

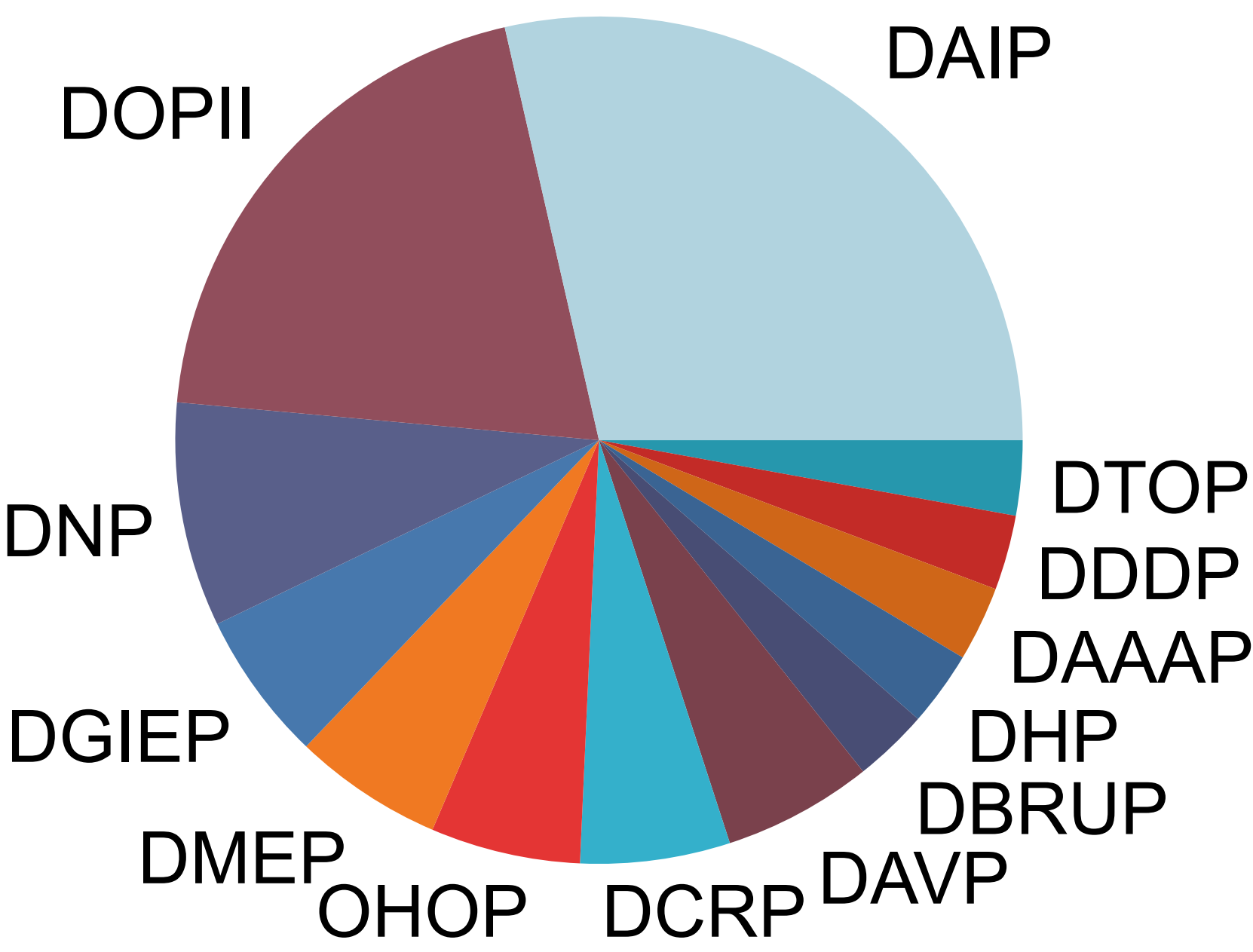
JumpStarting Review : Highlights

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ABSTRACT: The decision to accept a new drug application (NDA) or a biologics license application (BLA) for review is made on day 45 of the 21st Century Review process. JumpStart provides NDA/BLA Review Teams with data analyses early in the review process so reviewers can conduct an effective evaluation of the drug submission prior to the filing date. We summarize some common and impactful data quality issues described to reviewers. We also illustrate some customized analyses delivered in addition to standard safety explorations.

JumpStart has evaluated a total of 35 applications in FY14 and FY15. This is made up of 82 individual studies across 13 review divisions.

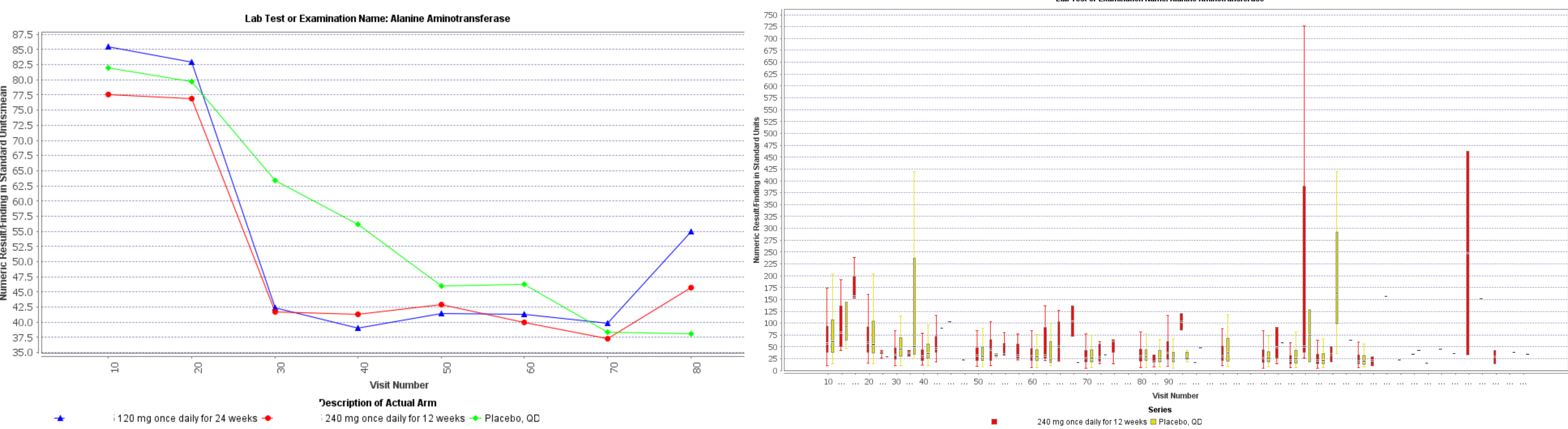
Total Applications by Division (FY14 & FY15)



JumpStart summarizes data quality and analyses issues in a consult, illustrates issues from the data submission, shows details of the methodology and provides an analytic output table shown below.

Analysis	Analysis Type	Study	
Data Fitness	Data Fitness Outputs	AE Code Matching .xls	AE Code Matching .xls
		- SUPP Contents .xls	ibs- - SUPP Contents .xls
		IE Subjects .xls	IE Subjects .xls
		Misallocation Report .xls	Misallocation Report .xls
Demographics	Demographics Analysis Panel	Demographics - 11-4-2014.xls	Demographics - 11-4-2014.xls
		moddm.sas7bdat	moddm.sas7bdat
Subject Disposition	Subject Disposition Analysis Panel	Disposition - 11-4-2014.xls	Disposition - 11-4-2014.xls
Adverse Events	MedDRA at a Glance Analysis Panel	MedDRA at a Glance - 11-17-2014.xls	MedDRA at a Glance - 11-17-2014.xls
		MedDRA at a Glance - 11-19-2014 (SAEs).xls	MedDRA at a Glance - 11-19-2014 (SAEs).xls
		MedDRA at a Glance - 11-19-2014 (Without Missallocated Subjects).xls	MedDRA at a Glance - 11-19-2014 (Without Missallocated Subjects).xls
		Missallocated Subjects .xls	Missallocated Subjects .xls
Adverse Events	AE Severity Grade Analysis Panel	AE Severity - 11-18-2014.xls	AE Severity - 11-18-2014.xls
	MAED Outputs	MAED General - 11-18-2014.xls	MAED General - 11-18-2014.xls
	AE Other	excluded_AEs .xls	excluded_AEs .xls
Liver Labs	Liver Labs Analysis Panel	Liver Labs - 11-18-2014.xls	Liver Labs - 11-18-2014.xls

Examples of customized data outputs for the Division of Antivirals



Secretary’s Pick for 2014 – HHS Innovates

Snapshot of Findings Discussed During Data Fitness Session

SDRG/ Define/Supp Info	Not including a good SDRG or Define file greatly increases the amount of time a review division must spend understanding an application. <i>See accompanying poster for more details!</i>
Controlled Terminology	Variables feature ambiguous values not present in the codelist which lead to confusion during review. <i>Issue found in 60% of FY15 Applications</i>
Deaths	Death summaries are provided to reconcile death records across an application. Typically issues stem from inconsistencies between DM, DS, AE, and CO domains.
Missing Data	Missing dates in the DS domain make it impossible to perform time to discontinuation event analyses. <i>See accompanying poster for more info!</i>
CDER Common Issues	EPOCH variable or Trial Summary domain is missing. <i>EPOCH and Trial Summary domain are missing in 90% and 30% of FY15 Applications respectively.</i>
Duplicates	Duplicate records in the LB, VS, and EG domain with potentially contradictory information make it difficult to summarize results. <i>Seen in 40% of FY15 applications.</i>
Term Matching	AEDECODs are missing or DSTERMs inappropriately coded to DSDECOD “OTHER”. <i>Found in 40% of FY15 applications.</i>
Standard Units	Standard Units inconsistent for a particular test making it necessary to manually convert before summarizing. <i>Found in 30% of FY15 applications.</i>
Safety Population	Inconsistencies found between DM, EX and clinical study report. Issues are presented to the review team to ensure safety analyses are done on the proper groups.
Race/ Ethnicity	<i>See accompanying poster for more info!</i> <i>Issues with Race or Ethnicity found in 80% of FY15 applications.</i>

Other Analytic outputs : reconciliation between the Sponsor’s report and different methodologies

Example of Treatment Emergent subject counts for most frequent adverse events using different methodologies

Adverse Event	CSR		Reference Start Date		First Exposure Date*	
	Treatment	Placebo	Treatment	Placebo	Treatment	Placebo
Diarrhoea	82 (30.6)	92 (33.5)	84 (31.3)	96 (34.9)	73 (28.3)	91 (34.3)
Anemia	70 (26.1)	79 (28.7)	72 (26.9)	84 (30.6)	37 (14.3)	39 (14.7)
Urinary Tract Infection	66 (24.6)	67 (24.4)	73 (27.2)	71 (25.8)	71 (27.5)	67 (25.3)
Hypertension	62 (23.1)	62 (22.5)	65 (24.3)	66 (24.0)	39 (15.1)	48 (18.1)
Constipation	49 (18.3)	67 (24.4)	51 (19.0)	70 (25.5)	30 (11.6)	41 (15.5)