

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



Presentation of the CombiStats Online Application

CombiStats

Webinar 3 July 2024

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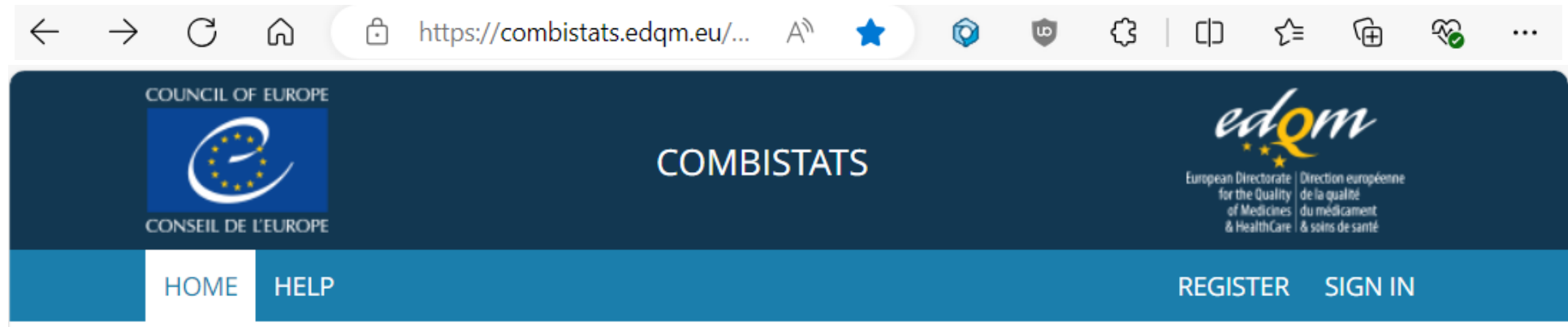
Q&A session

The CombiStats Software – Desktop

- 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

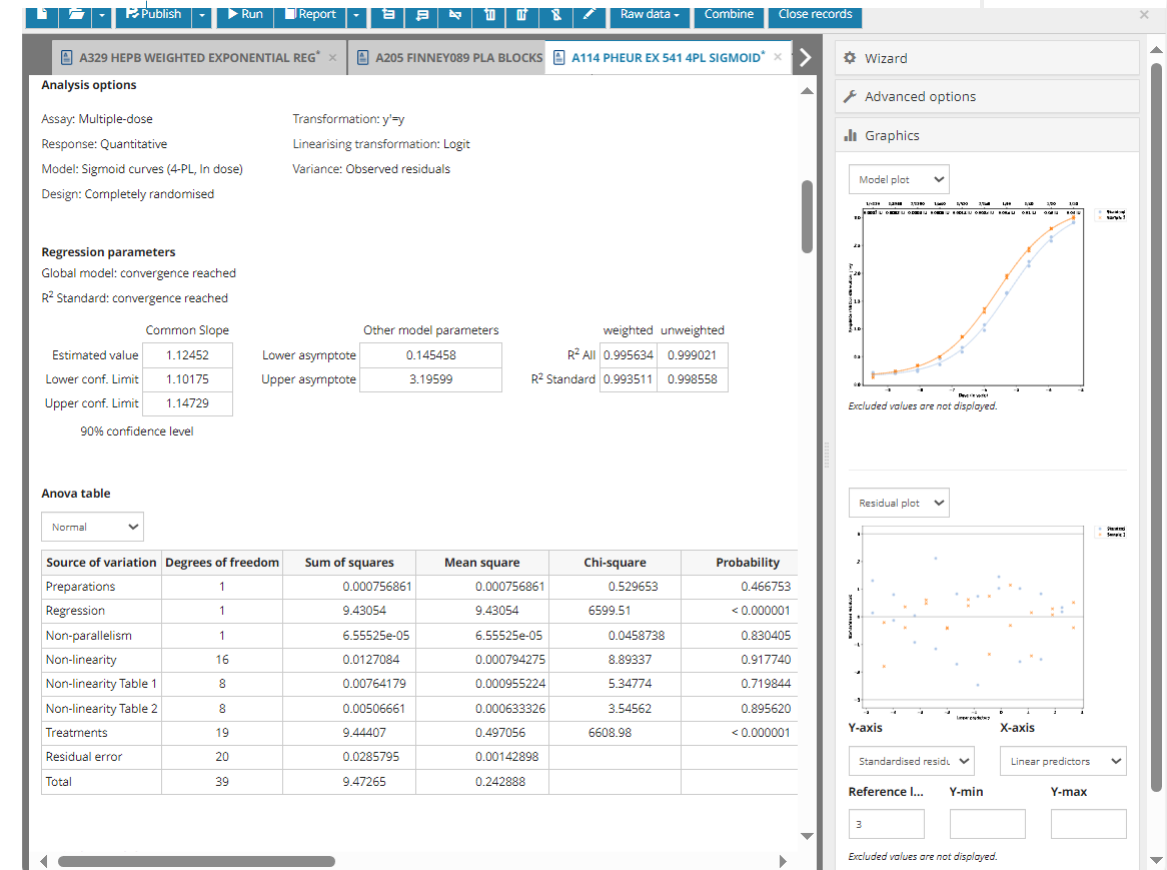
Dedicated workspace for your organisation

- 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 1 T	



The screenshot displays the CombiStats Online Application interface. The main window shows analysis options for a sigmoid curve fit. The analysis options include Assay: Multiple-dose, Response: Quantitative, Model: Sigmoid curves (4-PL, In dose), and Design: Completely randomised. The regression parameters section shows the global model convergence reached, with R² Standard: convergence reached. The anov table is also visible, showing the source of variation, degrees of freedom, sum of squares, mean square, chi-square, and probability.

Source of variation	Degrees of freedom	Sum of squares	Mean square	Chi-square	Probability
Preparations	1	0.000756861	0.000756861	0.529653	0.466753
Regression	1	9.43054	9.43054	6599.51	< 0.000001
Non-parallelism	1	6.55525e-05	6.55525e-05	0.0458738	0.830405
Non-linearity	16	0.0127084	0.000794275	8.89337	0.917740
Non-linearity Table 1	8	0.00764179	0.000955224	5.34774	0.719844
Non-linearity Table 2	8	0.00506661	0.000633326	3.54562	0.895620
Treatments	19	9.44407	0.497056	6608.98	< 0.000001
Residual error	20	0.0285795	0.00142898		
Total	39	9.47265	0.242888		

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		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

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

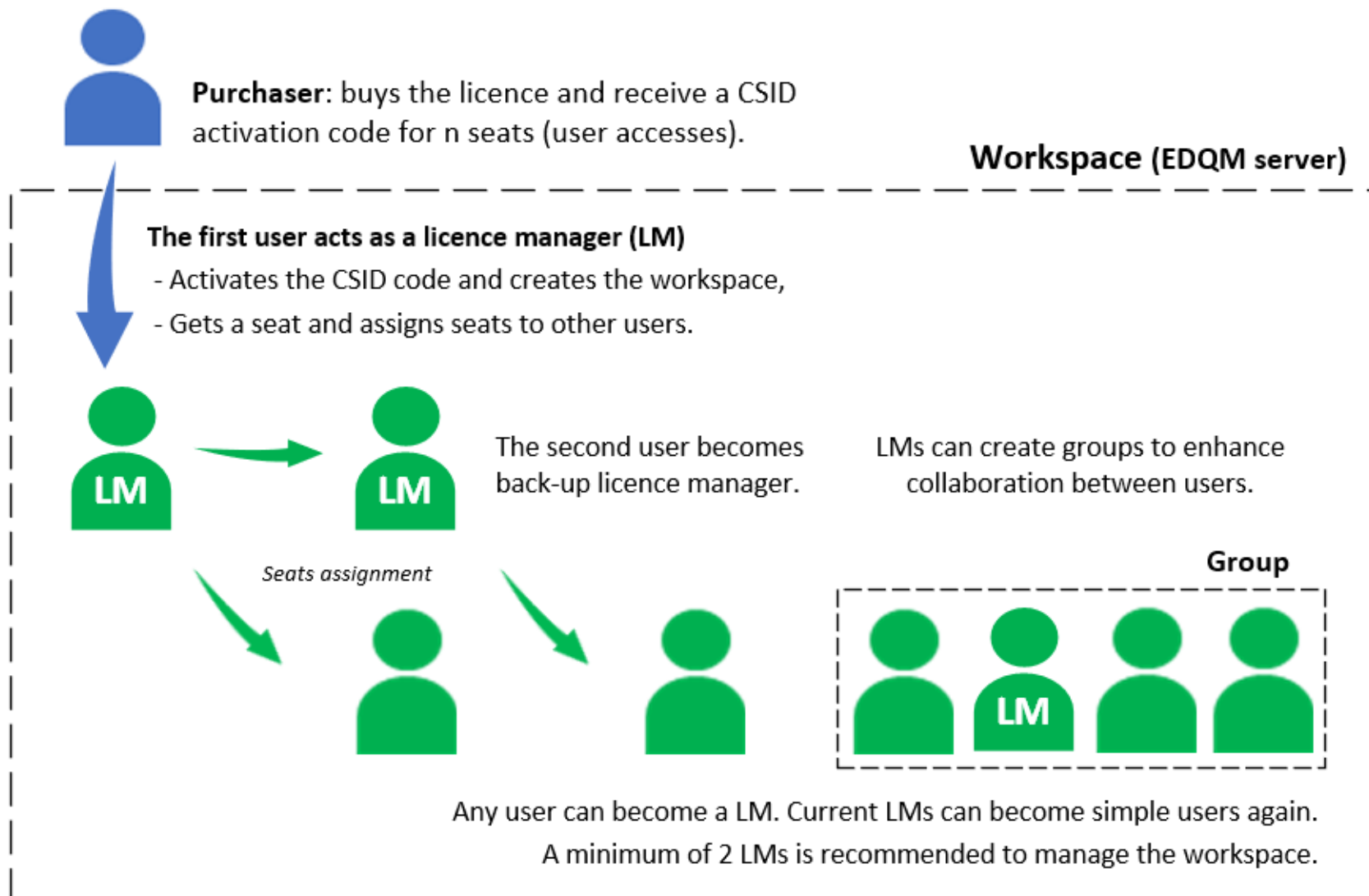
Password set. In order to finalise the activation of your account, you now need to log in.

Sign In

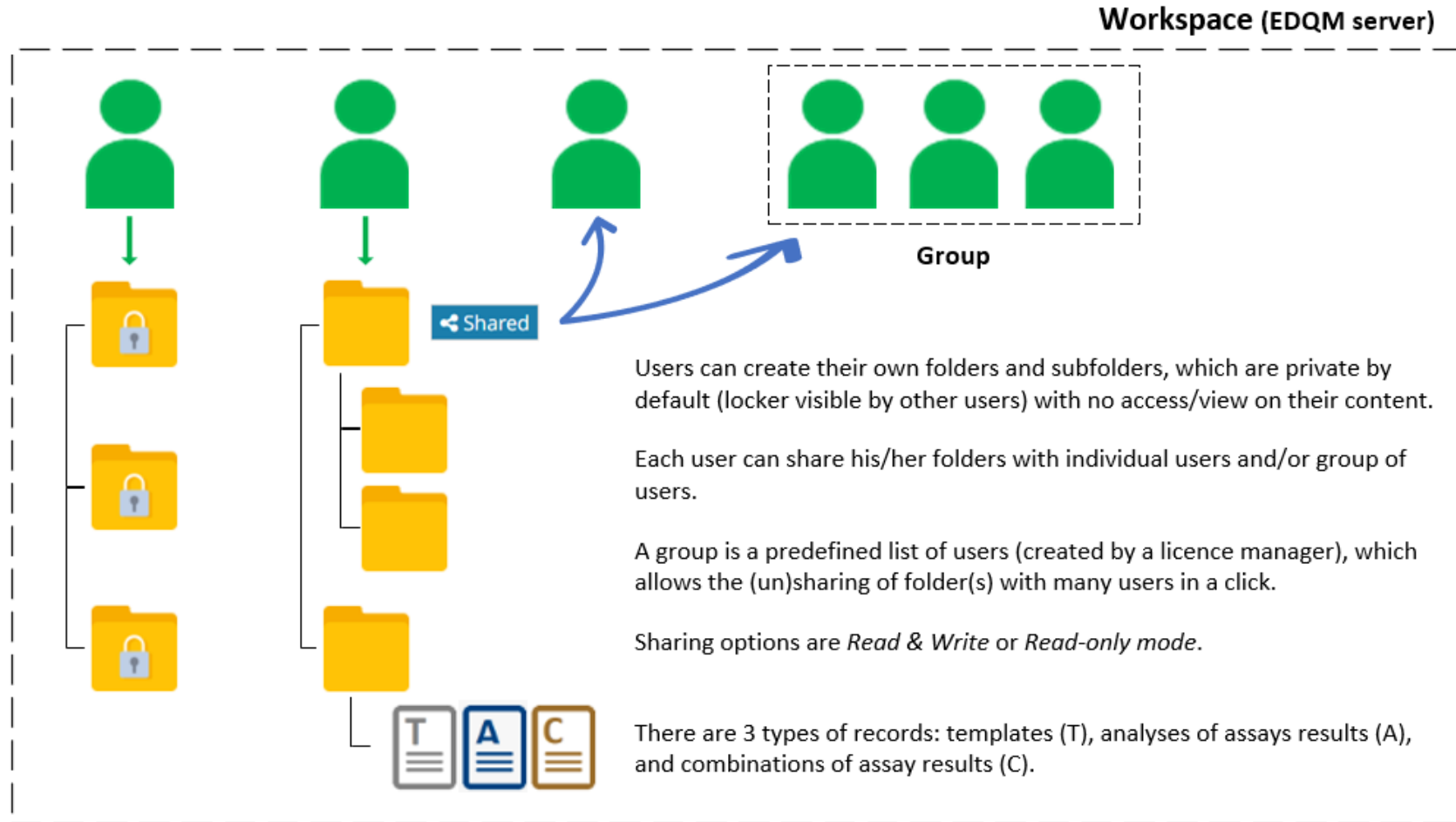
The Workspace

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)

From: Sales@edqm.eu <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](#).

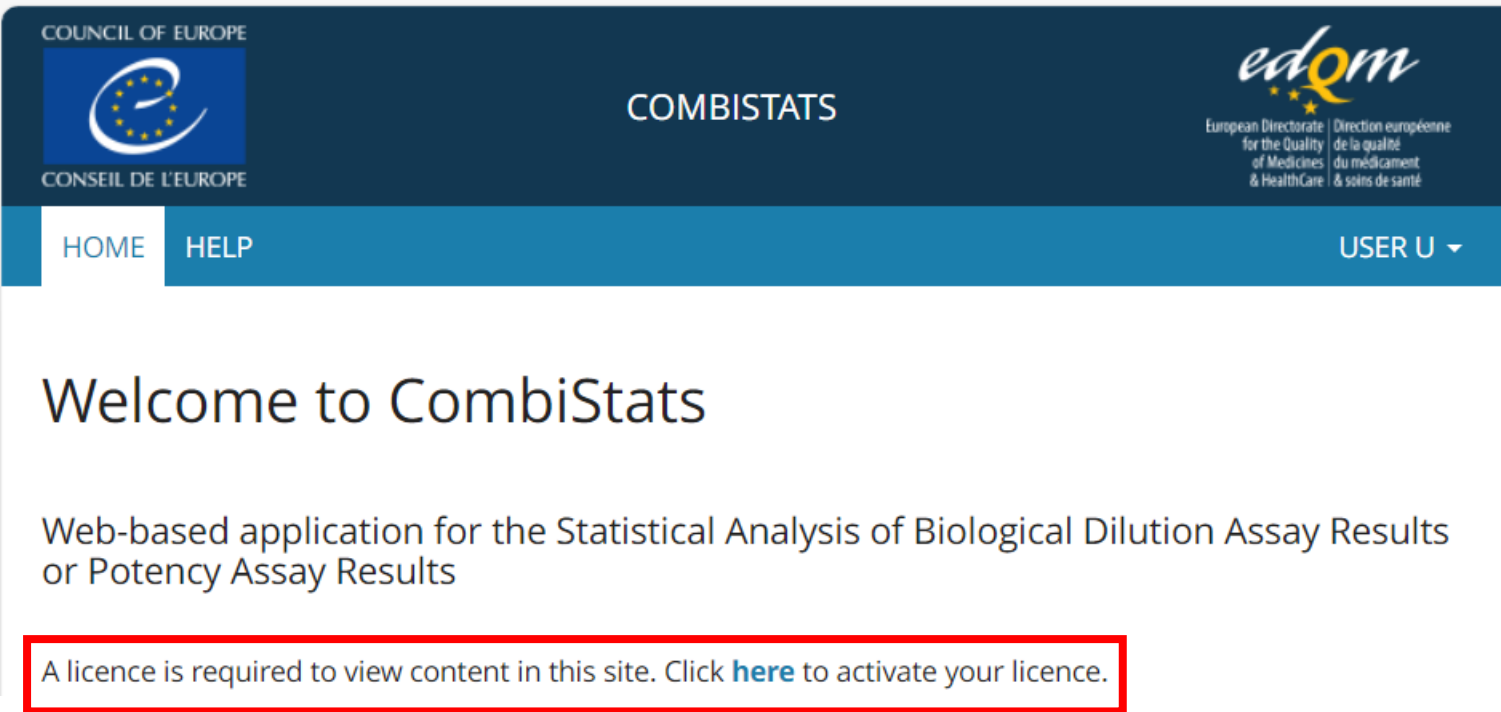
If applicable, please forward this message to the person responsible for managing CombiStats licences within your organisation.

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 dropdown labeled 'USER U'. 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

- 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

- 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/help/>

- Privacy, security notices

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

Validation

Ensure continuity

Online application results = Desktop version results

Validation based on:

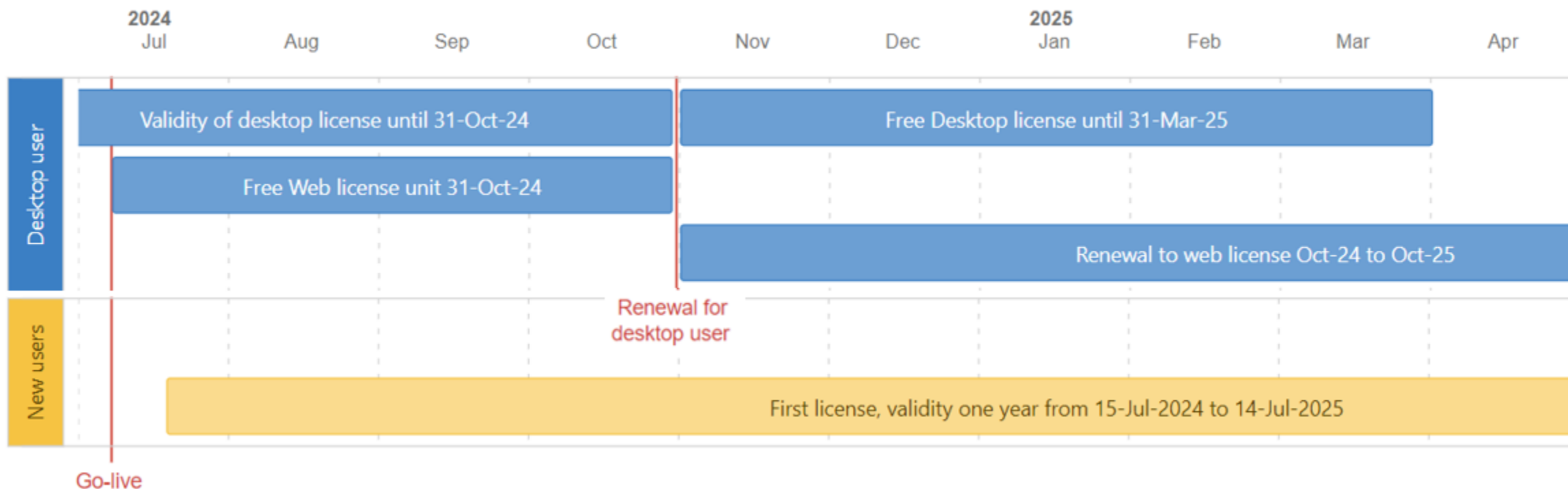
- all examples published in the **European Pharmacopoeia, chapter 5.3** 'Statistical Analysis of Results of Biological Assays and Tests'
- almost all numerical examples given **by D.J. Finney** in his standard work 'Statistical Method in Biological Assay, 3rd Edition, Grin, London (1978)'.

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: <https://store.edqm.eu/index.html>

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 the product details for 'Product Area: 0000000000'. It includes a description of CombiStats as a statistical analysis program, ordering information (English), and a table of discounts for multiple users. At the bottom, there is a table listing 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!



Thank you for your attention



Stay connected with the EDQM

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

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

X: [@edqm_news](#)

Facebook: [@EDQMCouncilofEurope](#)