› CASE STUDY

VERISTAT

A Refusal-to-File Prompts an Independent Quality Review of Clinical Data for an NDA Submission to FDA

Resubmission Accepted and Product Received FDA Approval

Background

A global pharmaceutical company submitted a New Drug Application (NDA) to the United States (US) Food and Drug Administration (FDA) for their product to treat a childhood disease. After its preliminary review, the FDA determined the application contained an incorrect version of the SAS datasets for a pivotal, Phase 3 clinical study and issued a Refusal-to-File (RTF). The FDA RTF letter stated the need for an extensive data quality assessment prior to resubmission.

Veristat was chosen to perform an independent, statistical, quality assurance (QA) review of the datasets for the pivotal study.

NDA was submitted for the treatment of a childhood disease

THE GOAL

Our client needed to review the corrected datasets for the resubmission of the NDA. Veristat was brought in to help by:

- Developing a plan for the independent review/audit of the datasets (including the process used to generate the datasets) and analyses for the NDA submission
- Preparing for and attending the FDA Type A Meeting
- Performing an independent review/audit of the raw, SDTM and ADaM datasets for the individual studies and the ISS/ISE, including the processes used to generate final datasets for submission
- Providing additional services as requested/required depending on the outcome of the audit of the datasets and discussions with the FDA during the Type A Meeting

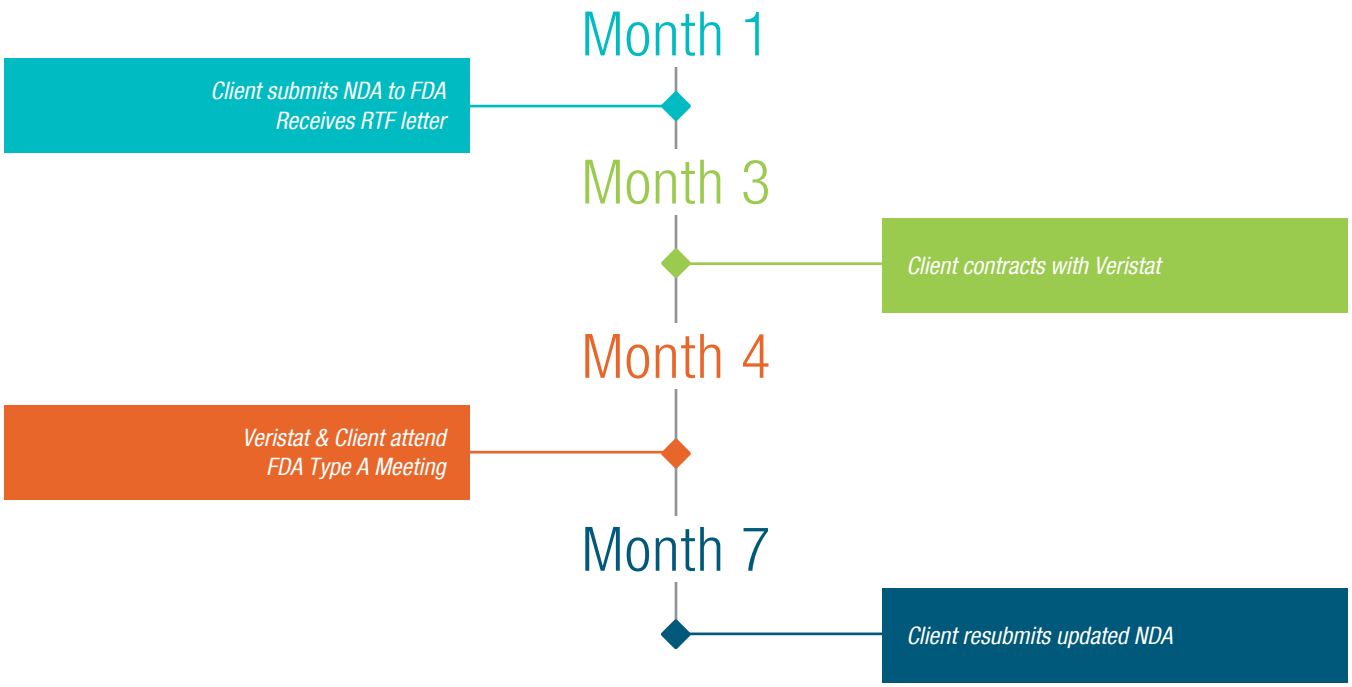
CHALLENGE/SOLUTION

The client, a small company, did not have in-house biostatistics expertise. The solution was a collaborative effort among Veristat, the client, and their primary CRO to share and review the data and the audit findings.

Veristat pulled together a cross-functional team of experts in the areas of regulatory affairs, programming and statistics. Our regulatory submission project director developed the project timeline and kept all parties aligned and on task. Our regulatory strategist helped determine the strategy for the Type A meeting and contributed to the briefing document explaining the data fixes for the resubmission. The lead statistician wrote a plan for review of the data that triaged where to focus our efforts based on regulatory history, the primary objectives of each analysis, and the highest likelihood of additional errors. Then, our lead programmer reviewed the dataset specifications and attempted to reproduce the analyses according to the documentation provided by the other CRO. Our programmers specifically reviewed the metadata, documentation, SAS programs, and datasets. We then worked with the client's CRO to address the dataset and programming issues in preparation for the resubmission.

Our statistical review of the datasets for the ISE identified a number of minor issues with the define.xml files, SDTM, and ADaM datasets. Veristat focused on the need for improved documentation and traceability in the files that are submitted to support the SDTM and ADaM analyses. In particular, the reviewer guides included in this data package were updated with improvements to support an effective review by the FDA. Veristat created a final report for our client on the steps we took to independently verify and correct the Phase III data package for resubmission.

Submission Timeline



RESULTS

Our client resubmitted their NDA application to the FDA with the corrected datasets seven months after their initial submission. It was accepted for filing and within nine months the product received FDA approval.

Meet Veristat

We understand that the stakes and pressures are high when you are preparing, submitting, and waiting for approval of your marketing application. The submission process is an overwhelming coordination effort. We have the experience, agility, and scientific-minded experts to help you navigate this process successfully. Get introduced to Veristat today.

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