND) and Investigational Device Exemption (IDE) submissions
4. Explain issues related to product clearance pertaining to New Drug Application (NDA), Abbreviated New Drug Application (ANDA), Biologics License Application (BLA), Device Premarket Approval (PMA) and 510(K) Premarket Notification
5. Describe clinical study design implementation and monitoring
6. Describe the roles of a regulatory affairs specialist within an organization and with the health authorities

Course Content

Definition of policy, law and regulation. Branches of government (legislative, judicial, executive). Variations between countries.

FDA History, Structure and Roles:

The Food and Drug Act of 1906. Elixir of Sulfanilamide Scandal 1937. 1938 Federal Food, Drug and Cosmetic Act (FD&C Act). Thalidomide Scandal in the late 1950s and early 1960s. Kefauver-Harris Drug Amendment in 1962.
Product classes from FD&C Act are as follows: food, dietary supplement, cosmetic, drug, biologic, device, tobacco products.
Center for Food Safety and Applied Nutrition (CFSAN): Foods, dietary supplements, cosmetics.
Center for Veterinary Medicine (CVM): Veterinary products which include livestock feeds, pet foods, veterinary drugs and devices.
Center for Drug Evaluation and Research (CDER): Drugs which include prescription drugs, generic drugs and over-the-counter (OTC) drugs and some biologics such as well-characterized proteins and antibodies.
Center for Biologics Evaluation and Research (CBER): Vaccines, gene therapy with vectors, blood clotting factors, engineered tissues, blood products.
Center for Devices and Radiological Health (CDRH): Devices, Xray machines and facilities, television, *in vitro* diagnostics.
Center for Tobacco Products (CTP): Tobacco products such as cigarettes, cigars and e-cigarettes.

Introduction to the Code of Federal Regulations (CFR). Title 21 – Food and Drugs.
International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH).
International Organization for Standardization (ISO).

Regulatory landscape: Basic Research → Preclinical Development → Early Clinical Development (Phases I and IIa) → Late Clinical Development (Phases IIb and III) → FDA Review → Post-marketing Trials (Phase IV).

Regulations Governing Drugs/Biologics Development, Registration and Marketing: IND, NDA/BLA, ANDA, GLP (21CFR58), GMP (21CFR210-211), GCP (21CFR11, 50, 54, 56, 312, 314, 320, 812, 814).

Expedited Development and Review of New Drugs: Accelerated Approval, Priority Review, Fast Track, Breakthrough Therapy.

Medical Device Regulations. Definition of Device. Classification of Devices. Types of Controls by Device Class. Design Control, Testing Requirements, Non-Clinical Studies, Clinical Trials, Applications and Submissions.

Marketing Medical Products: Drugs, biologics, devices, and combination products.

Introduction to Medical Product Quality. Definition of Quality and Risk to do with Quality. Quality by Design for the Manufacturing Life Cycle. Quality Risk Management and Continuous Improvements. Quality in Bio-manufacturing, Batch Record, Automation and Cleaning. Future of Quality Metrics. Warning Letters as Examples.

Definition of Clinical Trial, Importance of Clinical Trials, Historical Background, Legal Basis for Conducting Clinical Trials, Per IND Requirements, Phases of Clinical Trials (I-IV), General Study Designs and Objectives, Content and Format of a Clinical Study Report (ICH E3).

Organization of Small and Large Biomedical Companies.
Roles include Clinical Quality Assurance Associate or Specialist, Clinical Research Associate,

Drug Regulatory Affairs Specialist, Medical Writer, Pharmacologist, Product Safety Specialist, Quality Assurance Documentation Coordinator or Specialist, Quality Assurance/Regulatory Affairs Specialist (QA/RA Specialist), Quality Engineer, Regulatory Affairs Analyst, and Regulatory Affairs Associate, Scientist.
Responsibilities involve maintaining data in information systems or databases, ensuring compliance with regulations, advising others on regulatory and compliance matters, evaluating applicable laws and regulations to determine impact on company activities, providing technical review of data or reports, coordinating regulatory documentation activities, identifying and interpreting relevant regulatory guidelines.

Assessment (includes both continuous and summative assessment)

Component	Course LO Tested	Related Programme LO or Graduate Attributes	Weighting	Team/Individual	Assessment Rubrics
1. In-class online assignment	1, 2, 3, 4	Competence, Creativity, Civic-mindedness	15%	Individual	Point-based marking (not rubrics based)
2. Midterm test	1, 2, 3	Competence, Creativity, Civic-mindedness	20%	Individual	Point-based marking (not rubrics based)
3. Final term paper	1, 2, 3, 4	Competence, Creativity, Civic-mindedness	40%	Individual	Point-based marking (not rubrics based)
4. Group research project and presentation	1, 2, 3, 4, 5, 6	Competence, Creativity, Communication, Civic-mindedness	25%	Team	Appendix 1
Total			100%		

Formative feedback

You will be given feedback in four ways:

1. By working through examples provided during lectures
2. By response to postings on the course discussion board
3. By attending consultation hours
4. By studying the comments provided by the instructors after the grading of the in-class quizzes and midterm tests

Learning and Teaching approach

Lectures	Face-to-face lectures will be employed to enable you to interact directly with the instructor.

Reading and References

United States Food and Drug Administration (US FDA): https://www.fda.gov/home
Electronic Code of Federal Regulations (eCFR): https://gov.ecfr.io/cgi-bin/ECFR?page=browse
International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH): https://www.ich.org/
International Organization for Standardization (ISO): https://www.iso.org/home.html

Course Policies and Student Responsibilities

(1) General

You are expected to complete all assigned readings and activities, attend all lectures punctually, participate in discussions, and take all scheduled assignments and tests by due dates.

(2) Absenteeism

Absence from the midterm without a valid reason will affect your overall course grade. Valid reasons include falling sick supported by a medical certificate and participation in NTU's approved activities supported by an excuse letter from the relevant bodies. There will be no make-up opportunities for CA components.

All project assignments must be submitted on time. Failure to do so will affect your score.

Academic Integrity

Good academic work depends on honesty and ethical behaviour. The quality of your work as a student relies on adhering to the principles of academic integrity and to the NTU Honour Code, a set of values shared by the whole university community. Truth, Trust and Justice are at the core of NTU's shared values.

As a student, it is important that you recognize your responsibilities in understanding and applying the principles of academic integrity in all the work you do at NTU. Not knowing what is involved in maintaining academic integrity does not excuse academic dishonesty. You need to actively equip yourself with strategies to avoid all forms of academic dishonesty, including plagiarism, academic fraud, collusion and cheating. If you are uncertain of the definitions of any of these terms, you should go to the academic integrity website for more information. Consult your instructor(s) if you need any clarification about the requirements of academic integrity in the course.

Course Instructors

Instructor	Office Location	Phone	Email
Loh Zhi Heng	SPMS-CBC-01-19A	6592-1655	zhiheng@ntu.edu.sg

Planned Weekly Schedule

Week	Topic	Course ILO	Readings/Activities
1	Policy, Law and Regulation	1	Lecture
2	FDA History, Structure and Roles	2	Lecture
3	21CFR, ICH and ISO	3	Lecture, in-class online assignment
4	Regulatory Landscape	4	Lecture
5	Regulations Governing Drugs/Biologics Development, Registration and Marketing	5	Lecture
6	Revision and midterm	1,2,3,4,5	Midterm test
7	Expedited Development and Review of New Drugs	6	Lecture
8	Medical Device Regulations	7	Lecture
9	Medical Product Quality	8	Lecture
10	Marketing Medical Products	9	Lecture, final term paper
11	Clinical Trials	10	Lecture
12	Organization of Small and Large Biomedical Companies. Career Options.	11	Lecture
13	Group Project Presentations	12	Presentations

Appendix 1: Rubrics for Group research project and presentation (25%)

Grading criteria by instructor

Performance Level	Criteria
Excellent	Demonstrates complete achievement of the learning outcomes 1 – 6. Able to connect to the topics covered and how it can be used to solve the problem. Able to organize the team to present the assigned topic and answer the comments/questions after the oral presentation. Show good communication ability to lead the team members.
Good	Demonstrates complete achievement of the learning outcomes 1 – 6. Able to connect to the topics covered and how it can be used to solve the problem at hand. Able to present the assigned topic and have good communication with the team members.

Satisfactory	Demonstrates partial achievement of the learning outcomes 1 – 6. Able to apply the technique or methodology taught in class only in direct way. Able to present the assigned topic but may not be precise or concise enough.
Unsatisfactory	Demonstrates minimal achievement of the learning outcomes 1 – 6. Not able to apply the knowledge to the problems or not able to present the assigned topic well or have difficulty to maintain good communication with the team members.
Poor	Do not possess sufficient understanding of problem and lack solution for it. Not able to complete presentation and join team study.

Peer evaluation

Your instructor has no way to assess the contribution of each student to the final project. Hence, each team needs to include a contribution statement at the end of the presentation to state the individual team members' contributions.

In addition, each student is required to rate the contribution of each of the other group members with a peer assessment score out of 10. Peer assessment should consider attendance at group meetings (3 points), contributions to the project analyses (4 points), and contribution to the preparation of the final presentation (3 points).

All peer evaluation scores will be kept strictly confidential and will not be revealed to the other group members. You are to evaluate other group members fairly and objectively, as your evaluation will affect other group members' grades (explained below). It is essential for you to submit your peer evaluation form to get marks for the final project. To account for peer evaluations, the final grades for the final project will be calculated as follows:

Based on the instructor's evaluation of the presentation, the entire group will receive the same grade, before peer evaluations are considered.

If a student receives an averaged peer evaluation rating of 8 or more, that student receives 100% of the group's grade.

If a student receives an averaged peer evaluation rating of less than 8, that student receives a percentage of the group's grade as calculated by the formulae below:

- An average rating of 7 to <8 = 90% + (average rating – 7) × 10
- An average rating of 6 to <7 = 80% + (average rating – 6) × 10
- An average rating of 5 to <6 = 70% + (average rating – 5) × 10
- An average rating of 4 to <5 = 60% + (average rating – 4) × 10
- An average rating of 3 to <4 = 50% + (average rating – 3) × 10
- An average rating of 2 to <3 = 40% + (average rating – 2) × 10

Example

Assume the group receives 20 marks from the instructor for the project. A student with an average rating of 8.90 gets 100% of 20 marks, i.e., 20 marks. An average rating of 6.29 means that a student gets 82.9% [or 80% + (6.29 – 6) × 10] of 20 marks, i.e., 16.58 marks.

An average rating <2 will be investigated by your instructor, and the student may receive 0% of group grade.

Your instructor reserves the right to review the student ratings if in doubt, including if malice or discrimination are suspected. Similarly, if one student is not listed in the contribution statement and the instructor suspects that the student did not contribute at all, that student may receive 0% of the group grade regardless of the peer evaluation score.

Here is an example of the peer evaluation score table:

Criteria	Yourself	Member 1	Member 2	Member 3	Member 4
Contributed a fair share of work (Y/N)					
Attendance at group meetings (3 points)					
Contributions to the project analyses (4 points)					
Preparation of final products (3 points)					
TOTAL					
Comments, if any					

CBC Programme Learning Outcome

The Division of Chemistry and Biological Chemistry (CBC) offers an undergraduate degree major in Chemistry that satisfies the American Chemical Society (ACS) curricular guidelines and equips students with knowledge relevant to the industry. Graduates of the Division of Chemistry and Biological Chemistry should have the following key attributes:

1. Competence

Graduates should be well-versed in the foundational and advanced concepts of chemical science, be able to evaluate chemistry-related information critically and independently, and be able to use complex reasoning to solve emergent chemical problems.

2. Creativity

Graduates should be able to synthesize and integrate multiple ideas across the curriculum, and propose innovative solutions to emergent chemistry-related problems based on their training in chemistry.

3. Communication

Graduates should be able to demonstrate clarity of thought, independent thinking, and sound scientific analysis and reasoning through written and oral reports to audiences with varying technical backgrounds. They should also be able to effectively engage other professional chemists in collaborative endeavours.

4. Character

Graduates should be able to act in responsible ways and uphold the high ethical standards that the society expects of professional chemists.

5. Civic-mindedness

Graduates should be aware of the impact of chemistry on society, and how chemistry can be applied to benefit mankind. They should also be aware of and uphold the best chemical safety practices.