

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



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# Presentation of the CombiStats Online Application



## Webinar 3 July 2024

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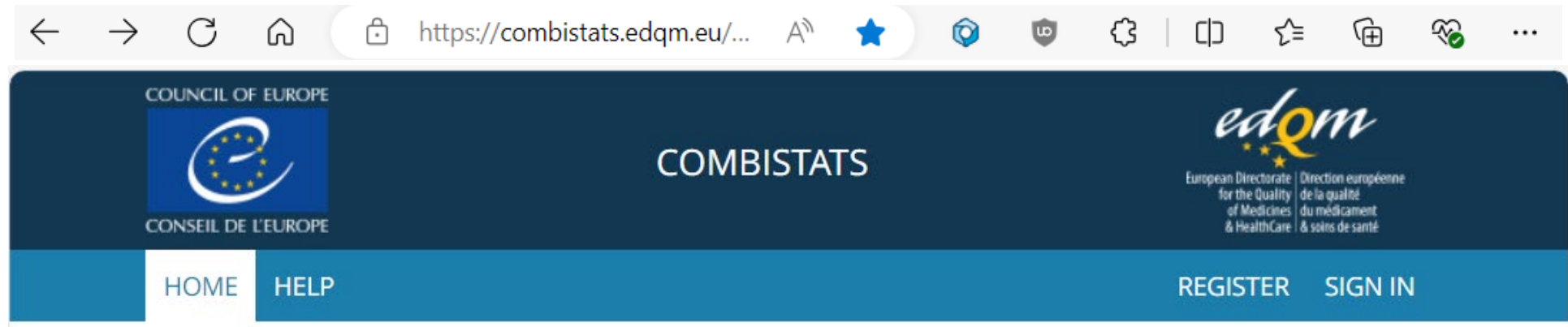
# The CombiStats Software – Desktop

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- Statistical analysis of data of biological dilution assays in accordance with Ph. Eur. Chapter 5.3
- First release in 1999 to OMCLs, in 2005 to non-OMCLs
- Used by 394 organisations (960 licences) worldwide in 2023
- Users' expectations (top 3)
  - Audit trail
  - Login/password (user identification)
  - More interactivity (e.g. information/error messages)

# CombiStats Online Application

- Go live: July 2024
  - Meet user's expectations, offering a new & interactive interface
  - Build a sustainable tool using a modern programming language



## 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

# CombiStats Online Application

## Flexible licence management system

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

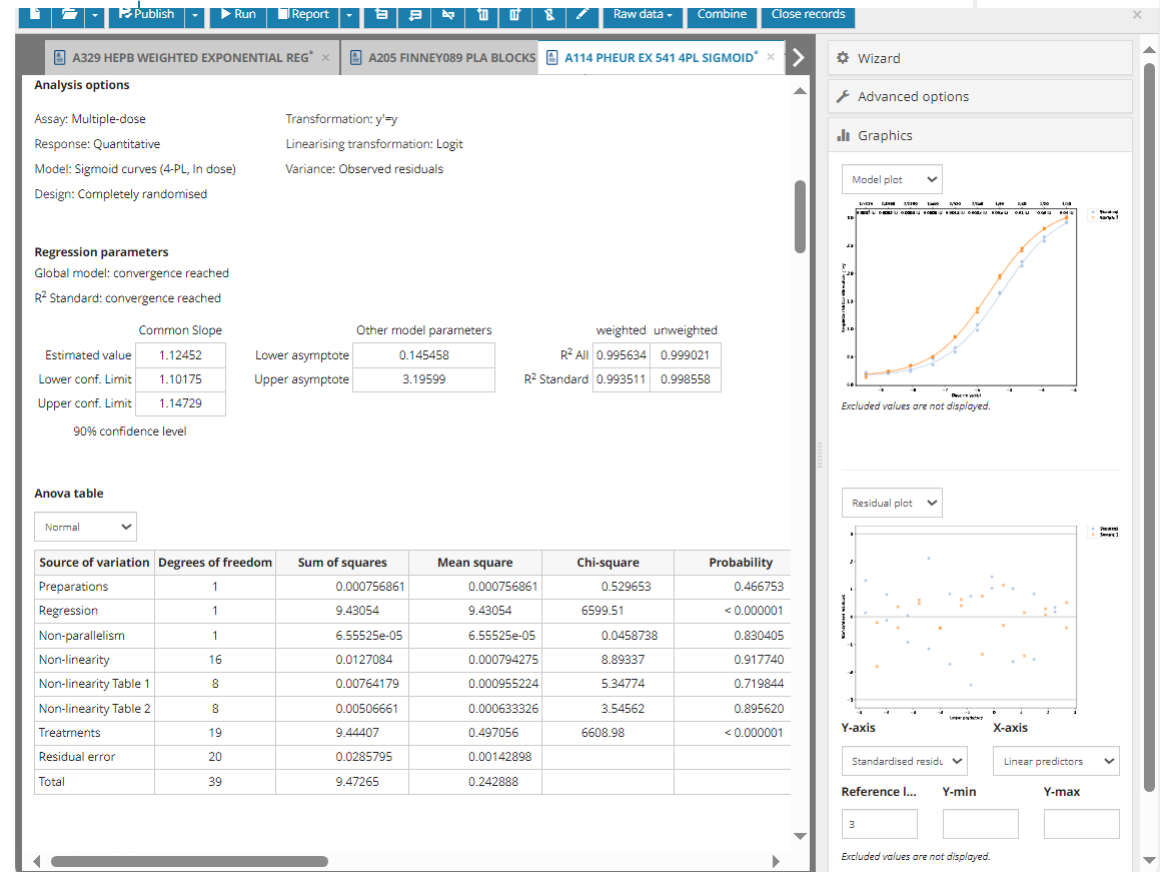
## Dedicated workspace for your organisation

- 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

<input type="checkbox"/>	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	



# Statistical Design & Analysis

## Desktop options (wizard & advanced)

### Size of tables

Number of tables, info. Lines  
Number of pre-dilutions  
Number of doses, replicates

### Orientation of tables

Doses vertical/horizontal

### Doses notation

Explicit/Implicit

### Design

Completely randomised  
Randomised block  
Latin square > show design

### ANOVA

No ANOVA to Complete  
Equivalence

### Model

Parallel lines, Slope ratio  
3-parameter exponential curves  
4- & 5-parameter sigmoid curves  
Single-dose assay  
Spearman-Kaerber approach

### Transformation

Dropdown list/user-defined

### Variance

Dropdown list/user-defined

### Fixed parameters

slope, addition, multiplication

### Prediction

Effective doses, inverse prediction

### Weight function

Table of blank results (+ stats)  
Multiple-dose (standard only) model  
Subset analysis (PLA)  
Confidence level: 80 to 99%  
Plot of linearised data/reg. lines  
Plot of studentised residuals  
PDF 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				
Estimated value	-111.255	R <sup>2</sup> All	0.982922	
Lower conf. Limit	-116.501		R <sup>2</sup> Standard	0.977164
Upper conf. Limit	-106.009			

95% confidence level



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# How to create your user account


 Sign in

Continue



[Forgot your password?](#)

# Create your account

COUNCIL OF EUROPE  
  
CONSEIL DE L'EUROPE

COMBISTATS

  
European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé


HOME HELP REGISTER SIGN IN

## 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.

# Validate your account

- 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.

- Enter 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\*

- Log in to finalise the activation

## One last step

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

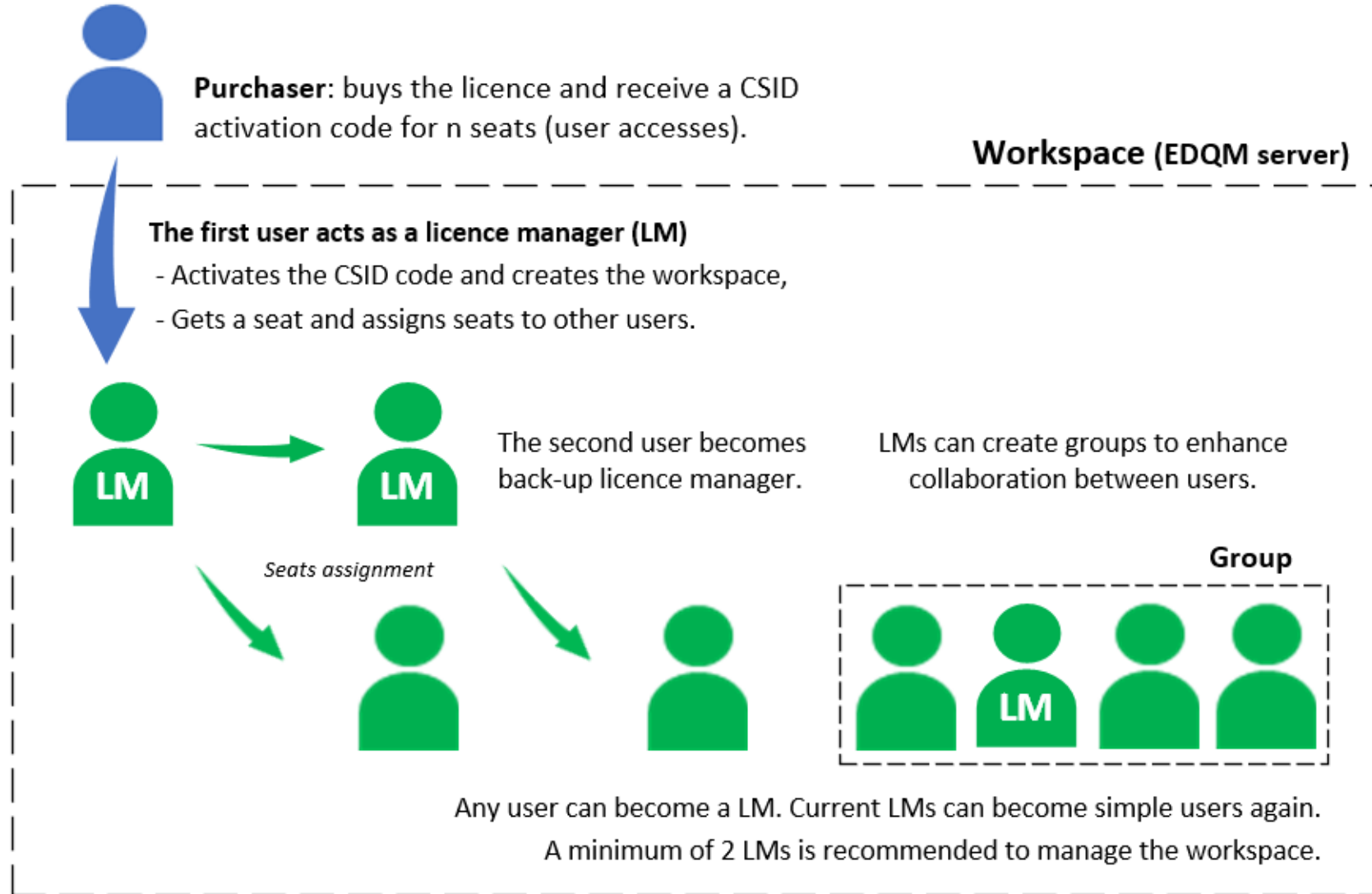
Sign In

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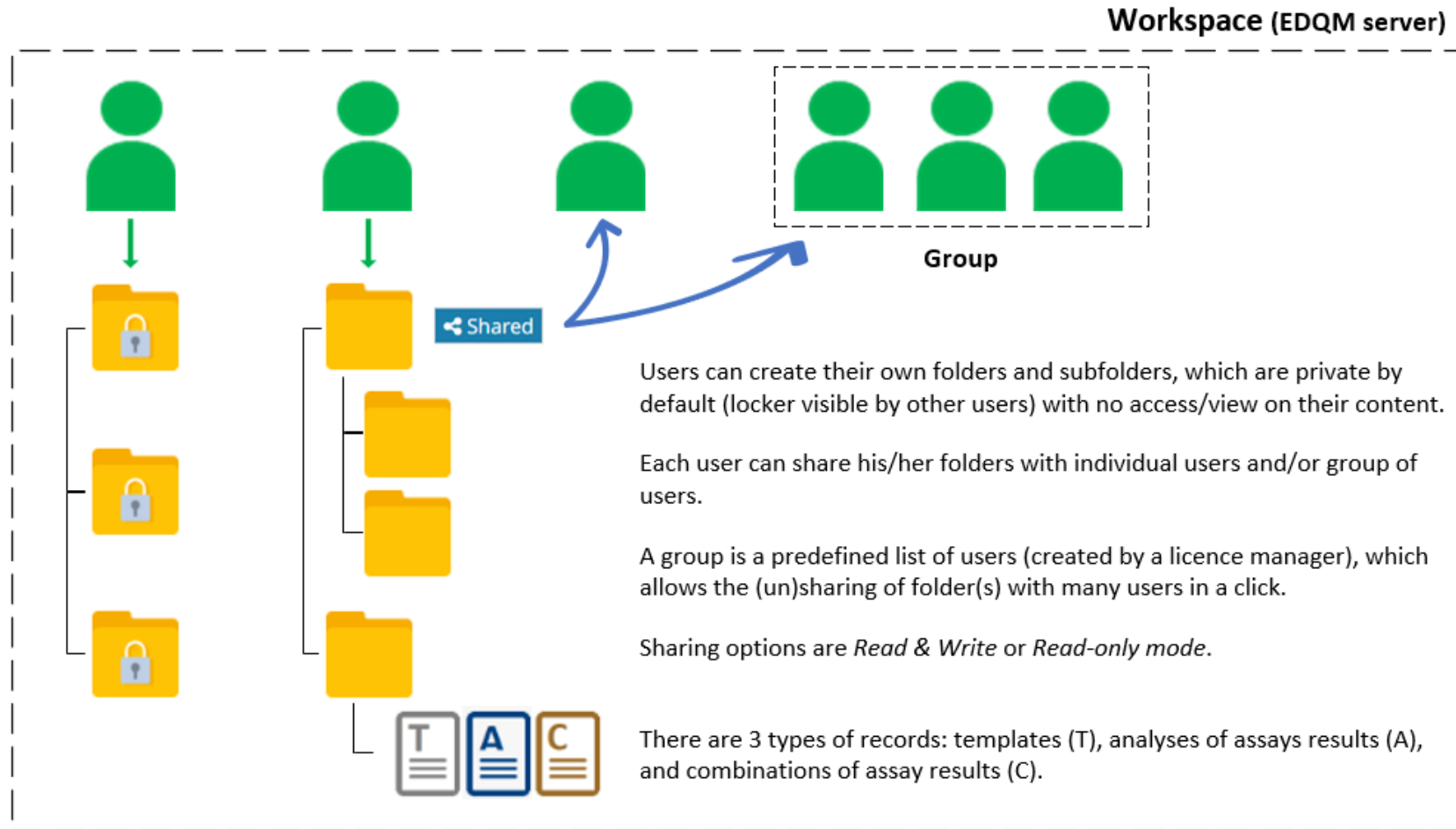
# The Workspace

Secure & collaborative  
working environment

# Workspace activation



# Collaborative environment



## Actions

Create

Search, rename

Copy, move to

Export (zip file) / import

Add to my Favourites

Share (read-only or read and 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.

# Ordering: CSID code for n seats (users)

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**From:** [Sales@edqm.eu](mailto:Sales@edqm.eu) <[Sales@edqm.eu](mailto:Sales@edqm.eu)>

**Subject:** CombiStats - Order 000000

Your CombiStats licence - Your order YYYYYY - Our order confirmation OOOOOO

DO NOT REPLY TO THIS MESSAGE

Dear Customer,

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

**COMBISTATS: STATISTICAL ANALYSIS OF DATA: access for N user(s)**

**CSID-AAAAA-BBBBBBBBBB-CCCCC-DDDD**

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

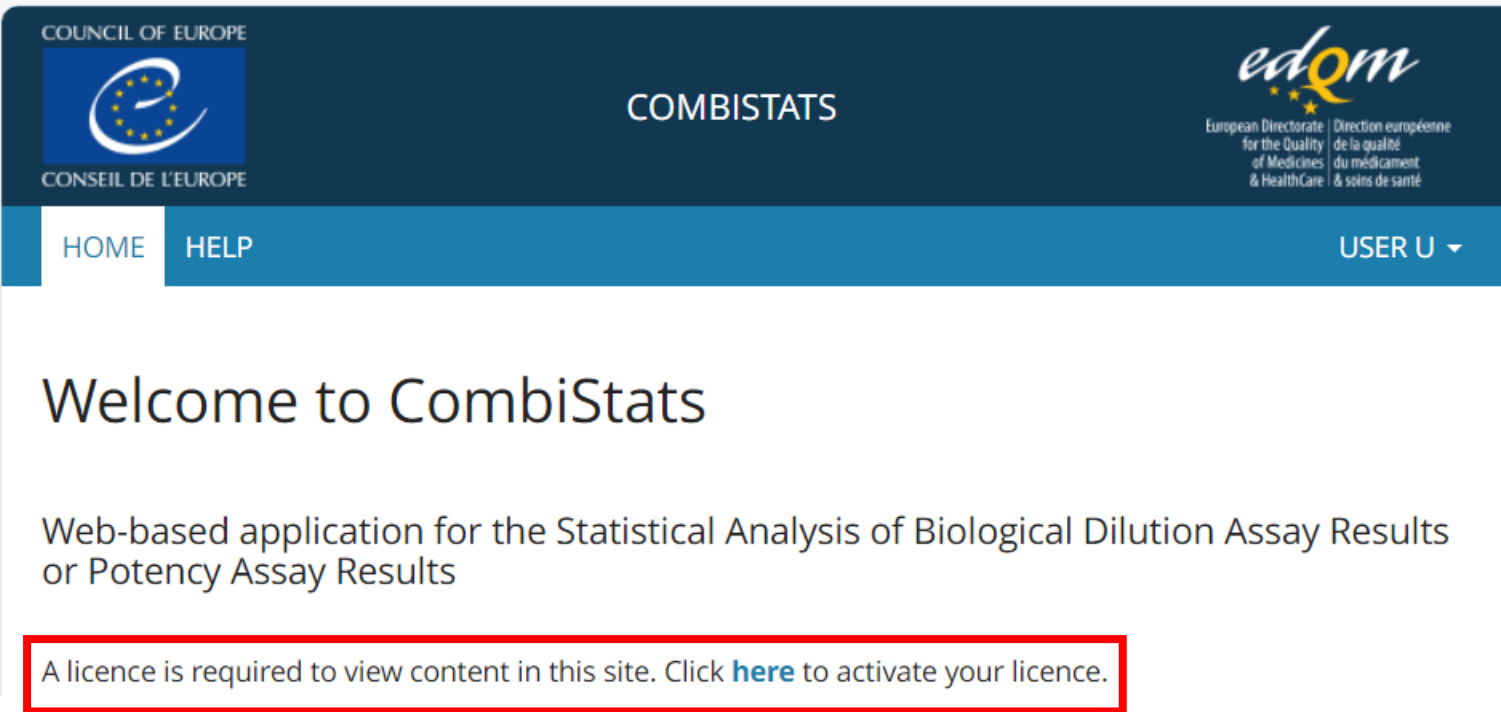
If applicable, please forward this message to the person responsible for managing CombiStats licences within your organisation.

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

Kind regards,

The EDQM Sales Section

# 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 text 'COMBISTATS' is centered in the header. Below the header, there are navigation links for 'HOME' and 'HELP', and a user profile indicator 'USER U' with a dropdown arrow. The main content area features a large heading 'Welcome to CombiStats' and 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.'

## 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



# Users' access management

## LICENCE

Workspace ID: 5BNDLNKJ

Number of access: 4 assigned - 3 available

Expiration date: 01 July, 2025

## 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 single user

Can manage

Assign single

Choose file\*

Assign multiple users in a click



Assign multiple

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

## GROUPS

Add

# Demos

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- Workspace
- Import of files created in Desktop version
  - Overview of analysis options & results
  - Subset analysis, show design
- CombiStats online application
  - Creation of an assay
  - Template, protection
  - PDF report, revision & audit trail
  - Combination of assay results

# Useful links

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- Institutional website

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

- User guide and FAQs

[https://combistats.edqm.eu/user-manuals/combistats\\_user\\_guide.pdf/](https://combistats.edqm.eu/user-manuals/combistats_user_guide.pdf/)

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

- Privacy, security notices

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

# Validation

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## Ensure continuity

**Online application results = Desktop version results**

## Validation based on:

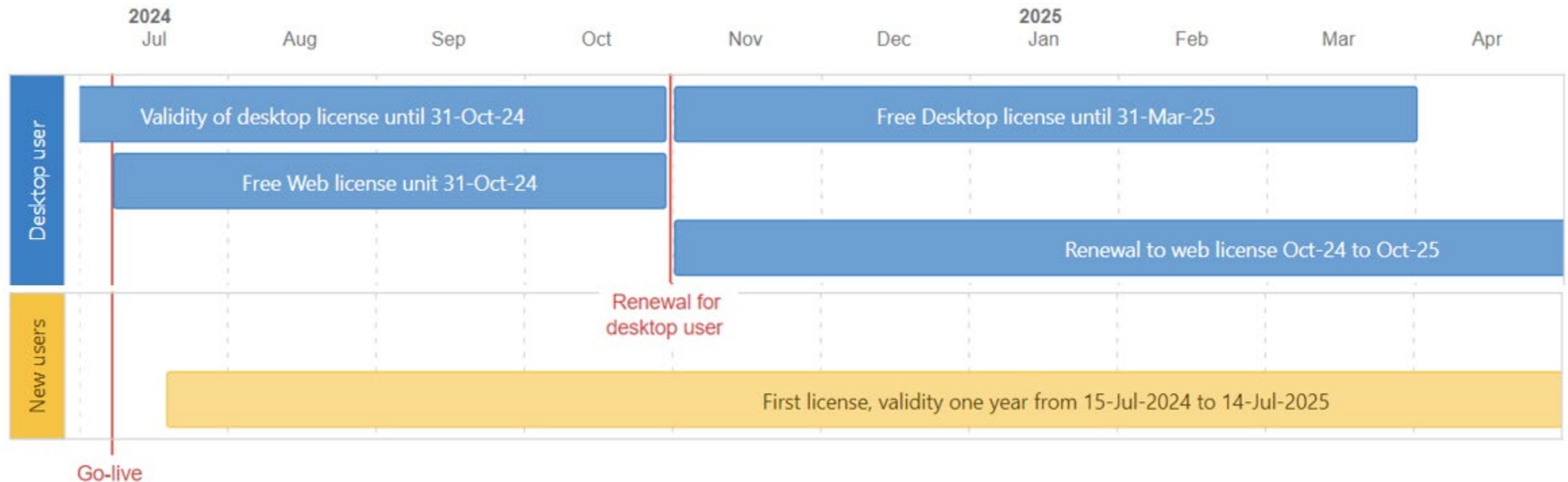
- all examples published in the **European Pharmacopoeia, chapter 5.3** 'Statistical Analysis of Results of Biological Assays and Tests'
- almost all numerical examples given **by D.J. Finney** in his standard work 'Statistical Method in Biological Assay, 3rd Edition, Grin, London (1978)'.

**Calculated results and published results are equal**

In addition, **beta-version testing** by several OMCLs in March 2024

# Toward a smooth transition

- Go-live in July 2024
- Licence renewal in Oct. 2024 (webshop)
- CombiStats Desktop will be available until March 2025



# How to order CombiStats

- From 5 July 2024, it will be possible to order CombiStats licence directly from EDQM webshop: [www.store.edqm.eu](http://www.store.edqm.eu)

The screenshot shows the EDQM webshop interface. On the left is a navigation menu with categories like 'EUROPEAN PHARMACOPOEIA 11th EDITION', 'BIOLOGICAL STANDARDISATION PROGRAMME', etc. The main content area displays 'Product Area: 0000000000'. Below this, there is a 'DESCRIPTION' section explaining that CombiStats is a calculation program for statistical analysis of data from biological dilution assays. It also lists 'Languages: English' and 'Ordering' details, including discounts for multiple users (5% for 2-4 users, 10% for 5-10 users, 20% for 11-20 users, 30% for 21+ users). A 'Technical requirements' section notes that the software runs on modern browsers and reports are exportable in PDF and Excel-compatible formats. At the bottom, a table lists the products for sale:

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

1	No discount
2-4	5%
5-10	10%
11-20	20%
21+	30%

- Price: 600 euros per licence
- 2 types of licence :
  - Normal / renewable
  - Extension

# The floor is yours!

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# Thank you for your attention

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## Stay connected with the EDQM

EDQM Newsletter: <https://go.edqm.eu/Newsletter>

LinkedIn: <https://www.linkedin.com/company/edqm/>

X: [@edqm\\_news](#)

Facebook: [@EDQMCouncilofEurope](#)