PP19: Statistical Programming Team Contributions for Real-World Evidence Regulatory Submission

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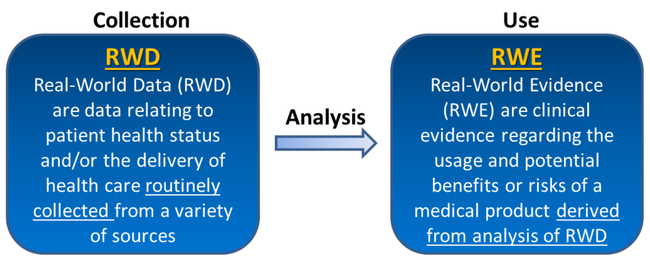
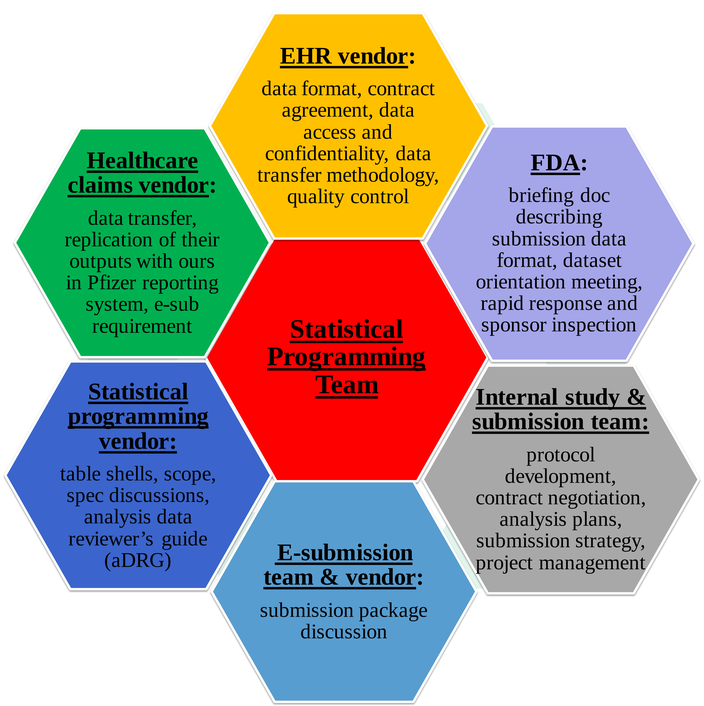
ABSTRACT: Use of Real-World Evidence (RWE) data in regulatory submissions is relatively new and FDA guidelines are still in draft stage. One of the early Pfizer submissions using Electronic Health Record (EHR) and Healthcare Claims data for label expansion was successfully approved by the FDA. Using RWE data for regulatory submissions has challenges which required earlier and broader involvement of the programing team, such as interaction with multiple organizations, study documentation development, FDA briefing document development, data analysis and finalizing the submission package to FDA. The purpose of this poster is to illustrate the involvement and contribution of the statistical programming team in each aspect of the process for successful regulatory submission, and to help other programmers who may need to use RWE data for regulatory submission before FDA guideline is finalized.

INTRODUCTION:



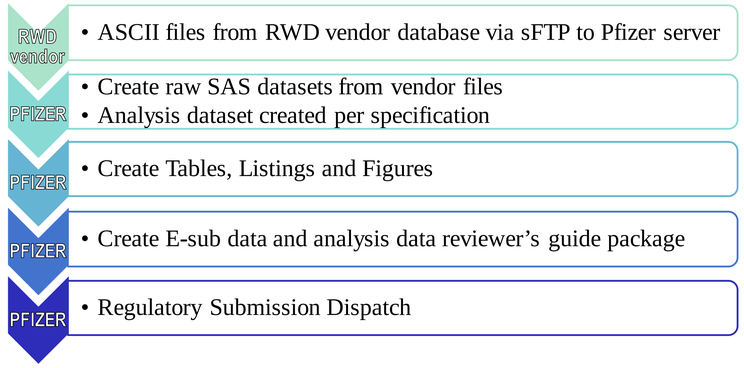
INTERACTIONS WITH MULTIPLE ORGANIZATIONS:



DATA TRANSFER:

- Deidentified data: understanding what Pfizer will be receiving from the vendors (e.g. how patients were selected for analysis; understanding the nature and format of EHR data to be transferred)
- Traceability of the data transfer and data security: documentation to record each data transfer per vendor, data transfer method, evidence of limited access to the sFTP sever, QC methodology of the transferred data

RWD FLOW IN PFIZER SYSTEM



SHARE AND EDUCATE RWD VENDORS WITH THE TECHNICAL REQUIREMNETS FOR FDA E-SUBMISSION:

SAS Dataset (.xpt) structures and attributes of variables
- Dataset name
- Dataset size
- Variable name
- Variable length
- Variable label length

Data Traceability
- Raw datasets
- Analysis datasets
- TLFs

Supportive documentations
- Define.pdf
- aDRG

SUBMISSION:

- Briefing Document: authored the dataset section for the briefing document to describe how the data was submitted (map EHR vendor legacy data structure to meet e-sub technical requirement).
- Analysis support: collaborated with study statistician and created targeted analysis datasets to support summary tables as well as simplified aDRG.
- FDA Orientation Dataset Meeting (timing was right after submission dispatch): participated teleconference with FDA and presented high level data flow included in the submission package.

POST SUBMISSION:

- FDA review queries: biostatistics queries, clinical queries, safety queries and label negotiations.
- FDA sponsor inspection: supported inspection with statistics and clinical line to review each raw patient data with inspector.
- FDA Post-Approval Feedback meeting: participated and raised questions on submitted datasets.

CHALLENGES/LESSONS LEARNED:

- Early engagement with RWD vendors to discuss submission expectation
- Have in-house experts familiar with source data from RWD vendors to be able to answer FDA inspector queries
- Understand and manage differences in RWD source data compared to expected data from a clinical trial
- Set up appropriate sFTP to ensure the data traceability
- Need to create Analysis Plan at early stage to have clear scope of supportive TLFs
- Table shells were ready before vendor data were available so first team exposure to the production data was at the time of draft TLF review, which led multiple modifications to refine TLFs
- Early engagement with FDA to seek agreement on the e-submission package
- Timeline alignment of TLF creation and submission package preparation
- Key messages should be determined as early as possible to help finalize the submission scope

CONCLUSIONS:

There will always be new and innovative technologies for data collection tools, which will bring many challenges (e.g. differing data quality standards, the often lack of robust data documentation) associated with using data collected through such tools for regulatory submission activities. Statistical programmers can play a key role in this ever-changing environment and in bridging multiple functional lines, as we have the experience to understand challenges associated with various data collection methods and their usage for analysis and reporting events. In order to overcome challenges in new submission strategies such as RWE requires statistical programmers' contribution to guide the team.

ACKNOWLEDGEMENT:

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REFERENCES:

FDA RWE information:

"Framework for FDA's Real-World Evidence Program", December 2018. https://www.fda.gov/media/120060/download

"Submitting Documents Utilizing Real-World Data and Real-World Evidence to FDA for Drugs and Biologics", May 2019. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/submitting-documents-utilizing-real-world-data-and-real-world-evidence-fda-drugs-and-biologics

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