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In-Licensing Projects from a Programming Perspective

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ABSTRACT

Over the past few years, the Pharmaceutical industry has seen many acquisitions or divestments of products so companies can focus on strategic niches. As a result, the receiving company finds itself inheriting another company's clinical work. To make that a success, it is key to understand what clinical data are already available and what needs to be done at its current status. The programming function plays a valuable role in ensuring that inherited data are workable/reusable and assessing how closely it aligns with Clinical Data Interchange Standards Consortium (CDISC) standards to help plan for future deliverables. This paper shares some experiences, challenges faced, and lessons learned as a programmer in the "in-licensing" process for two projects at different transition stages, including topics on transferring files, inventorying what has been received, assessing submission readiness, and quickly becoming data experts.

INTRODUCTION

In-licensing is the partnership of one company giving another company permission to use its property. For example, if a company produced a drug and did not have the resources to continue with clinical trials, they may out license the patents to a larger pharmaceutical firm for them to complete development. There are several steps taken prior to the data brought in-house before a company inherits a product. Licensing has been an integral part of commercial biotechnology since its inception. "Big Pharma companies spend a third of their R&D budget on early-stage drug development, which is an odds-makers' nightmare. Only one in 10 early-stage drugs make it to the market, with the odds rising to 20 percent at Phase II and 50 percent at Phase III. Maximum returns favor late-stage bets, which is where in-licensing can be most effective**" [1].** Marketing strategies may also favor in-licensing to take advantage of an organizations specialization in certain Therapeutic Area (TA). Joint licensing agreements are considered as well to take advantage of regional expertise. Once a project is inherited, the programmer being key to unlocking the full development value of the acquired data would improve accuracy and still convey impact.. The benefit of acquiring large amount of completed work comes with slight disadvantage – not having personal experience or history of what has already been done, decisions made and also reliant on the completeness/quality of the documentation and specification behind that work. Programming needs to actively work to bridge that gap.

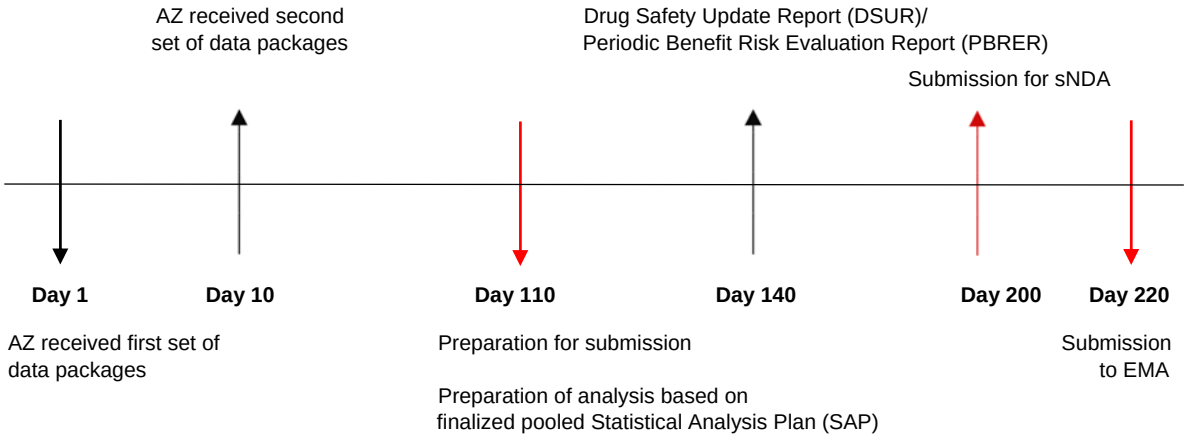
This paper presents two projects inherited at different phases with different paths for upcoming deliverables, including but not limited to regulatory submission/response, safety update reporting, etc. The projects encompass various challenges related to submission timings, quality of data, and missing information.

Example: In-Licensing Project I:

AstraZeneca (AZ) acquired this project from another company. The scope of the work included 70+ studies varying from Phase I to Phase III data. The majority of the 70+ studies were submitted to Federal Drug Administration (FDA) and European Medicines Agency (EMA). However, AZ was responsible for submitting an additional few studies as part of a Supplemental New Drug Application (sNDA) and Marketing Authorization Application (MAA). The partnering company used an outsourcing model with multiple vendors to accommodate analysis and reporting, and had the additional complication of inheriting several studies from another company. The AZ programming team had limited access to the partner

company as the personnel involved in these studies had already left or planned to leave in the near future.

The figure below outlines the timeline of major milestones for Project I such as preparation for submission to FDA and EMA:



1. **Challenge - Data size:**

   AZ received two sets of deliveries. The first set was a large transfer (~90 GB) via a secured file transfer portal. The second set of deliverables included a few recently completed studies without size issues. AZ could not use the conventional file transfer portal due to large data size. An additional challenge was assigned space within AZ internal servers to avoid any run time issues for other study work ongoing in the system.

   AZ solutions:

   After several discussions with the internal Information Technology (IT) team and partnering company, it was decided to use an external hard drive and sent to AZ IT team. Upon receiving, IT ran checks on the hard drive to make sure that all studies are intact and delivered per expectations. On delivery, IT made those studies available on AZ private servers without storage limitations and placed into AZ reporting environment as requested by the Lead Programmer.

2. **Challenge - Inventory/Due diligence:**

   The tight timelines of getting required studies to be available for FDA and EMEA submission was a challenge. Initial conversation with the partner company was related to the size of the data and formats but AZ programming team started finding additional gaps (e.g., missing dataset programs and macros programs) once due-diligence work commenced. Programmers were on a tight timeline to deep dive and understand all the gaps not only for submission planning, but also because the partner company was going out of business soon.

   AZ solutions:

   AZ programming worked on a few options in order to have an efficient and constructive dialogue with the partner company.

- Created a data standardization sheet to understand what was sent and the gaps. This sheet covered topics such as delivery of ADAM/SDTM datasets, define files, reviewers guide, open CDISC validator reports, and version of MedDRA used, etc.
- Created a Quality Assurance (QA) checklist looking into pivotal study datasets to make sure all components related to datasets, macro programs, output programs are available and re-usable within AZ systems.

- Discussed with internal study team members to understand what would be needed for upcoming submission work and added that to the QA checklist if not already covered.

- Cross-checked the vendor data with the FDA Study Data Technical Conformance Guideline document for submission readiness [2].

3. Challenge - Unforeseen risks:

There might be situations where projects could face unforeseen risks despite best due diligence activities.

One example was related to concomitant medication information. It was realized during the pooling process that there were inconsistencies in Anatomical Therapeutic Chemical (ATC) code used for two studies.

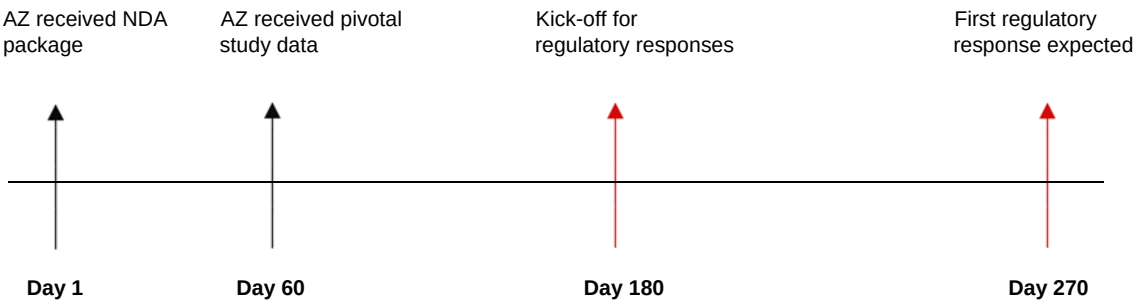
AZ solutions:

After several meetings with internal study team and input from the standards group, it was decided that pooling would not be possible which led to deletion of few reports from the pooled SAP.

Example: In-Licensing Project II:

AstraZeneca (AZ) acquired this compound late last year. The scope of work included in-licensing of an already marketed product. AZ was expecting to receive 20+ studies in batches. The partner company used a vendor to do their reporting work. AZ received a New Drug Application (NDA) package with 17 studies that were submitted by the partner company. It was discussed and decided to receive study level data as not all data information was submitted for all studies. AZ was responsible for the rest of the world submission and any regulatory response questions for countries (e.g., US, Switzerland, Canada) previously submitted by the partner company.

The figure below outlines the timeline of major milestones for Project I such as kick-off meetings for regulatory response and actual first expected regulatory response:



1. **Challenge - Limited time for transition:**

   AZ programming was racing against the clock to prepare for the rest of world submissions and upcoming regulatory responses. AZ initially received 17 study packages sent for NDA approval by the partner company. The programming team realized that the Study Data Tabulation Model (SDTM) and Analysis Data Model (ADAM) datasets were only submitted for 3 pivotal studies, and remaining studies only had table/listing/figures reports submitted. This significantly limited the internal due-diligence process. In addition, there were 6 ongoing studies that were required for possible use in the rest of the world submission.

   AZ solutions:

   AZ's lead programmer took a few approaches to expedite the review process:

   - Directly reached out to the vendor who did the initial programming to understand what was submitted.
   - Produced a timeline to start receiving study level data for the remaining studies batch wise, and also discussed the status of the ongoing studies and delivery timelines.
   - In parallel, AZ programming started working on a data standardization sheet (similar to Example 1, Challenge 2 solutions).

2. **Challenge - Resourcing:**

   In addition to understanding the scope of deliveries and planning for submission, there were competing activities related to review of specifications/datasets for ongoing studies received from partner's vendor. This placed a constraint on resourcing.

   AZ solutions:

   AZ's lead programmer worked proactively with different team members to address resourcing needs:

   - Discussed with study team/manager to plan peak and trough of required resources.
   - Discussed with vendor responsible for programming to understand the timelines and plan resources accordingly.
   - Worked closely with AZ regulatory team to understand what would be needed for the rest of the world submissions in order to plan scope of work and proper resources availability.

CONCLUSION

The pharmaceutical industry is moving towards more in-licensing scenarios. Programming needs to be agile and ready to receive work from other companies, and organize it and make it reusable as quickly as possible. In a few AZ in-licensing scenarios, the programming team has experienced some challenges and developed practical, effective solutions. A few key highlights from AZ's solutions include:

1. Advanced planning to file delivery strategy.

2. Open communication related to setting expectations.
3. Strategic foresight to resourcing and future deliverables.

Following the above recommended solutions, programmers can better manage future in-licensing projects more successfully.

REFERENCES

1 Carroll, John. "Experts advise Big Pharma to shift to in-licensing". Feb 1, 2010. Available at: *http://www.fiercebiotech.com/biotech/experts-advise-big-pharma-to-shift-to-licensing*

3. FDA website: FDA Study Data Technical Conformance Guide. March 2017. Available at: https://www.fda.gov/downloads/ForIndustry/DataStandards/StudyDataStandards/UCM384744.pdf

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SUGGESTED READING

Study Data Technical Conformance Guide v. 3.3 (PDF - 1.17MB) (Mar. 2017) or latest version.
CDER/CBER Study Data Standardization Plan Recommendations (PDF - 51.74KB) or latest version.

CONTACT INFORMATION

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