PLA 3.0

PLA 3.0 SOFTWARE FOR BIOSTATISTICAL ANALYSIS

PRODUCT OVERVIEW

PLA 3.0

INTRODUCTION TO PLA 3.0

PLA 3.0 - a generic platform for biostatistical analysis

PLA 3.0 is a software platform for biostatistical analysis in GxP and non-GxP environments. It supports the biostatistical analysis of your product from the early stages of product development to production.

The new architecture of PLA 3.0 delivers all functionality required for regulated environments by the platform, while all statistical functionality is delivered by PLA Document Packages.

DOCUMENT PACKAGES

Powerful extensibility

A document package contains one or more document types and calculation routines as well as required report templates and data for operational qualification (OQ).

The PLA 3.0 base system comes fitted with

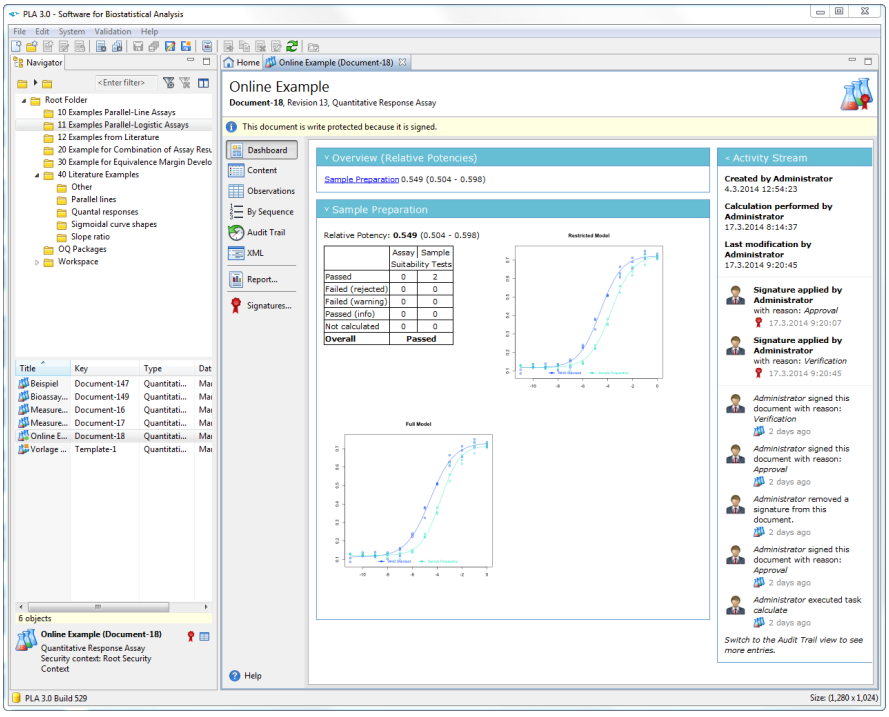
- Document Package for Biological Assays
- Document Package for Measurement Documentation
- Document Package for General Documents

Additional document packages can be installed into the platform. Additional document Packages may be available for download or they are created on demand.

MIGRATION PROJECTS

Framework for the migration of legacy systems to current standards.

With its extensibility PLA 3.0 gets an ideal tool for the migration of legacy software. Many companies make use of individual software solutions with validated but non-standard routines. The PLA platform can be extended to support these calculations. You receive the power of a commercial off-the-shelf product with all features required for regulated environments are already built-in, allowing the migration to focus calculation methods. In other words: migration projects get very cost and time efficient.



PLA 3.0 Screen Overview

DATA MANAGEMENT

The basic idea of the platform is the concept of electronic documents directly derived from the requirements of the FDA 21 CFR part 11 regulation. All data and meta data is kept in one single information unit - the document.
The structure and capabilities of a document are defined in the document packages. Documents are protected by the platform with electronic and digital signatures according to the 21 CFR part 11 regulation. Documents are organized in folders where several restriction can be applied (permissions, privileges, and mandatory templates.

The basic concept of the platform:
Handle data as documents!

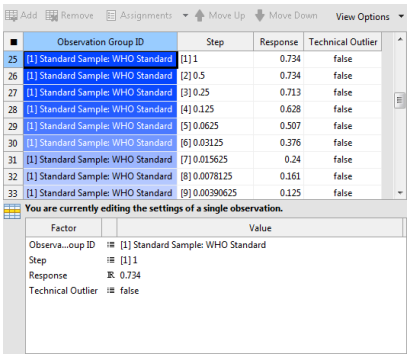
EDITORS

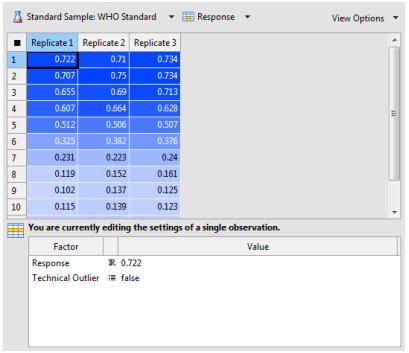
The ElasticForms Editor is the central editor for PLA 3.0. It is capable of editing documents of any complexity in a fast and efficient way. Context sensitive help for every field support the users with valuable information. The built-in template support allows to create and protect powerful templates to simplify usage and to support efficient standard operating procedures.

DATA EDITORS

The system is fitted with three data editor perspectives. They allow different views on your data sets. The user can decide wether it is more efficient to view or edit data points line by line, or per sample along a dilution series or in a position factor perspective. Powerful tools like color-coding of fields help reducing any input errors.

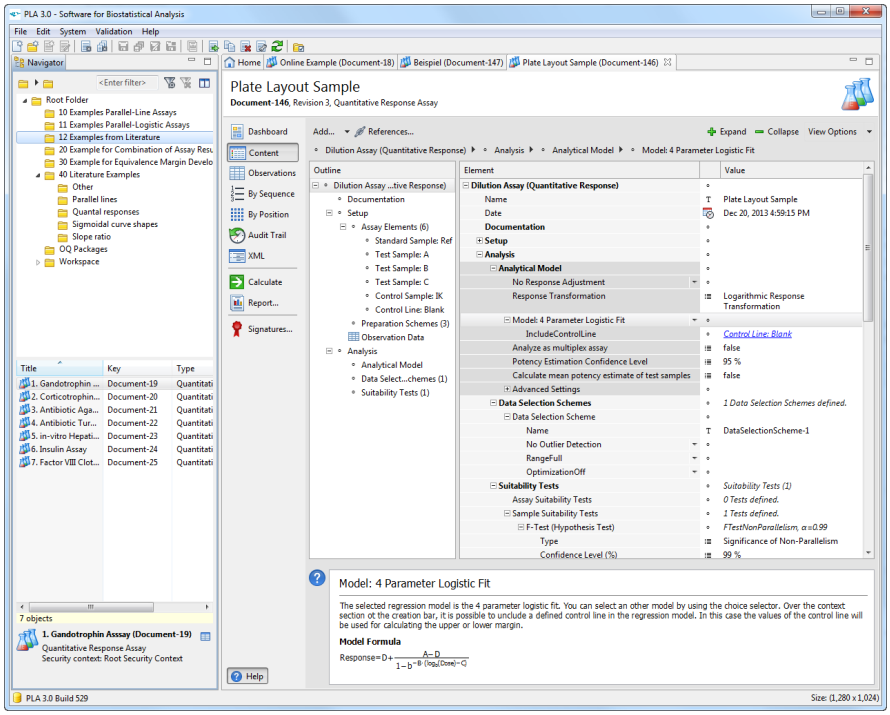
Data Editor Perspectives:

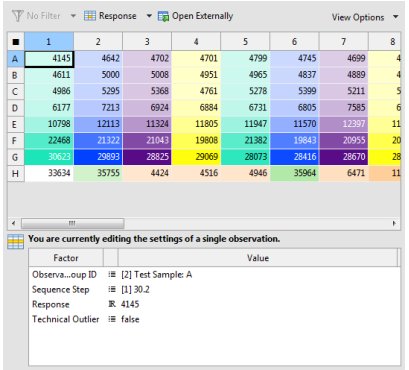




REPORTING

Correct and validated reporting is critical in controlled environments. The system supports validated reports to ensure a valid and trustable reporting of results.





PLA 3.0 - ElasticForms Editor

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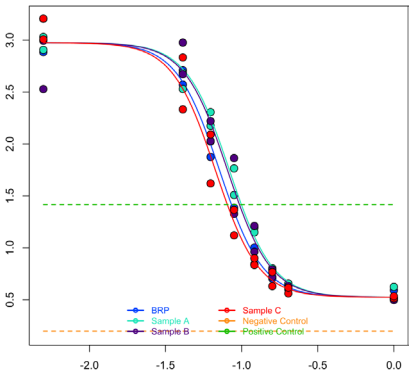
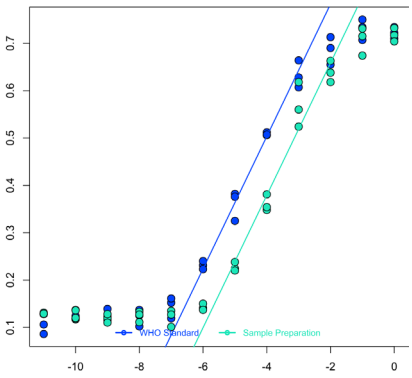
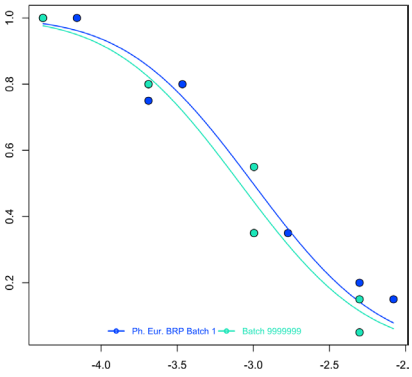
BIOLOGICAL ASSAYS

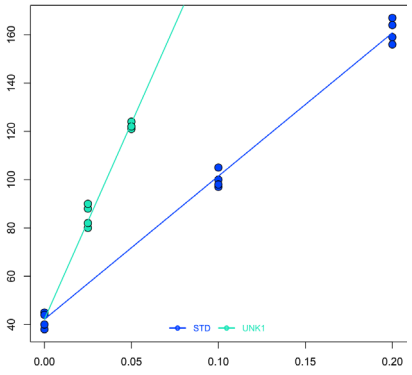
PLA 3.0 supports all types of Biological Assays according to European Pharmacopoeia chapter 5.3 and US Pharmacopeia <111> ,<1032>, <1033>, <1034>: Quantitative Response Assays (Parallel-Line, Parallel-Logistic, Slope-Ratio) and Dichotomous Assays (Quantal Response, Binary Assays). Results can be combined for the calculation of reportable values. Additional document types are available for Equivalence Margin Development, Control Charts and a Basic Bioassay Protocol.

Supported Assay Methods:









QUANTITATIVE RESPONSE ASSAYS EXTENDED

Biological or potency assays are frequently analyzed with the help of the parallel-line or parallel-logistic (3-, 4- or 5- parameter fit) as well as slope-ratio assays NEW. These methods have major advantages over traditional single-point assays:

- The linear or sigmoidal dose-response correlation is not only assumed but confirmed in each calculation.
- A dose-independent potency in terms of the standard's potency is calculated for each assay, and its validity is statistically proven.
- Test samples can be analyzed one-by-one or in a multiplex setup in a single regression. NEW
- Block effects are supported in the ANOVA. NEW

DICHOTOMOUS ASSAYS NEW

Dichotomous Assays (which are also called quantal response assays or binary assays) are assays based on binary outcome. E.g. a number of specimens shows a given response at a specific dose of an active ingredient. These assays are usually analyzed using the probit- or logit-method.

STATISTICAL TOOLS

FLEXIBLE ASSAY SETUP EXTENDED

The assay setup in PLA 3.0 is very flexible. You can setup any assay system with free number of test or control samples and control lines as well as free numbers of replicates and dilution steps. Symmetric and asymmetric assay setups are supported.

OUTLIER DETECTION

PLA supports four optional outlier detection methods: Dixon Test, Grubb's Test, Studentized Residual and a test based on the standard deviation.

CONFIGURATION OPTIMIZATION

While the parallel-logistic assay (full curve fit) describes the whole dose-response correlation, parallel-line assays focus the significant part of the dose-response relationship. PLA is able to locate the significant parts of the dose-response correlation automatically to determine the optimal assay configuration.

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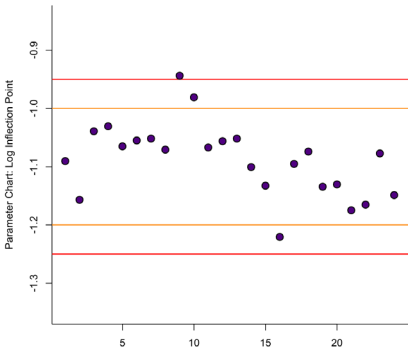
CURVE FITTING

In quantitative response assays both Parallel-Line Assays and Parallel-Logistic Assays (3–, 4– and 5-parameter sigmoidal functions) are implemented. For all models transformation functions for the response values are available to reduce heteroscedascity. The 3-parameter logistic curve fit is a constraint 4-parameter function, where either the lower or the upper asymptote is bound to a fixed value or to control lines. This allows truncated data to be analyzed.

Control Chart from PLA 3.0



SOPHISTICATED TEST SYSTEM

Testing can be done either by difference/hypothesis testing or by similarity/equivalence testing, which was introduced by the US Pharmacopeia chapters <1032>, <1033> and <1034>.

COMBINATION OF ASSAY RESULTS EXTENDED

The European Pharmacopoeia and the US Pharmacopeia describe different methods of combination calculations for independent assay results to obtain a reportable values for the potency. PLA supports all different weighting methods for combination calculations. PLA supports automatic data aggregation of independent assay data.

EQUIVALENCE MARGIN DEVELOPMENT EXTENDED

The development of equivalence margins for use according to the US Pharmacopeia is a challenging task. PLA is able to aggregate your reference data and calculate candidate equivalence margins.

CONTROL CHARTS NEW

The Control Chart document type in PLA 3.0 allows the trending of different parameters of your biological assay. Define any number of trending parameters and different limits to keep your assay under control.

The Control Chart document can be used in two ways. You can edit or import data from any source, allowing to use the trend chart universally. Or you can directly aggregate the corresponding data from your calculation results as required in regulated environments.

Equivalence Margin Development in PLA 3.0:

Result

	Basic Statistics				Equivalence Margins		
	n	mean	stderr	CV	upper	lower	reference mean
Difference of parameter (Test - Standard)							
Difference of slopes (Parameter B)	24	-0.617	1.090	176.7%	5.206	-5.206	
Difference of upper asymptotes (Parameter A)	24	-908.814	1292.377	142.2%	4070.914	-4070.914	
Difference of lower asymptotes (Parameter D)	24	-82.220	510.350	620.7%	3359.463	-3359.463	
Difference of asymmetry parameter (Parameter G)	24	-0.110	0.212	193.2%	1.117	-1.117	
Ratio of parameter (Test / Standard)							
Ratio of slopes (B Test/B Standard)	24	1.280	0.470	36.7%	3.486	0.496	
Ratio of upper asymptotes (A Test/A Standard)	24	0.980	0.027	2.8%	1.037	0.911	
Ratio of lower asymptotes (D Test/D Standard)	21	1.007	0.311	30.8%	4.545	0.027	
Ratio of asymmetry parameters (G Test/G Standard)	23	0.867	0.441	50.8%	5.398	0.187	
Scaled Parameter Range (Test - Standard)/reference mean (Standard)							
Scaled slope range (Parameter B)	24	0.245	0.432	176.7%	2.064	-2.064	-2.522
Scaled upper asymptote rage	24	-0.020	0.028	142.2%	0.088	-0.088	46254.702
Scaled lower asymptote range (Parameter D)	24	-0.036	0.221	620.7%	1.457	-1.457	2305.061
Scaled asymmetry parameter range (Parameter G)	24	-0.194	0.374	193.2%	1.974	-1.974	0.566
Curve Shape Tests							
Slope (B Standard)	24	-2.522	0.414	16.4%	-1.390	-4.619	
Upper asymptote (A Standard)	24	46254.702	1917.782	4.1%	50867.155	43308.579	
Lower asymptote (D Standard)	24	2305.061	590.841	25.6%	4720.635	-415.061	
EC 50 (C Standard)	24	-1.607	0.185	11.5%	-0.731	-2.265	
Asymmetry parameter (G Standard)	24	0.566	0.158	28.0%	1.426	0.124	
Difference of asymptotes ((A Standard - D Standard))	24	43949.641	1647.653	3.7%	49619.632	40217.242	
Ratio of Asymptotes (A Standard / D Standard)	21	21.517	6.310	29.3%	95.910	10.534	
Scaled asymptote range ((A Standard - D Standard)/reference mean (Std))	24	0.950	0.036	3.7%	1.073	0.869	46254.702
Additional Tests							
Nonlinearity sum of squares	24	4035127.525	2790311.252	69.2%	9501925.426	0.000	

BASIC BIOASSAY PROTOCOL NEW

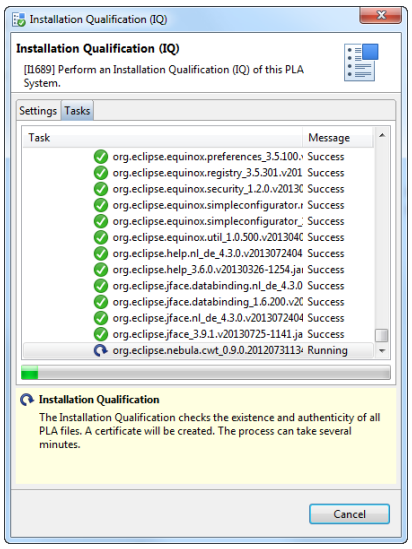
The Basic Bioassay Protocol implements a simple workflow. The protocol document links several independent quantitative response assays to one or more combination calculations.

PLA 3.0

FIT FOR THE ENTERPRISE

VALIDATION AND GXP COMPLIANCE

According to GAMP software has to be validated on the customer's computer system. The software vendor is only able to verify the software in his labs. The optional Validation Package helps you to manage the tasks of installation qualification, operational qualification and performance qualification (IQ, OQ, PQ) fast and efficiently.



INTEGRATION EXTENDED

PLA has a full set of interfaces for the import of raw data from data acquisition systems, for the export of data to e.g. documentation systems and for the reporting into many target systems. Individual modules can be created at low cost.

Import Modules are now distinguished into Document Import Modules creating a complete document with all settings and Data Acquisition Modules. Data Acquisition Modules are able to import data into the data table of any document type. (Note: They replace the former PLA 2.x Import Modules.)

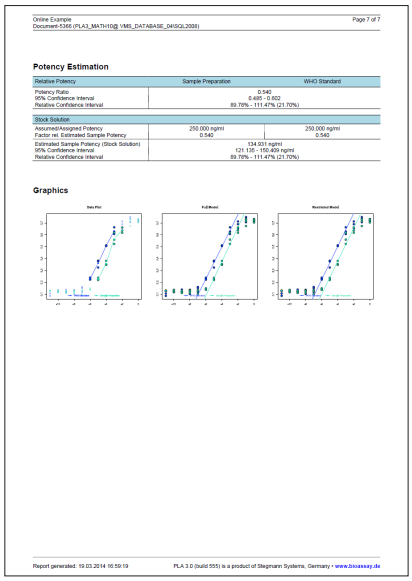
TRANSFER OF DATA AND TEMPLATES EXTENDED

PLA allows to transfer data and templates between projects, sites and companies in a secure manner.

The trustability and integrity of the data is assured by a combination of electronic signatures, that are preserved in the transfer, and cryptographically secured data transfers. PLA secures the information with the help of its own integrated PKI (Public Key Infrastructure). This operation is completely transparent for the user. It assures the secure communication of data and templates to different projects, sites or CROs.

ROLES AND PERMISSIONS EXTENDED

PLA 3.0 comes with an updated sophisticated permission system scalable from single seat to global installations. Typical roles are predefined in the system but can be altered to match your companies needs. All the settings are combined together in named security contexts, that can easily be applied to new folders.



TEMPLATES EXTENDED

PLA 3.0 comes with a new template engine. Templates can be defined by authorized users. They decide about the visibility, access level and default values in a document. Assays can be signed electronically and the administrator can define the mandatory use of specific templates in the database or in database sections. The template engine was designed to support the easy implementation of standard operating procedures (SOPs) within PLA.

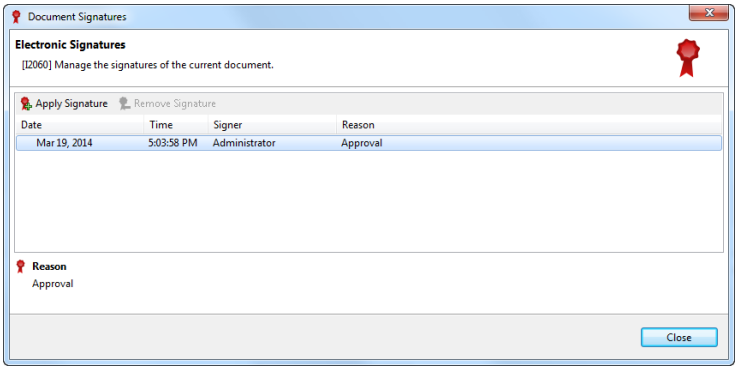
21 CFR PART 11 COMPLIANCE

ADVANCED SECURITY FEATURES

In accordance with the FDA 21 CFR part 11 PLA has its own security infrastructure that requires users to log into the system. User accounts and their roles are defined with an easy-to-use interface. The accounts and their roles are database specific. In addition to this account management PLA is fitted with the full range of security options required by the 21 CFR Part 11. The PLA Administrator can define security policies for each database in accordance to regulatory or your company's need. The feature includes password complexity, password aging, password blocking and password history rules. You may also define inactivity locks to prevent from unauthorized access to the system.

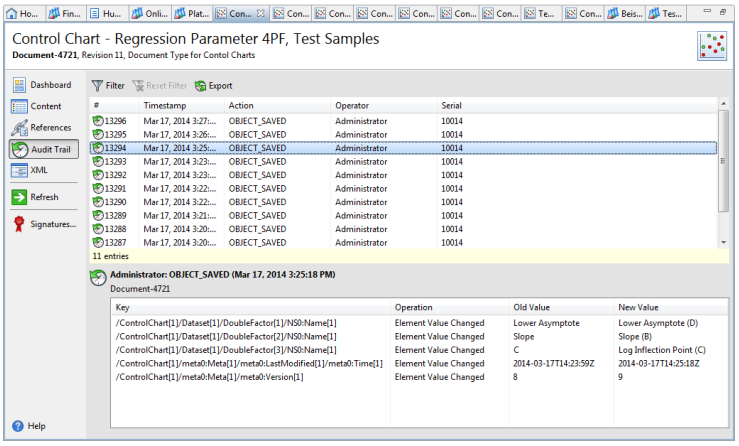
ELECTRONIC SIGNATURES

Electronic signatures can be applied to all documents in PLA. The application of electronic signatures is a requirement of the 21 CFR part 11. With PLA's advanced data storage technology electronic signatures can even be moved between different installations of PLA (e.g. between your CRO and your company).



AUDIT TRAIL EXTENDED

PLA has its own audit trail that covers all changes of data and properties of your documents and of all security features inside PLA. The audit trail can be inspected on a per-database and a per-document level. Filter and export functions have now been included into the base features of PLA 3.0



DIGITALLY SIGNED ELECTRONIC RECORDS

PLA benefits from the XML industry standard for the storage of electronic records. This very flexible format has the main advantage that it is human readable, which is another requirement for compliance.

PLA makes use of the XML Signature 1.0 Industry standard to assure the integrity of all the data that PLA works with. The XML Signature Standard applies a digital cryptographic signature to each data package. With the help of this signature the integrity of the electronic records is checked every time PLA makes use of them. This integrity check prevents any unauthorized or unwanted data modification, e.g. by computer defects.


STEGMANN
SYSTEMS