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Sabarinath Sundaram has more than a decade of statistical programming experience across multiple therapeutic areas, working on FIH studies through Phase III trials. His expertise includes CDISC standards, leading programming teams, regulatory submissions, handling NONMEM, ER, PK/PD, and ADA datasets. He holds a Ph.D. in Life Sciences (Biochemistry). Currently, He is a Senior Manager in the PKPD Programming Team at Pfizer Inc.



Divya Kommuru is Manager in Statistical Data Sciences and Analytics at Pfizer where she supports PK/PD Data Programming and manages respective external partner teams. She has worked across all phases of drug development with deep expertise in PK/PD Analysis Dataset Development and Regulatory Submissions. She has over 10 years of experience in programming and reporting in Pharmaceutical & CRO environments. Prior to joining Pfizer, Divya worked as a Lead PK/PD & SAS Programmer for CSL Behring and Eliassen.



Luai Alzoubi has worked in the pharmaceutical industry for almost 30 years in a statistical programming capacity, supporting CSR TLFs and for the past 19 years PK/PD deliverables. His experience spans many therapeutic areas, supporting clinical trials across all phases of development. Luai is a Director at Pfizer and leads the Global PK/PD Programming Team, which is comprised of both internal and external team members. His team's core deliverables include regulatory submissions and information request responses, delivery of NONMEM datafiles (PopPK, Exposure Response, PK/PD, etc.) as well as the loading of PK concentration data. He holds a M.S. in Computer Information Systems along with Computer Science and Mathematics undergraduate degree.

SA05: Electronic Submission of Population PK Analysis Files...What's Your Modus Operandi?

Stream: Submissions & Agencies (SA)

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Agenda

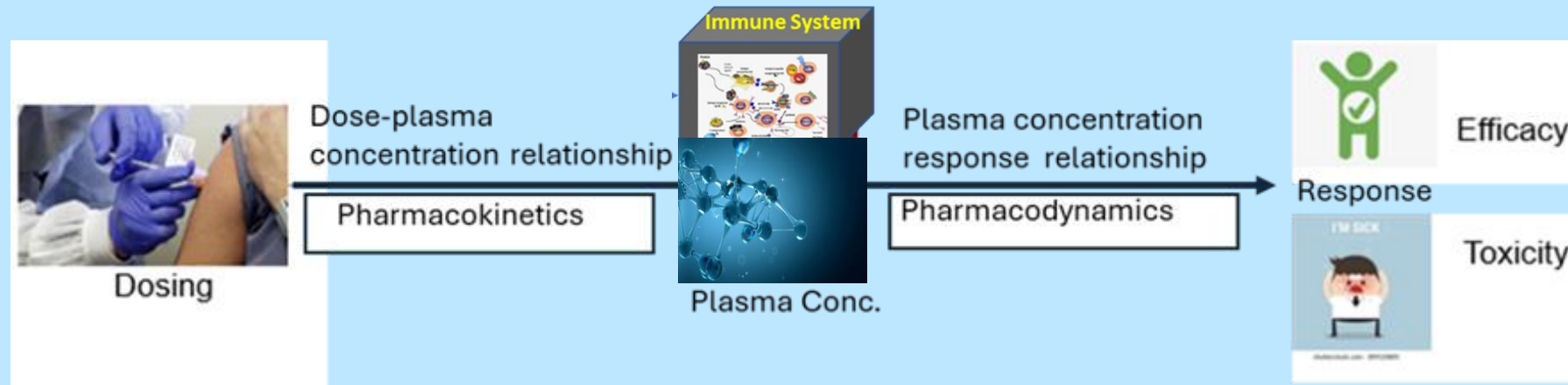
- Background
- Compiling the PMAR eSub Package
- PMAR eSub Package
- Conclusion

SA05: Electronic Submission of Population PK Analysis Files...What's Your Modus Operandi?

DISCLAIMER

The opinions expressed in this presentation and on the following slides are solely those of the presenters and not necessarily those of Pfizer Inc.

Conceptual PK/PD Framework Linking Drug Administration to Quantifiable Clinical Outcomes

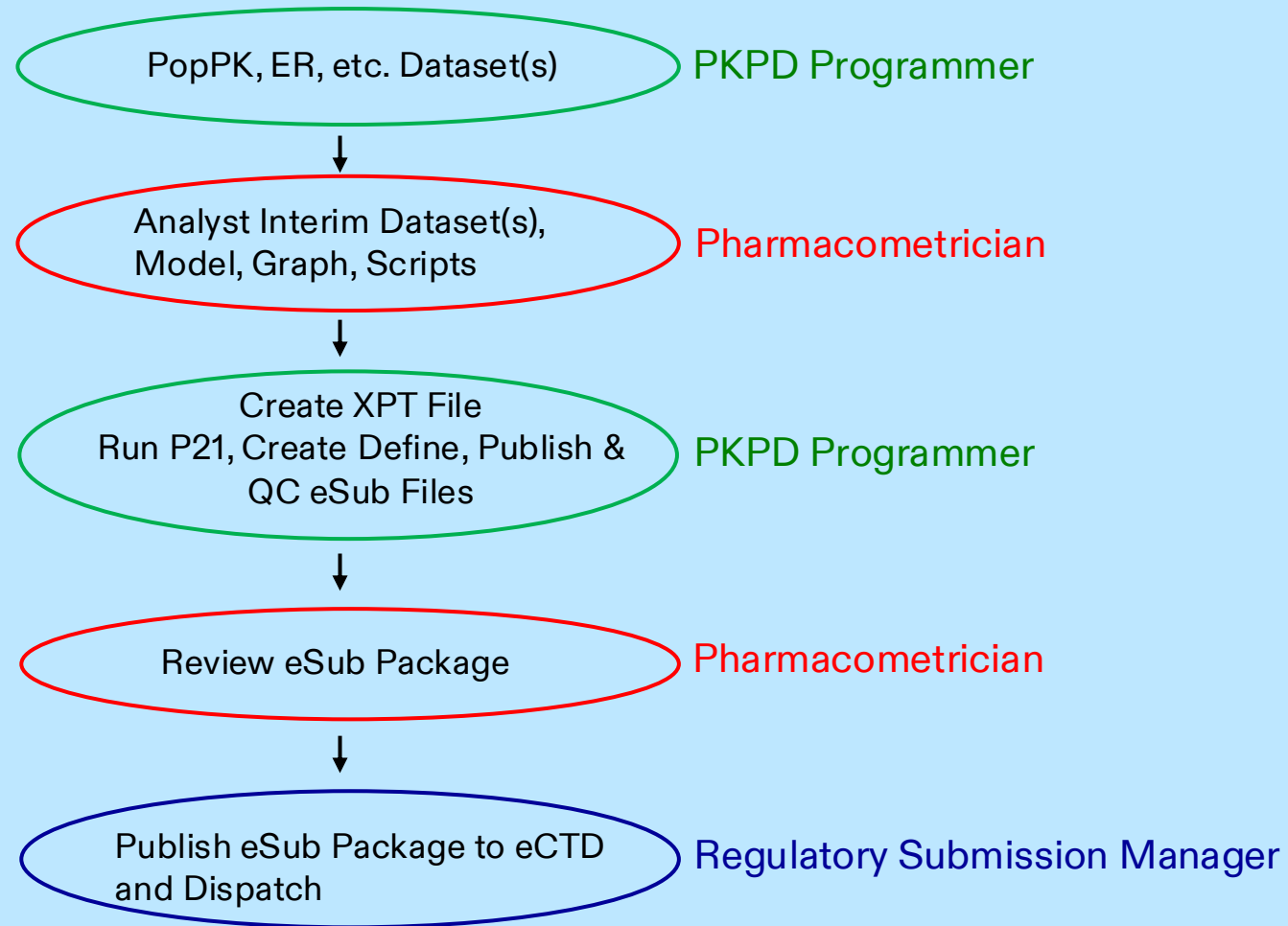


- Population Modeling Analysis Report (PMAR)- Summarize PopPK or ER analyses
- PMAR promotes bridging pharmacokinetic data from one population or formulation to another through modeling and simulation
- PMAR describes the modeling workflow in sufficient detail to allow interpretation of results

Summary of key distinctions in the use of Population Modeling Analysis Reports (PMARs) across early-stage (Phase I/II) and late-stage (Phase II/III) studies

Aspect	Early-Stage Development (Phase I/II)	Late-Stage Development (Phase IIb/III & Registration)
Objective	Guide starting doses, dose escalation, and initial safety	Confirm and refine dosing, support labeling and regulatory decisions
Population	Small, controlled cohorts; often healthy volunteers or limited patient populations	Large, heterogeneous patient populations reflecting intended use
Dose Selection	Establish safe starting doses and escalation schemes	Optimize therapeutic dose, account for inter-patient variability, support dose adjustments
Covariate Analysis	Evaluate key intrinsic/extrinsic factors (age, weight, organ function)	Quantify variability across broader populations, refine special population dosing
Bridging	Extrapolate adult data to pediatrics or special populations	Bridge across formulations, global populations, or real-world settings
Safety Evaluation	Early identification of exposure-safety relationships	Confirm safety margins, identify thresholds for adverse events
Efficacy Assessment	Exploratory exposure-response for efficacy endpoints	Quantitative support for label claims, dose-response validation
Regulatory Use	Inform early clinical development plans and trial design	Support regulatory submissions, labeling, risk management, and post-marketing strategy
Modeling Approach	Focused PK/PD modeling to guide trial design	Comprehensive population PK/PD modeling integrating exposure-response and covariate effects

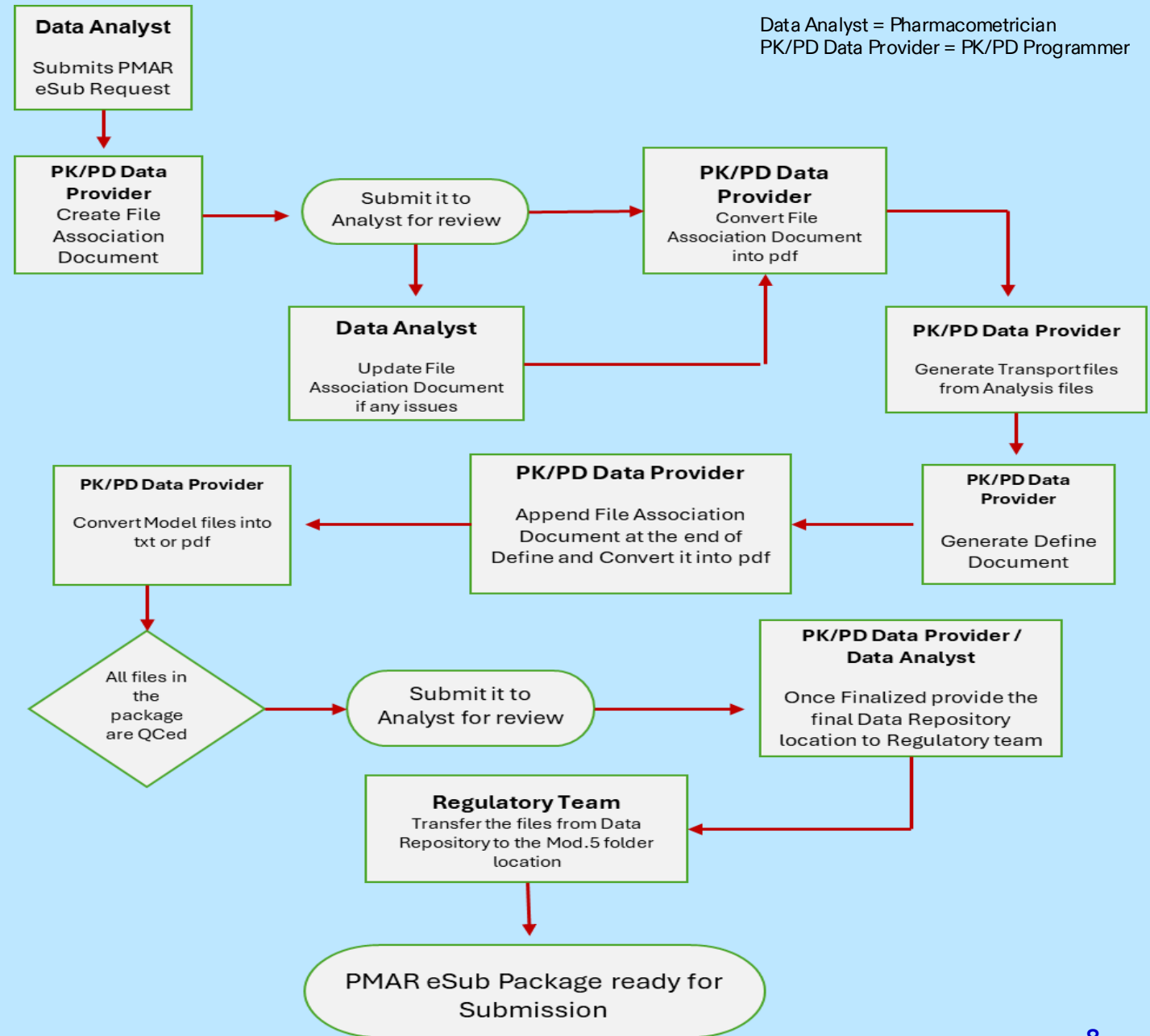
Major Role and Responsibilities



Overall Workflow to Support PMAR eSUB Delivery

Data Analyst = Pharmacometrician
PK/PD Data Provider = PK/PD Programmer

- Planning and Coordination
- Data Preparation
- Cross-functional Review
- Quality Check
- Deliverable



File Association Document

- Helps reviewers navigate and understand the background, structure and content of the submission package.
- Purpose is to provide an explanation of the various files submitted with the PK component.

PMAR EQDD CXXXi Other 1734 eSUB PKPD Analysis Data File Association					
Report Number	Report Description	Included Studies	Associated Files		
			File Type	File Name in Report ¹	File Name in Submission Package
PMAR-EQDD-CXXXi-Other-1734	Analysis dataset for Population PK analysis	103 105 106 107 110 111 112 117 118	Analysis Data file	finalppk.csv	N/A
			Transport file	N/A	pppdk.xpt
			Post Processing and Data Manipulation Scripts	PrepSimDataset_v7_pmar1734.R	prep-sim-dataset-v7-pmar1734-r.txt
				SummarizeSimResult_v7_pmar1734.R	summarize-sim-result-v7-pmar1734-r.txt
			Post Processing and Data Manipulation Output Scripts	PK Profile of ODT 75 mg EOD vs QD.png	pk-profile-of-odt-75-mg-eod-vs-qd-png.pdf
				PK Profile of ODT 75 mg EOD with FLCZ vs QD.png	pk-profile-of-odt-75-mg-eod-with-flcz-vs-qd-png.pdf
				SimulatedRimegepant Scenario Summaries for PPKREport_pmar1734_latex.csv	simulated-rimegepant-scenario-summaries-for-ppkre-port-pmar1734-latex.csv
			Base Model File	N/A	N/A
			Base Output File	N/A	N/A
			Final Model File	N/A	N/A
			Final Output File	N/A	N/A
			Simulation(s) File	run7.mod	run7-mod.txt
			Simulation(s) Output File	run7.lst	run7-lst.txt

File names indicated in the report have been modified to conform to eCTD guidelines for the submission package

Define Document

- Structure and Content
- Datasets
- Variables
- Metadata and Code lists

Dataset	Description	Class	Structure	Purpose	Keys	Location	Documentation
CNPPK	Analysis dataset for Population PK analysis	SYSTEM		Analysis		cnppk.xpt	

Go to the [top](#) of the define.pdf

★ Appendix I: Format Code Lists Footnoted in Descriptor Tables

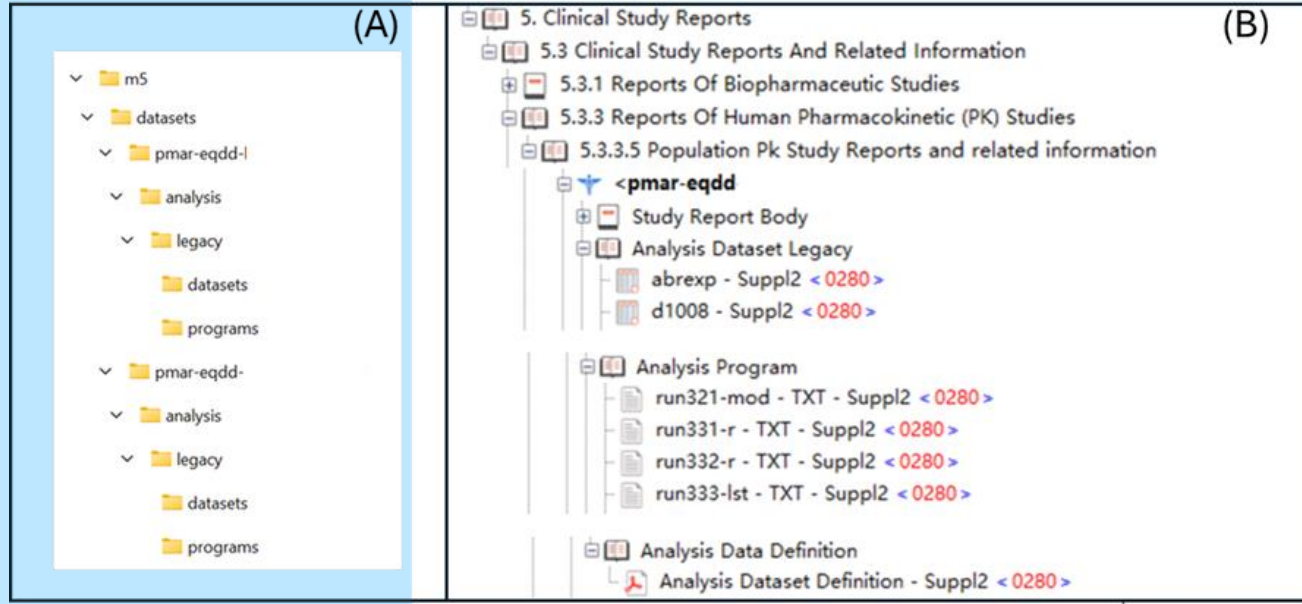
★ Appendix II: PMAR EQDD C - - - - - her 1734 eSUB Analysis Data File Association

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Analysis dataset for Population PK analysis (CNPPK) Location: cnppk.xpt					
Variable	Label	Type	Length / Display Format	Controlled Terms or Format	Source/Derivation/Comment
C	Comment	text	\$1	null	Pre first dose PK sample Placebo dose "C": Excluded from final model
STUD	Study number	integer	BEST12		
ID	Unique subject identifier	integer	BEST12		Sequential number starting at: 101 201 301 401 501 601 701 801 USUBJID without non-numeric values Unique number starting with 1181050
TIME	Actual time from first dose (hr)	float	BEST12		Relative actual time since first RHB-104 dose (hr) rounded to 3 decimals
NTIM	Nominal time from first dose (hr)	float	BEST12		Relative nominal time since first RHB-104 dose (hr) rounded to 3 decimals
TAD	Actual time from last dose (hr)	float	BEST12		Units: hours
NTAD	Nominal time from last dose (hr)	float	BEST12		Relative nominal time since last dose (hr) rounded to 3 decimals
EVID	Event identification	integer	BEST12		0: Observation record 1: Dose administration
CMT	Compartment	integer	BEST12		1: Dose administration 2: PK concentration record
AMT	Dose amount received (mg)	integer	BEST12		0: Observation records
DV	Dependent variable (ng/mL)	float	BEST12		0: Dosing records
LNDV	Log transformed dependent variable	float	BEST12		Log(DV) 0: If BLQ observations
MDV	Missing dependent variable	integer	BEST12		1: When DV=0 (except pre first dose PK sample) or ismissing 0: Otherwise
DOSE	Actual dose (mg)	integer	BEST12		0: Pre first dose records

eCTD Folder Structure

- The eCTD Module 5 (M5) folder structure (A) organizes clinical study reports and related data for regulatory submissions
- M5 folder structure is largely harmonized across major regulatory agencies including US FDA, PMDA, Health Canada
- (B) shows how these corresponding components appear in the regulatory eSub package, organized under Clinical Study Reports and associated analysis files



Challenges in PMAR Submissions

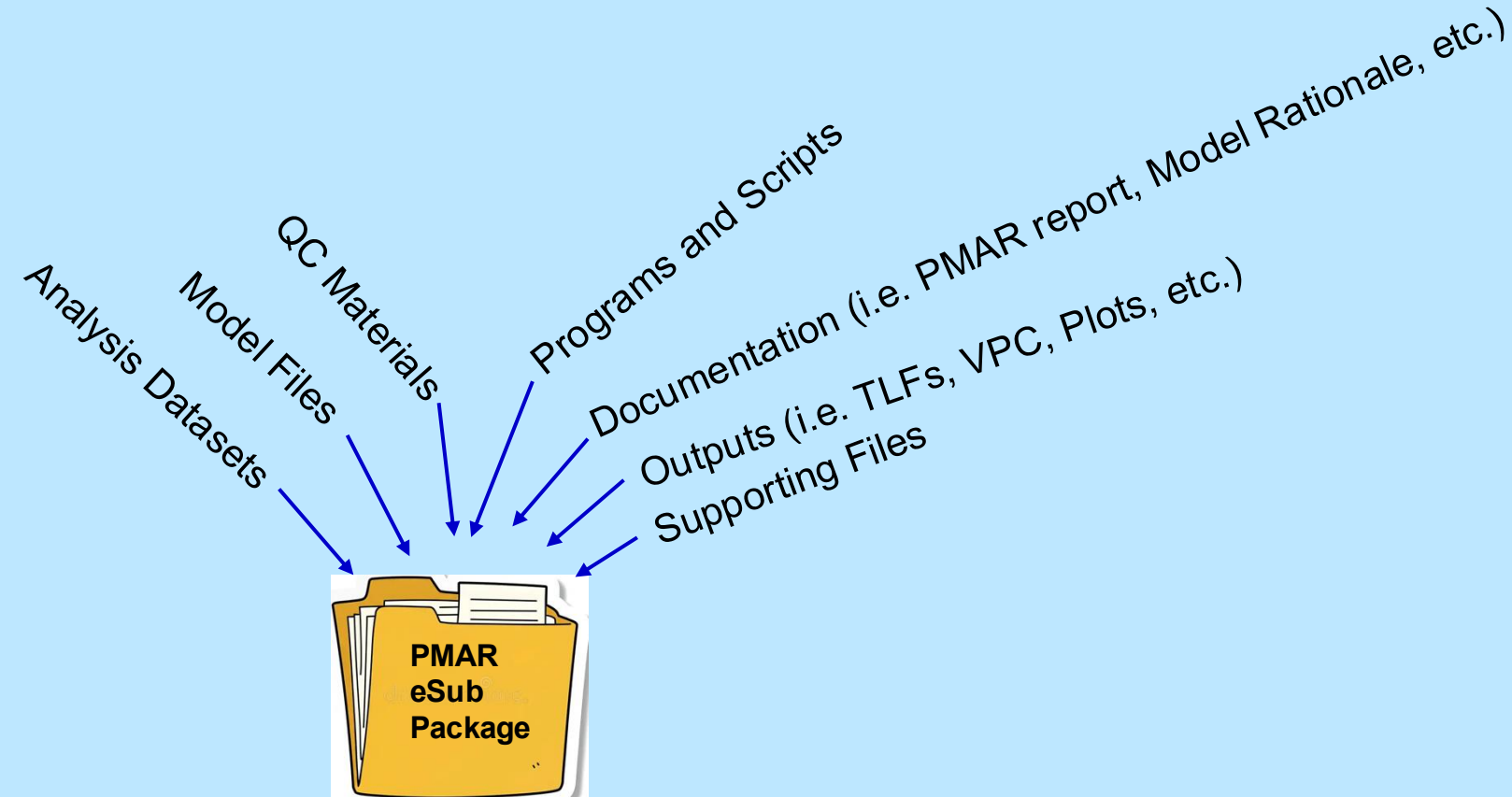
- Data Set Size and Complexity with the potential to result in long data processing times for large, integrated datasets spanning many clinical trials.
- Time Constraints: The urgent or quick turnaround timelines.
- Awareness of different submission requirements between agencies (some examples are shown below)

	US	Japan	Canada
Agency	FDA	PMDA	Health Canada
File format	csv, xpt, r, txt, pdf, png	csv, pdf, txt	.inf and .dat
Documentation	Define	Define, Programming Procedure	Supporting Documentation
Agency Website Providing Details on eCTD and eSubmission	U.S. Food and Drug Administration	Pharmaceuticals and Medical Devices Agency	Health Canada - Canada.ca

PMAR eSub Package



- PMAR eSub Components are submitted via the eCTD, in Modules 2 (Summaries) and 5 (Clinical Study Reports)



Conclusions

- Close collaboration remains essential to ensure accuracy, traceability, and compliance with eCTD requirements.
- High Quality PMAR Submission: eSub data packages rely on clear documentation, reproducible datasets, and modeling files that facilitate transparent and efficient regulatory review and their decision.

Future Direction:

- ✓ Increased automation of data preparation and model packaging to reduce manual intervention, shorten timelines, and improve reproducibility in submissions.
- ✓ AI enabled document generation and validation will streamline the development of model reports, traceability in packages, data reviewer's guides, and technical appendices. As these technologies mature, AI driven workflows are expected to further integrate and accelerate key steps within the submission preparation process, ultimately enhancing both efficiency and consistency.

Thank you

