Continuation/Research Progression Projects Form (7)

Required for projects that are a continuation/progression in the same field of study as a previous project.
This form must be accompanied by the previous year's abstract and Research Plan/Project Summary.

Student's Name(s) Ashley O'Neill

To be completed by Student Researcher: List all components of the current project that make it new and different from previous research. The information must be on the form; use an additional form for previous year and earlier projects.

Components	Current Research Project	Previous Research Project: Year: 2018-2019
1. Title	Comfortable Breathing Duration (CBD) of Fentanyl Using a Three-Compartment Model	A Mathematical Exploration Applying th e Number e to Pharmacokinetic Modelin g of Opioids
2. Change in goal/ purpose/objective	To develop a more realistic, three-compartment model for fentanyl instea d of the one-compartment model used in the previo us project	The goal was to create a project that cre ates a compartment model to analyze h ow different dosages and other factors i nfluence the probabilities of opioid attrib uted lack of breathing and pain relief.
3. Changes in methodology	Nested loop, Piecewise log-linear model, Analyzes the appropriate dosing range among alpha, beta, and g amma ranges of elimination	This methodology involved collection of data from a standardized medical textb ook and creating the basic compartment model in Microsoft Excel using various mathematical formulas and analyzing th e resulting data
4. Variable studied	Comfortable breathing duration as func tion of initial concentration and three ha lf-times.	Different dosages of four different opioid s, different volume distributions of these opioids, different half times (beta and ga mma), the probability of apnea (no breat hing), and the probability of analgesia (p ain relief)
5. Additional changes		

Attached are:
☑ Abstract and Research Plan/Project Summary, Year 2018-2019

I hereby certify that the above information is correct and that the current year Abstract & Certification and project display board properly reflect work done only in the current year.

Ashley O'Neill — Student's Printed Name(s)
ashley o'neill — Signature
01/28/20 — Date of Signature (mm/dd/yy)

3. The Research Plan/Project Summary should include the following:

a. RATIONALE: The opioid epidemic is a widespread issue that affects every one of us, whether directly or indirectly. Thousands of people die every year from opioid overdoses, and much of this is due to significant respiratory depression, which ultimately leads to no breathing at all (apnea). Part of the other issue is that since the goal of opioids is to provide pain relief, there is ambiguity with how much drug to provide given that each person processes the drug differently. The long term goal with this research is to determine a way to alter administration variables so that it can positively impact the probabilities of both apnea and analgesia (pain relief) and prevent frequent overdosing. This would greatly impact society because the rates of opioid overdose and death could decrease significantly, and a successful alteration could save many lives throughout the country and the world.

b. RESEARCH QUESTION(S), HYPOTHESIS(ES), ENGINEERING GOAL(S), EXPECTED OUTCOMES: Some research questions I ask are, “How can different dosages, volume distributions, half times, and types of drug impact the probabilities of apnea and analgesia after a single dose?” “How does a second dose impact the probabilities of apnea and analgesia? Does the time at which the second dose is administered have a significant impact on these probabilities? Are the probabilities impacted differently with a second dose based on the type of drug administered?” The hypothesis for the first question would be that by using exponentials, logarithms, opioid formulas, and statistical equations, the benefits and drawbacks of different variations of the four different opioid administrations (fentanyl, sufentanil, alfentanil, and remifentanil) could be analyzed. The hypothesis for the second question would be that the probabilities would likely increase due to the proven superposition effect of the drugs (where the drugs stack on top of each other). The hypothesis to the third question would be that the probabilities may increase if the second dose is administered sooner because there is less time for the initial dose to be processed throughout the body before the second administration. The hypothesis to the fourth question is that fentanyl will have the highest probability of apnea and analgesia after the second dose because fentanyl is a very potent drug, even more potent than morphine, and thus, it may produce the highest probability after the second dose. Throughout this project, I hope to gain more expertise in coding, specifically with Python, and I hope to learn more statistical tests to support my research in the long term.

c. Describe the following in detail:

• Procedures: First, a review of literature will be performed to obtain pharmacokinetic data on the four opioids and their effects on respiratory depression and pain relief. Next, using various pharmacokinetic formulas, statistical formulas, and derivations/substitutions based on these equations, a Python compartmental model will be generated using variables and functions to allow input of different variables and its immediate results. This will be a baseline model focused on allowing input of different variables that may impact the probabilities of apnea and analgesia after the first dose and the times at which the probabilities of apnea and analgesia reached 50%. After creating this baseline Python simulation, the model will expanded to allow for the second dose to be inputted and recorded. This data may include the probabilities of apnea and analgesia after the first dose, the new probabilities of apnea and analgesia after the second dose, the time at which the probabilities of apnea and analgesia reached 50%, etc. Statistical testing will be performed on the data, which will analyze the statistical significance of the variables altered during the research. After this, the results will be analyzed, discussed, and concluded.

• Risk and Safety: There are minimal to no risks in this computer-based research. One possible risk would be eye strain from exposure to computer screens for lengthy periods of time, and this could be prevented by taking frequent breaks and minimizing computer use at night or in the dark.

• Data Analysis: After the compartment model is generated using Python, there will be various statistical tests performed to analyze the results. The mean and standard deviation of the times at which probabilities of apnea and analgesia reach 50% based on different dosages and volume distributions. Graphs will be generated by the Python model and analyzed after obtaining data. Various statistical tests will be performed for further analysis. There may be additional graphs generated based on further manipulation of data to aid data analysis.

d. BIBLIOGRAPHY:

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OFFICIAL ABSTRACT and CERTIFICATION

A Mathematical Exploration Applying the Number e to the Pharmacokinetic Modeling of Opioids

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Opioids, a class of drugs used medically as painkillers, are one of the leading causes of drug related deaths in the United States [Stein]. The probability of apnea is a function of opioid concentration, and a pharmacokinetic model involving the number e was developed in Python using pharmacokinetic data from the published literature to determine the probability of apnea and analgesia as a function of time. A second Python model was generated to compare a different representation of the comfortable breathing duration (CBD) to the first python model, which was estimated to better understand the factors that determine the clinical "sweet spot" for opioid dosing. The two models (A vs B) were compared for fentanyl average CBD using the T-test for the difference between the means of two independent samples. The T test was determined to be statistically significant (p=0.0093), which represents the inherent variability in the underlying biological parameters plus the arbitrary selection of input values in the simulations. Ultimately, this project functions as a useful tool in pharmacokinetics.

Category
Pick one only — mark an "X" in box at right

- Animal Sciences
- Behavioral & Social Sciences
- Biochemistry
- Biomedical & Health Sciences
- Biomedical Engineering
- Cellular & Molecular Biology
- Chemistry
- Computational Biology & Bioinformatics ■
- Earth & Environmental Sciences
- Embedded Systems
- Energy: Sustainable Materials and Design
- Engineering Mechanics
- Environmental Engineering
- Materials Science
- Mathematics
- Microbiology
- Physics & Astronomy
- Plant Sciences
- Robotics & Intelligent Machines
- Systems Software
- Translational Medical Sciences

1. As a part of this research project, the student directly handled, manipulated, or interacted with (check ALL that apply):

   ☐ human participants ☐ potentially hazardous biological agents

   ☐ vertebrate animals ☐ microorganisms ☐ rDNA ☐ tissue

2. I/we worked or used equipment in a regulated research institution or industrial setting: ☐ Yes ■ No

3. This project is a continuation of previous research. ☐ Yes ■ No

4. My display board includes non-published photographs/visual depictions of humans (other than myself): ☐ Yes ■ No

5. This abstract describes only procedures performed by me/us, reflects my/our own independent research, and represents one year's work only ■ Yes ☐ No

6. I/we hereby certify that the abstract and responses to the above statements are correct and properly reflect my/our own work. ■ Yes ☐ No

This stamp or embossed seal attests that this project is in compliance with all federal and state laws and regulations and that all appropriate reviews and approvals have been obtained including the final clearance by the Scientific Review Committee.