ALIS - DMA/DMPRA: A NEW LC/MS PHARMACEUTICAL & AGROCHEMICAL DATA REPORT WRITER

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Summary

ALIS-DMA/DMPRA is a software package specifically designed to process and report LCMS data generated in support of drug metabolism, pharmacokinetic and field dissipation studies. Four key design features were identified during prototype development neccessary for consistent study management of pharmacokinetic and field dissipation studies.

1

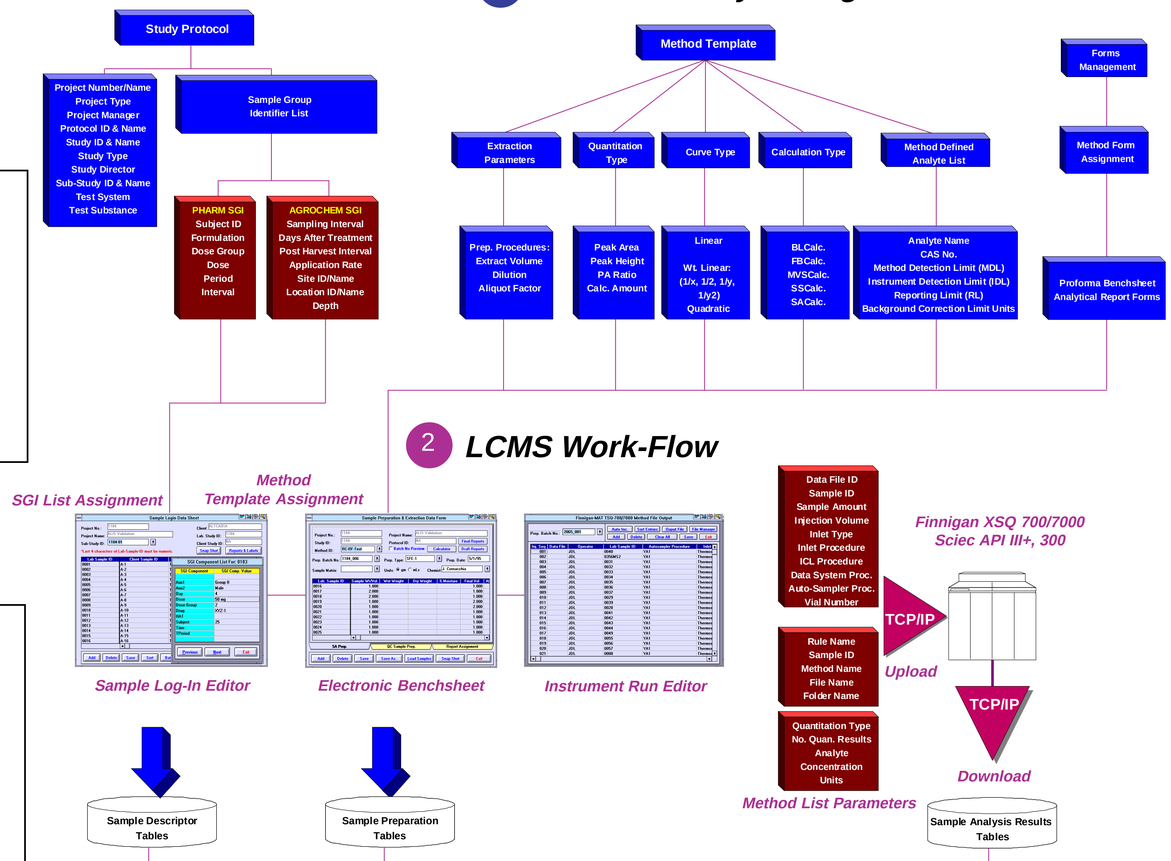
Study/Protocol Management

ALIS relies on an extensive set of utilities to ensure that samples are processed based on a consistent set of protocol driven controls. During study set-up, samples may be grouped into experimental sets (sub-studies) and assigned a list of sample log-in parameters - the Sample Group Identifier (SGI) list. The SGI list is customizable allowing the user to assign up to 12 treatment fields based on the experimental design. The SGI data is linked with analytical results and processed in the Pharmacokinetic Modeling portion of ALIS.

2

LCMS Work-Flow

The ALIS user interface is designed to automate typical CRO work flow operations and includes a Sample Log-In Editor, Electronic Benchsheet, Instrument Run List Editor and bi-directional Automated Instrument Data Transfers. Sample processing is controlled via a method template assigned during sample preparation. Method templates encode most quantitation and reporting parameters including calibration regression types, instrument control scripts and laboratory report forms.



Compartment Independent Model

The plasma drug concentration C_t at any given time t following a single intravenous bolus can often be described by:

$$C_t = C_0 e^{-\lambda_z t}$$

This implies that the plasma concentration of drug is linearly related to the dose and the profile C_t versus t, is the result of one or more linear rate processes.

Compartment independent model parameters are described below.

$$T_{1/2} = \frac{0.693}{\lambda_z}$$ ----[Half Life]

$$AUC = \frac{C_0}{\lambda_z}$$ ----[Area Under Curve]

$$AUMC = \frac{C_1}{\lambda_1}$$ ----[Area Under Moment Curve]

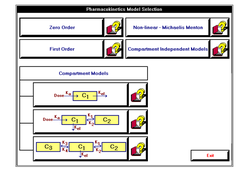
$$V_d = \frac{D_{IV}}{AUC * \lambda_z}$$ ----[Apparent Volume of Distribution]

$$V_{ss} = \frac{D_{IV} * \frac{C_0}{\lambda_z}}{(AUC)^2}$$ ----[Steady State Volume of Distribution]

$$CL = V_d * \lambda_z$$ ----[Total Body Clearance]

$$MRT = \frac{AUMC}{AUC}$$ ----[Mean Residence Time]

$$VRT = \frac{AUMC}{AUC} - (MRT)^2$$ ----[Variance of Residence Time]



3

Pharmacokinetic Module

The pharmacokinetic module incorporates zero-order, first-order, non-linear (Michaelis-Menton), compartment (one, two and Three) and compartment independent models (refer to adjacent figure).

4

Report Generation

Laboratory reports are designed and produced using programs within the MS Office Suite (MS Access, MS Excel and MS Word) or any ODBC compliant third party report writer such as Crystal Report Professional (CRP), the default ALIS report writer. Summary data tables are extracted from the database using SQL based graphical query builders and written to MS Word and/or MS Excel for reporting or export as an electronic deliverable.

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