DDMoRe Standalone Execution Environment (SEE) Version 1.2.0

Features and Known Issues

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1   Introduction and overview of the release

This is a Public Beta Release of the MDL IDE and Interoperability Framework.

The purpose of the release is to allow access to DDMoRe Consortium members and the General Public to assess the deployment, features and usability of the system.

2 Interoperability framework features by release

		Beta release SEE Version 1.2.0	Future release(s)
High-level overview			
Language standards		MDL v. 7	TBD
		PharmML v. 0.6.1	
Key software components		MDL-IDE Demonstrator 1.2.0	TBD
		Monolix v. 4.3.2	
		NONMEM v. 7.3	
		R v. 3.0.3	
		Xpose v. 4.5.3	
		PsN v. 4.4.8	
		Simulx v. 2.1.1 (mlxR) / 1.1.0 (mlxLibrary)	
Distribution/deployment			
Stand-alone execution environment		x	x
Integration within existing IT infrastructure			x
Features/tasks			
Estimation	Monolix	x	x
	NONMEM	x	x
	winBUGS		x
Graphical diagnostics	R (user-defined)	x	x
	Xpose	x	x
Re-sampling/simulation-based diagnostics	Bootstrap in PsN (+NONMEM)	x	x
	VPC in PsN (+NONMEM)	x	x
Simulation	MATLAB		x
	SimCyp		x
	Simulx	x	x
Optimal design	PFIM		x
	PopEd		x
Models supported			
Outcome types	Continuous	x	x

	(single or multiple)		
	Binary		x
	Count	x [1]	x [2]
	Categorical		x
	Time-to-event	x [3]	x [4]
Ways to describe the model	ODEs (user-defined)	x [5]	x [5]
	Closed form analytical solutions (user-defined)	x [6]	x [6]
	Short-hand macro notation	x [7]	x [8]
	One-line PK library functions		x [9]
Administration/dosing/resetting support	Single or multiple dosing schedules	x	x
	Single or multiple administration routes	x	x
	Zero- or first-order input	x	x
	Steady-state dosing (SS, II, ADDL)	x [10]	x [10]
	Non-dosing related compartment resetting		x
Variability model types	Inter-individual variability	x	x
	Inter-occasion variability	x [11]	x
	Higher levels of variability		x
	Correlation between random effects	x [12,13]	x

				x
	Prior distributions			x
	Mixture models			x
Covariate types	Continuous (constant or time-varying)		x	x
	Categorical		x	x

Notes

1 : Poisson-type.

2 : Non-Poisson type.

3 : Exact/right-censored type. NOTE: It is currently not possible to combine a PK model directly with a time-to-event PD model. PK concentrations should instead be included as a column in the data set.

4 : Incl. interval-censored type.

5 : Resolves to: ADVAN 13 + $DES in NONMEM; ODEs in Monolix.

6 : Resolves to: $PRED in NONMEM; analytical solution in Monolix.

7 : Resolves to: ADVAN 13 + $DES in NONMEM; PK macros in Monolix.

8 : Resolves to: ADVAN 1-4/10-12 in NONMEM if of these types, otherwise to ADVAN 13 + $DES; PK macros in Monolix.

9 : Resolves to: ADVAN 1-4/10-12 in NONMEM if of these types, otherwise to ADVAN 13 + $DES; PK macros in Monolix.

10 : There is a known bug in the current version of Monolix, which means that ADDL is not handled properly.

11: Inter-occasion variability is not currently supported in the translation to Monolix.

12 : There is a limitation in the current translation to NONMEM, which means that random effects parameters for inter-individual as well as inter-occasion variability have to be defined in MDL in an order that ensures that the resulting OMEGA matrix in NONMEM is a block-diagonal band matrix.

13 : There is a known bug in the current translation to NONMEM, which means that the OMEGA BLOCK statement for correlated parameters will always appear before the OMEGA statements for un-correlated parameters. To ensure a correct model in NONMEM, the user must make sure to define the correlated random effects parameters before the uncorrelated random effects parameters in MDL.

3   Known issues with this release

Additionally, the following are either known issues revealed during ad-hoc testing or areas of functionality that are known to be incomplete. These are due to this being a beta release.

1. Installation of the SEE into a path containing spaces will result in failures when attempting to execute any third-party tools. Installing the SEE into a path without spaces will resolve the problem. Similarly, installation of the SEE into a deeply-nested folder will cause path length issues, usually when copying execution output files back to the workspace project directory, so it is strongly suggested that the recommended location mentioned in the Installation Guide is used.
2. There have been instances observed where memory has been exhausted on a 4GB RAM environment with multiple projects loaded. Restarting the MDL IDE resolved the problem.
3. There have been instances observed where the R Console has hung and eventually an error ('RMI – R server not found') was displayed. Restarting the R Console resolved the problem.
4. Only a subset of models has been validated (see Section **Error! Reference source not found.**). Other similar models may be supported but no guarantees can be made as to the level of this support.
5. Auto Completion of MDL code is not fully functional for all language elements.
6. Syntax Highlighting relies on the defined grammar for MDL which has not been exhaustively tested so may have some highlighting omitted.
7. The set of Errors and Warnings that are detected by the MDL Editor may not be complete.
8. The R console has been seen to 'disappear' following an MDL-IDE shutdown, possibly related to attempting to move the workspace. Restarting the IDE resolved the issue. In any case, attempting to use a workspace other than the default may work to some extent but with limited functionality, primarily in that the R console and attendant servers will not automatically start up.
9. Executions on a MOG object (as opposed to an MDL file) must be invoked from the location in which the data file sits.
10. The error messages produced in the R console when failures occur in task execution can be cryptic or not specific enough to be helpful. To identify the root cause, the contents of the relevant files within the working directory or workspace directory may need to be examined.
11. The parsing of the Standard Output object into the R environment can produce a number of warning messages if the 3rd-party tool has not populated the object as expected.
12. It is not possible to create an XPose database object following all model executions. One example is for discrete data models.
13. It is not possible to cancel 'in-progress' jobs.

The execution of models via third party tools is limited to NONMEM, Monolix, PsN and Simulx (depending on the plugins installed).