An Approach to Mitigating Challenges of Data Sharing in the Development of Biomarkers

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Abstract

BACKGROUND
Biomarker integration into drug development can happen through various pathways. These pathways are often executed in parallel with one and other and are not mutually exclusive.

PURPOSE
This project, beginning January 2020, aims to help address barriers seen with the integration of biomarkers in drug development and to assess if we can use IND/NDA/BLA biomarker data submitted to FDA to answer new drug development questions. Historically access to data has been the largest challenge due its proprietary nature and lack of consistency in data collection, analysis, and interpretation between groups. Therefore, can we explored using data previously submitted to the FDA during the application process to form a metadata repository that can be queried to address specific drug development specific, while defining the context for which this data might be appropriately used.

METHODOLOGY
The authors chose to use fecal calprotectin as a test case since here is interest both internally and externally, large amounts of data has been collected by multiple programs. Additionally, FDA staff have discussed possible utility for a fecal calprotectin but has been unable to draw definition conclusions about its use.

RESULTS
Of the three trials identified for this case study, we focused our efforts on the one with the largest number of patients and the longest duration. Preliminary data showed a modest correlation between the raw fecal calprotectin levels and the raw endoscopy score.

CONCLUSION
Since beginning this project in January 2020, it is encouraging that through this process we have learned there is accessible data that could be utilized to answer current drug development questions. Future steps and challenges of this project include:

1) Identify analysis methods and clinical trial protocol used for fecal calprotectin testing and endoscopy scoring.
2) Data standardization/normalization.
3) Collaborating with experts to identify appropriate cut offs points.

Introduction

BIOMARKER INTEGRATION INTO DRUG DEVELOPMENT
Biomarker integration into drug development can happen through various pathways. These pathways are often executed in parallel with one and other and are not mutually exclusive.

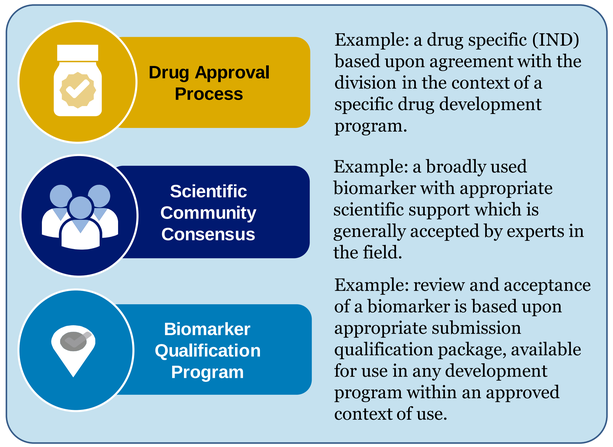

Figure 1. Pathways to Facilitate Biomarker Integration

OVERCOMING BARRIERS TO SUCCESS WITHIN THIS SPACE
This project, beginning in January 2020, aims to help address two main barriers seen with the integration of biomarkers in drug development. Basically, can we use data we have to answer new drug development questions.

- Access to Data: historically, this has been the largest challenge, due to the proprietary nature of the data. Therefore, can we help address this challenge by using data previously submitted to the FDA during the application process (INDs/NDAs/BLAs) to form a metadata repository that can be queried to address drug development specific needs that the industry is facing.
- Addressing Drug Development Specific Needs: is this data sufficient to address FDA regulatory needs, and what is the context in which this can be and not be applied.

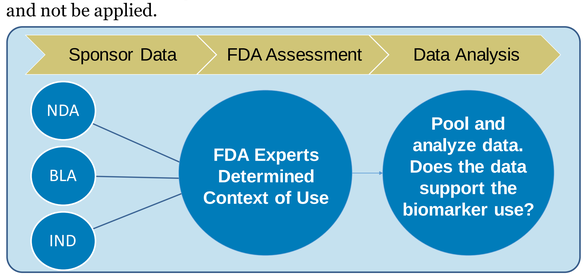

Figure 2. Project Process

Materials and Methods

FOCUS ON FECAL CALPROTECTIN
- Multiple external groups expressed interest
- Encouraging preliminary search, as you can see in Table 1 the data type spans a wide range trial types, providing a more comprehensive assessment
- Survey results from divisions showed internal interest
- Discussion with Subject Matter Experts at the FDA focused the analysis on the correlation of the fecal calprotectin level with the endoscopy score

Application	Study Type	Number of Subjects
BLA 761044	Maintenance Trial	624
BLA 125476	Phase 2	47
BLA 125476	Maintenance Trial	895
NDA 201830	Pediatric Trial	72
BLA 125289	Maintenance Trial	1228

Table 1. Sample of Trials from Each Application

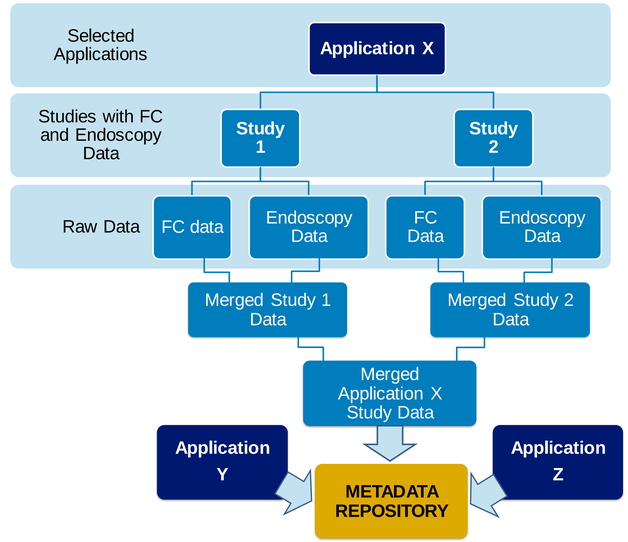

Figure 3. Application Data Integration Pathway

Results and Discussion

PILOT DATA FOR BLA 125289
Three trials were identified for this application. Of the three, two were eventually combined into a Extension/Maintenance Trial. We extracted data from the Extension Trial, because it had the largest number of patients and the longest duration of the three trials.

Preliminary data showed a modest correlation between the raw fecal calprotectin levels and the raw endoscopy score.

Conclusion

From the start of this project in January 2020, we have, through this process learned there is accessible data that could be utilized to answer current drug development questions. We have determined that the following steps below will be necessary to utilize this data for addressing any drug development needs.

FUTURE STEPS
Below we have listed some of the future steps and challenges of this project which are still to come.

- Identify analysis methods and clinical trial protocol used for measuring fecal calprotectin levels and endoscopy scoring. This includes hundreds of different testing level cut off/significant value points for fecal calprotectin, including those which are specific to a single lab/site, and identifying methods to avoid double counting patients.
- Data standardization/normalization. This includes grouping analysis methods, time frames, standardizing by time frame, endoscopy score type on methods.
- Identify appropriate cut offs points, via collaboration with experts.