

Implementing NONMEM POP PK Specifications and Data Standards through the Use of a Browser-based Order Form

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Objectives

Population pharmacokinetic modeling (POP PK) has become a routine analysis to support internal decision making and regulatory submission. Yet, the process for preparing data is often met with frustration due to the differences in individual approaches and the lack of standards, processes and specifications. The result is a process that can be time and resource consuming often taking several weeks to months to complete.

Methods

In order to streamline the POP PK data build process, a browser based order form utility has been developed that standardizes the specification layout and enforces the use of standard variable names in a natural way. The tool is flexible enough to allow updates to variable names and definitions. It also provides on-the-fly instructions (pop-ups) for new users. It manages code lists, formulae and drop-down selection lists with admin privilege.

Results

The browser-based order form eases the pharmacometrician's and programmer's burden in developing the programming specifications. It produces fast and reliable data instructions with consistent variable definitions that can be efficiently applied across studies and drugs with minimal modification. It enables programmers to develop generic SAS code for data set generation and for diagnostic data summaries and diagnostic plots. These standardized summaries and plots aid in efficient data inspection not typically reviewed during data collection.

Conclusions

Implementing the browser-base order form is currently undergoing review and further development to support data diagnostics. The order form significantly streamlines the processes for POP PK modeling and facilitates higher quality model-based drug development and decision making.

End User

QCP Data Request

Project: AZD9999
Study: D9999C00001
Analysis Type: PKPD-Safety
Therapeutic Area: PKPD-Efficacy
Purpose: Internal Decision
Project Directory: \\Usophdevcanda1\PM_1
Pharmacometrician (Lead): Al-Huniti, Nidal
Programmer (Lead): Fox, Robert

Data Specifications: Select an analysis type to view corresponding variables

Get For Later Submit Request

QCP Data

Data Specifications:

Identifier: Example defined by PM; 1-dosing event 2-Parent Concentration 3-Metabolite

Demographics: Example defined by PM; 1-dosing event 2-Parent Concentration 3-Metabolite

Timing: Example defined by PM; 1-dosing event 2-Parent Concentration 3-Metabolite

Dose: Example defined by PM; 1-dosing event 2-Parent Concentration 3-Metabolite

NMID: Example defined by PM; 1-dosing event 2-Parent Concentration 3-Metabolite

Required Variable Label Code List Method Analyst Instructions

Variable: DV, DV Identifier, 8, Num, BestB, Example defined by PM; 1-dosing event 2-Parent Concentration 3-Metabolite

Variable: DV, DV Identifier, 8, Num, BestB, Example defined by PM; 1-dosing event 2-Parent Concentration 3-Metabolite

Variable: MDV, Missing Data Value, 8, Num, BestB, 0=Observation 1=Missing observation or dose

Variable: BLQ, Below Limit of Quantification, 8, Num, BestB, 1=BLQ 0=above LQ

Variable: LLQ, LLQ, 8, Num, BestB, 1=BLQ 0=above LQ

QCP Data

D9999C00001 Data Specifications v.1 - ACTIVE

Analysis Type: PKPD-Safety
Pharmacometrician (lead): Nidal Al-Huniti
Programmer (lead): Robert Fox
Project Directory: \\Usophdevcanda1\PM_1

Therapeutic Area: Internal Decision
Purpose: Project/Study

Onco/Pharm: AZD9999 D9999C00001

Edit Copy Specs To New Request Download SAS Program

Variable	Label	Code List	Method	Instructions	Length	Type	Format	Category
C	NONMEM Exclusion Flag	c=C			1	Char	\$1	Identifier
OPROJID	Original Project Identifier				20	Char	\$20	Identifier
PROJID	Numeric Project Identifier				8	Num	BestB	Identifier
OSTUDYID	Original Study Identifier				25	Char	\$25	Identifier
STUDYID	Numeric Study Identifier				8	Num	BestB	Identifier
SITEID	Numeric Centre Identifier				8	Num	BestB	Identifier
OSID	Original Subject Identifier				8	Num	BestB	Identifier
SID	Numeric Subject Identifier				8	Num	BestB	Identifier
NMSEOSID	Sequential Subject Identifier				8	Num	BestB	Identifier
AGE	Age				8	Num	BestB	Demographics

QCP Data

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Early Clinical Development QCP Quantitative Clinical Pharmacology NONMEM Order Form

New Data Request Update / Copy from Prior Study

1. Click Update/Copy from Prior Study or New Data Request

2. Manually enter data or select drop-down options
3. Analysis type triggers default categories (Identifier, Demographics, Timing, etc) each of which expands out to display the variables.

POP-UPS and code lists provide definitions and information for end user

4. Analyst can enter study-specific instructions

5. A specification is produced and stored within the tool and also as a pdf or word file; email notifications are sent to the programmer and pharmacometrician

Click on the details button to open specification for edit or to copy specification to a new study

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List of existing requests

Requests

Created	Project	Study	Analysis	Pharmacometrician	Programmer	Purpose	Current Version	Delivered
2015-12-11	AZD7594	03740C00001	PKPD-Safety	Nidal Al-Huniti	Huan Liu	Internal Decision	2	Not set
2015-11-05	AZD9999	D9999C00001	PopPK	Nidal Al-Huniti	Robert Fox	Internal Decision	1	2015-11-05
2015-11-05	AZD9999Demo	D9999C99999	PopPK	Nidal Al-Huniti	Robert Fox	Internal Decision	1	Not set
2015-09-29	AZD9999	D9999C00001	PopPK	Nidal Al-Huniti	Robert Fox	Internal Decision	1	2015-11-15
2015-10-01	AZD1337	HAPPYSTUD00	PopPK	Nidal Al-Huniti	Robert Fox	Internal Decision	3	Not set

Administrator

Manage Tab is displayed when logged in as administrator. Administrators can edit any of the categories listed.

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Variables

Category	Variable	Label	Code List	Methods	Description	Length	Type	Format	Default Unit	Action
NMID	DVID	DV Identifier			Example (defined by PM); 1-dosing event 2-Parent Concentration 3-Metabolite	8	Num	BestB		
NMID	DV	Dependent Variable				8	Num	BestB		
NMID	MDV	Missing Data Value			0=Observation 1=Missing observation or dose	8	Num	BestB		
NMID	BLQ	Below Limit of Quantification			1=BLQ 0=above LQ	8	Num	BestB		
NMID	LLQ	LLQ					Num	BestB		
NMID	EVID	NONMEM Event Identifier			Example: 0=observation event 1=dose event 2=other-type event 3=reset event 4=reset-and-dose event	8	Num	BestB		

Add variable

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Variable Codes

Variable	Code	Value	Description	Standard	Action
ROUTE	1	ORAL		FDA	
ROUTE	2	RESPIRATORY (INHALATION)		FDA	
ROUTE	6	INTRAVENOUS DRIP		FDA	
ROUTE	7	INTRAVASCULAR		FDA	
ROUTE	8	NASAL		FDA	
ROUTE	9	RECTAL		FDA	
ROUTE	10	SUBCUTANEOUS		FDA	
ROUTE	11	SUBLINGUAL		FDA	
ROUTE	12	INTRACULAR		FDA	
ROUTE	13	INTRADERMAL		FDA	

Add Code

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Derivation Methods

Variable	Method	Unit	Formula	Default?	Action
TBW	Watson (>18)	L	Male: TBW = 2.447 * (0.09156 * Age) + (0.1074 * Height(cm)) + (0.3362 * Weight(kg)) Female: TBW = -2.097 * (0.1069 * Height(cm)) + (0.2466 * Weight(kg))	Yes	
TBW	Hume (>18)	L	Male: TBW = (0.194786 * Height(cm)) + (0.296785 * Weight(kg)) - 14.012934 Female: TBW = (0.34454 * Height(cm)) + (0.183809 * Weight(kg)) - 35.270121	No	
TBW	Mellitis-Cheek (<16)	L	Boy: TBW = -1.927 * 0.465 * Weight(kg) + 0.045 * Height(cm), for Height < 132.7 cm; Girl: TBW = 0.076 * 0.507 * Weight(kg) + 0.013 * Height(cm), for Height < 110.8 cm; = -10.313 + 0.252 * Weight(kg) + 0.154 * Height(cm), for Height > 110.8 cm	No	

Add Method