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OSI Packages: What you need to know for your next NDA or BLA Submission

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ABSTRACT

The FDA's Office of Scientific Investigations (OSI) has responsibility to select sites for on-site inspection as part of the FDA's Bioresearch Monitoring (BIMO) program and needs each sponsor's help in order to perform this selection quickly and efficiently. Sponsors are asked to provide a variety of site-level information so the OSI can identify sites of interest - for example, high enrolling sites, sites whose data may be swaying the results, sites with prior inspection issues, etc. In late 2012, the FDA released new OSI materials (draft guidance for industry, dataset specifications, and a webinar) that describe what sponsors should include in their NDA/BLA submissions to support the OSI's efforts. This paper provides an overview of the released OSI request components (Parts I, II, and III), and it describes how AstraZeneca prepared an OSI package for a recent NDA submission. The emphasis will be on programming deliverables with attention towards Part II (subject level data listings by site) and Part III (summary level clinical site dataset). This paper includes examples of Q&A with the OSI, timings for delivery, the need for cross-functional input, and some lessons learned. After reading it, you will be better prepared to put together an OSI package for your submission.

INTRODUCTION

The Food and Drug Administration (FDA) launched a Bioresearch Monitoring (BIMO) program to perform on-site inspections.[1] "The overarching goals of the agency's BIMO program are to protect the rights, safety, and welfare of subjects involved in FDA-regulated clinical trials; to determine the accuracy and reliability of clinical trial data submitted to FDA in support of research or marketing applications; and to assess compliance with FDA's regulations governing the conduct of clinical trials, including those for informed consent and ethical review."[1] The BIMO program spans several centers at the FDA such as the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), the Center for Devices and Radiologic Health (CDRH), and the Center for Veterinary Medicine (CVM).[1]

Specifically for New Drug Applications (NDAs) and Biologic Licensing Agreements (BLAs) submitted to CDER (as well as supplemental applications for each), the OSI has responsibility for on-site inspection planning including site selection and preparation of background inspection materials for inspectors.[2] The Office of New Drugs and the Office of Biostatistics aid the OSI in site selection. Once sites are selected, the FDA's Office of Regulatory Affairs is responsible for conducting the inspections using the background materials provided by the OSI.

Historically, the OSI made information requests to sponsors after a submission was filed, so the requests were considered 'on the clock'.[2] In 2010, the OSI developed information requests and began asking for them as part of the pre-NDA and pre-BLA process/meeting with the intent that the requested information be provided in the NDA or BLA. According to the FDA Webinar, with the enactment of PDUFA V, there are new inspection completion goals that require the OSI to make site inspection decisions sooner, such that for submissions on a standard review clock, the goal is for the OSI to select sites for inspection within 45 days of a submission being filed. For submissions on a priority review clock, the goal is even more ambitious with the OSI aiming to select sites within 30 days.[3] With such goals, there is a need for the OSI to receive requested information sooner and in a standard format. The OSI has also begun to pilot the use of a risk-based model to accelerate the site-selection process.[4]

In late 2012, the FDA released materials (webinar, draft guidance for industry and dataset specifications) to clarify the OSI's information requests for sponsors. The materials detail the what, how and when regarding Sponsor's delivering OSI information requests within a submission. Going forward, the OSI's information request is referred to as the OSI request and the body of work that AstraZeneca prepared is called an OSI package.

In this paper we share one AstraZeneca (AZ) NDA submission team's experience planning and preparing an OSI package. Note that for the AstraZeneca experience cited in this paper, the FDA provided specific requirements about the OSI request at our pre-NDA technical meeting. This occurred shortly before the release of the 2012 materials, but the request was similar. For the purpose of this paper, the public 2012 FDA OSI request materials are used as a reference, unless otherwise noted. Also, at our pre-NDA technical meeting, the FDA offered that AstraZeneca could arrange a teleconference with the FDA's OSI if we had any questions about the requested information. AstraZeneca

prepared several questions and had a teleconference with the OSI. Throughout this paper, we share relevant questions and answers (Q&A) for your consideration.

Disclaimer: please note that the materials presented in this paper are not intended to represent the views of the FDA. We are providing an example of one AstraZeneca submission team's experience preparing to satisfy the FDA's OSI request. The responses that the OSI gave to our questions may not be applicable for your submission. It is advised to seek clarification and agreement from the FDA and OSI if you have questions about preparing an OSI package for your submission.

OSI REQUEST - OVERVIEW

The OSI request is explained in three key FDA materials released at the end of 2012:

FDA Webinar: "Overview of Information requested by CDER's Office of Scientific Investigations (OSI) for NDA and BLA Submissions" (Oct 2012)

FDA Draft Guidance: "Draft Guidance for Industry Providing Submissions in Electronic Format – Summary Level Clinical Site Data for CDER's Inspection Planning" (Dec 2012)

FDA Dataset Specification: "Specifications for Preparing and Submitting Summary Level Clinical Site Data for CDER's Inspection Planning" (Nov 2012)

The References section of this paper contains links to these documents.

Per the FDA Webinar, the OSI request consists of three main parts referred to as Parts I, II, and III, plus a reviewer's guide. They contain:

Part I	Tabular listings of site information (5 items)
Part II	Subject data listings by site (10 listing titles)
Part III (optional)	Summary level clinical site dataset (clinsite.xpt, define.pdf)
BIMO Reviewer's Guide	Documentation about the location of Parts I, II, and III within the submission

Note that the FDA Webinar provides details about Parts I, II, and III, while the draft guidance and dataset specifications give information about Part III only.

AstraZeneca's Experience - Overview

At AstraZeneca, the first step in preparing the OSI package for one NDA submission was to assemble a cross-functional team with the expertise to lead and deliver all parts. Key team members included representatives from Statistics, Programming, Regulatory, Study Delivery, and Publishing. The table below identifies which AstraZeneca functions were key contributors for each part of the request. The cross-functional team reviewed the entire OSI request to evaluate the scope of work, prepare questions, assess resource needs, and plan timings.

OSI Information Request	Description	Key AZ Function(s) Involved
Part I	Tabular list of site information (.pdf)	Study Delivery
Part II	Subject data listings by site (.pdf)	Programming, Statistics
Part III (optional)	Summary level clinical site dataset (clinsite.xpt)	Statistics, Programming, Study Delivery
BIMO Reviewer's Guide (optional)	Location of each item for Parts I, II, III in the submission	Regulatory, Publishing
	Placement of OSI Parts into eCTD submission per OSI request	Publishing

Table 1. Key AstraZeneca Functions Involved in each Part of OSI Request.

OSI REQUEST PART I – TABULAR LISTINGS OF SITE INFORMATION

OSI Request Part I is Tabular Listings of Site Information. In general this part contains key logistics for planning and scheduling inspections (contact information and location of documents and data), counts of subjects at each site, and two important study level documents, the protocol and the annotated CRF. Specifically, the information requested in Part I is divided into five items. The OSI suggests that the first three items could be captured as tabular listings in a single pdf. The last two items are separate study documents. For details, see below:

Item	Content
Item 1	List of clinical sites where studies were conducted (including address and contact information)
Item 2	High level summary information for each site (number of subjects screened, enrolled, randomized, discontinued)
Item 3	List of responsible entity for key study functions contracted by sponsor and current location of study-related documents (e.g. monitoring, randomization, data management) Location of all source data generated by CROs (Specifically mentioned in specific request from FDA to AZ)
Item 4	Annotated Case Report Form (CRF)
Item 5	Protocol and all amendments

Table 2. OSI Request Part I Tabular Listings of Site Information Items 1-5, from FDA Webinar [3] and AZ'S OSI request from FDA

To support inspection planning, Items 1 and 3 are about logistics -- who were the investigators and CROs involved in each study, where are they located, and how can the OSI contact them if they want to schedule an inspection? Additionally, where are key study documents physically located so the OSI knows where to inspect specific files? The FDA webinar clarifies that if the study documents in Items 4 and 5 are already available in another location in a submission, then they do not need to be redelivered for the OSI request. Instead, simply specify that location in the BIMO Reviewer's Guide.

ASTRAZENECA'S EXPERIENCE WITH PART I

At AstraZeneca, Study Delivery led the preparation of Part I. In the FDA's specific request to AstraZeneca, we were asked to provide the items in Part I for all completed Phase III studies. After review of Part I of the request, we had one follow up question for the OSI:

- Regarding Part I Item 3, Location of source data generated by CROs: What is meant by 'source data' generated by CROs?
  The OSI reply was any study-specific documentation created, maintained or retained by the CRO. (This could include many things including, but not limited to, monitoring plans, data management plans, monitoring records, training records, contracts, work orders, etc.) Additionally, if a CRO was involved in generating source data, then provide the location where the source data could be inspected and provide diagrams to capture data flow.

In general, Study Delivery was able to gather and prepare most of the information for Part I, but the mention of data flow diagrams for Part I Item 3 sparked additional work for AstraZeneca. A single pdf was created that contained the data flow diagrams for each study for each CRO's data. Note that in some cases, the diagrams were available from the CROs, and in other cases Study Delivery created them in consultation with the CRO. For our AstraZeneca studies, some examples of CRO generated source data included laboratory data, blinded external central review data, electronic diary data, and randomization data.

Below is an example of AstraZeneca's data flow diagram for laboratory data to support Part I Item 3:

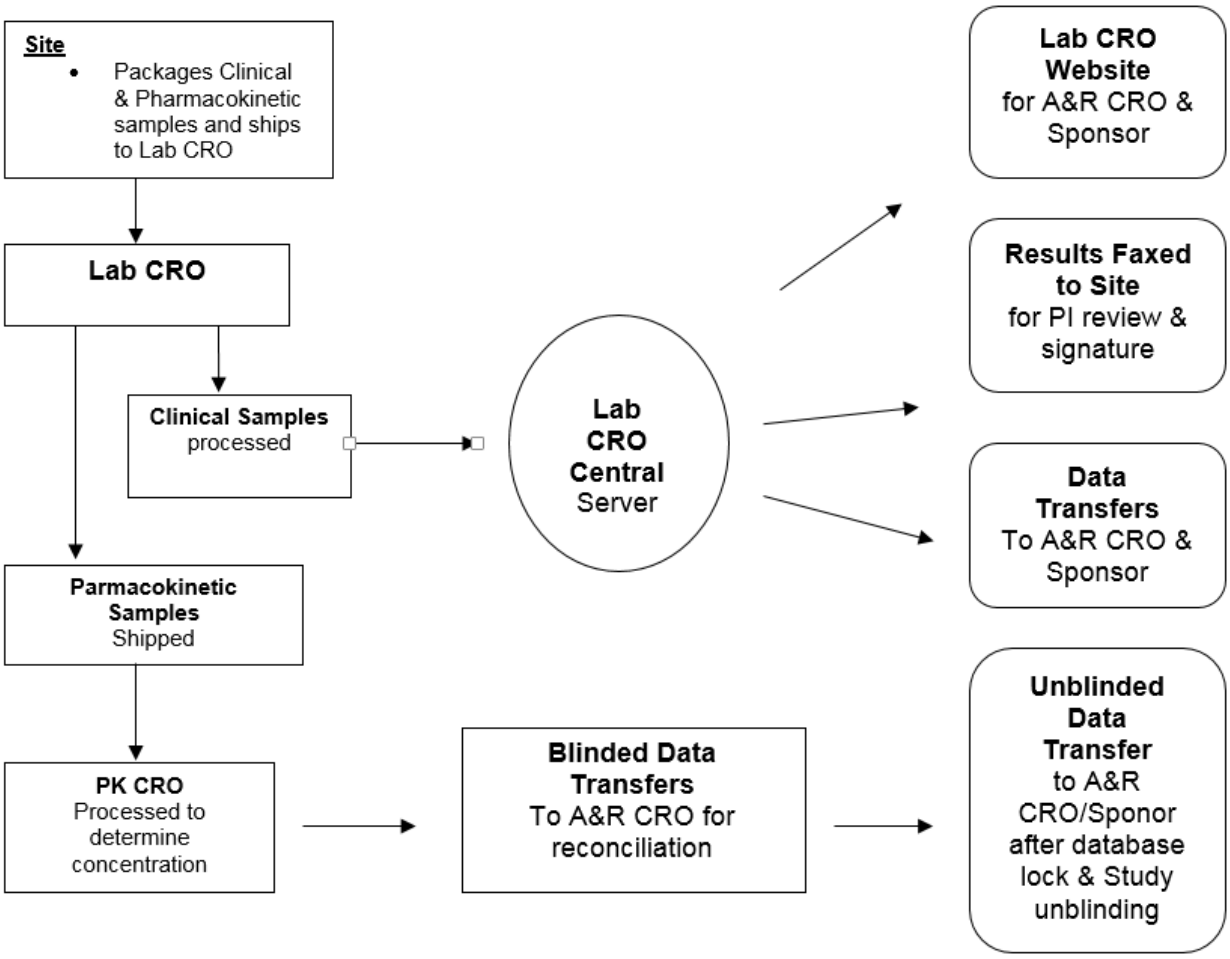

Figure 1. AstraZeneca's Sample Data Flow Diagram for Laboratory Data for Part I Item 3.

The source for each study's subject counts for Part I Item 2 was the completed Clinical Study Report (CSR). For Part I Items 4 and 5, AstraZeneca had already provided the annotated CRF and protocols in another part of the submission, so the location of those files was simply mentioned in the BIMO Reviewer's Guide. As a lesson learned, plan to have data flow diagrams prepared at the beginning of a study as a standard deliverable from each CRO that generates source data. This will provide clarity and ensure the diagrams are readily available for the OSI request. Regarding timing for Part I, the tabular listings of addresses and contact information could be started during study conduct, with a reminder that the investigator contact information is expected to be current. Therefore, just prior to submission, the investigator contact information would need to be double-checked to ensure it is still current. The subject counts by site that are requested in Item I Part II can only be finalized after the study is complete.

OSI REQUEST PART II – SUBJECT-LEVEL DATA LISTINGS BY SITE

OSI Request Part II should contain subject-level data listings by site. The purpose of the listings is to provide background material for inspectors to use during inspections for comparison versus source data. The FDA Webinar indicates that Part II listings are requested for each pivotal study.[3] Sponsors should ensure agreement with the Review Division about which studies are considered pivotal. The OSI provides 10 titles for subject data listings by site. To most programmers and statisticians, a listing 'by site' means the listing is 'sorted by site'. ***That is not the case for this request.*** Instead, the OSI asks that the 10 listings are created *separately* for each site. If a study has 50 sites, you may need to create 500 separate listings. Per the FDA Webinar, the 10 listings titles are below: Note that the webinar refers to the listings as "1" to "10" (in the list of titles) and also refers to them as "a" through "j" (in the screen shot of the pdf bookmarks for the listings). For completeness, we have shown both.

Listing Reference (numeric)	Listing Reference (character)	Subject Level Data Listing Titles
1	a	Listing for each subject/number screened and reason for subjects who did not meet eligibility criteria
2	b	Subject listing for treatment assignment (randomization)
3	c	Subject listing of dropouts and subjects that discontinued with date and reason
4	d	Evaluable subjects/ non-evaluable subjects and reason not evaluable
5	e	By subject listing of eligibility determination (i.e.; inclusion/exclusion criteria)
6	f	By subject listing(s), of AEs, SAEs, Death, and dates
7	g	By subject listing of protocol violations and/or deviations reported in the NDA, description of the deviation/violation
8	h	By subject listing of the primary and secondary endpoint efficacy parameters or events **For derived or calculated endpoints, provide raw listings used to generate the derived/calculated endpoint.**
9	i	By subject listing of concomitant medications (as appropriate to the pivotal clinical trials)
10	j	By subject listing(s), of laboratory tests, radiologic tests, etc. performed for safety monitoring

Table 3. OSI Request Part II - Subject Level Data Listing Titles, from FDA Webinar[3]

Note that Part II contains a minimum of 10 listing titles because Listing “8” or “h” may require additional supportive raw listings if the primary or secondary efficacy endpoints are derived or calculated.

The listing titles cover typical clinical trial subject data that most programmers are familiar with. The OSI materials do not contain mock shells for the listings, but some of the titles mention specific content to include such as: reason not evaluable and dates for adverse events. FDA webinar clarifies that the format for delivering these listings is one pdf for each study with all listings included. The OSI requests bookmarks for the study number, then beneath that a bookmark for each site, and for each site bookmarks for each of listings for that site. Below is an image from the FDA Webinar showing the suggested bookmarks:

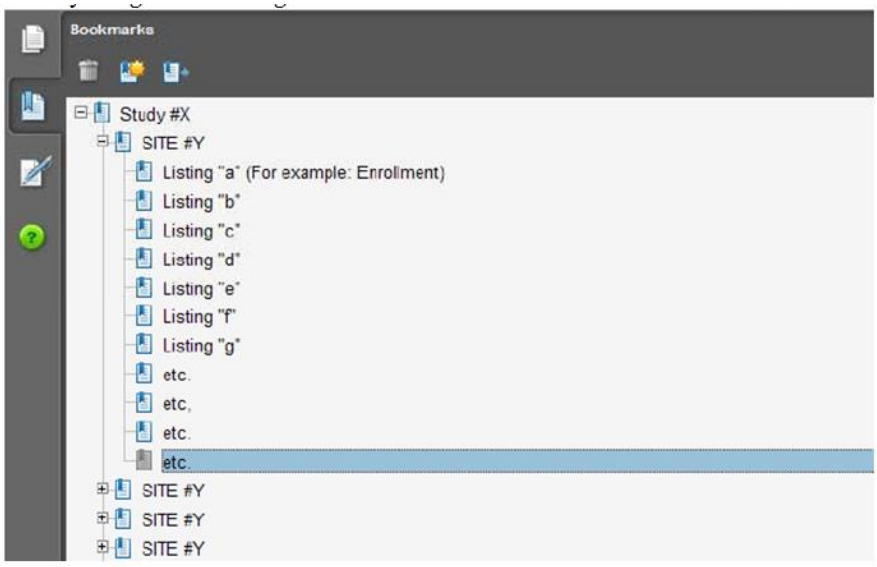

Figure 2. OSI Part II Sample .pdf Bookmarks for Subject Level Data Listings, from FDA Webinar[3]

ASTRAZENECA'S EXPERIENCE WITH PART II

At AstraZeneca, Programming and Statistics together led the preparation of Part II. After review of Part II of the request, AZ had several follow up questions for the OSI, some general and some specific to particular listings:

- Since we have approximately 130 sites per pivotal study, AZ proposed to prepare 10 listings sorted by site to avoid producing approximately 1300 separate listings.
  The OSI reply was that our proposal was not acceptable, but the OSI offered that we could initially produce listings only for sites with >=5 randomized subjects, with the caveat that they could ask for listings for lower enrolling sites at a later date, if needed. AZ declined the offer concluding that it would be more efficient to do all of the work at one time.
- Which patient population should be displayed on each listing?
  The OSI reply was that the safety set (i.e.; subjects who took one dose of study medication) should be displayed for all listings, except for listings "a" and "d".
- Listing-specific questions:
  - For listing "d", Subjects evaluable/non-evaluable: Evaluable for which analysis set?
    The OSI reply was that it is evaluable for the per protocol analysis set.
  - For listing "f", Subjects with AE, SAEs, Death: Should this be one listing or three listings?
    The OSI reply was that one listing is preferred.
  - For listing "h", Subject primary and secondary efficacy endpoints: Regarding the request to providing raw listings to support primary or secondary efficacy endpoint derivations/calculations. Do we need to have raw listings for all secondary endpoints points (we have many) or only secondary endpoints defined prospectively as key?
    The OSI reply was to just provide supportive raw listings for primary and *key* secondary endpoints.
  - For listing "g", Protocol Deviations/Violations: We had a question about the logic for protocol deviations/violations and placed it with questions in Part III for the "number of protocol deviations" variable.

After the requirements for each listing were clear, the next step was deciding the mock shell for each. At first glance, it seemed that the listings were a repeat of AstraZeneca's study level CSR listings. That perhaps it would be a mere copy of the CSR listing programs with slight updates to create separate listings for each site. For some listings that was the case, but for others it required a little more mock shell work. As a starting point, programming did a comparison of the OSI listing titles versus the AstraZeneca CSR listings to identify which CSR listing(s) contained the information of interest. In a few cases (i.e.; listings "a", "b", "c", "e", "f") there was a one to one match where one CSR listing contained relevant data for one OSI listing title, with the caveat that the patient population might need to be updated to match the OSI-requested patient population. In other cases (i.e.; listings "d", "g", "h", "i", "j"), the data for one OSI listing was spread across two or more CSR listings. We noted our findings about which CSR listings had data for the OSI listings and how those CSR listings should to be combined or reformatted to satisfy the OSI request. Our notes formed the working instructions for producing each OSI listing.

For our AZ submission, the primary and key secondary efficacy endpoints were derived, so two additional listings of raw efficacy data were needed to support listing "h". We referenced the efficacy listings as "h1", "h2", and "h3".

The source for the Part II subject level listings by site was each pivotal study's analysis datasets. The intent was that the OSI listings and the CSR listings are based on the same source data. Also, the analysis datasets had the population flags and the raw and derived efficacy data that was necessary for the listings. Regarding the timing for Part II, the OSI listings could be programmed on draft analysis datasets for each pivotal study, but they could not be finalized until after a pivotal study's analysis datasets were deemed final. As a lesson learned, plan resources to decide mock shells for the OSI listings and resources to program these additional study-level listings. Also, consider planning CSR listings with OSI listing requirements in mind, so in the future there might be more one to one matches between CSR listings and OSI listings.

OSI REQUEST PART III – SUMMARY LEVEL CLINICAL SITE DATASET (OPTIONAL)

OSI Request Part III is an optional summary level clinical site dataset. The OSI asks sponsors to provide the dataset with all pivotal studies included. Similar to Part II, sponsors should ensure agreement with the Review Division about which studies are pivotal. If a sponsor opts to provide this dataset, it will be used to do risk-based modeling to aid in site selection. The dataset aids in site selection because it contains the investigators and the studies they are involved in and provides characteristics and outcomes at the site level. The dataset structure is one record per study

per site per treatment arm with 39 variables. The FDA's specification document provides detailed information including variable names, variable labels, type (character or numeric), format, comments, and sample values. Some variables contains study level information (i.e.; study title, sponsor name, NDA number). Other variables contain site level information (i.e.; investigator name, contact information, and financial disclosure amounts). Lastly, some variables provide summary information per site and/or treatment arm (i.e.; number of subjects enrolled, number of SAEs, and several efficacy related variables). Below is a list of the 39 variables requested per the specification:

#	Variable Name	Variable Label
1	STUDY	Study Number
2	STUDYTL	Study Title
3	DOMAIN	Domain Abbreviation
4	SPONNO	Sponsor Number
5	SPONNAME	Sponsor Name
6	IND	IND Number
7	UNDERIND	Under IND
8	NDA	NDA Number
9	BLA	BLA Number
10	SUPPNUM	Supplement Number
11	SITEID	Site ID
12	ARM	Treatment Arm
13	ENROLL	Number of Subjects Enrolled
14	SCREEN	Number of Subjects Screened
15	DISCONT	Number of Subject Discontinuations
16	ENDPOINT	Endpoint
17	ENDPTYPE	Endpoint Type
18	TRTEFFE	Treatment Efficacy Endpoint
19	TRTEFFS	Treatment Efficacy Endpoint Standard Deviation
20	SITEEFFE	Site-Specific Treatment Effect
21	SITEEFFS	Site-Specific Treatment Effect Standard Deviation
22	CENSOR	Censored Observations
23	NSAE	Number of Non-Serious Adverse Events
24	SAE	Number of Serious Adverse Events
25	DEATH	Number of Deaths
26	PROTVIOL	Number of Protocol Violations
27	FINLMAX	Maximum Financial Disclosure Amount
28	FINLDISC	Financial Disclosure Amount
29	LASTNAME	Investigator Last Name
30	FRSTNAME	Investigator First Name
31	MINITIAL	Investigator Middle Initial
32	PHONE	Investigator Phone Number
33	FAX	Investigator Fax Number
34	EMAIL	Investigator Email Address
35	COUNTRY	Country
36	STATE	State
37	CITY	City
38	POSTAL	Postal Code
39	STREET	Street Address

Figure 3. OSI Request Part III Partial Dataset Specification (names and labels), From FDA Specification [5]

ASTRAZENECA'S EXPERIENCE WITH PART III

At AstraZeneca, Programming, Statistics, and Study Delivery collaborated for the planning and preparation of the Summary Level Clinical Site Dataset. After review of Part III of the request, AZ had several follow up questions for the OSI:

- There are many sites within the pivotal studies that only randomized small numbers of patients. As such, site level treatment efficacy and effect results will be difficult to interpret, and in many cases, treatment efficacy standard deviations and site specific efficacy effect size/variability may not be estimable.
  The OSI reply was that the OSI acknowledges this potential, but we request that all data for all sites be presented as requested.
- AZ proposed the content/logic for the efficacy variables.
  The OSI reply was that our proposal is acceptable.
- For the variable DISCONT (Number of Subject Discontinuations): Please confirm if this contains all discontinuations (after informed consent) or only discontinuations after randomization.
  The OSI reply was that DISCONT includes all subjects that were randomized.
- For the variable SAE (Number of Serious Adverse Events): Should this include all SAEs (not just those deemed treatment related or treatment emergent)?
  The OSI reply was yes.
- For the variable PROTVIOL (Number of Protocol Violations): For the CSR, protocol violations leading to exclusion from the per protocol analysis set were tabulated, as per the Statistical Analysis Plan (SAP). What additional violations, if any, does the FDA expect to be included over and above what is above?
  The OSI reply was that if there are additional significant violations as defined in the monitoring or data management plans, plan to include these violations.

After further review of the variables, it was determined that some information requested to be in the dataset was **not** in the clinical database. Instead, Study Delivery would gather the information (such as study title, NDA number, investigator name and contact information, financial disclosure information, etc.) and provide it in a spreadsheet to Programming. Meanwhile, Programming would use the pivotal studies' analysis datasets to generate the information from the clinical database (summary variables such as number of subjects enrolled, number of SAEs, and various efficacy variables). Specifically, Study Delivery would provide source data for variables 1-11 and 27-39 (with the help of AZ's Financial Disclosure group) and Programming would provide variables 11-26. The overlapping variable for merging was variable 11 SITEID. Ultimately, Programming used the spreadsheet from Study Delivery to produce the complete clinsite.xpt dataset.

In addition to the dataset, Programming provided a define.pdf file to document the contents of the dataset and the logic used for any calculations. The creation of the summary level clinical site dataset can begin when a draft spreadsheet from Study Delivery and draft study level analysis datasets are available for the pivotal studies. The dataset could not be finalized until the pivotal studies' analysis datasets and Study Delivery's spreadsheet were deemed final. As a lesson learned, it is important to have collaboration between Programming, Statistics, and Study Delivery in order to gather all of the necessary information for preparing the dataset. Also, plan resources for this additional programming work. Note that several versions of the FDA Specifications document have been released. In November 2012, the version 1.2 was released. Please check the FDA website link in the References section to locate this version.

BIMO REVIEWER'S GUIDE (OPTIONAL)

The Reviewer's Guide is an optional document requested to clarify the content and location of each of the Parts of the OSI Request within a submission. Note that the OSI materials suggest where to place the various OSI files within the eCTD within Module 5 Clinical Study Reports. For example, the OSI suggests that the summary level clinical site dataset be placed in the following m5 folder structure: m5/datasets/bimo/site-level. [5]

ASTRAZENECA'S EXPERIENCE WITH BIMO REVIEWER'S GUIDE

At AstraZeneca, Regulatory led the creation of the BIMO Reviewer's Guide in close collaboration with Publishing. The Reviewer's Guide restated key agreements between AZ and the OSI from our question and answer exchange.

The guide also listed each of the parts of the OSI request and clarified for each study the location where the OSI package information was been placed.

SUMMARY OF LESSONS LEARNED FROM ASTRAZENECA'S OSI EXPERIENCE

There were several lessons learned from preparing the OSI package for our AstraZeneca NDA submission:

1. View the FDA Webinar to learn about Parts I and II. The Draft Guidance & Specifications only cover Part III.
2. Assemble cross-functional team of Programming, Statistics, Study Delivery, Regulatory and Publishing
3. Allow adequate time and resources for the planning, preparation and programming of the OSI package
4. Ensure cross-functional review of all OSI request materials early in the process and identify questions
5. Reach out to the FDA/OSI with questions. The FDA Webinar provides OSI email contacts for questions.
6. Arrange for CROs to provide data flow diagrams at the beginning of a study if CRO is generating data.
7. Consider OSI listings when planning CSR listings to enable reuse.
8. Plan for close collaboration between Study Delivery, Programming, and Statistics for summary level clinical site dataset to confirm variable logic and to ensure availability of information not in clinical database.
9. Could start OSI programming work when draft analysis datasets are available for pivotal studies.
10. Could only complete the OSI programming work after all pivotal studies' analysis datasets are deemed final.

CONCLUSION

The FDA released OSI materials in 2012 to help sponsors better understand what information the OSI is requesting in order to efficiently and effectively plan on-site inspections. The FDA's OSI Webinar, Draft Guidance for Industry, and Dataset Specification documents form a strong foundation to inform sponsors about the information the OSI would like included with an NDA or BLA (or supplemental) submission to CDER. Sponsors are encouraged to make provisions to prepare the various components of the OSI Request: Part I Tabular Listings of Investigator information, Part II Subject Data Listings by Site, Part III Summary Level Clinical Site Data, and a BIMO Reviewer's Guide. One AstraZeneca Team's OSI experience was shared throughout this paper, including our questions to the OSI and our strategies for preparing our OSI package. We hope you have learned from our effort and that you'll share your experience and lessons learned in the future. If sponsors deliver OSI Packages in their NDA and BLA (or supplemental) submissions as requested, then the OSI is better positioned to meet aggressive PDUFA V inspection timelines. Together, if we can contribute to the Agency meeting PDUFA V timelines, then we are helping get new medicines to patients who need them.

REFERENCES

1 FDA Website: http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm228722.htm

2 FDA OSI Slides: Okwesili, Paul. **"**Summary level data and information for CDER's inspection planning". Date unknown. Available at http://www.fda.gov/downloads/drugs/developmentapprovalprocess/smallbusinessassistance/ucm361329.pdf

3 FDA OSI Webinar: Meeker-O'Connell, Ann and Kassim, Sean "Overview of Information Requested by CDER OSI for NDA and BLA Submissions". Oct 2012. Available at https://collaboration.fda.gov/p44198603/

4 FDA Draft Guidance: "Guidance for Industry - Providing Submissions in Electronic Format – Summary Level Clinical Site Data for CDER's Inspection Planning". Dec 2012. Available at http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/UCM332468.pdf

5 FDA Specifications: "Specifications for Preparing and Submitting Summary Level Clinical Site Data for CDER's Inspection Planning". Nov 2012. Available at http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/UCM332466.pdf

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SUGGESTED READING

We suggest viewing the FDA's OSI webinar and reading the reference materials (Draft Guidance for Industry, Specifications, and OSI Slides) listed in the Reference section above.

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