Biomedical Engineering

BME460

Biomedical Product Development II

Jayson Parker

Fall Term, 2024

Dr. Jayson L. Parker

Associate Professor (teaching stream)
Dept. of Biology
MBiotech Program (Digital Health)
University of Toronto Mississauga

Biomedical Engineering (BME; cross appointment)
University of Toronto

Email: jayson.parker@utoronto.ca
Twitter: @Jayson_Parker
Cell: 647-929-5315

PhD (University of Toronto)
MSc (University of Toronto)
MBA (Wilfrid Laurier University)

Professional Interests

Digital health technology, medical device regulation, clinical trial design, biomarkers, health and wellness.

My publications: https://www.researchgate.net/profile/Jayson_Parker/

Impact

My interests stem from my time conducting research in medical imaging, brain trauma and drug addiction. My commercial experience in investment banking and the pharmaceutical industry also animate my research goals.

Research on clinical trial failure rates in the context of new medicines and biomarkers is one of my main areas. Recently, we have started to combine this with advanced tools in machine learning.

The “Dark Data” project is my main activity in the context of digital health. We are looking at lifestyle choices can predict improved health and wellness outcomes within 24 hours. This project makes extensive use of wearable technology.

Digital health and more broadly medical device regulation, are active areas of research.

Miscellaneous

Hobbies include: Dungeons and Dragons, 3D-printing, digital modelling, tabletop wargaming (Warhammer 40k), computer games (MMOs, Fallout) and miniature painting.

Class Location: WB130

Class Times: Tuesdays (10:10 AM - 2:00 PM)

Instructor: **Dr. Jayson Parker, *M.B.A., M.Sc., Ph.D.***

Office Hours: Office meetings are by appointment.

TA: Ms. Kate MacQuarrie. k.macquarrie@mail.utoronto.ca

Course Description

The goal of the course is to understand medical device product development with a strong emphasis on medical device regulation.

Students will be able to:

1. Given a medical device, identify and argue for possible pathways for medical device regulation for product approval.
2. Reverse engineer from a regulatory pathway to create a medical device.
3. Apply hazard analysis to medical devices in support of your arguments.
4. Navigate the FDA website and use FDA guidance documents and medical literature appropriately.
5. Forecast future thinking by the FDA on emerging innovative medical device issues.

Course Overview:

Course Element	Weighting
Course Engagement	5%
Tutorial I: ICD Hazard Analysis	10%
Tutorial II: ICD 510k Submission	10%
Major Project:	
Customer Need Identification	5%
Feedback on your Design from Experts	10%
Final Report and Presentation	25%
Final Exam	35%

Assignment	Due Date	Mode of Submission
Team Formation	Sept 17th before class	Coordinate with the TA.
Tutorial I: ICD Hazard Analysis	Sept 24th before class	Email to both TA and instructor. CC all team members.
Tutorial II: ICD 510K Submission	Oct 8th before class	Email to both TA and instructor. CC all team members.
Major Project: User Feedback	Nov 5th	Email to both TA and instructor. CC all team members.
Major Project: Design and Expert Feedback.	Nov 12th before class	Email to both TA and instructor. CC all team members.
Major Project Due	Nov 24th by Noon	Email to both TA and instructor. CC all team members.
Major Project Slide Deck Due	Nov 25th 5:00 PM	No animations and no "links" to presentations. **Upload to Dropbox link (link TBA)**. I need to centralize all talks on the podium on a single laptop.

Late penalties: 10% initially and 20% if late ≥24 hours.

Course Activity Schedule:

Date	Lecture Topic	Tutorial
Sep 10	Hazard analysis; Implantable cardioverter defibrillator case introduction; MAUDE database.	In class Hazard analysis exercise; Tutorial #1 assigned.
Sep 17	Medical Device Regulatory Overview **(12:30 - 2 PM by Zoom)**	Submission pathways
Sep 24	Guest Speaker. Medical Device Standards in Design. Dr. Paul Santerre. **No Device use during lecture.** 2nd half: 510k Pathway (Dr. Parker).	Tutorial #1 due. 510k exercise in class Tutorial #2 assigned.
Oct 1	Digital Health Regulation. Screening & Diagnosis.	Tutorial 2 group work.
Oct 8	Unlocked Neural Networks in Device Regulation & AI Regulation (Dr. Parker). Major Project Introduction; user needs; market analysis; expert feedback	Tutorial #2 Due. Major Project Start.
Oct 15	Large Language Models in Clinical Decision Making (Dr. Parker) 2nd half: Drug Regulation Primer.	Major Project group work.
Oct 22	Patent Primer (Dr. Parker) Lecture by **Zoom** (10 AM - Noon).	
Oct 29th	Reading break	
Nov 5	**Major Project Work**. Instructor meetings Teams 1, 2 and 3.	
Nov 12	Major project work.	Angela Henshilwood patent searching (tentative) at 11 AM. . Instructor meetings Teams 1801-2 and 1801-3

Nov 19	Guest Speaker. Human factors Device Design. Dr. Joe Cafazzo. **No Device use during lecture.** 2nd half: AI patents Damian Wolf 12:30 PM.	Major project work
Nov 26	**Major Project Presentations**	Major project work ** **10:10 AM start time.** Talks will be stopped at the 10 minute mark - reminder. Judging: Drs Santerre, Fekr and Cafazzo confirmed.
Dec 3	Final Exam review; course evaluations; course wrap up.	

Peer Evaluation - Group Projects

For each group project (both tutorials, major project) all team members will send a private email to the teaching assistant and instructor scoring their other team members, using the table below (title the email "Peer Evaluation").

If the instructor concludes there is a student that does far more than their fair share of work relative to their peers, that person will receive a higher grade for the same project.

If the instructor concludes there appears to be a pattern where one student is not keeping up with their fair contribution to then group project, their project score will be lower than the rest of their team.

Email: This is sent each time a group assignment is due. *Send the TA your scores and a few sentences as to why. Title your email "Peer Evaluation" the day your submission is due. Indicate which assignment your peer evaluation is about.*

Score	Meaning
9-10	Student team member went well and beyond what was expected to help the team. The team member made a big effort to help the team.
8-9	Student team member made very helpful contributions to the team.
7	The student team member did the bare minimum to help the team.
< 7	The student often did not meet the most basic work requirements needed to help the team.

< 5	For all intents and purposes, the team member was absent and the work was largely done by the rest of the team. Or the work done was of such low quality it had to be repeated by other team members.

Class Engagement

This score represents participation in class as well as contribution to group assignments.

Course Readings

Please come prepared to answer the questions based on the course reading.

Date	Lecture Topic	Reading & Questions
Sep 10	ICD introduction; Hazard analysis; Safety & MAUDE.	Unpublished book chapter on Drug Safety. - What is a safety event reported? When is it associated with a product?
Sep 17	Medical Device Regulatory Overview	Go to the FDA website and download the guidance document titled: The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510k]. Read pages 1- 5. • What was the MDA? • What is a post-amendment device? • What are the risk classes? • What is a risk class? • What is the 510k pathway?

Sep 24	Medical Device Standards in Design. Guest Speaker Dr. Paul Santerre. 2nd half: 510k Pathway (Dr. Parker).	Go to the FDA website and download the guidance document titled: The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510k]. Read pages 5-16 (you can ignore multiple predicates). • What is an NSE determination? • What is a predicate? • What if you cannot find a predicate? • What is intended use?
Oct 1	Digital Health Regulation. Screening & Diagnosis.	Go to the FDA website and download the guidance document titled: Policy for Medical Software Functions and Mobile Applications. Guidance for Industry and Food and Drug Administration Staff. • What is the history of this guidance document? • What is meant by SaMD? • Why isn't a smartphone considered a medical device? • When is an accessory a medical device? • When does the FDA intend to apply "enforcement discretion"? • How are simple calculations in healthcare practice classified in this guidance document? • Why would mobile apps that provide GPS location information for asthmatics be considered a medical device, according to this guidance? • Why would the FDA consider software functions that display messages for a substance abuser who wants to stop addictive behaviour, subject to potential oversight as a medical device?

Oct 8	Unlocked neural networks in device regulation & Al (Dr. Parker)	1. "Proposed Regulatory Framework for Modifications to Artificial Intelligence / Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)". https://www.fda.gov/media/145022/download
Oct 15	Large Language Models in Clinical Decision Making (Dr. Parker) 2nd half: Drug Regulation Primer.	From the FDA website: Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan. https://www.fda.gov/media/145022/download - Unpublished book chapter "Clinical trial design".
Oct 22	Patent Primer	- Book chapter "What can be Patented" on Quercus - Unpublished book chapter "Patents and Gorillas" on Quercus.
Oct 29	**Fall Break**	None.
Nov 5		
Nov 12	Guest Speaker. Patents on Software and Artificial Intelligence Primer. Mr. Damian Rolf.	Review the book chapter "What can be Patented" on Quercus. Review tests for novelty, non-obviousness and the concept of prior art from our prior lecture.
Nov 19	Guest Speaker. Human factors Device Design. Dr. Joe Cafazzo.	None.
Nov 26	Major Project Presentations	None.
Dec 3	Course exam review & wrap up.	

Course Management

Devices In Class - Laptops, phones, Tablets

There is a problem made worse by COVID remote learning where everyone, including some faculty, are distracted by their devices when others are giving a talk. This is deeply disrespectful to our guest speakers who come to us voluntarily.

Therefore: when this course has guest speakers, no electronic devices of any kind are permitted to be used or on your desk. This includes laptops, phones and tablets. If you need to take notes, use a pen and paper.

These measures have dramatically improved class engagement for our guest speakers. Adherence to this rule is part of your Class Engagement mark.

Use of Large Language Models (LLM) / Chat GPT in the Course

LLM use is fully encouraged in the course. As young professionals you have to start using these tools to your advantage. However, you are entirely responsible for accuracy of content gleaned from LLMs. You can never cite an LLM result to back up your assertions. Use this as an opportunity to learn how to engineer prompts to make LLMs more useful while at the same time learning the limitations of LLMs.

Caution: GPT / Large language models will miss critical information needed for a question. You are responsible to know such findings and thus if you only use LLMs you do so at your peril. You still need to do library and FDA searches to be thorough.

Figures and Report Guidelines "Document Specifications"

All course submissions should have pages numbered, a proper title page, identifiers on the title page (course, students, title, date, instructor, date). Font is Times New Roman with standard margins, 1.5 line spacing.

No figures should be drawn by hand. Everyone should have basic proficiency in graphics and 3D modelling programs to depict their design concepts.

Tutorials

Tutorial and tutorial reports:

Overview. *An example of a tutorial assignment from previous years will be available in Quercus – these reports, while good, are not perfect so do not expect emulation will achieve a perfect grade*. We expect you to surpass the quality of these reports – use them as a starting point.

Submission. Students will be graded on their performance in tutorial based on a 1-page written summary of their responses to these issues for each group.
Write concisely. Your 1-page report needs to state your arguments and rational. The appendix is not to be used to "explain" things you never discussed in your 1-page description.

First Tutorial Rubric Factors: This tutorial is the foundation for your second tutorial. You will construct a hazard analysis of the base product you will modify eventually in the second tutorial.. You will need hazard analysis for both risk class.

Format. A sample hazard tutorial assignment is posted on Quercus. There are minor changes in format for each year. You can have as many figures and tables as you like in the appendix.

1. What are the hazards and clinical outcomes?
2. Have hazards and clinical outcomes been correctly distinguished?
3. What evidence have you used for your clinical risk estimates? Is this evidence acceptable for the FDA?
4. What clinical outcomes, if any, are unknown and therefore require a clinical study?
5. Have mitigations been reflected in clinical outcomes for your hazards?
6. Has the report followed course requirements for document specifications?

Second Tutorial Rubric Factors: This tutorial builds upon the first tutorial. It is a much larger submission. Your design may change from the first trial and that's perfectly fine. You need to adjust your hazard analysis accordingly etc.

Like the first tutorial, the submission should follow "document specifications" for the course.

Format. A sample tutorial assignment is posted on Quercus. There are minor changes in format for each year. The three sections are Regulatory, Design and Value proposition all on a single page. You can have as many figures and tables as you like.

Please see the elements below.

Regulatory Tutorial Guide (2nd Tutorial).

1. Risk class argument. Don't assume that the instructors know the risk class – explicitly state your risk class in the document, telling us what it is - and on what basis you are arguing it belongs to that risk class. The risk class should be based on hazard analysis comparisons to a product of a known risk class. While you can show similar products at the FDA and their risk class, this is not enough. You have to dow your own work and justify your risk class with hazard analysis.

2. Reference to FDA decision history of related or identical products. This is part of your supporting arguments and key to talking to the FDA. Be sure your table has a "comment" column stating what your conclusion is for each product example.

3. ***Side by side tabular comparisons of features for predicate identification vs. the new device.*** This is a must and you will be docked marks for not presenting detailed comparisons. Where are they same and where are they different? Where differences exist, interpret the meaning of those differences with respect to safety or efficacy that can invalidate a substantial equivalence argument or demand a higher risk class. Just don't give us a technical summary - tell us what differences are important and why.

4. Safety is a concern even if it looks like an IMPROVEMENT, which demands some form of testing and discussion to address this point. Provide relevant Standards in the appendix, related to the testing. The bigger the safety *change*, the more likely the risk will increase.

5. Hazard analysis. Hazard analysis is expected. The book chapter by Dr. Parker in Tong gives you an idea of how to get started (however, our in class exercise will have more detail) However, unlike the book chapter you need to take this farther and compare the hazard score of your proposed device to your base product (that could be a predicate as appropriate). You will need assumptions but look at the clinical literature for to get a sense of probability for different kinds of safety events.

7. What are all the relevant guidance documents supporting your regulatory argument?

8. What kind of evidence is needed to explore any safety or efficacy issues? (animal, cell culture, written description or clinical study). Why? If you are saying such work is important, then does this underscore a safety uncertainty that would make your product look like a class III? What aspects of your hazard analysis are

unknown, if any, and need to be addressed by a clinical study? What is the endpoint?

9. Screenshots of FDA device website - just don't give us references - show us the actual screens / quotes / tables you are referring to in your appendix from the sources you cite. ***Your document should be able to act as a reference sheet to help you on a phone call to the FDA with all the information you need readily available.*** Simply giving a reference does not do this - show us the actual information you plan to use.

10. Study requirements. Your regulatory pathway will likely require some kind of study. Do your best to find out what this may be (animal model, small clinical study etc.). Check clinicaltrial.gov and the peer reviewed literature for your product area. Check FDA guidance documents and related submissions to your product category. You can summarize all of this is in 1-2 sentences.

11. Product label. What is the label for your proposed product? This can be put in appendix. Think carefully about your wording. This can also be "intended use" but see lecture notes on the difference.

Design Tutorial Guide (2nd Tutorial).

1. Is there a focus on the quality and credibility of engineering proposed designs?

2. A knowledge base for engineering: Demonstrated competence in university level mathematics, natural sciences, engineering fundamentals, and specialized engineering knowledge that they are applying to the project, appropriate to the program.

3. Problem analysis: An ability to use appropriate knowledge and skills to identify, formulate, analyze, and solve complex engineering problems in order to reach substantiated conclusions.

4. Investigation: An ability to conduct investigations of complex problems by proposed methods that include appropriate experiments, analysis and interpretation of data, and synthesis of information in order to reach valid conclusions.

5. Design: An ability to design solutions for complex, open-ended engineering problems and to design systems, components or processes that meet specified needs with appropriate attention to health and safety risks, applicable standards, and some consideration of the economic, environmental, cultural and societal considerations.

Major Project

**** 50% of mark is individual (closely supervised) and 50% is team**. This applies to the final submission of the major project (not the milestones).

Your team decides work allocation but each team member is responsible for one section below. **The section author must be indicated in the table of contents.** If you have more or less than the number of sections below, decide how to divide up the work.

1. FDA decision history; Regulatory path argument (510k Etc)
2. Risk class argument & hazard analysis
3. Intended use analysis & proposed product label; technology description
4. Design feedback & User feedback & Competitor Analysis
5. Market analysis
6. Patentability; Development time line

Your major project design proposal, modifying a base device (assigned in class), must contain the following elements:

1. Use of AI as part of your design submission. The AI should use must look plausible technically and the regulatory strategy has to look compelling.
2. Usability / human factor enhancements.
3. Additional design changes permissible but be selective. Intended use changes are also permitted to the base device.
4. Your submission must look like a real improvement to the device that could plausibly get approved by the FDA and attract users.

Description

In brief, this project will require students to take an existing medical device product line and propose a change. The change is expected to be commercially competitive, meet commercialization timelines, offer congruence to physician needs and be of sound science.

The entire class will work on predefined products that will be assigned by the instructors early in the term.

Grading of the final submission will be in two parts: 50% of the grade each student in the team receives will be based on the entire submission and 50% of the grade will be based on the specific section a student was responsible to take lead on for the final report. So your grade on this will be half group grade and half individual grade.

Project milestones:

1. User feedback. We want you to conduct research on actual users of this technology – this is not about speaking to experts. **Interviews with caregivers and patients**, surveys and Internet forums are all potential sources – see instructors for details. Conclude your survey of feedback with clear needs you think needs to be addressed in your design. Every team is expected to go beyond analyzing data from the internet and talk to people. Your market size should reflect the severity of the disease and whether such patients are eligible for reimbursement.

   Format: (This report is up to 1 page followed by an unlimited appendix; standard margins; title page; pages numbered; 1.5 line spacing; Times New Roman font; proper identification on the document noting team members, course, instructor).

2. Design & Expert feedback. What kind of feedback did you get from experts on your proposed design? How many experts did you speak to? On what basis are they considered experts for the questions you are asking? What design features appeared problematic and how did you address the issues? Don't forget to mention design standards you are following. Be prepared, and it is likely, you will need to modify your design idea based on this feedback.

   Format: (This report is up to 2 pages followed by an unlimited appendix; standard margins; title page; pages numbered; 1.5 line spacing; Palatino font; proper identification on the document noting team members, course, instructor).

Major Report Format:

- 10 pages text /1.5 line spacing/ 12 point Times New Roman font
- Unlimited appendix size at the end of your report
- Talk is 10 minutes (1 minute per slide minimum); all team members must present; one figure per slide; don't read from a script

Examples of sections we expect to see in your report – but is not limited to:

1. Executive Summary (250 words not part of total word count)
2. FDA decision history; Regulatory path argument (510k Etc)
3. Risk class argument & hazard analysis
4. Intended use analysis & proposed product label; technology description
5. Design feedback & User feedback & Competitor Analysis

6. Market analysis
7. Patentability; Development time line

Final Exam

The final exam will draw heavily on your product development skills you have applied through the tutorials and cases discussed in class. The exam is open book.

APPENDIX: BME 1801, Fall term
Final project document and presentation of the proposal.

	1	2	3	4	Total
(a) Knowledge of customer needs, market potential and limitations of market access with respect to design considerations (document)	insufficient customer survey and/or knowledge with respect to the market selection for the considered design(s)	Some evidence from customer survey and/or knowledge with respect to the market selection for the considered design(s), but superficial	reasonable level of detail from customer survey and/or knowledge with respect to the market selection for the considered design(s), supported with some level of detail	Well designed survey questions and knowledge retrieval and analysis with respect to market selection for the considered design(s), supported by an appropriate level of detail	/20

(b)Regulatory strategy (document)	Lack of evidence of using appropriate regulatory pathways	Some evidence of using regulatory pathways as per the course syllabus, lack of justificatio n	Reasonable level of details in regulatory pathway selection and justification as per the course syllabus	Excellent selection and application of regulatory strategies in the design, well justified as per course syllabus; insight into regulation for uncertain issues.	/40
(c) Design strategy(Commercially competitive, meet commercialization timelines) Does the design qualify as novel and inventive based on patentability criteria? (document)	Lack of quality and creativity of proposed design. Unrealistic with respect to practical knowledge in the field.	Some evidence of quality and uniquenes s of the design, with some considerat ion of practical limits in the field as per course syllabus. Lacks of justificatio n of design decisions, and questiona ble application . Missing standards. Unclear passes patentabili ty tests.	Design shows good quality/ creativity and a clear appreciatio n for practical limitations in the field as per course syllabus. Reasonable level of details in design selection, justification, and described standards for testing. It passes the patentability tests.	Design shows great quality and a high degree of creativity. Well defended arguments, as per course syllabus. Shows consideratio ns to health and safety risks, provides comprehens ive necessary standards, and assesses relevant cultural and societal consideratio ns.	/20

Organization, flow and balance (document)	Reader cannot understand the presentation of the work because there is no sequence of information. Too much text devoted to particular individual parts of the research process.	Reader has difficulty following text because student jumps around. Some sections are over- or under-emphasized	Student presents information in a logical sequence by which the reader can follow. Overall, the amount of information allotted to each section is appropriate	Logical, intuitive progression of ideas with clear and direct reference to information in the literature, tables and figures. Reader can easily follow the flow of ideas and will be able to see the support for the conclusions.	/5

Appearance (document)	Sections in text are cluttered or unreadable from the reader's perspective. Irrelevant figures. Insufficient text supporting data (figures or tables). Distracting background. Blocks of text too lengthy; spelling/ grammatical errors; poor use of graphics to support text and presentation	Some sections provide a readable and appropriate balance of text and graphics, while many do not. Student occasionally uses graphics that partially supports text and conclusions; text has some misspelling and/or grammatical errors.	Most text is balanced with supporting figures, tables, appendices and references. Text does not have extensive white space and is readable throughout the document. Student's graphics relate to text and conclusions; Document has very few misspellings and/or grammatical errors.	Text has an excellent balance figures, tables, appendices and references. Text does have innappropriate white spaces or cluttered background. Figures and tables are clear with appropriate captions. Blocks of text is well organized and referenced. Tasteful layout. Fonts readable throughout the document. Headings obvious, appropriate. Student's graphics explain and reinforce text and conclusions; text has very few misspellings or grammatical	/5

Presentation (slides and oral)	Poor delivery. Slides are not clear and content is not appropriately relevant. Students read report with no eye contact or constantly faces screen; Student voices are not clear or spoke too softly or too quickly and without clear enunciation; incorrectly pronounces terms	Content in slides is good but information is poorly presented on the slides. Student occasionally uses eye contact, but still reads from the report; Student's voice is low. Student incorrectly pronounces terms. Audience members have difficulty hearing the presentation.	Slides appropriately convey message and format is appealing. Student maintains eye contact most of the time but sometimes returns to notes; Student's voice is clear. Student pronounces most words correctly. Most of the audience members can hear presentation and are engaged.	Slides are visually impactful and concisely convery the message. Presenter guides audience through presentation. Enthusiastic, animated. Eye contact with audience. Spoke loudly and at a reasonable pace. Did not read from script. Controlled use of laser pointer. Slide transitions simple and direct. Student maintains eye contact with audience, seldom returning to notes;	/5

Subject Knowledge (document [5]); and Response to Audience Questions (oral [5])	Student does not have a working grasp of information; student cannot answer questions about subject. Answers are incorrect, evasive, defensive, incoherent.	Student is uncomfortable with information but attempts to answer when cued, but is able to only answer rudimentary questions.	Student is at ease with expected answers to all questions, but fails to elaborate. Had difficulty engaging discussion beyond the direct question.	Student demonstrates full knowledge (more than required) by answering all class questions with explanations and elaboration. Answers were direct, clear, on-target, no-nonsense, and engaged discussion.	/5
				Total Points:	/100