

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



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# CombiStats online Training module 1

## Introduction to the online application

# Content

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- 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.

1. introduction
2. randomisation and independence of individual treatments
3. assays depending upon **quantitative responses**
  - 3.2. the parallel-line model
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  - 3.4. extended sigmoid dose-response curves
4. assays depending upon **quantal responses**
  - 4.2. the probit method
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  - 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

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- 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

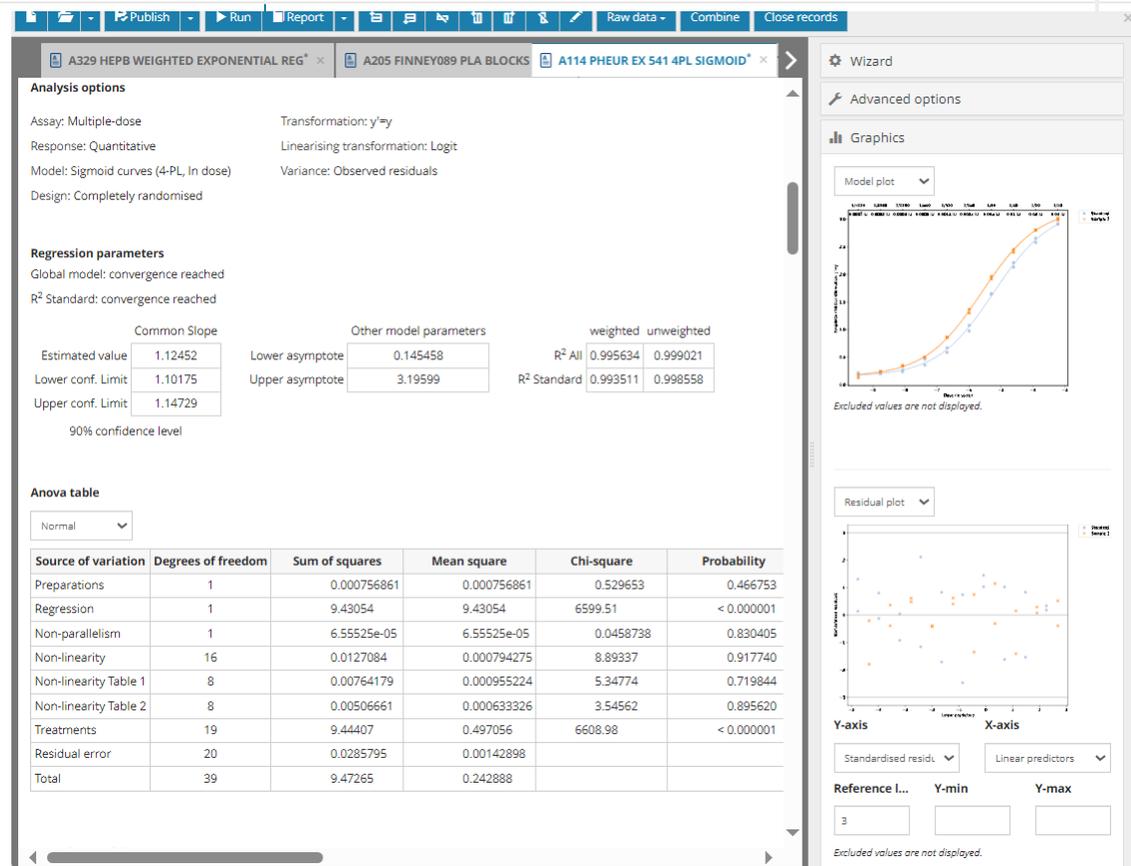
## Dedicated workspace for your organisation

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

## Modern & interactive interface

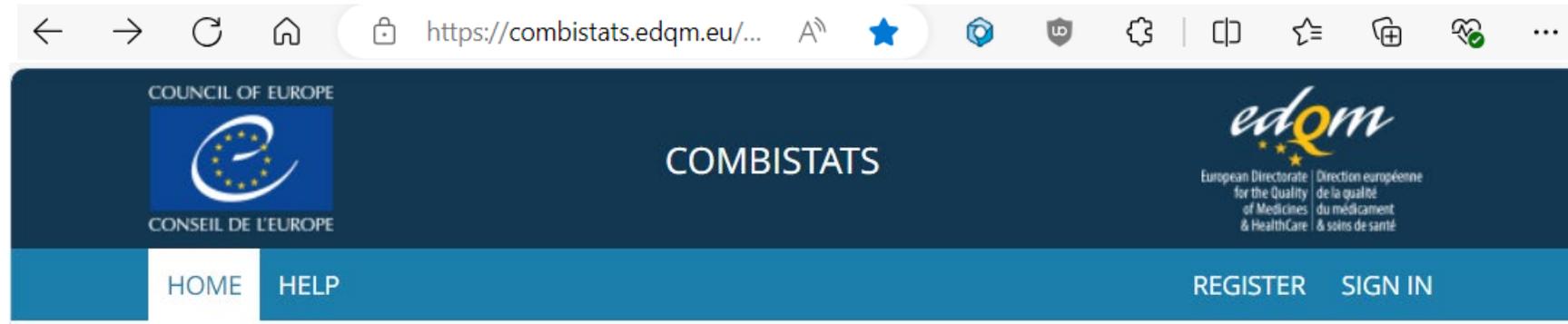
- Better flow of analysis options
- Enhanced graphical views
- Information and error messages
- Template, file protection
- PDF report, audit trail

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 11 



# Notes for guidance in free access

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



## 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

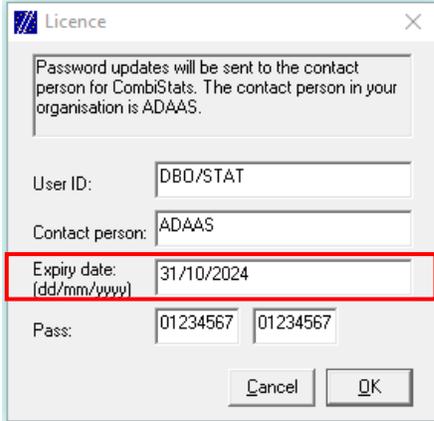
## Technical requirements

- 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



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](mailto:Sales@edqm.eu) <[Sales@edqm.eu](mailto: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,

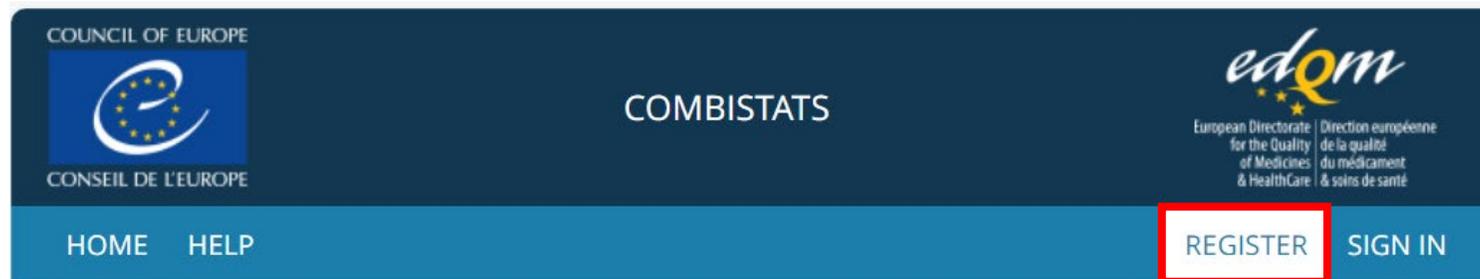
The EDQM Sales Section

# Content

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- 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](mailto: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
<input checked="" type="checkbox"/> EUROPEAN PHARMACOPOEIA 11th EDITION
<input type="checkbox"/> BIOLOGICAL STANDARDISATION PROGRAMME
<input type="checkbox"/> BLOOD TRANSFUSION
<input type="checkbox"/> COSMETICS
<input type="checkbox"/> COUNTERFEIT MEDICINES AND SIMILAR CRIMES
<input type="checkbox"/> FOOD CONTACT
<input type="checkbox"/> ORGANS, TISSUES AND CELLS
<input type="checkbox"/> PHARMACEUTICAL CARE
<input type="checkbox"/> QUALITY MANAGEMENT FOR BLOOD ESTABLISHMENTS
<input type="checkbox"/> TATTOOS AND PERMANENT MAKE-UP
<input checked="" type="checkbox"/> <b>CombiStats</b>

## 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	
<b>CombiStats licence</b>	<b>600.00 EUR</b>	1 <input type="text"/> PCE 	
<b>CombiStats licence - Extension</b>	<b>600.00 EUR</b>	1 <input type="text"/> PCE 	

**Enter the number of seats (users) here.**

# Example

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

Name	Price	Quantity	
<b>Combistats licence</b>	600.00 EUR	<input type="text" value="2"/> PCE	
<b>Combistats licence - Seat Extension</b>	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	
<b>Combistats licence</b>	600.00 EUR	<input type="text" value="0"/> PCE	
<b>Combistats licence - Seat Extension</b>	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	
<b>Combistats licence</b>	600.00 EUR	<input type="text" value="3"/> PCE	
<b>Combistats licence - Seat Extension</b>	600.00 EUR	<input type="text" value="0"/> PCE	

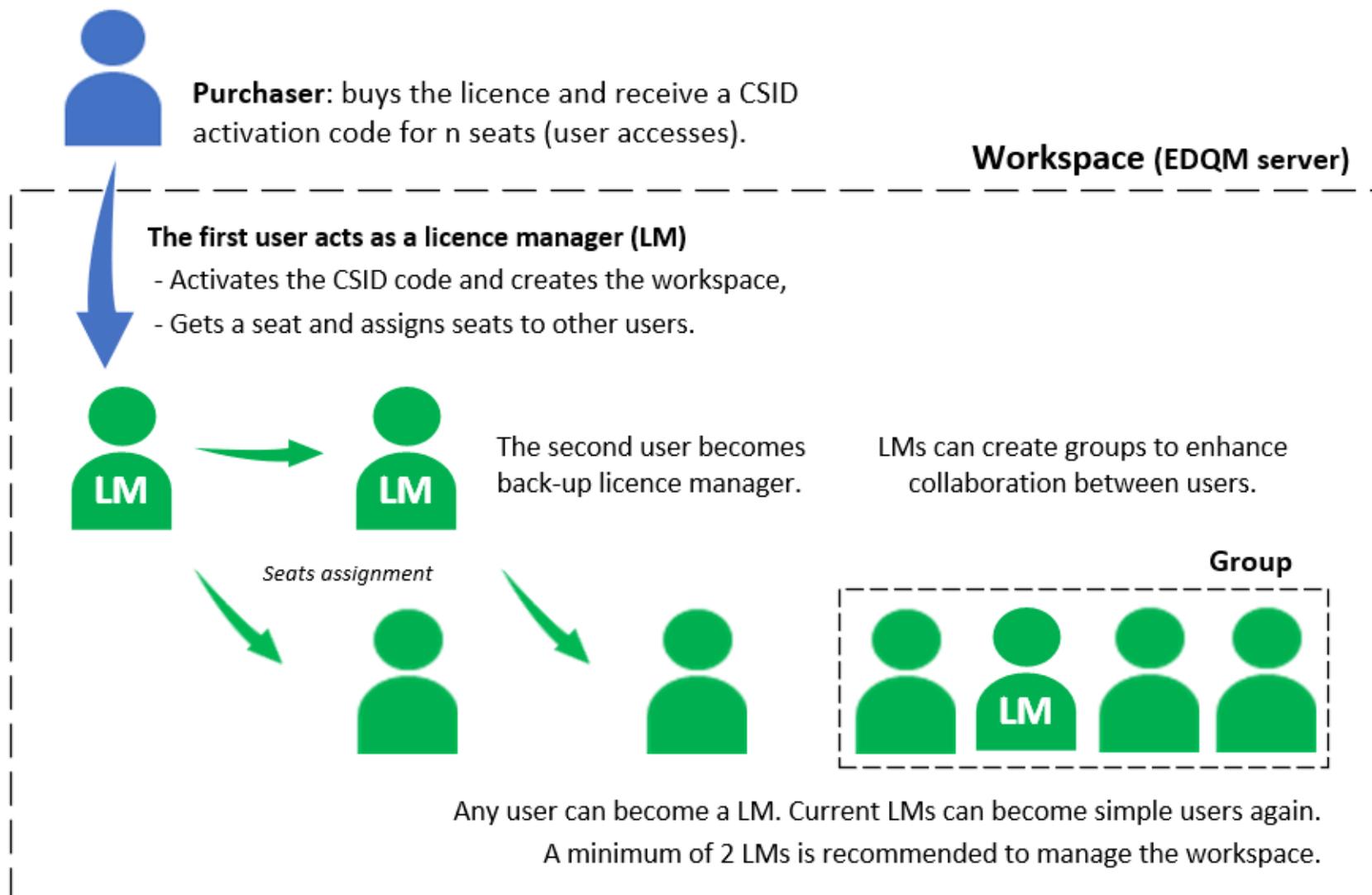
CSID code to activate the workspace

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 sub-heading '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](mailto:Sales@edqm.eu) <[Sales@edqm.eu](mailto: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	<a href="#">user1@CS.org</a>
2	<a href="#">user2@CS.org</a>
3	<a href="#">user3@CS.org</a>
4	...

You can download a template to fill in here

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

# Licence manager (LM role)

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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>



Order Combistats

To place an order, visit our online store at [www.edqm.eu/store](http://www.edqm.eu/store) or send your order to [orders@edqm.eu](mailto:orders@edqm.eu)

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\*:

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.*

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

Renewal after expiry still possible

#### RENEW ACCESS

Licence key (CSID)\*:

Renew

*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](#)

### Registration

First name\*

Last name\*

Professional organisation\*

Country (of organisation)\*

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

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



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

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

# Remarks

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- 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

## 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.

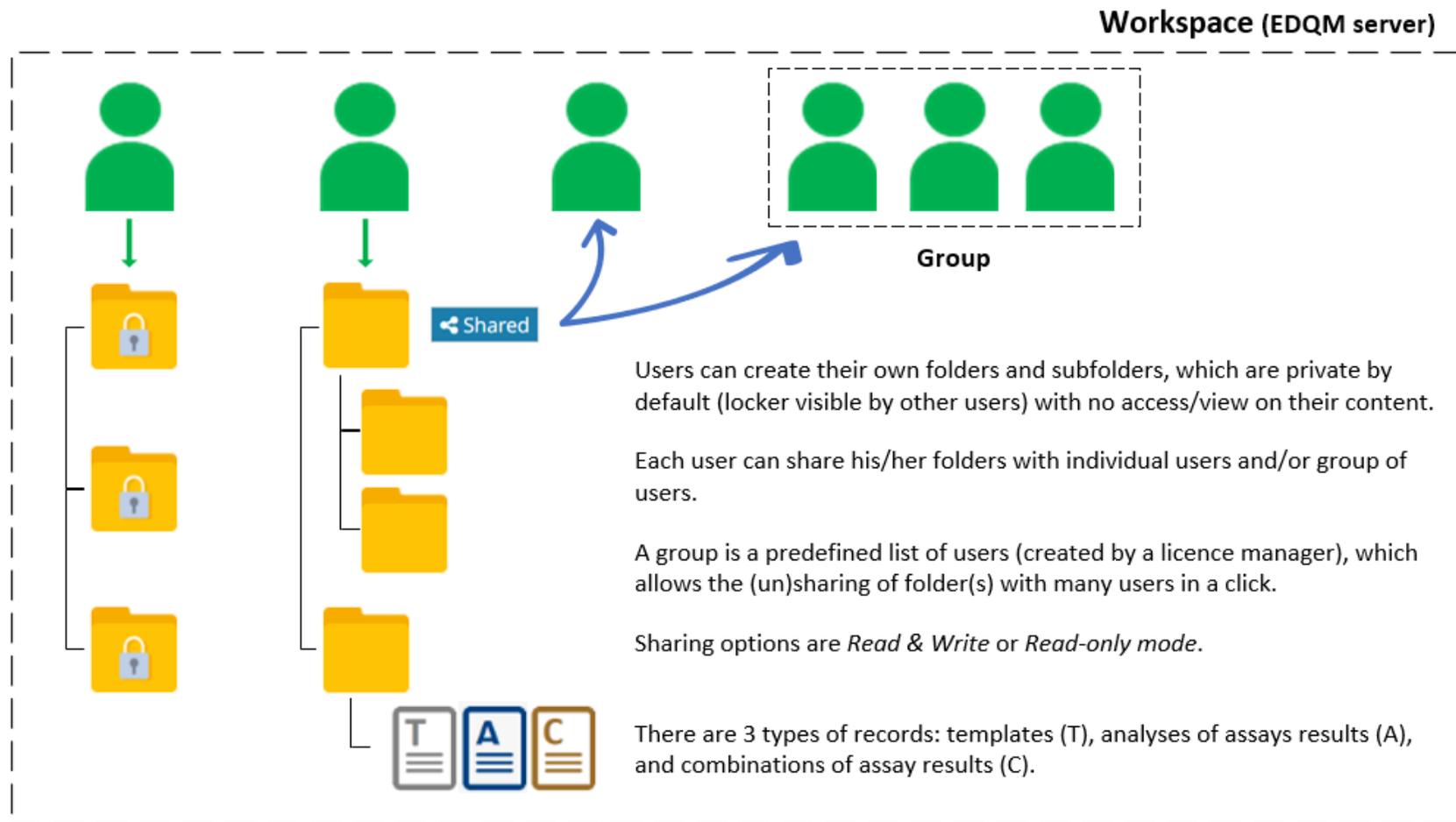
<https://combistats.edqm.eu/faq/link/87/>

# Content

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

# 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)



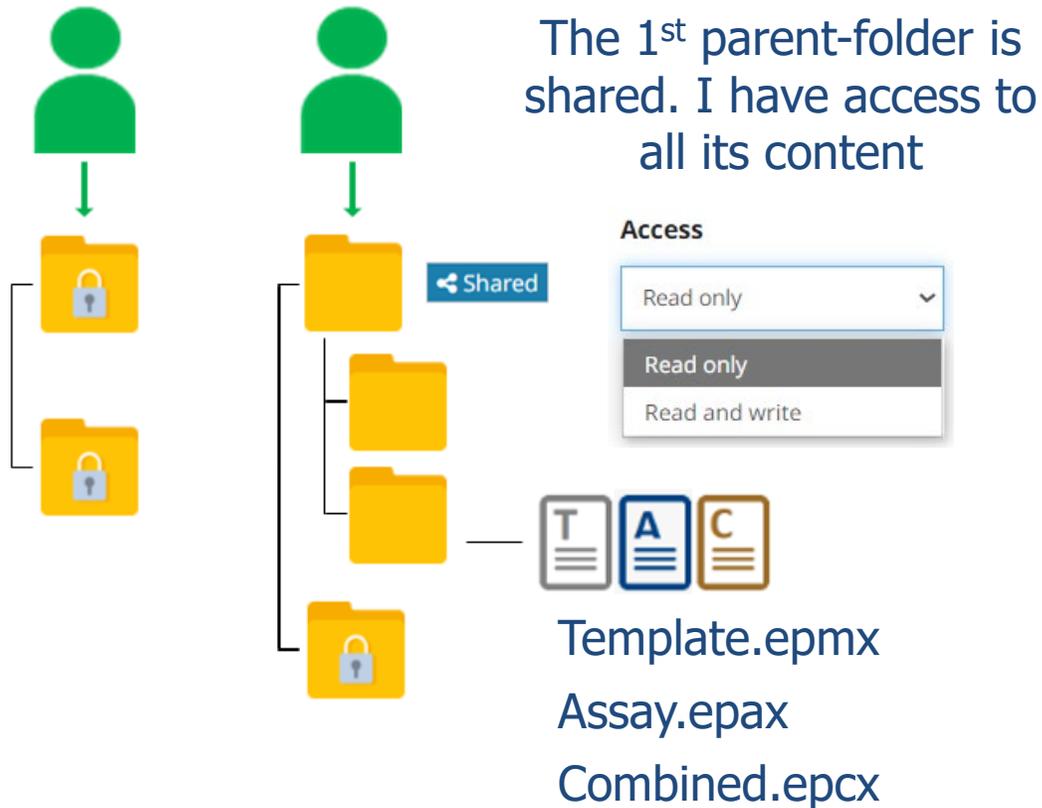
Analysis, combination reports as PDF.



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

# Content

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- Introduction
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# Features

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

# 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)

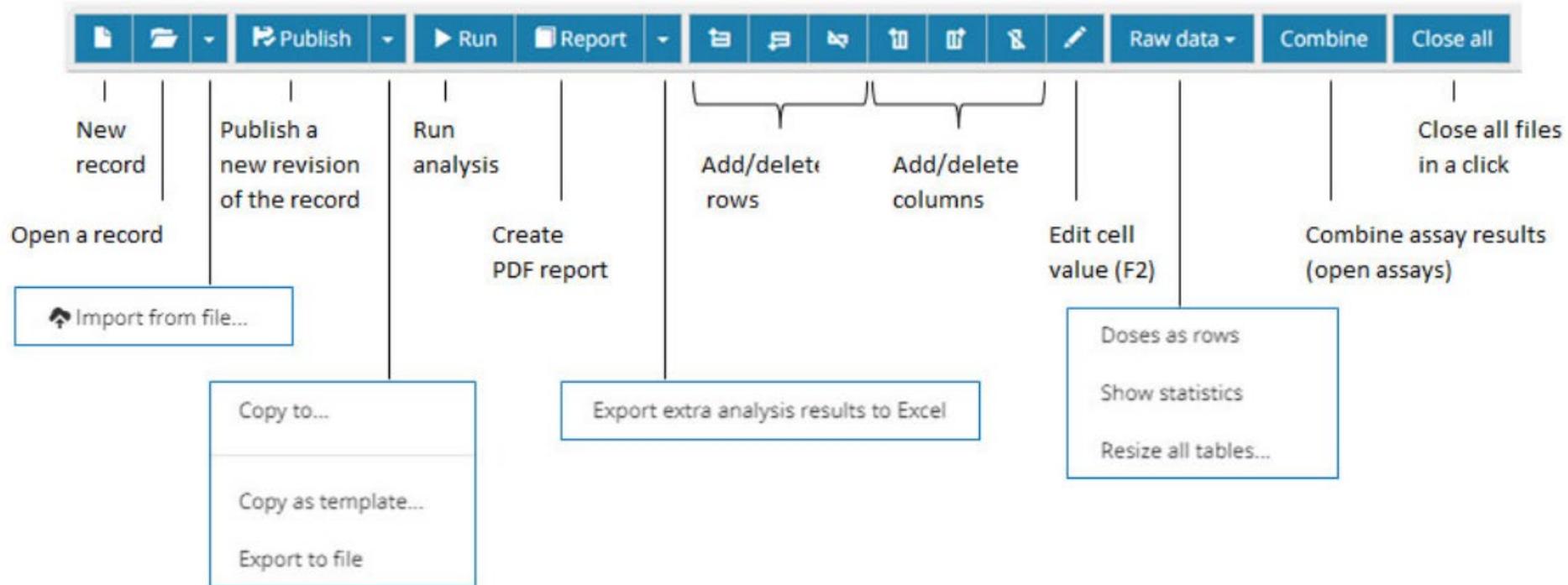
Common slope(factor):  $b = -111.255$  (-115.612 to -106.898)  
 Correlation | r |: 0.991424

## Online application (95% conf. level)

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

95% confidence level

# Taskbar and analysis options

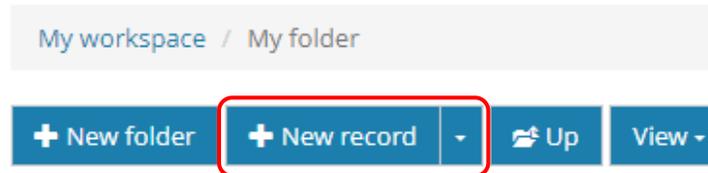


The Wizard configuration panel is a vertical sidebar on the right side of the interface. It contains several sections, each with a dropdown menu for configuration. The sections are:

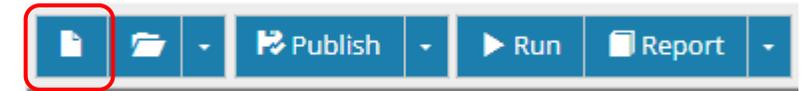
- Assay:** Multiple-dose
- Type of design:** Completely randomised
- Response variable:** Quantitative
- Model:** Sigmoid curves (4-PL, ln dose)
- Transformation:** No transformation:  $y'=y$
- Linearising transformation:** Logit
- Variance:** Observed residuals
- Dose entry:** Manual
- Show design:** 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

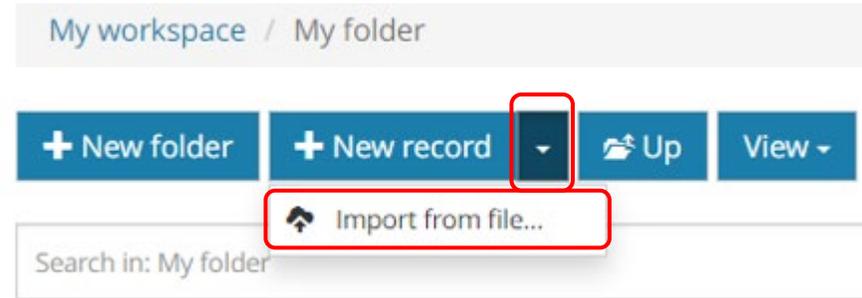
3

Cancel

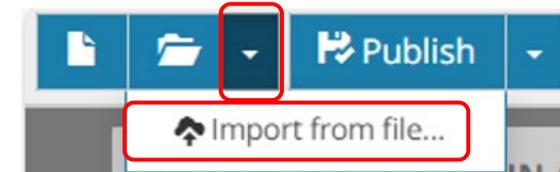
Create

# Import a record

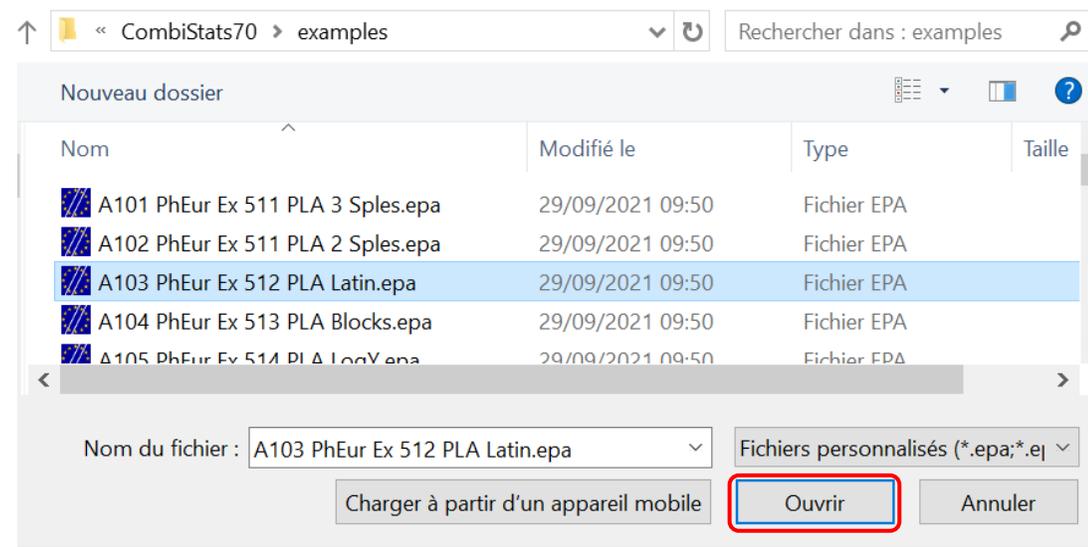
## 1. Import from file...



## 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  Automatic

**Show design**

No  Yes

**Show blank results**

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

Mean SD RSD%

0.038 0.010 26.2

**Dose entry**

Automatic

**Highest dose**

Last dose  First dose

**Dilution step**

1.5

Dose	1/1	1/1.5 <sup>1</sup>	1/1.5 <sup>2</sup>
Dose	1/1.5 <sup>2</sup>	1/1.5 <sup>1</sup>	1/1

**Dose entry**

Automatic

**Highest dose**

Last dose  First 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

R<sup>2</sup> Standard: convergence reached

	weighted	unweighted
R <sup>2</sup> All	0.991457	0.998112
R <sup>2</sup> 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

## Anova table

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			

## 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.

# Potency and effective dose values

Potency estimates		Potency		Precision		Recovery	
		Estimate	(LCL, UCL)	Rel. To Est.	(LCL, UCL)	Rel. To Ass.	(LCL, UCL)
Preparation	Units	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)

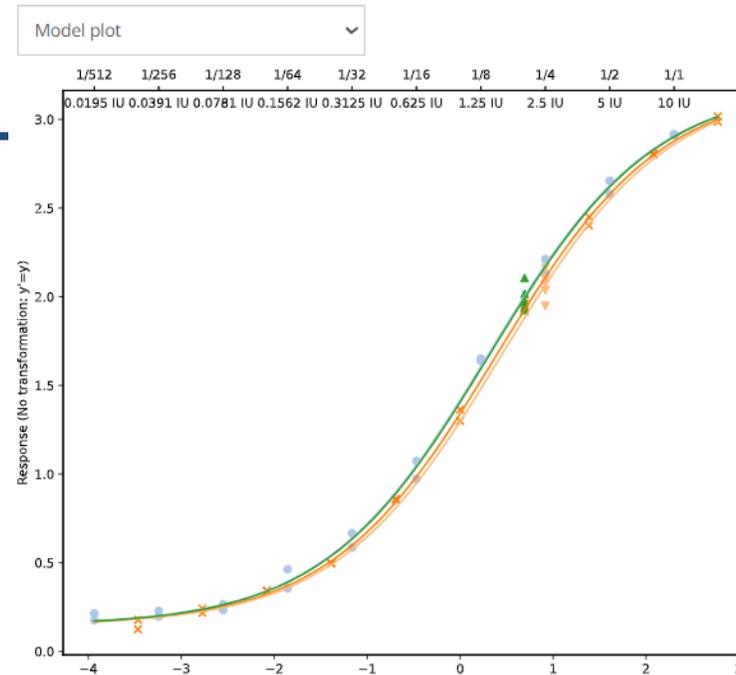
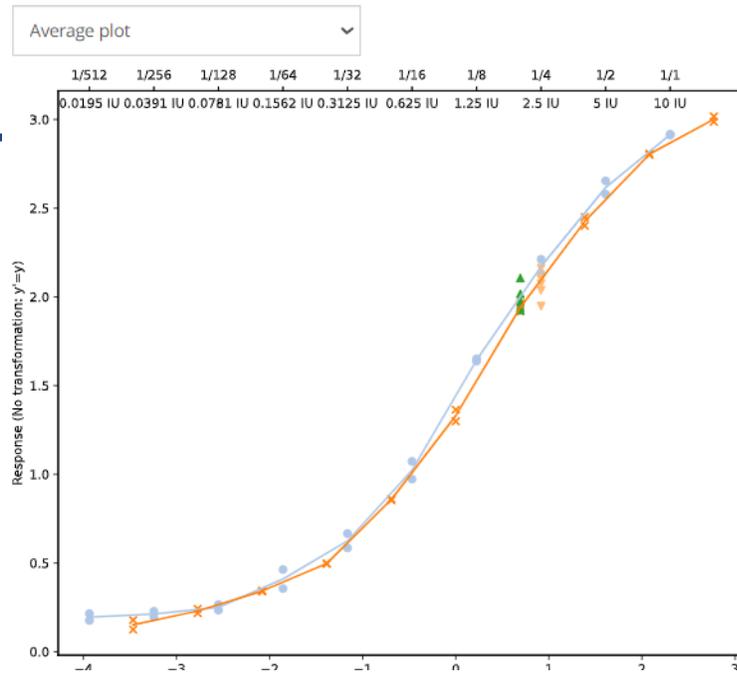
Confidence limits (in brackets) calculated for a 95% confidence level (advanced options).

## Inverse predictions

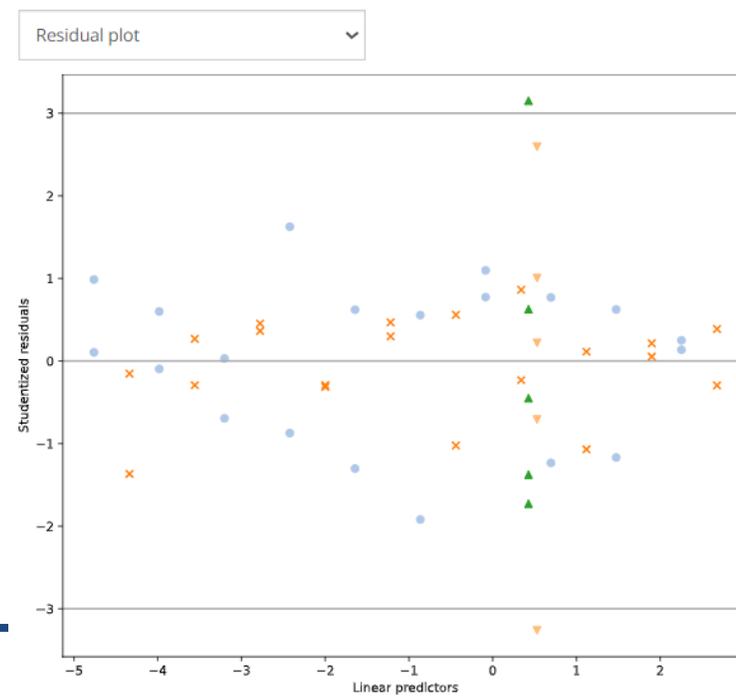
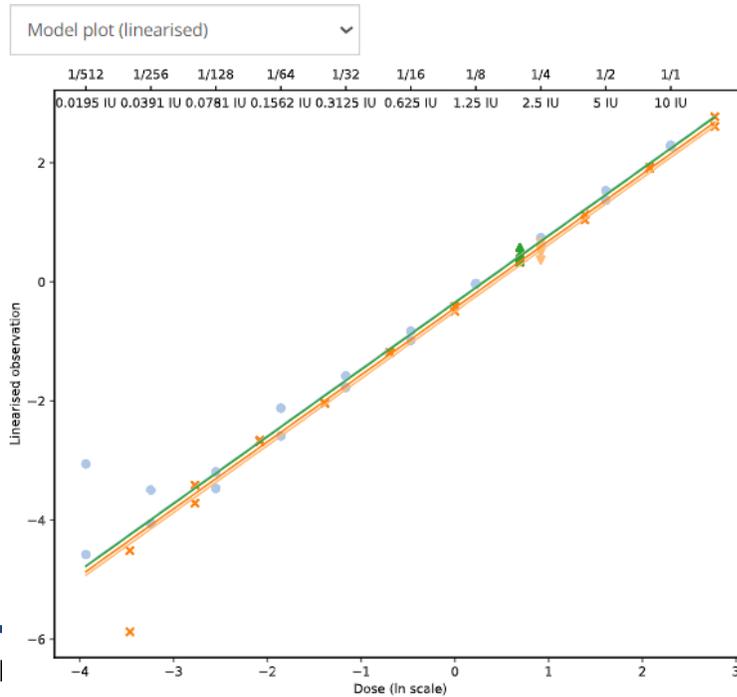
Preparation	Units	Estimate	y-value(s)		
			1	1.5	
Preparation	Units	Estimate	(LCL, UCL)	Estimate	(LCL, UCL)
Standard: S	IU	0.582207	(0.551716, 0.613296)	1.10348	(1.05369, 1.15521)
Sample 1: T	IU	0.638534	(0.604979, 0.672733)	1.21024	(1.15569, 1.26686)
Sample 2: C1	IU	0.674564	(0.627048, 0.723594)	1.27853	(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"  
this is a copy
- 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

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

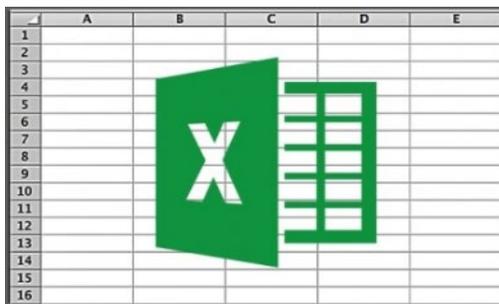
# How to automate data entry into .epax files?

E.g.

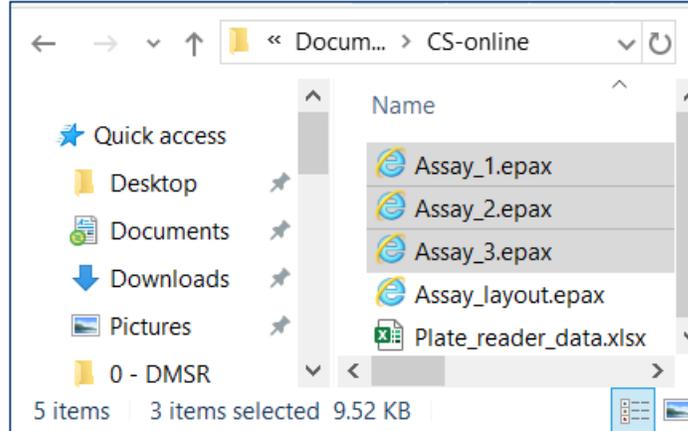
## 1. Microplate reader



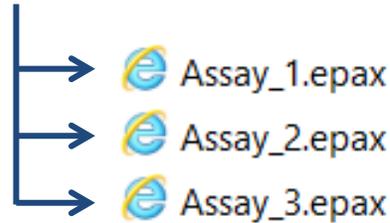
## 2. Plate\_reader\_data.xlsx



## 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

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



