Regulatory Plan for Kal-PDx, a maternal diagnostic tool

This plan was developed by Innovations in Maternal Health Diagnostics (IMHD)

Team Members: Mitali Bhandari, Dushyanth Gopichand, Sara Khalil, Linnan Li, Sejal Purohit, Raghvendra Shaktawat, Jiaying Zheng

April 21, 2021

Project- high level description:

IMHD has developed this plan for Kalia Health's preeclampsia diagnostic, Kal-PDx. Kalia Health is a health justice company dedicated to improving access to maternal health care through early detection of preeclampsia, a pregnancy complication. They are in the early stages of developing their product, Kal-PDx, and will use this plan to guide their regulatory submissions. IMHD researched the FDA requirements for submitting requests to register a new medical device and determined the relevant requirements needed for each stage of the regulatory process.

Contents

I. Project Overview

Our Objective:

The main objective of this project is centered around providing Kalia Health with a detailed regulatory plan which will drive their meetings, submissions and overall effort for seeking FDA approval for their new diagnostic tool, Kal-PDx.

Project Scope:

This project will result in an exhaustive list of required documents and a detailed regulatory plan needed to better prepare Kalia Health for the FDA regulatory process. Preparations for pre-market regulatory submissions and interactions with regulatory authorities will help achieve commercialization milestones and are included in the scope of this project.

As part of our project, the plan will help in doing the following: **(1)** identifying key documents needed, **(2)** developing a flowchart outlining requests and applications applicable to Kalia Health's medical device, and **(3)** prioritizing deadlines and anticipated application fees.

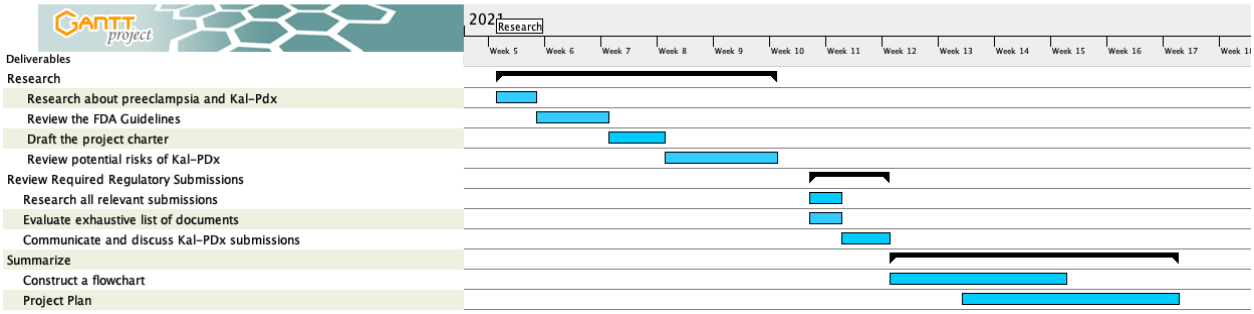
Out of Scope:

Product development and related clinical studies needed to collect safety and effectiveness data will not be included in this project. Furthermore, implementation of this regulatory plan and ongoing data collection are also out of the project's scope.

II. Timeline

This project will require 3 months for completion and involve three main phases: (1) Research, (2) Review Required Regulatory Submissions, and (3) Summarize.

Task	Task Description	Start Date	Duration (days)	End Date
	Research	01/25	35	03/22
1	Research the company's mission, clinical implications of preeclampsia & their design for a diagnostic device for early detection of pregnancy complications	01/25	5	01/29
2	Review Code of Federal Regulations (CFR) for new medical devices and determine key documents needed to be submitted and filing fees	01/30	9	02/07
3	Draft the project charter	02/08	7	02/13
4	Review potential risks of Kal-PDx	02/15	14	02/28
	Review Required Regulatory Submissions	03/01	14	03/14
5	Research all relevant submissions needed for Kal-PDx: 510(k) pre-market, De-Novo 513(g) - all of which will be needed for regulatory clearance of Kal-PDx	03/01	14	03/14
6	Come up with an exhaustive list of documents needed for Kal-PDx submissions	03/05	4	03/08
7	Brainstorm ideas for how to effectively communicate and discuss Kal-PDx submissions	03/09	6	03/14
	Summarize	03/15	36	04/19
8	Construct a flowchart that summarizes the regulatory process for registering Kal-PDx. This flowchart will be to be used as a visual tool when communicating with stakeholders	03/15	22	04/05
9	Synthesize research findings and come with a project plan	03/24	27	04/19



III. Budget

Given that Kalia Health is a small business, we made sure to include all applicable fees for small businesses. These fees are typically less than standard fees required for regulatory submissions. Moreover, since Kal-Pdx is still in its early stages of development, we wanted to account for different potential device classifications, class II and III. Listed below are all possible anticipated fees as referenced by the FDA's most updated official fees (for 2021). This budget should be used for guidance at this stage of the project.

*Fee type: small business fee

Application Type	Fee
Establishment & Registration for Medical Device Listing	$5,546
Small Business Certification Request	$0
513g Request	$2,468
510(k)	$3,108
De Novo Classification Request (NSE devices)	$27,424
Pre-Market Approval (PMA) (Class III high risk devices)	$91,414
Total Fee (Class II moderate risk device)	**$11,122**
Total Fee (Class II moderate risk & NSE)	**$38,546**

Total Fee (Class III high risk)	**$102,536**
Total Fee (Class III high risk & NSE)	**$129,960**

**Note: a small business is eligible for a "first premarket application/report" fee waiver*

IV. Procurement

This section will not be applicable to our project plan since our project mainly focused on developing a plan for FDA submissions. We did not directly interact with vendors at this stage of the project. These interactions may happen afterwards.

V. Quality Management

Quality Management ensures that the project will satisfy the documents needed for the regulatory submissions for Kal-Pdx and that the device meets FDA requirements and specifications. Required documents that are particularly important include those that evaluate the medical device for regulatory clearance and highlight the benefit-risk considerations. For example, adequate device testing and documentation is needed to demonstrate the efficacy and safety of Kal-Pdx. Additional descriptive information is needed to clearly articulate intended use(s), warnings, benefits, health-risks and any other relevant information.

In conjunction with the regulatory requirements, the project team has identified the following documents needed by Kal-PDx for regulatory submissions:

- **Establishment Registration & Medical Device Listing – 21 CFR Part 807:** Registering the organization with the FDA to be able to market and sell any medical device. Registration information must be verified every year (any time between Oct.1- Dec. 31). * no exemptions- fixed fee for all establishments

- **Small Business Request:** The Small Business Determination (SBD) Program determines if a business is both certified and qualified as a “small business” and eligible for reduced submission fees – forms needed: Form 3602 and/or 3602A

- **513(g):** Formal device classification information provided by the FDA

- 510(k) Pre-market Submission (21 CFR Part 807 Subpart E): For medical devices intended for human use, regardless of class- This is needed to demonstrate that the device is safe and effective. Exemptions may apply (i.e class I devices). The FDA provides a clearance letter specifying if the device is substantially equivalent (SE), safe and effective to be legally marketed.

a) Evaluation of Medical Device for Regulatory Clearance: To review performance factors- adequate performance testing and documentation is needed to demonstrate the efficacy and safety of the device.

b) CDRH Total Product Life Cycle: To evaluate the intended use of the medical device for device clearance

c) Labelling requirements – 21 CFR Part 801: Descriptive information (ie. manual, box inserts etc) needed to be included in the label highlighting intended use(s), warnings, reactive ingredients, appropriate storage information, manufacturer info, etc- needs to be evaluated

d) Benefit-Risk Considerations: discuss controls, benefits and health-related risks to end-users. Risk management: risks (assessment, mitigation, contingency planning, tracking and reporting ie. risk registry), contingencies and impacts

- De Novo classification request (Device Classification Under Section 513(f)(2): The 510(k) review is followed by revision under the De Novo Classification Process (risk-based classification process). This happens only after the FDA determines that the device is not substantially equivalent (NSE).

- Premarket Approval application (PMA)- 21 CFR Part 814: To market a medical device intended for human use- typically required for Class III high risk medical devices only. This is the scientific review process that more closely evaluates device safety and effectiveness. *Note: a small business is eligible for a "first premarket application/report" fee waiver*

- Investigational Device Exemption (IDE) for Clinical Studies – 21CFR Part 812: This can be used to support the PMA application. It allows manufacturers to present safety and effectiveness data for the device prior to commercialization

- Quality System (QS) Regulation 21 CFR Part 820: Quality management to ensure that the device meets FDA requirements and specifications. Device Master Record (DMR), Device History Record (DHR), Device History File (DHF), document control- monitoring and controlling performance.

- **Pre-Submissions (Pre-Sub):** Submit a formal investigational and marketing application for the pre-submission meeting. Include a cover letter, premarket review submission cover sheet, thorough description of the device, specific questions and type of requested feedback. Also prepare a presentation identifying meeting topics and questions, to be shared with the FDA prior to the meeting.
- **Medical Device Reporting (MDR) – 21 CFR Part 803:** Detecting and reporting back to the FDA in case any problems were experienced by device users.

Additional documents required include:

- **DMR (Device Master Record)**: A compilation of the procedures and specifications for designing the finished device and testing it. Design specifications include design drawings, composition, components or specifications. Additional documentation may be required to outline production methods, environment specifications, inspection procedures, quality assurance (acceptance criteria, QA equipment), labeling and packaging, and service details.
- **Design History File**: Documentation of the iterative process of product design and development, tracking the evolution of the device design to meet user needs and in response to different design inputs, revisions, risk assessment, troubleshooting, verification, and validation reports.
- **DHR (Device History Record)**: The production history of a finished device. Includes: UPCs (important for complaint investigations) or lot#, manufacturing dates, quantity manufactured and distributed, acceptance records that show the design followed the DMR, and labeling for each unit.
- **Documentation control:** Tracking important technical documents that the project depends on to accomplish its objectives. We have a controlled internal iterative process, which depends on changes made to the device design and updates obtained from clinical trials.
- **Clinical trials:** Detailing clinical trials designs, timelines, validation and early background research.
- **Quality Assurance:** Project quality assurance is one of three parts of a larger project quality system that ensures the project deliverables meet the planned quality standards.

VI. Resources & Project Team

Human resources management is an important element in this project. The human management resources plan is a tool which will help in managing human resource activities throughout the

project until closure. The purpose of this plan is to identify and document project roles, responsibilities, required skills, team member performance, provide feedback, resolve issues, and manage changes to optimize project performance. This section does not only shed light on required technical skills but also recognizes the importance of interpersonal skills in helping in facilitating collaborations and exchange of ideas. The working environment and culture strengthened relationships between team members and fostered a supportive internal network.

Roles	Responsibility
Project Sponsor	- Provide key documents, preliminary data, and overview of the project - Schedule Biweekly meetings with the team leader and members - Review and approve project deliverables
Project Manager	- Organize the project in accordance with the project plan - Lead team members toward project objectives - Provide overall project direction - Coordinate project deliverables - Report project status to the project sponsor
Project Team Members	- Provide knowledge and recommendations - Participate in team discussions - Work on project deliverables

VII. Communication

Communication is key in ensuring project success. Not only is good communication important for keeping key stakeholders well informed about the project, but it also encourages project discussions and collaborations within the team.

Stakeholder	Main Contact Person	Mode of Communication	Strategy	Message

Project Sponsor	Team leader (Sara Khalil)	Biweekly virtual meeting with the entire team via Google Meet	Providing updates on the team's progress and anticipated project direction and expectations	Inform, educate, and gain agreement
Kalia Health	Project sponsor (Happy Ghosh)	Meetings, email	Provide funds and make decisions	Involve
FDA/ Regulatory Agencies	Project sponsor (Happy Ghosh)	Email, pre-sub meeting (presentation)	Submissions & presubmissions (meetings & feedback)	Inform and gain agreement
Kalia Health's product development team	Project sponsor (Happy Ghosh)	Email	Keep updated	Involve and inform
Hospitals/Healthcare organizations	Vendors, research institutions and academic affiliates	Email, advertisement	Keep informed	Inform, gain buy-in, educate, update
Customers (clinicians and patients)	N/A	Advertisement	Keep satisfied	Gain buy-in, educate
Non - governmental organizations	FDA	Email, meetings	Educate and develop strategies to target all affected communities and maximize device utility	Involve, educate and support

VIII. Risk Management

Risk management aims to identify risk, plan responses and manage risk that are under our control. The purpose of our risk management plan is to document potential risks and strategies

to better prepare and manage them. This document will also include a contingency plan, which elaborates on risks we eliminated early in our project.

Roles and Responsibilities

Risk	Risk Owner	probability	Impact	Description	Root Cause	Triggers
Insufficient funds available	PS/ Kalia Health	medium	medium	Kalia Health is a small company, and we are not fully aware of its budget. They might not have enough funds to cover anticipated expenses or additional required fees	Kalia Health is a small company with a limited budget	Any changes made to the device classification, which will require additional submissions and costs
Final product does not match the original design	PS	medium	high	Although product development is out of our project scope, still the final device will affect our regulatory plan. If the final product does not match the company's original expectations, then the regulatory plan will require drastic revisions.	The device does not pass the testing needed to prove its efficacy	Negative clinical study results, incomplete or unsuccessful product design
Competitor Ready To Market a Similar Device	N/A	medium	medium	To our knowledge and based on our research, there are no similar devices in the market. However, according to reports obtained from the project sponsor, there is another company that is working on releasing a similar product. We have no information on their progress and specifics related to their project design. If this product gets released before Kal-Pdx, then Kalia Health will no longer need to submit a De Novo request.	Competitive nature of the market	A competitor submits and registers its device before Kalia Health

Contingency plan:

1. *Incorrect device classification*

Kal-Pdx is still in its early stages of development. This device has not been formally classified yet by the FDA and therefore we cannot be 100% certain of its classification. As it stands, Kal-Pdx

can be either a class II or a class III device. Differences in classifications will affect required documents, submissions and application fees. To account for this uncertainty and eliminate this risk, we integrated alternative regulatory plans. In our flow chart, we created alternative pathways that accommodate for both class II and III devices.

2. *De Novo submission*

De Novo submissions are required when there are no similar products in the market. Up until now, there are no similar devices registered in the market and therefore we anticipate that the FDA will require that Kalia Health submit a De Novo request. However, according to reports from our project sponsor, a competitor has been working on a similar device and there is a possibility that their company may register their device before Kalia Health. So, the risk we are facing is that we cannot be certain about whether or not Kalia Health's Kal-Pdx will qualify as a NSE device and require De Novo submissions. We eliminated that risk by accounting for both De Novo-dependent and independent regulatory pathways.

VIIII. Stakeholders

Below is a list of key stakeholders:

Identifying Stakeholders

Stakeholder	Project Role	Power/ Interest	Influence/Impact
Project Sponsor	Leadership support, sponsorship	High/High	Provide project oversight/leadership, guidance and approval
FDA and other regulatory Agencies	Invisible stakeholder	High/Low	Mandate guidelines and specific requirements for releasing medical devices such as Kal-PDx into the market
Research Institutions and academic affiliates	sponsorship	Low/Low	These institutions will offer research opportunities for testing and optimizing Kal-PDx
Clinicians/ Hospitals	N/A	Low/High	Once Kal-PDx is released into the market, clinicians will use it to help in the early diagnosis of preeclampsia.

Non-profit organizations	N/A	Low/Low	Spreading awareness about preeclampsia and the need for diagnostic tools such as Kal-PDx for early detections so as to avoid any dire consequences.
Patients	N/A	Low/High	The patients are the main end-users of the medical device.

Stakeholder Management

It is especially important to develop a management plan to ensure that these listed stakeholders remain engaged throughout the project. Not only must they remain informed throughout the course of the project, but they should be updated adequately and consistently depending on their specific power and interest level. The stakeholders' contribution is critical for the success of the project.

Stakeholder Engagement

Project stakeholders have varying levels of contribution, however one unifying element to managing their engagement is communicating efficiently so as to also educate them and gain their agreement. Communication will help ensure that stakeholder expectations and needs are met, issues are addressed, and conflicts are avoided. The stakeholder communication plan will clearly define the type of information as well as the most suitable and agreed upon method and frequency of communication needed to be maintained. This communication plan might require adjustments in case of sudden changes to the availability or interest levels. Relatedly, establishing healthy relationships with stakeholders will be equally important and therefore their satisfaction must be prioritized and reviewed periodically.

X. Change Management

Change management is the process and techniques required to successfully navigate change, managing both the people side and technical side of change, both of which are needed to achieve the project's desired outcome. It accounts for both organizational and individual capabilities, helping individuals impacted by change in making successful transitions. Some of the considerations needed to be studied when managing change include levels of dissatisfaction with the status quo, practicality of change, cost of changing and desirability of the proposed changes. It is important that a project leader develops strategies to successfully manage change and resistance. More specifically, planning for changes will help the project move forward towards

its desired state where Kal-Pdx is FDA-registered, released into the market and distributed to hospitals, patients, noon-profit organizations and academic research institutions for use.

Effective communication between the project manager and team members allowed for needed changes to be incorporated into our project deliverables. In fact, poor communication would have negatively impacted the project's progress. For example, not receiving feedback from team members but rather solely depending on a one-way communication stream would have prevented the project manager from understanding how well changes are processed.

Furthermore, given that Kal-PDx is at its early stages of development and testing, change and uncertainty in predicting the project's final performance and classification was inevitable. Despite facing some changes, it was important to still achieve the desired solution. Deliverables were modified as more information became available to the team and key concepts related to the functionality of the product and its status in product development became clearer. Changes in deliverables required additional work and effort and team members met the project sponsor's standards with minimal resistance.

In addition to technical changes, it will be important to also consider the people or human side of change. Registering Kal-Pdx using well-defined and pre-set regulatory standards is the main goal. However, it will be important to keep an eye on updates to these submission criteria, and any changes or additions made to the requirements. These changes should be reflected in the project plan so as to properly prepare Kalia Health for FDA submissions and not risk submitting an incomplete application. Moreover, it is important to carefully consider hospitals and patients, stakeholders and end-user of the device. Kal-Pdx should ultimately be used as a diagnostic tool, targeting different populations around the world. Another important consideration would be to be aware of nuances in regulatory requirements in different countries so as to ensure that the device will be approved outside of the US as well.

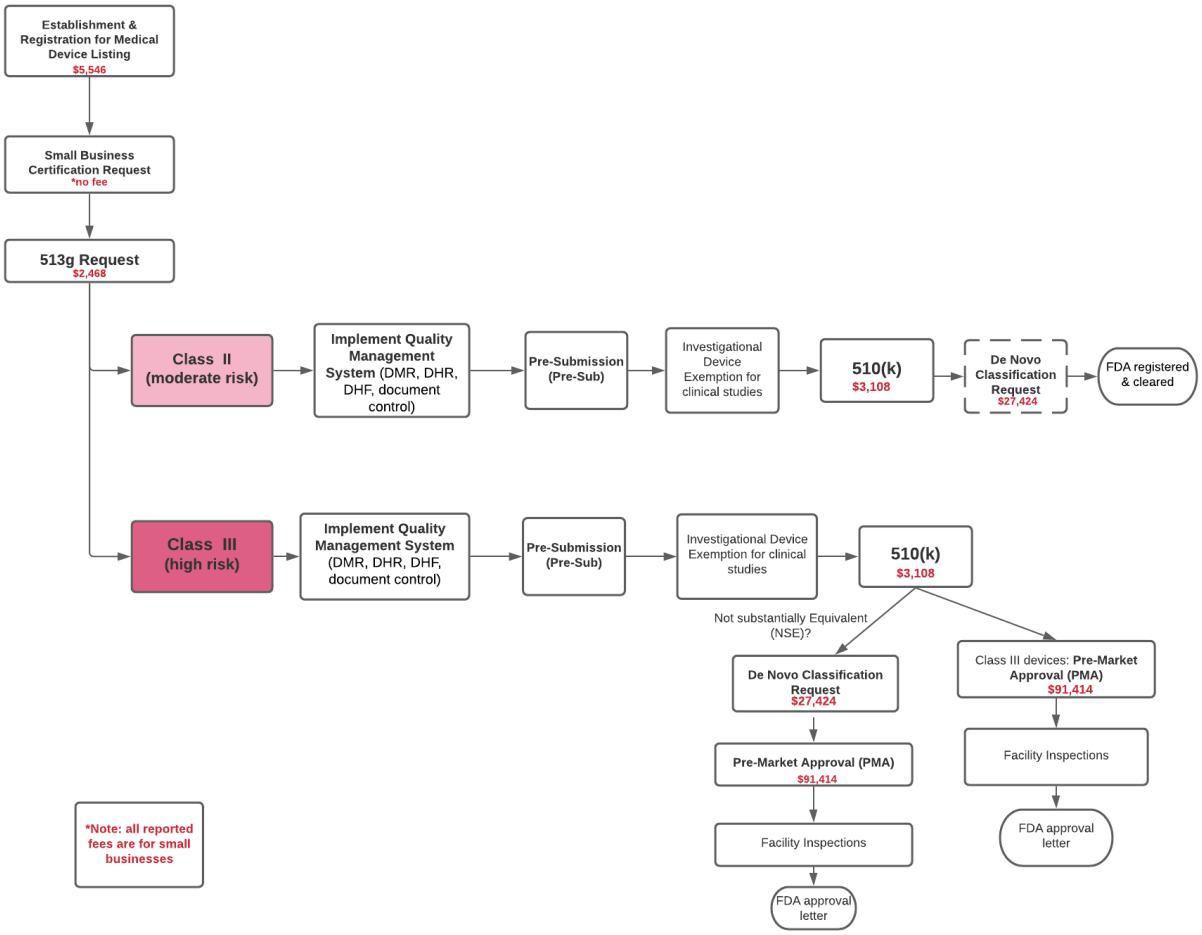
XI. Project Closing

Closing of the project began at the start of the project, specifically when our project sponsor clearly defined different project criteria and her overall expectations.

At the end of the project, a final project report was shared with our project sponsor. This report included an exhaustive list of regulatory documents that will be required to register Kal-Pdx and a flowchart summarizing the FDA regulatory process. The project report can also include more information stating completed tasks and issues dealt with while also including notes explaining why certain issues were faced. We sent the documents to our project sponsor prior to our last meeting with her. In our last meeting, we made sure that we met her expectations, and she was satisfied with what we delivered.

XII. Appendix

Flowchart of the Regulatory Plan



*The flowchart was made using a web-based platform: Lucidchart. It can be edited using this link:
https://lucid.app/lucidchart/invitations/accept/16bfe9e2-9e3d-4326-b843-5c756309dd7c?viewport_loc=-298%2C-62%2C2848%2C1402%2C0_0