

THE EUROPEAN DIRECTORATE FOR THE QUALITY OF MEDICINES & HEALTHCARE (EDQM)



CombiStats online Training module 1

Introduction to the online application

Content

- Introduction
- Workspace
- File and folder management
- Data entry, analysis options & audit trail
- Batch creating .epax files

- Statistical analysis of data of dilution assays in accordance with Ph. Eur. Chapter 5.3

5.3. STATISTICAL ANALYSIS OF RESULTS OF BIOLOGICAL ASSAYS AND TESTS

1. INTRODUCTION

This chapter provides guidance for the design of bioassays prescribed in the European Pharmacopoeia (Ph. Eur.) and for analysis of their results. It is intended for use by those whose primary training and responsibilities are not in statistics, but who have responsibility for analysis or interpretation of the results of these assays, often without the help and advice of a statistician. The methods of calculation described in this annex are not mandatory for the bioassays which themselves constitute a mandatory part of the Ph. Eur. Alternative methods can be used and may be accepted by the competent authorities, provided that they are supported by relevant data and justified during the assay validation process. A wide range of computer software is available and may be useful depending on the facilities available to, and the expertise of, the analyst.

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2. randomisation and independence of individual treatments
3. assays depending upon **quantitative responses**
 - 3.2. the parallel-line model
 - 3.3. the slope-ratio model
 - 3.4. extended sigmoid dose-response curves
4. assays depending upon **quantal responses**
 - 4.2. the probit method
 - 4.3. the logit method
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5. examples
6. **combination of assay results**
 - 6.2. combination of independent assay results
 - 6.3. unweighted combination of assay results
7. beyond this annex
8. tables and generating procedures
9. glossary of symbols
10. literature

Some figures

- Desktop version release in 1999 to OMCLs, in 2005 to non-OMCLs
- Used by 394 organisations (960 licences) worldwide in 2023
- **CS-online release in 2024**
- Users' expectations (top 3)
 - User identification (individual login/password)
 - More interactivity (e.g. information/error messages)
 - Audit trail

Sustainable tool using a modern programming language

Flexible licence management system


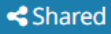



- EDQM Store: 1 licence = n users/seats
- Possibility to assign and revoke users

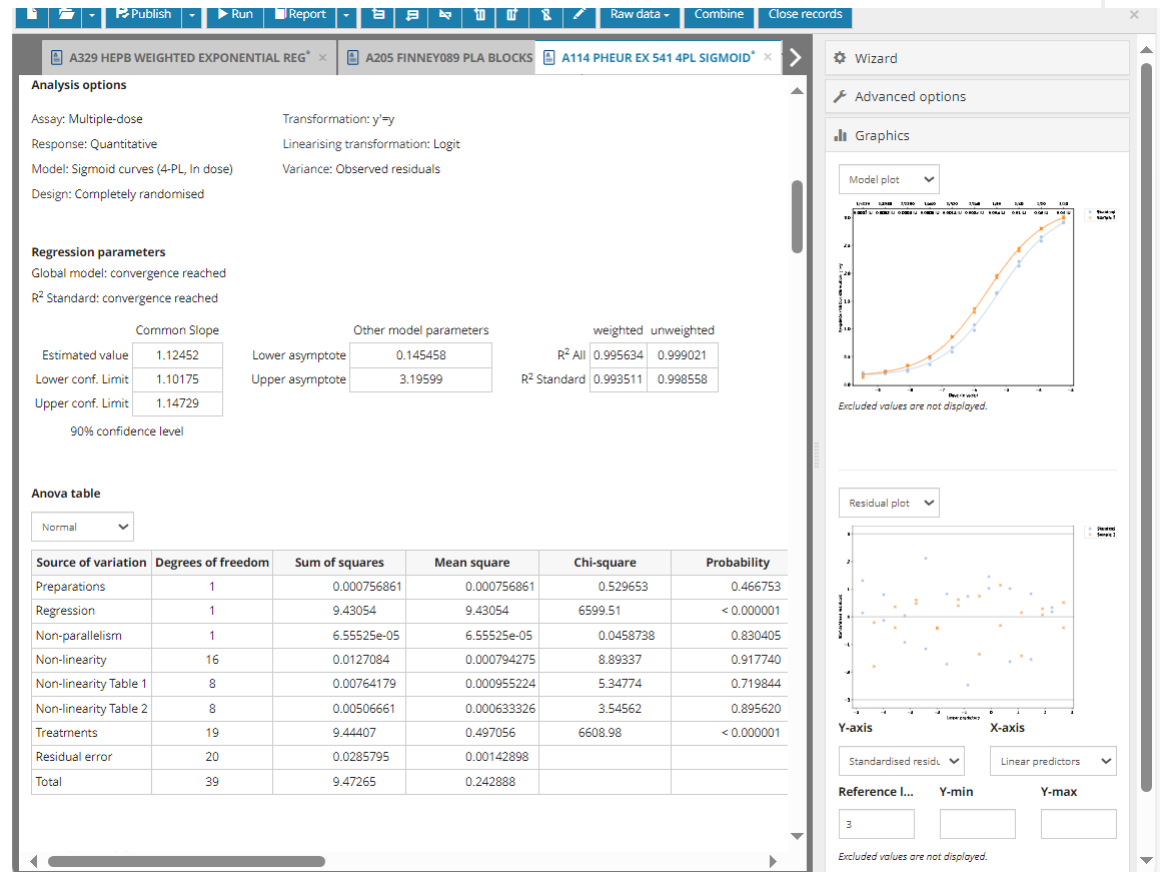
Dedicated workspace for your organisation

- Access by login/password
- Folders & files creation, management, sharing
- Import of CombiStats Desktop 5.0 to 7.0 files

Modern & interactive interface

- Better flow of analysis options
- Enhanced graphical views
- Information and error messages
- Template, file protection
- PDF report, audit trail

Type	Name	Created	Created by	Last modified	Last modified by	Owner
<input type="checkbox"/>	 A_folder01	31 May 2024	User U	today	User U	User U  
<input type="checkbox"/>	 A_folder02	25 Jun 2024	User U	today	User U	USER 1 T 



Notes for guidance in free access

- <https://combistats.edqm.eu/home/>

The screenshot shows the COMBISTATS website interface. At the top, there is a navigation bar with the Council of Europe logo on the left, the text 'COMBISTATS' in the center, and the EDQM logo on the right. Below the navigation bar, there are two main menu items: 'HOME' and 'HELP'. To the right of these are 'REGISTER' and 'SIGN IN' buttons. An arrow points from the 'HELP' menu item to a list of resources. The resources are organized into three sections: 'How to', 'Notices', and 'Notes for guidance'. The 'Notes for guidance' section contains a list of 24 items (EN00 to EN24). To the right of this list, there is a section titled 'Technical requirements' with two bullet points.

How to

- Create my account

Notices

- Privacy Notice
- Security Notice

Notes for guidance

- EN00 Release Notes
- EN01 Information And Remarks
- EN02 Taskbar
- EN03 Wizard Options
- EN04 Advanced Options
- EN05 Preparations Table
- EN06 Rawdata Tables
- EN07 Show Design
- EN08 Table of Blank Results
- EN09 Subset Analysis
- EN10 Regression Parameters
- EN11 ANOVA Table
- EN12 Equivalence of Slopes
- EN13 Graphical Representations
- EN14 Extra Analysis Results
- EN15 Potency Estimates
- EN16 Effective Dose & Prediction
- EN17 Combination of Assay Results
- EN18 Spearman-Kaerber Approach
- EN19 Single-dose Assay
- EN20 Multiple-dose Assay (Standard Only)
- EN21 Template & Protection
- EN22 Audit Trail
- EN23 Information & Error Messages
- EN24 Structure of epax & epmx files

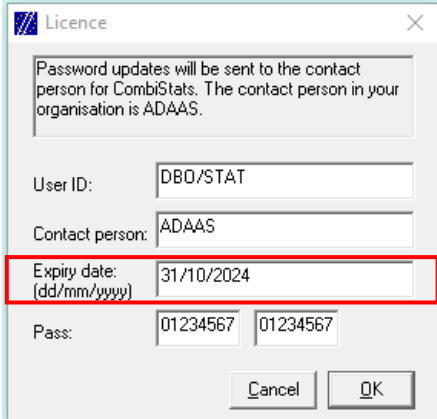
Technical requirements

- Computer with access to the Internet, Chrome or Edge browsers
- Acrobat Reader for viewing PDF reports, MS Excel for viewing extra analysis results

Timelines

- July 2024: Go live
 - Free licence until 31 Oct. 2024
- Q3 2024
 - No renewal: CombiStats stops on 31 Oct. 2024
 - Renewal: CS-online licence for 1 year + CS-desktop until 31-Mar-2025 (transition)
- Next year
 - No renewal: CS-online stops after 1 year (from the date of activation of the CSID code)
 - Renewal: CS-online available for 1 more year

CS-desktop



CS-desktop

Licence

Password updates will be sent to the contact person for CombiStats. The contact person in your organisation is ADAAS.

User ID: DBO/STAT

Contact person: ADAAS

Expiry date: 31/10/2024
(dd/mm/yyyy)

Pass: 01234567 01234567

Cancel OK

CS-online

From: Sales@edqm.eu <Sales@edqm.eu>

Sent: Wednesday, October 30, 2024 5:00:00 PM (UTC+01:00) Brussels, Copenhagen, Madrid, Paris

Your CombiStats licence - Your order 0123456789 - Our order confirmation 543210

DO NOT REPLY TO THIS MESSAGE

Dear Customer,

Thank you for your order. Please find your licence activation key below:

Combistats licence - Access for N user(s)

CSID-/////-----/////----/ → **Activation code**

The procedure for activating the licence key and registering users can be found [here](#).

If applicable, please forward this message to the person responsible for managing

CombiStats licences within your organisation.

If you experience any problems, do not hesitate to contact us via the [EDQM HelpDesk](#).

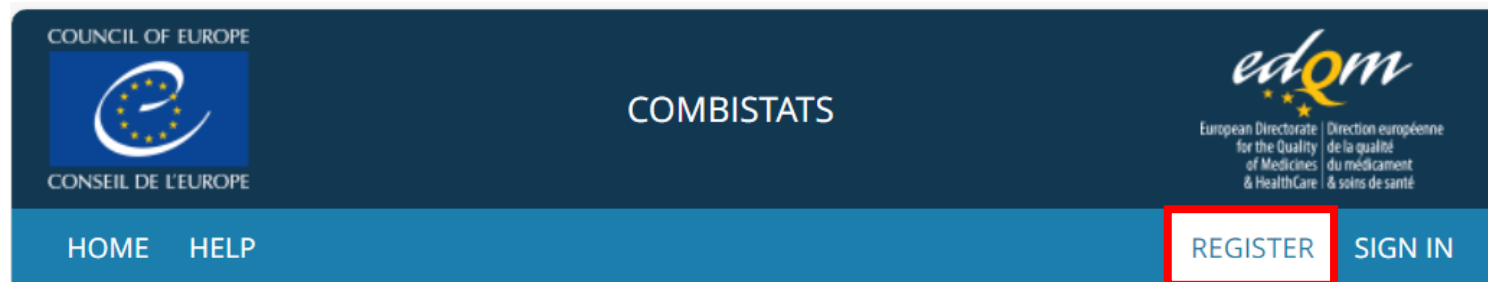
Kind regards,

The EDQM Sales Section

Content

- Introduction
- **Workspace**
- File and folder management
- Data entry, analysis options & audit trail
- Batch creating .epax files

User account creation



Registration

E-mail ID*

Please enter the e-mail address that will serve as login

Captcha*

[Back](#) [Next](#)

Registration

First name*

Last name*

Professional organisation*

Country (of organisation)*


[Back](#) [Register](#)

Your account has been created. You will shortly receive an e-mail with a link to define your password in order to finalise your registration.

You already have an EDQM account. Your access to this application has been granted. Please use your EDQM credentials to login.

User account activation

1. Click the link received by email

[EDQM-Account] Creating your account - Please define your password -- [Compte EDQM] Création de votre compte - Veuillez définir votre mot de passe 



From noreply-qual@edqm.eu on 2024-06-28 10:12

 Details  Headers  Plain text

Version française plus bas

*** This is an automatically generated e-mail, please do not reply ***

Dear My first name My las,

Welcome to the EDQM environment.

In order to activate your account, you will need to set your password. To do so, please follow the link below:

<http://sign-qual.edqm.eu/validation/MzExOA/6mb-fc6404052bcf121c90cc/?>

[lang=en&redirect=aHR0cHM6Ly9jb21iaXN0YXRzLXF1YWwuzWRxbS5ldS9hY2NvdW50cy9sb2dpcg](http://sign-qual.edqm.eu/validation/MzExOA/6mb-fc6404052bcf121c90cc/?lang=en&redirect=aHR0cHM6Ly9jb21iaXN0YXRzLXF1YWwuzWRxbS5ldS9hY2NvdW50cy9sb2dpcg)

Do not forward this link to other users, as it contains a token that is only valid for your e-mail address for 1 day.

Please be informed that your account will be deactivated if you do not set up your password and log in within 5 days.

For your information, your login is your e-mail address.

Permissions will be granted to your account, when necessary, for applications you need to access to. In this case, you will receive an automatic e-mail from the so-called applications.

2. Create a password

Enter your password

Please enter your password twice so we can verify you typed it in correctly.

New password*

- Your password must contain at least 10 characters.
- Your password must contain at least 1 uppercase character.
- Your password must contain at least 1 digit.
- Your password must contain at least 1 special character among !@#\$\$%^&*(){}[]-+.
- Your new password can not be identical to any of the 10 previously entered.
- Your password can't be a commonly used password.
- Your password can't be entirely numeric.
- Your password can't be too similar to your other personal information.

New password confirmation*

3. Sign in to activate your account

One last step

Password set. In order to finalise the activation of your account, you now need to log in.

[Sign In](#)

How many seats users (seats) for your organisation?

- EDQM webshop: <https://store.edqm.eu/index.html>

▼ Products

- EUROPEAN PHARMACOPOEIA 11th EDITION
- BIOLOGICAL STANDARDISATION PROGRAMME
- BLOOD TRANSFUSION
- COSMETICS
- COUNTERFEIT MEDICINES AND SIMILAR CRIMES
- FOOD CONTACT
- ORGANS, TISSUES AND CELLS
- PHARMACEUTICAL CARE
- QUALITY MANAGEMENT FOR BLOOD ESTABLISHMENTS
- TATTOOS AND PERMANENT MAKE-UP
- CombiStats**

DESCRIPTION

CombiStats is a calculation program for the statistical analysis of data from biological dilution assays according to Ph. Eur. general chapter 5.3.

You can find out more about CombiStats [on the dedicated webpage](#) and [FAQs](#) on the EDQM website.

Languages: English



Ordering: The following discounts are available for orders for multiple users:

- 5% for 2 to 4 users;
- 10% for 5 to 10 users;
- 20% for 11 to 20 users;
- 30% for 21 or more users.

These discounts will be applied after validation of your order/quotation.

Technical requirements :

CombiStats runs on recent versions of all modern web browsers including Chrome and Edge. Reports are exportable in PDF format and results in an Excel-compatible format. For more information on the technical requirements, please see the [EDQM FAQs](#).

Name	Price	Quantity	
CombiStats licence	600.00 EUR	1 <input type="text"/> PCE 	
CombiStats licence - Extension	600.00 EUR	1 <input type="text"/> PCE 	

Enter the number of seats (users) here.

Example

- First order: a licence for 2 seats (users)

Name	Price	Quantity	
Combistats licence	600.00 EUR	<input type="text" value="2"/> PCE	
Combistats licence - Seat Extension	600.00 EUR	<input type="text" value="0"/> PCE	



CSID code to activate the workspace



Validity: 1 year from licence activation date (anniversary date)

- Second order: 3 additional seats (same workspace)

Name	Price	Quantity	
Combistats licence	600.00 EUR	<input type="text" value="0"/> PCE	
Combistats licence - Seat Extension	600.00 EUR	<input type="text" value="3"/> PCE	

CSID code to extend the workspace

Validity: anniversary date of first order



- Licence for 3 seats **in another workspace**

Name	Price	Quantity	
Combistats licence	600.00 EUR	<input type="text" value="3"/> PCE	
Combistats licence - Seat Extension	600.00 EUR	<input type="text" value="0"/> PCE	

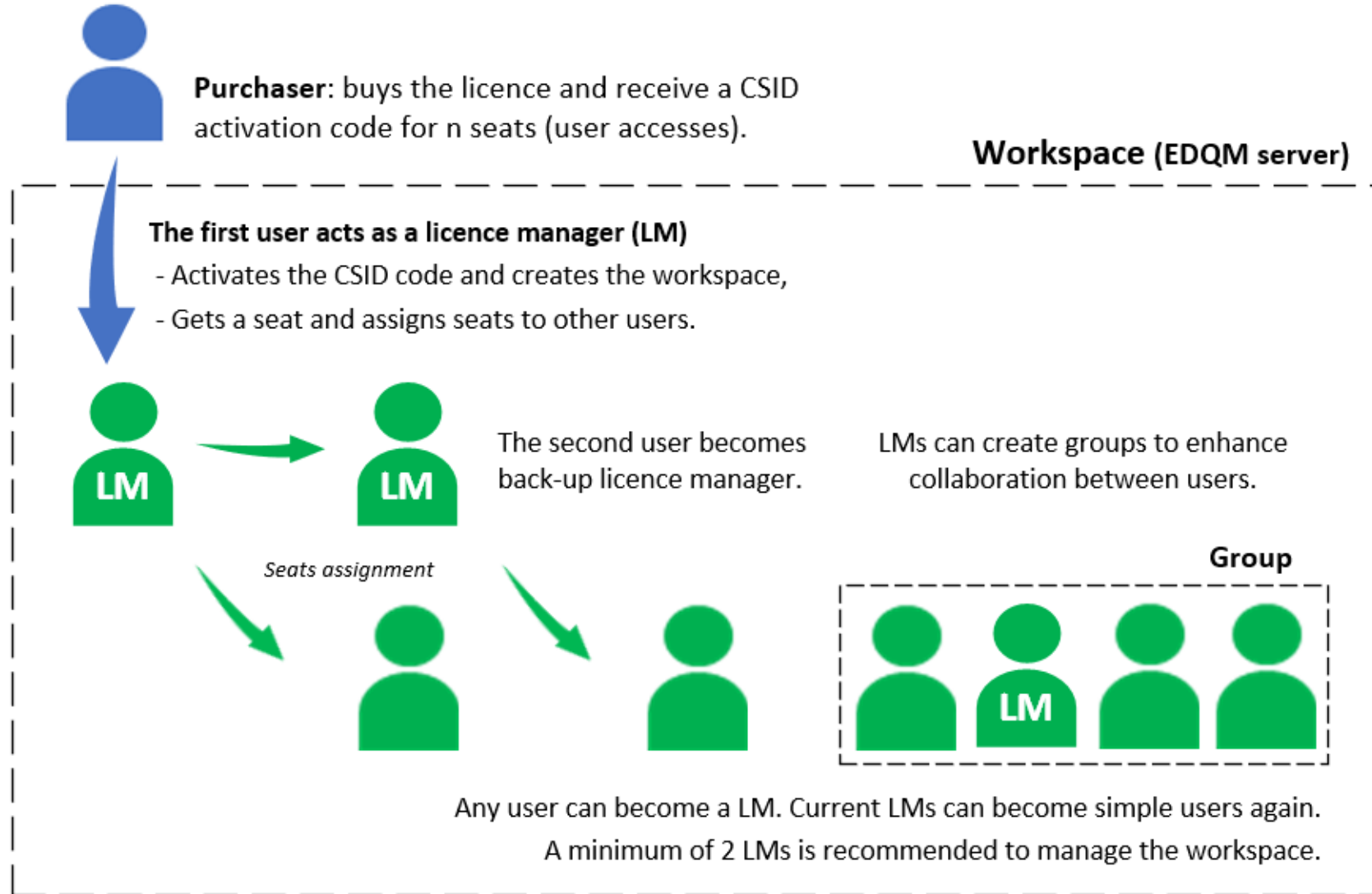
CSID code to activate the workspace

Validity: 1 year from licence activation date



Workspaces do not communicate between each other

Workspace: secure & collaborative working environment



Workspace activation

The screenshot shows the top navigation bar of the CombiStats website. On the left, there are logos for the Council of Europe and EDQM. The center of the header displays 'COMBISTATS'. On the right, there is the EDQM logo and its full name in English and French. Below the header is a blue navigation bar with 'HOME' and 'HELP' links on the left, and 'USER U' with a dropdown arrow on the right. The main content area features a large heading 'Welcome to CombiStats' followed by a subtitle 'Web-based application for the Statistical Analysis of Biological Dilution Assay Results or Potency Assay Results'. A red-bordered box highlights a message: 'A licence is required to view content in this site. Click [here](#) to activate your licence.'

From: Sales@edqm.eu <Sales@edqm.eu>
Sent: Wednesday, October 30, 2024 5:00:00 PM (UTC+01:00) Brussels, Copenhagen, Madrid, Paris
Your CombiStats licence - Your order 0123456789 - Our order confirmation 543210
DO NOT REPLY TO THIS MESSAGE
Dear Customer,
Thank you for your order. Please find your licence activation key below:
CombiStats licence - Access for N user(s)
CSID-///// -////////-///// -//// → **Activation code = licence key = CSID**
The procedure for activating the licence key and registering users can be found [here](#).
If applicable, please forward this message to the person responsible for managing CombiStats licences within your organisation.
If you experience any problems, do not hesitate to contact us via the [EDQM HelpDesk](#).

Licence Activation

If you have a licence key, activate it here to create your workspace.

Otherwise, contact the licence manager within your organisation.

Licence key (CSID)*:

Once activated, your licence key will be valid for a year.

Activate

Each organisation can manage access to the workspace

LICENCE

Workspace ID: 5BNDLNKJ

Number of access: 4 assigned - 3 available

Expiration date: 01 July, 2025

This page is accessible to licence managers only

NEW LICENCE ACTIVATION

CSID code*:

Activate

In case of renewal, your licence key will be valid for a year. In case of extension of the number of seats, the expiration date remains unchanged.

Licence key	Access count	Subscription	Activated on	Activated by
CSID-5D0QG-XV5YK16Q4C-TPB57-H8P0	7	until 2025-07-01	01/07/2024	bao lalala

ASSIGNEES

E-mail*

Assign user (one-at-a-time)

Can manage

Assign single

Choose file*

Assign multiple users (at once)



Assign multiple



	A
1	user1@CS.org
2	user2@CS.org
3	user3@CS.org
4	...

E-mail	Assignee	Can manage workspace	
baothanh.nguyenvan@edqm.eu	bao lalala	<input checked="" type="checkbox"/>	Revoke

Licence manager (LM role)

A user who can:

- Enter CSID codes to activate/renew the workspace
- Assign users to the workspace, give LM roles
- Revoke users from the workspace, revoke LM roles (including him/herself)
- Create, edit, delete user groups
- Manage files and folders

Note. Revoke a user...

E-mail	Assignee	Can manage workspace	
combistats@edqm.eu	Test User	<input checked="" type="checkbox"/>	Revoke

The user can give read/write access to their folders before being revoked. Alternatively, a LM can do it.

User group

How to share a folder with several users (in bulk):

- create a user group
- share the folder with the group

E-mail	Assignee
combistats@edqm.eu	Test User
david.le-taltec@edqm.eu	User U
elena.regourd@edqm.eu	ELENA REGOURD

Licence assignee history

GROUPS

Add

New group

Display name*

My_group

Is active

MEMBERS

Name

User U

Add another

Cancel

Save

Display name

Is active

My_group

✓



Share folder "User_1"

GENERAL

Owner

User U

SHARE TO

Name

My_group

Add another

Access

Read only

Read only

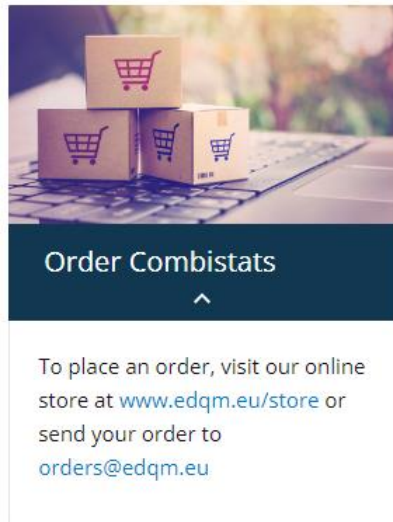
Read and write

Remarks

- You cannot access CS-online unless your account has been assigned to a seat. Assignment to a seat is managed by a licence manager (see previous slide)
- A same email address cannot be used with several workspaces
- Licence renewal: place an order (webshop or email)

E-mail	Assignee	Can manage workspace	
david.le-taltec@edqm.eu	> DLT	<input checked="" type="checkbox"/>	Revoke

<https://www.edqm.eu/en/lp-combistats>



E-mail notifications to licence manager(s) 1 month and 2 weeks **before expiry**

- Renewal: enter the new CSID code
- No renewal: workspace locked

NEW LICENCE ACTIVATION

CSID code*:

In case of renewal, your licence key will be valid for a year. In case of extension of the number of seats, the expiration date remains unchanged.

Homepage: **Your licence has expired. Please renew it in order to access your workspace.**

Renewal after expiry still possible

RENEW ACCESS

Licence key (CSID)*:

If you know that you will stop using CS-online for a long period, export files locally (files are automatically deleted 3 years after their date of creation).

Remarks

- In case where the workspace has only one seat (user is necessarily licence manager)

Licence key	Access count
CSID-AAAAA-BBBBBBBBBB-CCCCC-DDDD	1

If changing positions, this user should **transfer** the licence ownership to his/her replacement

TRANSFER LICENCE

E-mail*

The new licence manager will have full access to folders & files

- Notices

- [Privacy Notice](#)
- [Security Notice](#)

The EDQM processes your data based on the Council of Europe Regulations on the Protection of Personal Data (**CERPPD**).

Registration

First name*

Last name*

Professional organisation*

Country (of organisation)*

- [Privacy Notice](#)
- [Security Notice](#)



Data is processed by a server of the EDQM located in France.

1. **General aspects:** e.g. governance, development policy, risk & incident management
2. **Data protection:** e.g. user access, data encryption, data retention
3. **Infrastructure:** e.g. security, availability & resilience, recovery

Remarks

- Should I transfer all my epa files (CS-desktop) to the workspace? **NO**

After reviewing the user manual, I noticed that it only allows importing files one at a time. Given that we have over 15 years' worth of work in .epa format, this process would be quite time-consuming for us.

➔ Files are deleted 3 years after their creation (the EDQM server is not meant to become a database)

Option:

- Store legacy files (epa, epc) locally in case where you would need to import them to CS-online for reanalysis
- Export files (epax, epcx) on a regular basis unless PDF reports (raw data, analysis options, calculated results, audit trail) are enough

Validation

Release notes

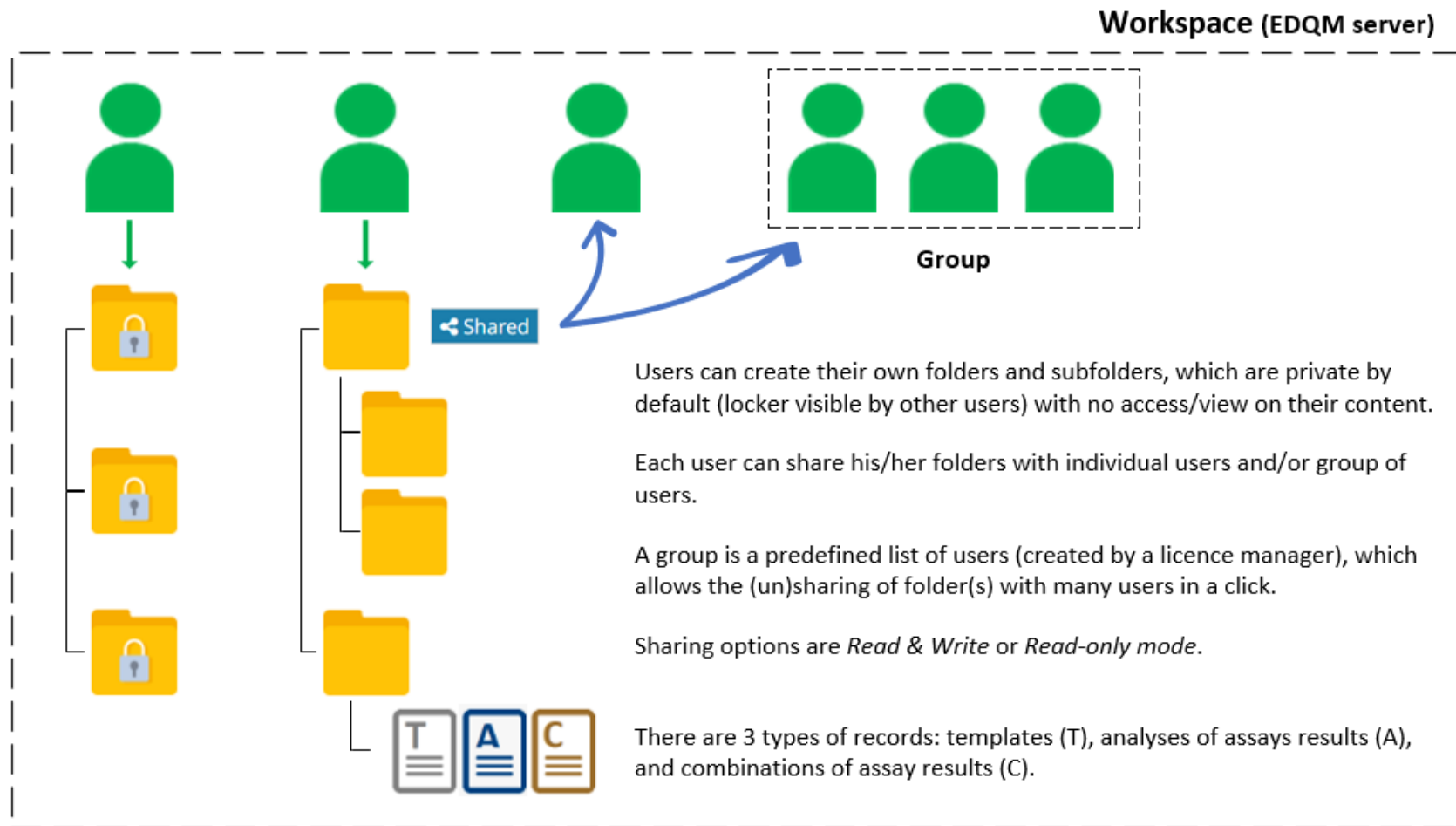
CombiStats has been successfully tested using the Chrome and Edge web browsers. The calculation modules previously available in the desktop version have been reproduced using more up-to-date language and terminology. Although the EDQM has not published any documentation pertaining to the validation of CombiStats Online, since the application is not certified, the examples from Ph. Eur. general chapter 5.3 and Appendix A of the desktop version user manual, as well as the majority of the examples provided in *Statistical Method in Biological Assay* by David J. Finney (3d ed., 1978, ISBN 0852642520), were tested and the results were successfully compared with those generated by the desktop version.

<https://combistats.edqm.eu/faq/link/87/>

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Overview



Actions

Import CS-desktop files

Create folders, files

Search, rename

Copy, move to

Export (zip file) / import

Add to my Favourites

Share (read-only or read-write)

Trash: items remain 30 days in the trash after deletion. Can be restored or deleted permanently

Outside the workspace, exports of files



Records are exported as XML files (.epmx, .epax, and .epcx)



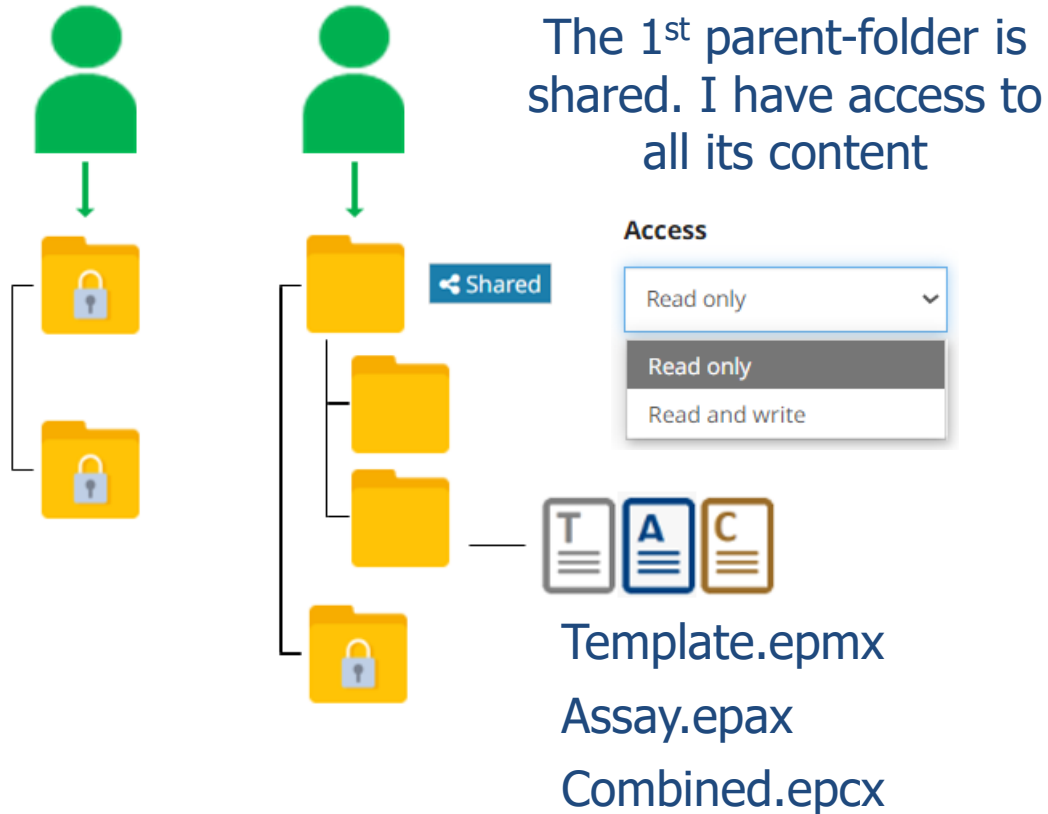
Analysis, combination reports as PDF.



Extra analysis results as Excel tables.

Remarks

- **Permissions** are set at the level of parent-folders



- **Templates (.epmx)**



Protection level

No protection

No protection

L1: Wizard and advanced options are protected

L2: L1 + number and dimension of tables are protected

L3: L2 + non-empty cells are protected

Only .epax files created from a template can inherit the protection level of the template

An .epax file created from scratch cannot be protected

However, at any time, a file can be published in 'read-only' mode

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Features

Data tables Preparations, labels, info. Potency value/pre-dilutions Number of doses, replicates Descriptive stat/dose	Quantal/quantitative response Model Parallel lines, Slope ratio 3-parameter exponential curves 4- & 5-parameter sigmoid curves Single-dose assay	Graphics Average plot Regression plot (linearised) Residual plot (incl studentised)
Orientation of tables Doses vertical/horizontal	Transformation Dropdown list/user-defined	Potency estimates precision, relative to assigned value
Doses entry Manual/automatic	Variance Dropdown list/user-defined	Prediction Effective doses, inverse prediction
Statistical design Completely randomised Randomised block Latin square > show design	Fixed parameters Slope, addition, multiplication	Confidence level From 80% to 99%
Show design Plate layout, block structure	ANOVA No ANOVA to Complete ANOVA Equivalence of slopes/intercepts	Weight function Dropdown list/user-defined
Table of blank results Descriptive stat (mean, sd, rsd)	Parallel-line analysis Subset analysis (dose selection)	Combination of assay results Homogeneity of potency estimates weighted, semi-weighted, unweighted
		Template & protection Statistical report & audit trail

Confidence levels, correlation/determination coefficients

Results	Desktop	Online application
	(fixed)	(range)
Common slope or intercept	90%	95% (80%-99%)
Potency estimates	95%	95% (80%-99%)
Effective doses, predictions	95%	95% (80%-99%)
Equivalence - individual slopes or intercepts	95%	95% (80%-99%)
Equivalence - differences or ratios	90%	90% (fixed)
Combination of results	95%	95% (80%-99%)

Desktop version (90% conf. level)

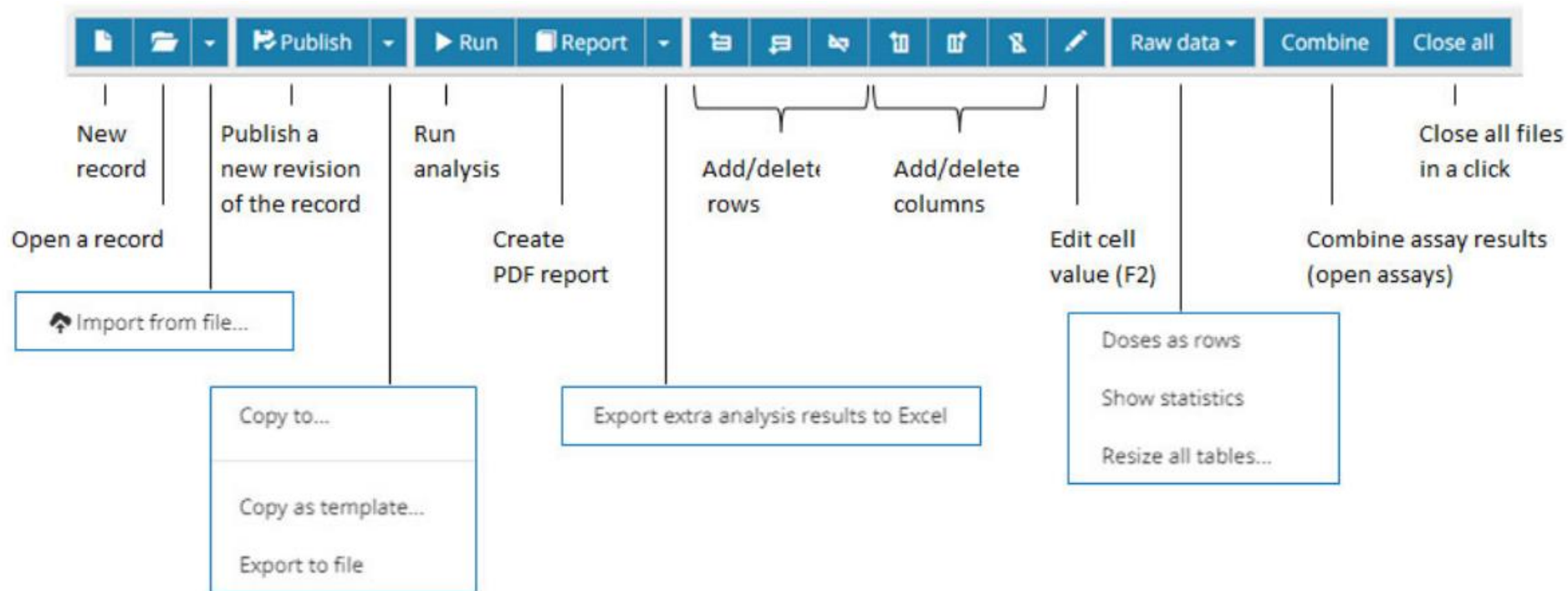
Common slope(factor): $b = -111.255$ (-115.612 to -106.898)
 Correlation | r |: 0.991424

Online application (95% conf. level)

Common Slope		R ² All	R ² Standard
Estimated value	-111.255		
Lower conf. Limit	-116.501		0.977164
Upper conf. Limit	-106.009		

95% confidence level

Taskbar and analysis options



Wizard

Assay
Multiple-dose

Type of design
Completely randomised

Response variable
Quantitative

Model
Sigmoid curves (4-PL, ln dose)

Transformation
No transformation: $y'=y$

Linearising transformation
Logit

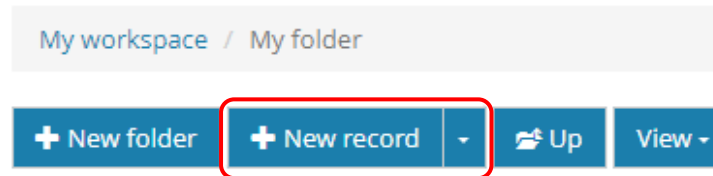
Variance
Observed residuals

Dose entry
Manual

Show design
Yes

Create a new record

1. Create a new record



Taskbar in editor



2. Enter the record type and name, select destination folder and assay set-up

New record

Type

Assay

Name

Assay1_4PL

To folder

David

Elena

My folder

Assay

Multiple-dose

Type of design

Completely randomised

Response variable

Quantitative

Model

Sigmoid curves (4-PL, In dose)

Preparations

2

Max doses

5

Max replicates

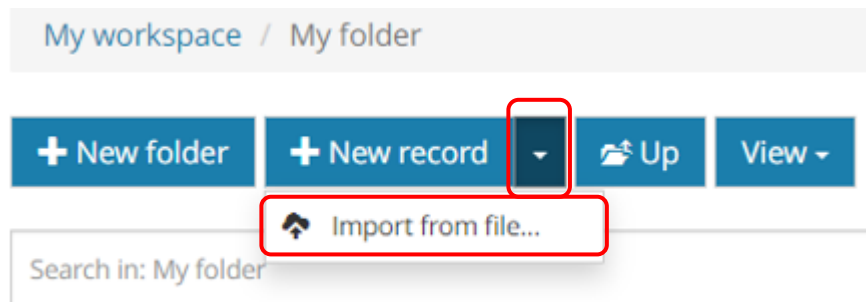
3

Cancel

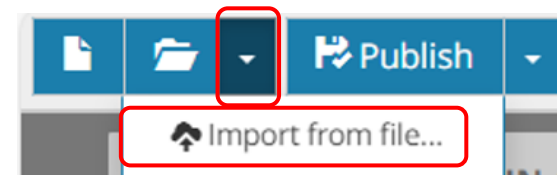
Create

Import a record

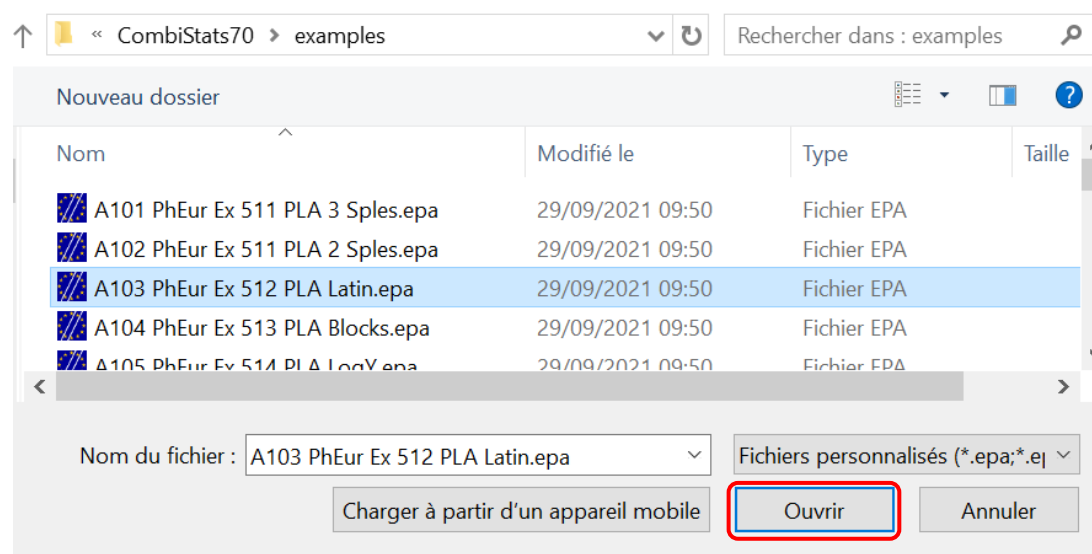
1. Import from file...



Taskbar in editor



2. Browse to and select the file you wish to import, then click on Open.



Data entry

Preparations

Table	Preparation	Information		Potency		Pre-dilution	
		ID	Long label	Potency	Value	Reconstitution	Stock solution
1	Standard ▾	S	standard	Assigned	100 IU/amp.	1 amp./mL	1 mL/10 mL
2	Sample 1 ▾	T	test sample	Assumed ▾	80 IU/vial	1 vial/0.5 mL	0.5 mL/5 mL
3	Sample 2 ▾	C1	Control 1	Assumed ▾	25 IU/mL		
4	Sample 3 ▾	C2	Control 2	Assumed ▾	120 IU/mL		

Observ.	c1	c2	c3	c4	c5	c6	c7	c8	c9	c10	c11	c12
r1												
r2	0.031	0.044	0.027	0.032	0.028	0.051	0.117	0.097	0.104	0.093	0.112	0.047
r3	0.046	2.912	2.579	2.130	1.651	1.073	0.585	0.463	0.266	0.228	0.176	0.031
r4	0.024	2.917	2.654	2.212	1.638	0.973	0.666	0.356	0.234	0.197	0.215	0.050
r5	0.030	3.017	2.801	2.401	1.918	1.364	0.861	0.497	0.340	0.242	0.178	0.035
r6	0.045	2.987	2.808	2.450	1.963	1.299	0.854	0.496	0.344	0.217	0.125	0.024
r7	0.051	2.105	2.074	2.162	1.948	2.037	1.974	1.925	2.017	2.106	1.938	0.038
r8												

Blank results

0.031	0.046	0.024	0.030	0.045	0.051
0.047	0.031	0.050	0.035	0.024	0.038

Mean *SD* *RSD%*
 0.038 0.010 26.2

<https://combistats.edqm.eu/help/>

Table 1					
Preparation	Standard				
ID	S				
Long label	standard				
Potency	Assigned				
Potency value	100 IU/amp.				
Reconstitution	1 amp./mL				
Stock solution	1 mL/10 mL				
Dose	Rep.1	Rep.2	Mean	SD	RSD%
1/1	2.912	2.917	2.914	0.004	0.1
1/2	2.579	2.654	2.617	0.053	2.0
1/4	2.130	2.212	2.171	0.058	2.7
1/8	1.651	1.638	1.644	0.009	0.6
1/16	1.073	0.973	1.023	0.071	6.9
1/32	0.585	0.666	0.626	0.057	9.2
1/64	0.463	0.356	0.410	0.076	18.5
1/128	0.266	0.234	0.250	0.023	9.1
1/256	0.228	0.197	0.213	0.022	10.3
1/512	0.176	0.215	0.196	0.028	14.1

EN01 Information And Remarks
 EN02 Taskbar
 EN05 Preparations Table
 EN06 Rawdata Tables
 EN07 Show Design
 EN08 Table of Blank Results

Data entry options

Wizard

Dose entry

Manual Manual
 Automatic

Show design

No No
 Yes

Show blank results

No No
 Yes

Taskbar

Raw data

Doses as rows

Show statistics

Resize all tables...

Show blank results

Yes

Number of rows

2

Number of columns

5

Blank results

0.031	0.046	0.024	0.030	0.045	0.051	
0.047	0.031	0.050	0.035	0.024	0.038	
						<i>Mean</i>
						<i>SD</i>
						<i>RSD%</i>
						0.038
						0.010
						26.2

Dose entry

Automatic

Highest dose

Last dose First dose Last dose

Dilution step

1.5

Dose	1/1	1/1.5 ¹	1/1.5 ²
Dose	1/1.5 ²	1/1.5 ¹	1/1

Dose entry

Automatic

Highest dose

Last dose First dose Last dose

Zero dose

Dose	2/2	1/2	0
Dose	0	1/2	2/2

Show design

Yes

Number of rows

8

Number of columns

12

Rawdata reference Table|Dose|Rep

Corresponding response

Design	c1	c2	c3	c4	c5	c6
r1	Pos	1 1 1	2 1 1			Neg
r2	Pos	1 2 1	2 2 1			Neg
Observ.	c1	c2	c3	c4	c5	c6
r1	2.222	2.879	3.025			0.125
r2		2.854	2.998			

Data analysis options

The list of the available Wizard and Advanced options depend on the Assay, Response variable and Model

For more details refer to <https://combistats.edqm.eu/help/>

EN03 Wizard Options
EN04 Advanced Options

Wizard

Assay

Multiple-dose

Type of design

Completely randomised

Response variable

Quantitative

Model

Sigmoid curves (4-PL, In dos

Transformation

No transformation: $y'=y$

Linearising transformation

Logit

Variance

Observed residuals

Advanced options

FIXED PARAMETER

Slope

Addition

Multiplication

PREDICTED VALUES

Effective dose

50 %

Reported as

Container / Effective Dose

Y values

You can specify up to 6 response values, separated by semicolons.

CONFIDENCE LEVELS

Slope / intercept

90 %

Potency / Effective dose / Inverse...

95 %

REGRESSION TYPE

Weighting

Unweighted regression

Maximum number of iterations

Summary statistics

Regression parameters

Global model: convergence reached

R² Standard: convergence reached

	weighted	unweighted
R ² All	0.991457	0.998112
R ² Standard	0.993511	0.998558

Common Slope

Estimated value	1.12452
Lower conf. Limit	1.08725
Upper conf. Limit	1.16179

95% confidence level

Other model parameters

Lower asymptote	0.145458
Upper asymptote	3.19599

Equivalence of slopes

Preparation	Slope	Difference with Standard	Ratio with Standard
Standard: S	1.12755 (1.07426, 1.18084)	0.000000	1.00000
Sample 1: T	1.12162 (1.06949, 1.17375)	-0.00593102 (-0.0684964, 0.0566344)	0.994740 (0.940903, 1.05171)

Slopes: confidence limits (in brackets) calculated for a 95% confidence level (advanced options).

Differences and ratios of slopes: confidence limits (in brackets) calculated for a 90% confidence level.

Anova table

Normal

Source of variation	Degrees of freedom	Sum of squares	Mean square	Chi-square	Probability	Level of significance
Preparations	3	0.813672	0.271224	301.79	< 0.000001	***
Regression	1	9.43054	9.43054	3497.77	< 0.000001	***
Non-parallelism	1	6.55525e-05	6.55525e-05	0.0243133	0.876090	
Non-linearity	16	0.0127084	0.000794275	4.71353	0.997004	
Non-linearity Table 1	8	0.00764179	0.000955224	2.83433	0.944320	
Non-linearity Table 2	8	0.00506661	0.000633326	1.8792	0.984494	
Treatments	21	10.257	0.488428	3804.3	< 0.000001	***
Residual error	28	0.0754923	0.00269615			
Total	49	10.3325	0.210867			

Potency and effective dose values

Precision Recovery

Potency estimates

Preparation	Units	Potency		Relative To Estimate (%)		Relative To Assumed/Assigned (%)	
		Estimate	(LCL, UCL)	Rel. To Est.	(LCL, UCL)	Rel. To Ass.	(LCL, UCL)
Sample 1: T	IU/vial	72.9429	(68.3897, 77.8023)	100	(93.76, 106.66)	91.18	(85.49, 97.25)
Sample 2: C1	IU/mL	21.5772	(20.0321, 23.2672)	100	(92.84, 107.83)	86.31	(80.13, 93.07)
Sample 3: C2	IU/mL	118.279	(109.978, 127.322)	100	(92.98, 107.65)	98.57	(91.65, 106.10)

Confidence limits (in brackets) calculated for a 95% confidence level (advanced options).

Effective dose estimates

Preparation	Units	Effective Dose (ED)		Relative To Estimate (%)	
		Estimate	(LCL, UCL)	Rel. To Est.	(LCL, UCL)
Standard: S	IU/ED50	1.34768	(1.28756, 1.41071)	100	(95.54, 104.68)
Sample 1: T	IU/ED50	1.47806	(1.41232, 1.54693)	100	(95.55, 104.66)
Sample 2: C1	IU/ED50	1.56146	(1.47123, 1.65552)	100	(94.22, 106.02)
Sample 3: C2	IU/ED50	1.36729	(1.29102, 1.44685)	100	(94.42, 105.82)

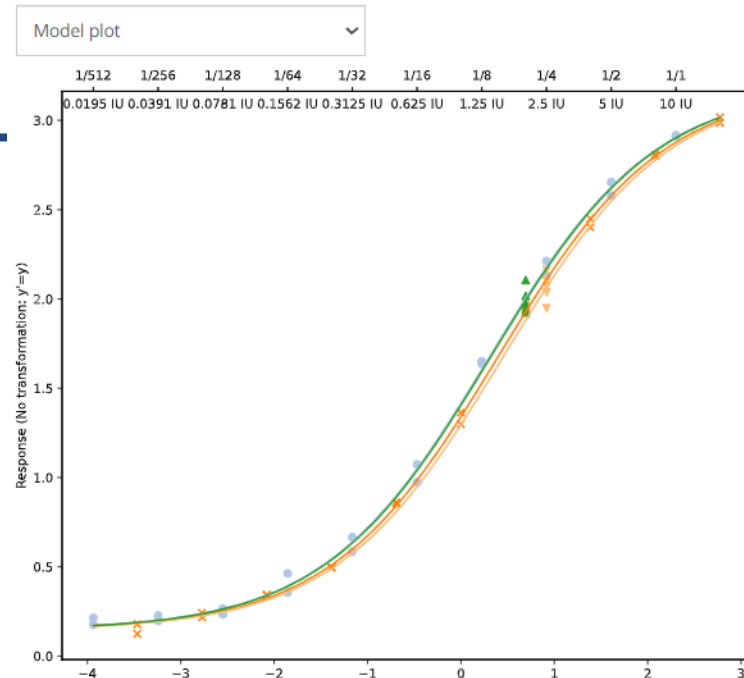
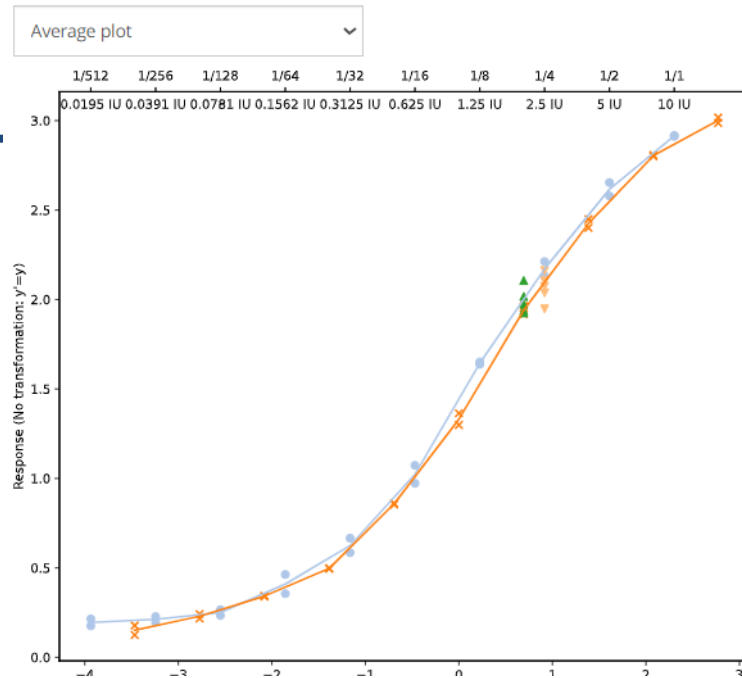
Confidence limits (in brackets) calculated for a 95% confidence level (advanced options).

Inverse predictions

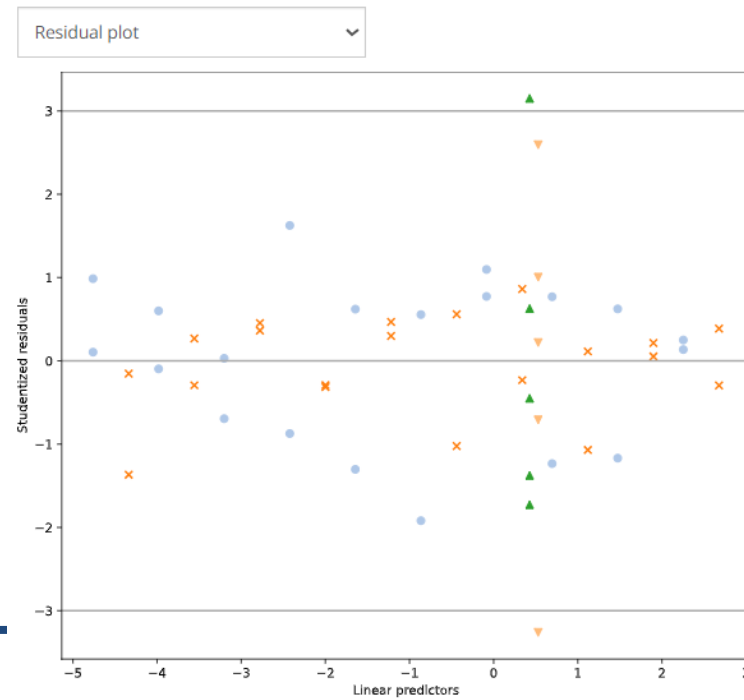
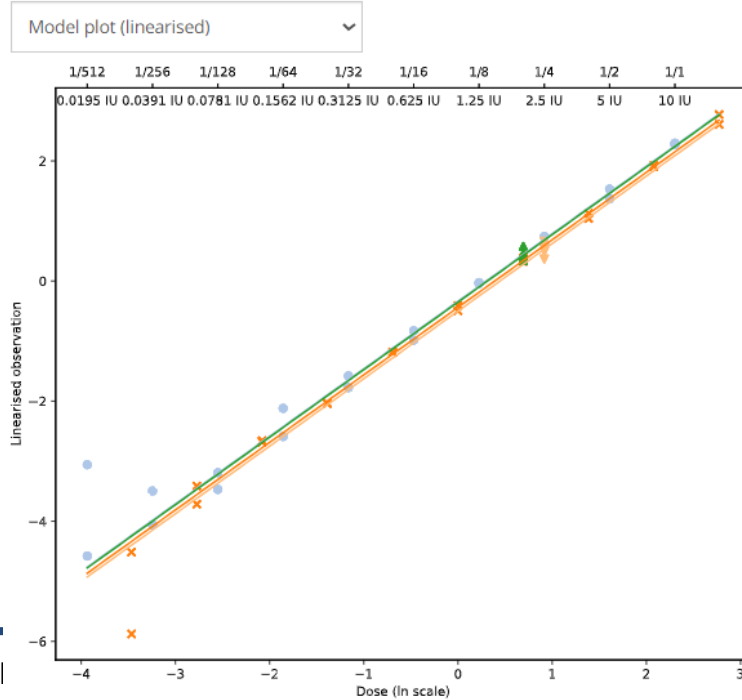
Preparation	Units	y-value(s)			
		1		1.5	
		Estimate	(LCL, UCL)	Estimate	(LCL, UCL)
Standard: S	IU	0.582207	(0.551716, 0.613296)	1.10348	(1.05369, 1.15521)
Sample 1: T	IU	0.638534	(0.604979, 0.672733)	1.21024	(1.15569, 1.26686)
Sample 2: C1	IU	0.674564	(0.627048, 0.723594)	1.27853	(1.20187, 1.35809)
Sample 3: C2	IU	0.590679	(0.550703, 0.631861)	1.11954	(1.05493, 1.18659)

Confidence limits (in brackets) calculated for a 95% confidence level (advanced options).

Graphics



- Standard: S
- Sample 1: T
- Sample 2: C1
- Sample 3: C2



- Standard: S
- Sample 1: T
- Sample 2: C1
- Sample 3: C2

- Wizard
- Advanced options
- Graphics
- Revisions

Each time the assay is published a new version is created and differences to previous published version are recorded

User can add a comment and protect the sheet

Meta-data for each version: date, GMT time and username

Publish a new version

Comment

this is a copy

Publish in read-only mode, the sheet can no longer be modified.

Publish Cancel

- v6 (Current) - 12/11/2024 at 18:08:59 - ELENA REGOURD**
No description
- v5 - 12/11/2024 at 18:08:49 - ELENA REGOURD**
No description
- v4 - 12/11/2024 at 18:03:40 - ELENA REGOURD**
Copy from "Test2 - v3 - 12/11/2024 17:58:09"
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- v3 - 12/11/2024 at 17:58:09 - ELENA REGOURD**
Restored from v1
No description
- v2 - 12/11/2024 at 17:57:34 - ELENA REGOURD**
No description
- v1 - 12/11/2024 at 17:57:05 - ELENA REGOURD**
No description

The modifications and comments for each version

- displayed in the report
- can be accessed by clicking in the version in the revisions section

V.4 (CURRENT) - PUBLISHED ON 12/11/2024 AT 18:03 BY ELENA REGOURD

Copy from "Test2 - v3 - 12/11/2024 17:58:09"
this is a copy

Field	Old value	New value
Wizard		
Transformation	y'=y	y'=sqrt(y)
Variance	Observed residuals	Deviation from model
Raw-data		
Table 1		
	Dose 1/30 Rep.5 176	Dose 1/30 Rep.5 400

Content

- Introduction
- Workspace
- File and folder management
- Data entry, analysis options & audit trail
- Batch creating .epax files

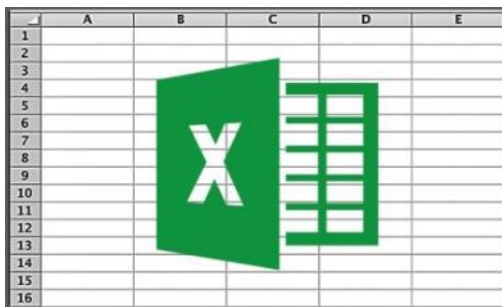
How to automate data entry into .epax files?

E.g.

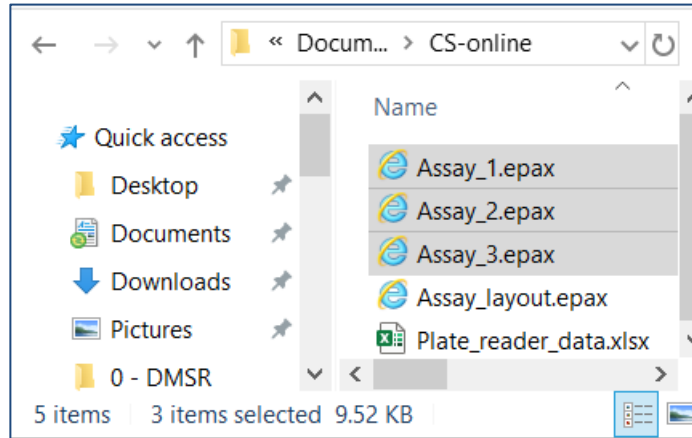
1. Microplate reader



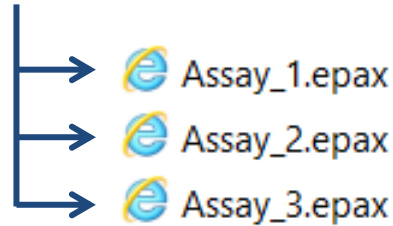
2. Plate_reader_data.xlsx



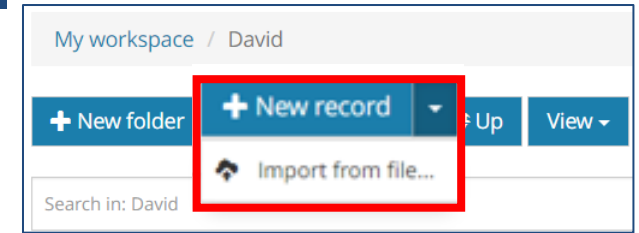
3.



Assay_layout.epax



4.



<input type="checkbox"/>	Type	Name	Created
<input type="checkbox"/>		Assay_1	today
<input type="checkbox"/>		Assay_2	today
<input type="checkbox"/>		Assay_3	today

[→ See demo](#)

Useful links

- Institutional website

<https://www.edqm.eu/en/lp-combistats>

- FAQs, privacy, security notices

<https://combistats.edqm.eu/help/>

- User guide (sign in first)

https://combistats.edqm.eu/user-manuals/combistats_user_guide.pdf/



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