DBI
Deep Breath Intelligence®

Instruction For Use

DBI-EPIbreath®

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Symbols used:

The following table displays the symbols used in this instruction for use.

SN	**Software version**
REF	**Catalogue Number**
🏭	**Date of Manufacture**
UDI	**Unique Device Identification**
🏭	**Legal manufacturer (Effectum Medical AG)**
EC REP	**European Community Representative**
IVD	**In-vitro diagnostic medical device**
📖	**Refer to instructions for use**
CE	**CE marking of product complies with the essential requirements of the relevant European health, safety and environmental legislation**
⚠	**Warnings and Precautions: Highlights information that is critical for optimal performance of the system. May also indicate that loss of data or invalid data could occur if the precautions or instructions are not observed.**

Contents

1. Overview

1.1. Intended use

DBI-EPIbreath® provides systemic valproic acid concentrations (total and free in mg/L blood) and probability scores for Risk of seizures and Risk of severe side effects (in low/moderate/high).

These results and values are supporting medical doctors to make decisions on treatment adjustments.

1.2. Product description

DBI-EPIbreath® is an application (“the Product”) to analyze breath samples from epileptic patients.

DBI-EPIbreath® provides Valproic acid (VPA) values (total and free VPA in blood), a predicted drug response likelihood, a predicted side-effects risk score to identify patients which are likely to benefit from the treatment and which ones are likely to suffer from unwanted side effects and therefore help medical doctors to decide how to treat people suffering from epilepsy and to choose appropriate drug dosage.

DBI-EPIbreath® is a user-end application, a cloud-based core system, and a management system for patient metadata.

DBI-EPIbreath® works in the following way.

High Resolution Breath Test for Epilepsy

PLEASE NOTE: THE RESULTS ARE CORRELATIONAL ESTIMATIONS. THEY SHOULD NOT BE USED AS DIAGNOSTIC FACTS.

Systemic Concentration of Valproate Acid

Total VPA
69.9 mg/L

Free VPA
6.4 mg/L

Drug Response

Risk of Seizures
High

Risk of Severe Side-effects
Moderate

On-site breath measurement

Real-time report

Supporting information

1. The patient exhales into the analytical device, into the mass spectrometer or into an offline sampler.
2. DBI-EPIbreath® analyzes the patient’s breath and generates a test report, a PDF file summarizing the results.
3. The test report is automatically sent to the healthcare provider to support treatment decisions.

The report contains the following information:

- Patient information
- Measurement related information
- Total Valproic acid (VPA)
- Free Valproic acid (VPA)
- Drug response prediction
    - Risk of seizures
    - risk of severe side effects

1.3. Scope

In scope of this document is the DBI-EPIbreath® software application.

Out of scope of this document DBI-EPIbreath® are third party instruments like the following peripheral devices that are used to acquire the breath samples:

- High-Resolution Mass Spectrometer (HRMS) Orbitrap Exactive from Thermo Fisher Scientific (TFS)
- Secondary electro spray ionization source (SESI) Super-SESI from Fossiliontech (FIT)
- EXHALION from Fossiliontech (FIT)

1.4. Limitations

⚠ DBI-EPIbreath® can only be used in patients of 6 years of age and older. Please account more time for the breath sampling using SESI-HRMS, if your patients are younger than 12 years and older than 70 years old.

⚠ DBI-EPIbreath® only supports data collected from the third-party instruments listed in 1.3 Scope.

⚠ DBI-EPIbreath® can only analyze patient data once a reference database has been created (4.1 Initialization SST). This reference database requires reference measurements with SESI-HRMS over the course of at least 21 days. The days do not have to be consecutive. For the reference measurement a standard gas (α-Terpinene) is injected into the SESI-HRMS and the molecular fingerprint of the environment is recorded in positive-ion mode.

The rationale behind the reference database is the following: the SESI-HRMS is very sensitive and does not only identify the molecules within the breath of the patient but also the ones in the environment. The reference database accounts for these environmental factors in the data and serves as a reference for the actual patient measurement.

⚠ DBI-EPIbreath® can only analyze patient data, when a reference measurement has been acquired on the same day as the actual measurement and actual data entry (4.2 Daily SST).

⚠ If DBI-EPIbreath® is used at different locations, the results may differ across the locations due to a batch effect. A batch effect refers to systematic technical differences, when samples are processed and measured in different batches/at different locations and which are unrelated to any biological variation.

The size of a potential batch effect and is mitigation is currently under investigation in post-market performance studies. To make sure that the performance of DBI-EPIbreath® is not affected by a batch effect, the first 20 measurements at a new location cannot be interpreted, before the size of the batch effect is assessed.

1.5. Third-party requirements

1.5.1. Operation of the SESI-HRMS

Please follow the instructions for use of the HRMS.

https://assets.thermofisher.com/TFS-Assets/CMD/manuals/man-bre0012255-exactive-series-manbre0012255-en.pdf

For pre installation requirements:

http://tools.thermofisher.com/content/sfs/manuals/1288110-Exactive-Series-Preinstallation-Requirements.pdf

1.5.2. Maintenance of the SESI-HRMS

Please follow the instructions for use of the SESI-HRMS.

HRMS is very sensitive and any changes in the environment could influence DBI-EPIbreath® result and should be therefore reported to DBI (support@dbi.ch).

Please take special care in the following situations:

1. Cleaning: frequent cleaning (at least once a month) with same reagents and not 3 hours before patient measurement.
2. Consumables: at least 2 gas bottles and capillaries on stock
3. Service contract with periphery devise technical support advised
    a. Thermo Fisher Scientific https://www.unitylabservices.com/en/home.html
    b. Fossiliontech (FIT) https://www.fossiliontech.com/
4. Environment changes/moving instrument.

1.5.3. Operation of the EXHALION

⚠ For correct results of DBI-EPIbreath®, a single-use mouthpiece without filter must be used. After each use, the breath inlet of the EXHALION must be cleaned with ethanol and air dried or dried with nitrogen to avoid contamination of the next user.

1.5.4. Data files

The following file types are required from the measurements with the periphery device instruments.

- Reference database:
    a. 21 SESI-HRMS RAW files from reference measurement recorded in positive-ion mode from different days (**positive RAW file**)
- New measurement:
    a. 1 SESI-HRMS RAW file from *reference measurement* recorded in positive-ion mode (**positive RAW file**, for 4.2 Daily SST)
    b. 1 SESI-HRMS RAW file from *patient measurement* recorded in positive-ion mode (**positive RAW file**)
    c. 1 SESI-HRMS RAW file from *patient measurement* recorded in negative-ion mode (**negative RAW file**)
    d. 1 EXHALION file related to b. (**positive CO_2 file**)
    e. 1 EXHALION file related to c. (**negative CO_2 file**)

⚠ Naming of the RAW file is important! System will check if the names are correct.

All RAW files shall have the following naming convention: Date (yyyymmdd), Index (2 digits integer), Polarity (Pos, or Neg.), user information, subject information

Exp. **20220515_02_Pos_TestProject_Subject003_Visit02.RAW**

⚠ The CO_2 files are automatically generated. If the time setting is correct. There is no need to rename the file.

1.6. Training requirements

To use DBI-EPIbreath® there is a training required. Every user shall get a training with the following topics:

Account settings, SST database creation, Daily SST, environment risks, breath sampling, periphery device handling specific for DBI-EPIbreath®, create new measurement, upload data, create a report, read the report.

After the training, a separate training record list will be filled out with the User's Name, Users Organisation, Date, Instructors Name, and a checklist which topics have been covered. This document then needs to be signed by the user and the instructor.

2. Get started

2.1. System requirements

The DBI-EPIbreath® application requires the following operating system:

- macOS version 10.15 or later
- Windows version 7 or later

The DBI-EPIbreath® application requires the following browser:

- Safari 15.0 or later
- Edge 84.0.522 or later
- Chrome 100.0.4896 or later
- Firefox 100.0 or later

⚠ Please note, this only represents the support at the time of release. We might stop supporting out-dated versions in the future.

⚠ The DBI-EPIbreath® application requires a stable internet connection.

⚠ The DBI-EPIbreath® requires access to DBI's cloud services. Please contact DBI for support (support@dbi.ch) if your firewall may block certain cloud services.

⚠ Daily back up will be performed.

2.2. Account set up

Administrator rights are within the system administrator of Deep Breath Intelligence (DBI). DBI will set up an account for your organization and the individual users within your organization. Once your account has been created, you will receive an email notification that allows you to set up your password.

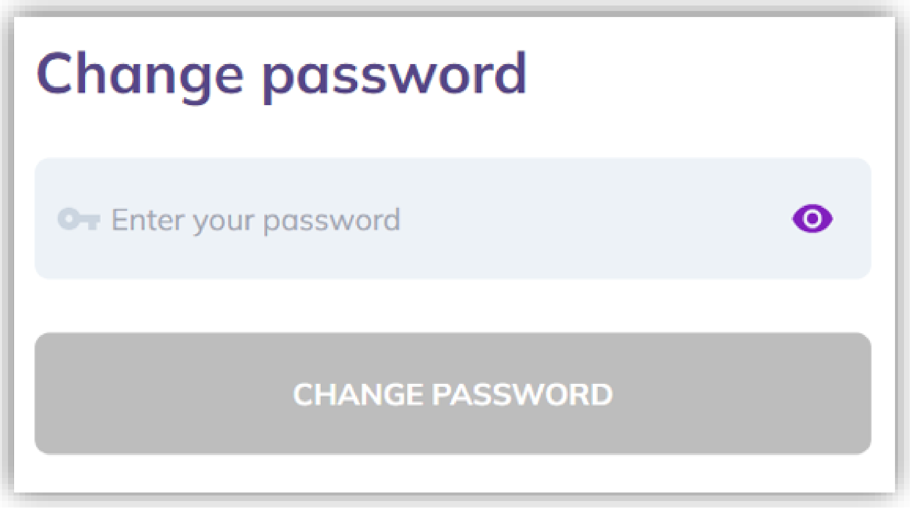
⚠ warning that login details shall not be shared between users. This applies also to users within the same organization.

2.3. Set up your password

Before you get started with DBI-EPIbreath® you will have to set up the password for your account. You will receive an email from Deep Breath Intelligence (DBI) with a link to set up your password.

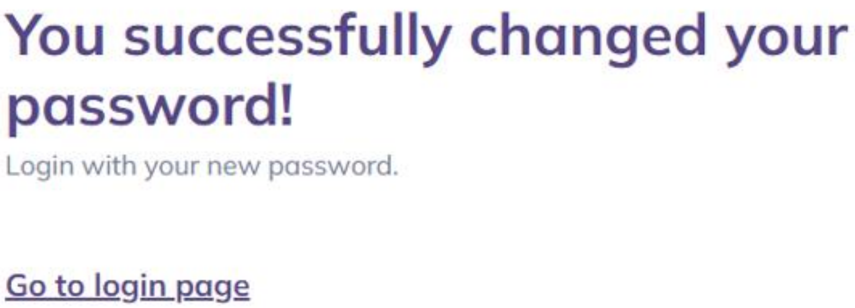
1. Check your inbox for an email from DBI technical support (support@dbi.ch).
2. Open the link in the email. It will take you to the change password screen of DBI-EPIbreath®.
3. Type in a password of your choice.

   You can click the show password 👁 button on the right at any time. This will display your password instead of dots.
4. Click **CHANGE PASSWORD**.



Change password

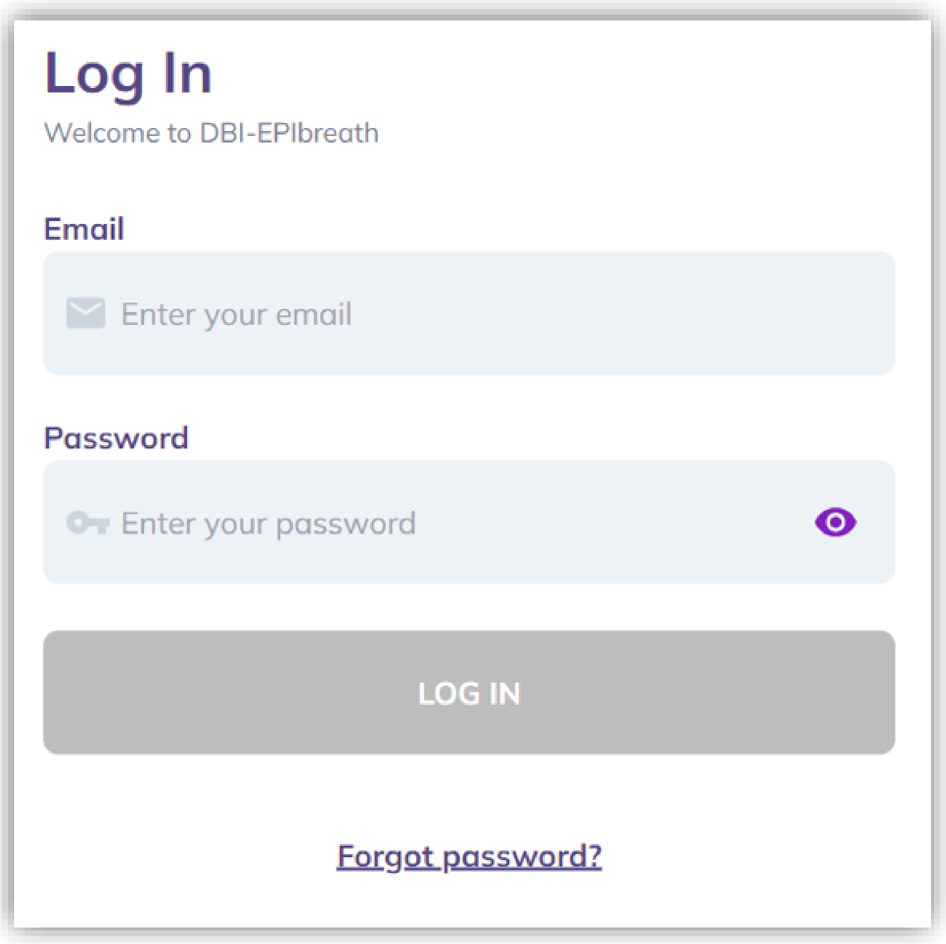
5. Click **LOG IN** on the success screen. You will be forwarded to the login page.



You successfully changed your password!

Login with your new password.

6. Enter your **email address**.

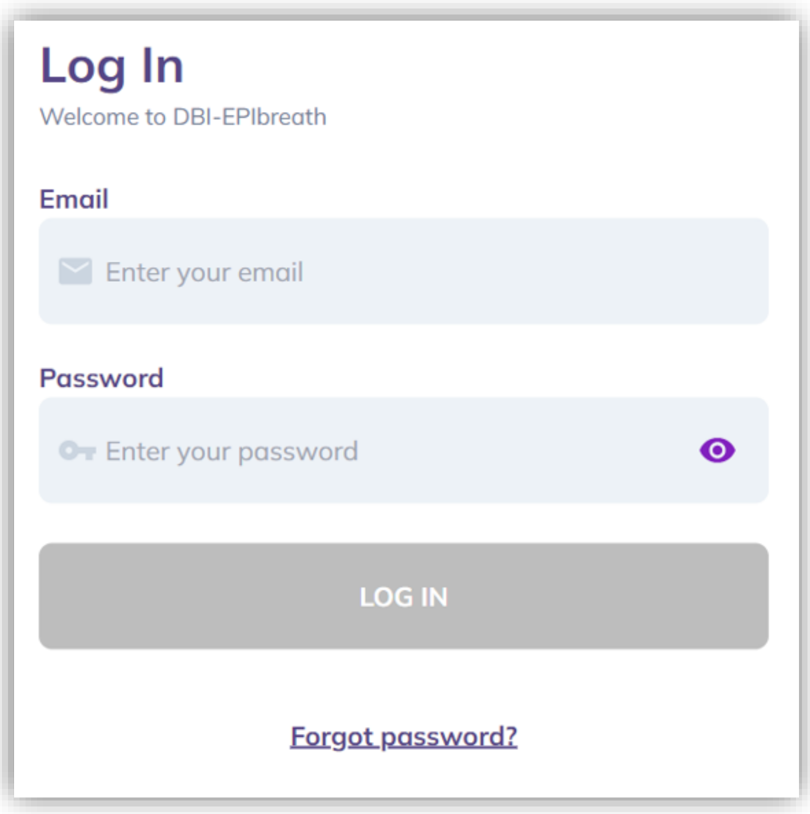


7. Enter your **new password**.
8. Click **LOG IN**.

2.4. Log in

1. Open a web browser.
2. Type in the following web address:
   https://epibreath.dbi.ch

9. Enter your **email address**.



10. Enter your **password**.
11. Click **LOG IN**.

3. System Suitability Test (SST)

3.1. Generation of reference database

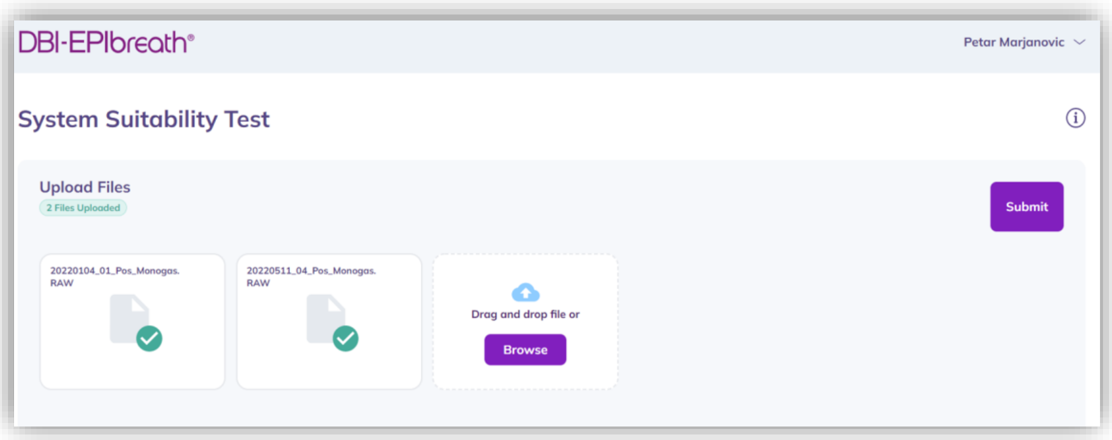
Before you can use DBI-EPIbreath® it is necessary to establish a reference database (1.4 Limitations). After having conducted enough reference measurements, the data need to be uploaded and DBI-EPIbreath® will compute a meaningful reference against which the actual patient measurements can be compared.

SST reference database does cover the baseline for the environmental conditions for the periphery devices.

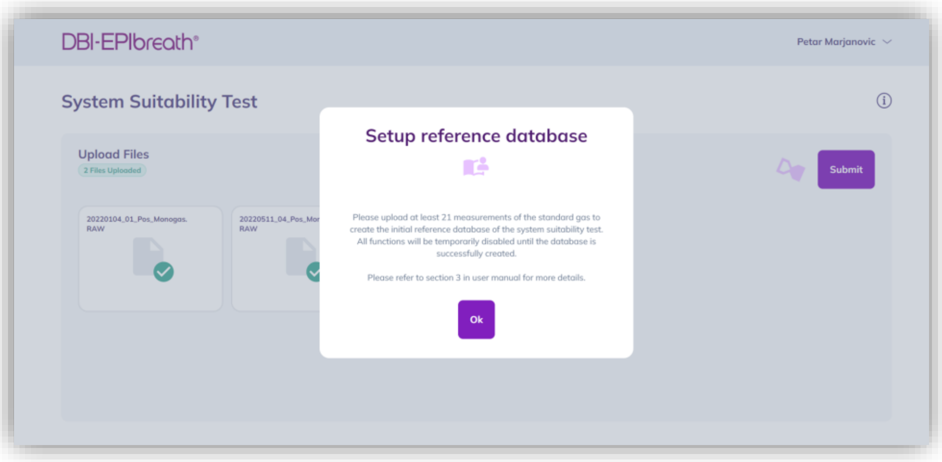
⚠ The final creation of the reference database can only be performed by DBI after manual data review and may take up to 3 business days. Please factor this in when scheduling the patient measurements.

Conduct a reference measurement by injecting a standard gas into the SESI-HRMS.

1. Once logged into the DBI-EPIbreath® application, upload the **positive raw file** from step 1. You can either select files by clicking **Browse** or simply drag and drop them into the corresponding field.



2. Repeat steps 1 and 2 until there are at least 21 measurements.
3. If you have less than 21 files uploaded this error massage will appear.

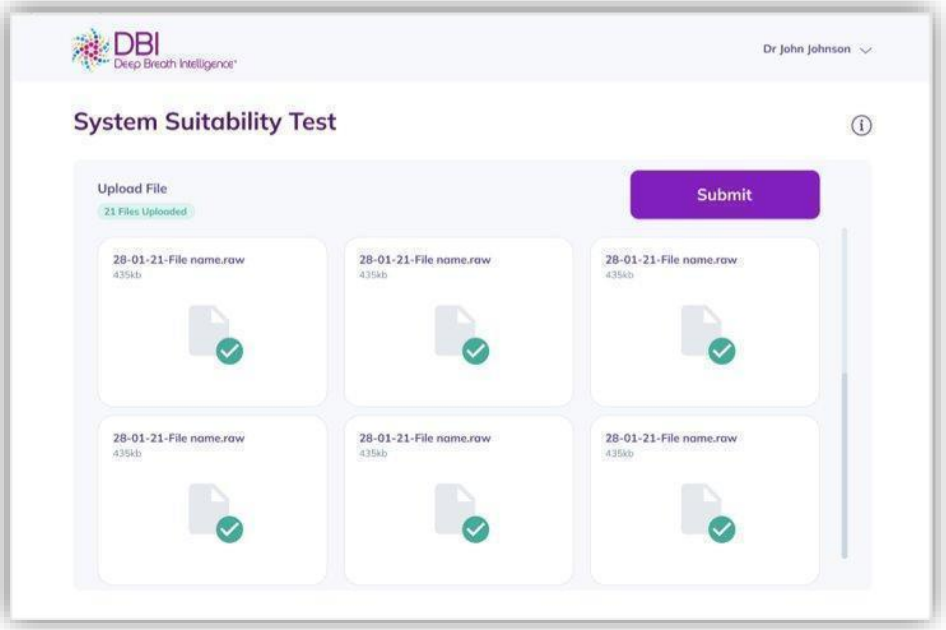


Please upload at least 21 measurements of the standard gas to create the initial reference database of the system suitability test. All functions will be temporarily disabled until the database is successfully created.

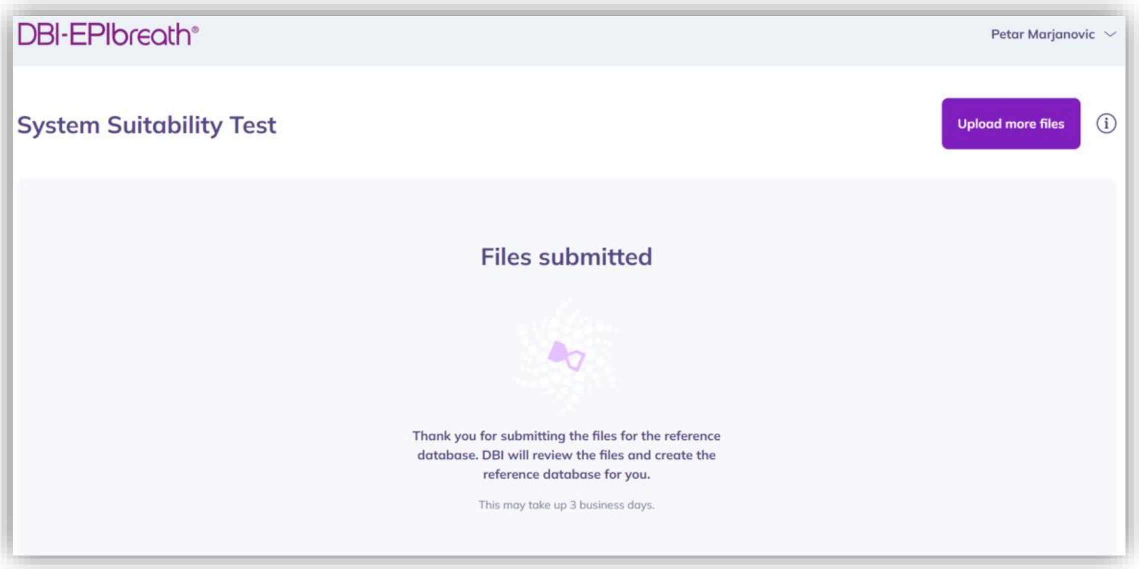
Please refer to section 3 in user manual for more details.

4. Once 21 files have been successfully uploaded, click **Submit**.
   Please note: the **Submit** button will only appear active once 21 files have been uploaded.

However, it is possible to conduct more reference measurements and upload more files.



5. The initialization SST is performed. Please be patient, this process can take up to **3 business days.**



Thank you for submitting the files for the reference database. DBI will review the files and create the reference database for you.

This may take up 3 business days.

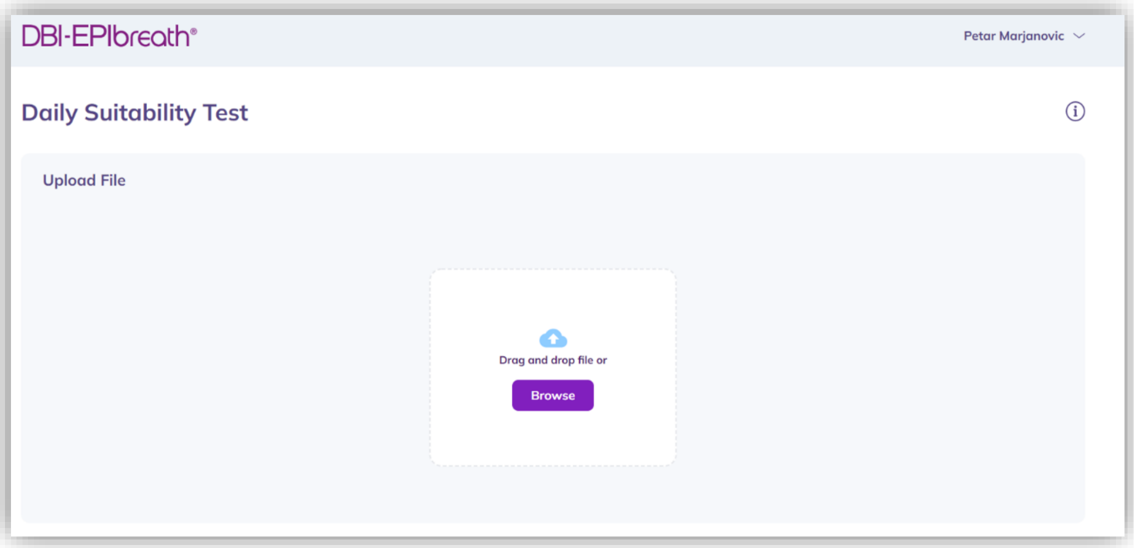
6. It may happen that some of the files were corrupted or of insufficient quality. In that case the application will ask you to upload additional files. Follow steps 1 to 5 to upload those files and complete the initialization SST.

7. Congratulations! Once the initialization SST process is passed successfully, DBI-EPIbreath® is ready for use.

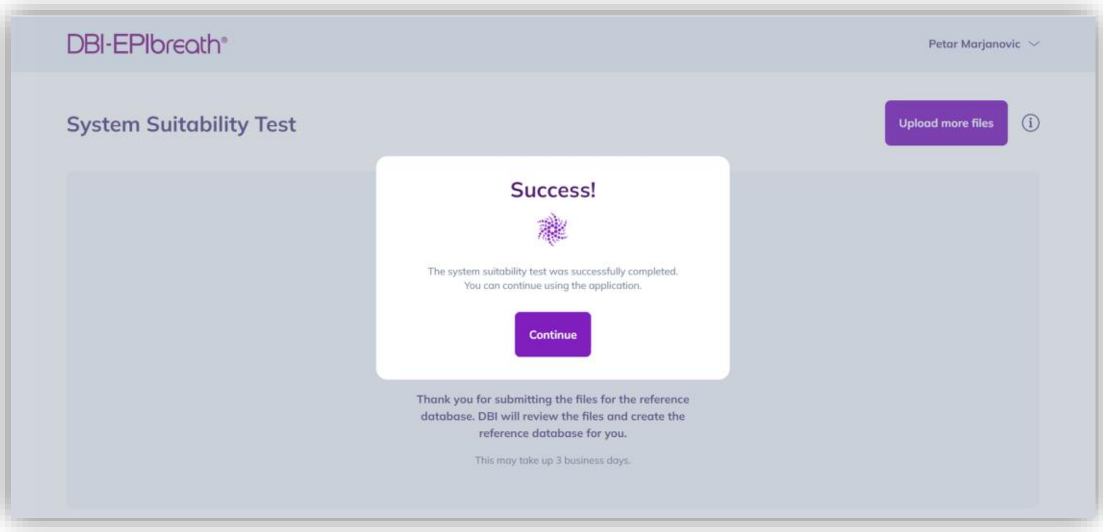
3.2. Daily System Suitability Test (SST)

The daily SST is a measurement done at the same day as the patient measurement and is needed for meaningful interpretation of the patient measurement.

1. Conduct a SST by injecting a standard gas into the SESI-HRMS.
2. After login into DBI-EPIbreath® on a new day, you will be asked to run the daily SST.
3. Click **the underlined text** in the top right corner of the dashboard. This will open the upload screen.
4. Upload only the **positive raw file** from step 1. You can either select files by clicking **Browse** or simply drag and drop them into the application.
   Please note that you won’t be able to create a new measurement before the daily SST has been successfully performed



5. The daily SST is performed. Please be patient, while the raw file is analyzed. This process might take a couple of minutes.
6. Congratulations! You are all set for today and able to create a new measurement.



System Suitability Test

Success!

The system suitability test was successfully completed.
You can continue using the application.

Thank you for submitting the files for the reference database. DBI will review the files and create the reference database for you.

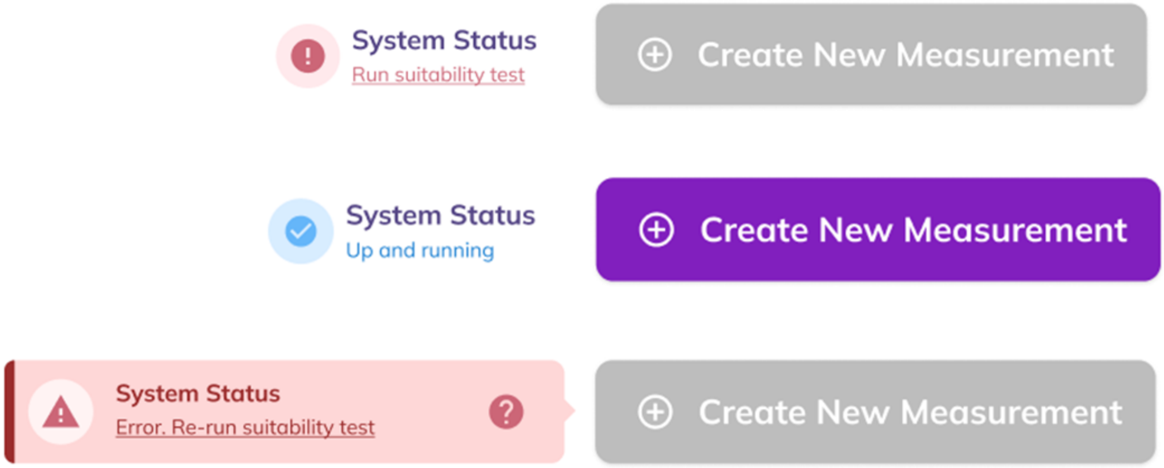
This may take up 3 business days.

3.3. Possible system status

Based on the outcome of the SST, the system status can be one of the following figures (also see screenshot below).

- Run suitability test: before file is uploaded
- Analyzing: during the time of analysis (not shown)
- Up and running successful daily SST

The system status is displayed in the top right corner of the dashboard next to the **Create New Measurement** button.



System Status
Run suitability test

System Status
Up and running

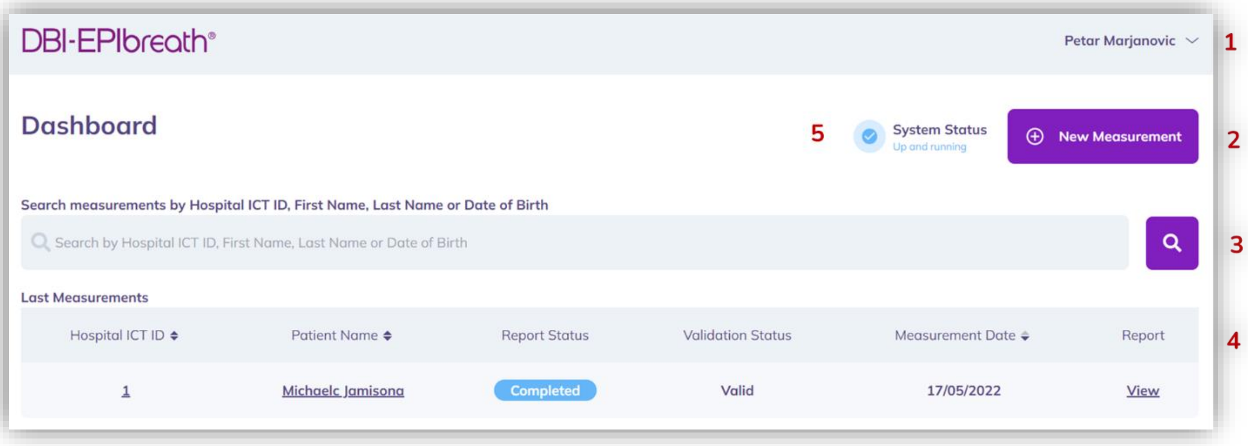
System Status
Error. Re-run suitability test

4. Operation

4.1. Dashboard

The dashboard is the central application screen with the following options:

1. **User Information (1)**
   This drop-down menu allows accessing your Profile, Settings, About, Help, and Logout.
2. **Create New Measurement (2)**
   This button initiates a new measurement flow.
3. **Search Bar (3)**
   The search bar allows you to search the database of existing measurements for patient ID, first name or last name.
4. **Recent Measurements (4)**
   The table lists all previous measurements by patient ID, patient name, report status, validation, date and report. The list can be sorted by any category.
5. **System Status (5)**
   This indicates if a reference measurement has been performed and the system is ready for creating a new measurement.



Hospital ICT ID	Patient Name	Report Status	Validation Status	Measurement Date	Report
1	Michaelc Jamisona	Completed	Valid	17/05/2022	View

4.2. User information

Log in with the user’s name and the personal set password.

4.3. Create new measurement

Click on **Create New Measurement** to guide you through data entry, data analysis and creation of a report.

4.3.1. Enter patient data

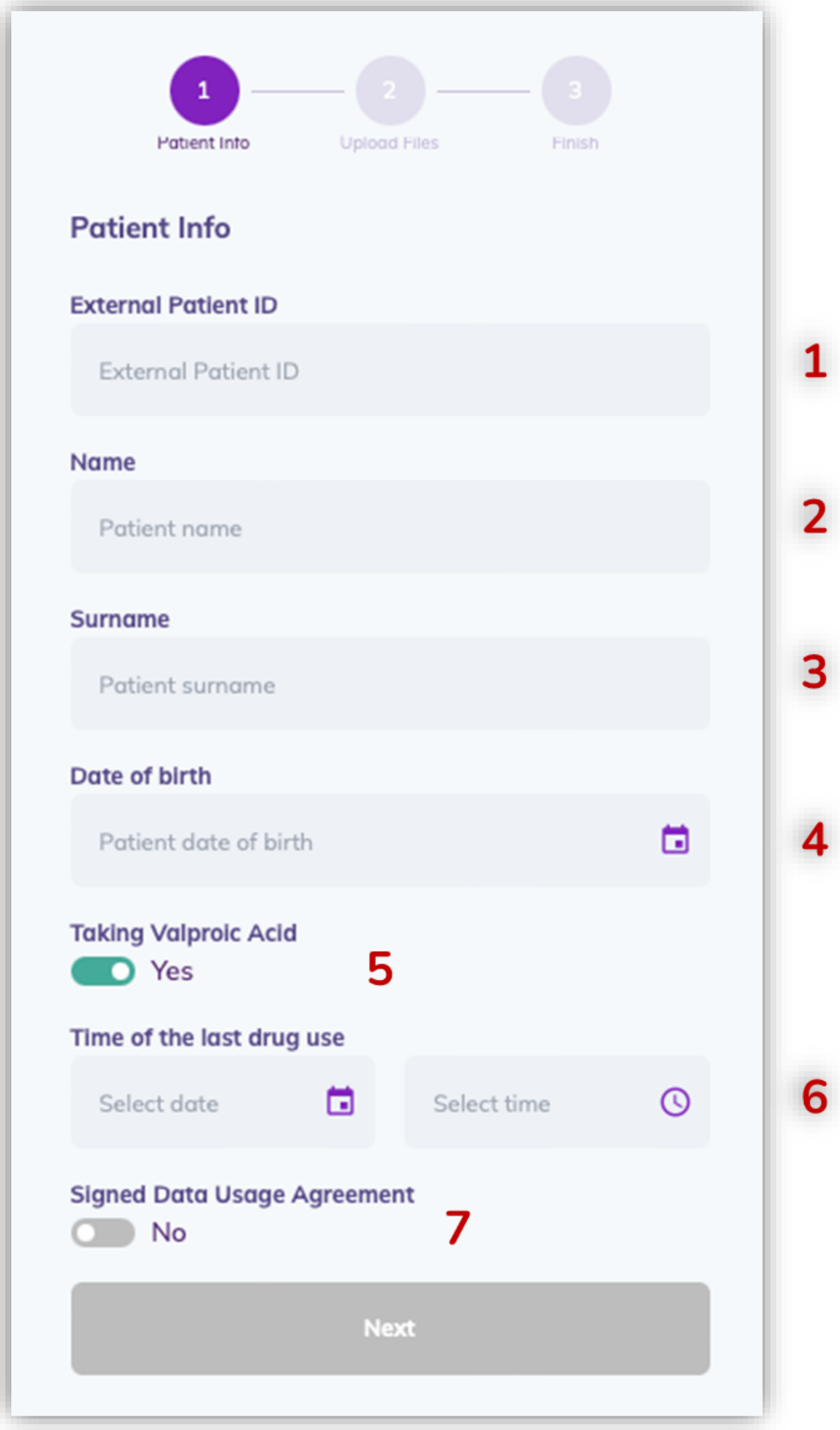
As a first step to create a new measurement you are asked to enter the patient’s data.

1. Enter the **External Patient ID (1)**.
   If you already collected data from a given patient, items 2. to 6. will be automatically filled upon entering the External Patient ID.
2. Enter the patient’s **Name (2)**.
3. Enter the patient’s **Surname (3)**.
4. Enter the patient’s **Date of Birth (4).**

5. Enter if **Taking Valproic Acid (5)**.
   The default for this is **Yes**. In case the patient did not take VPA before the measurement, toggle it to **No**.
6. If VPA was taken, **select time for drug usage (6)** and **Select Date** and **Select Time.**
7. In order to proceed with the measurement, accept the **Data Usage Agreement** by toggling to **Yes (7)**.

⚠ By accepting the **Data Usage Agreement**, the patient does allow to use his/her data to create a result file including patients personal data for the health care professional.

8. Click **Next** to proceed with the data upload.

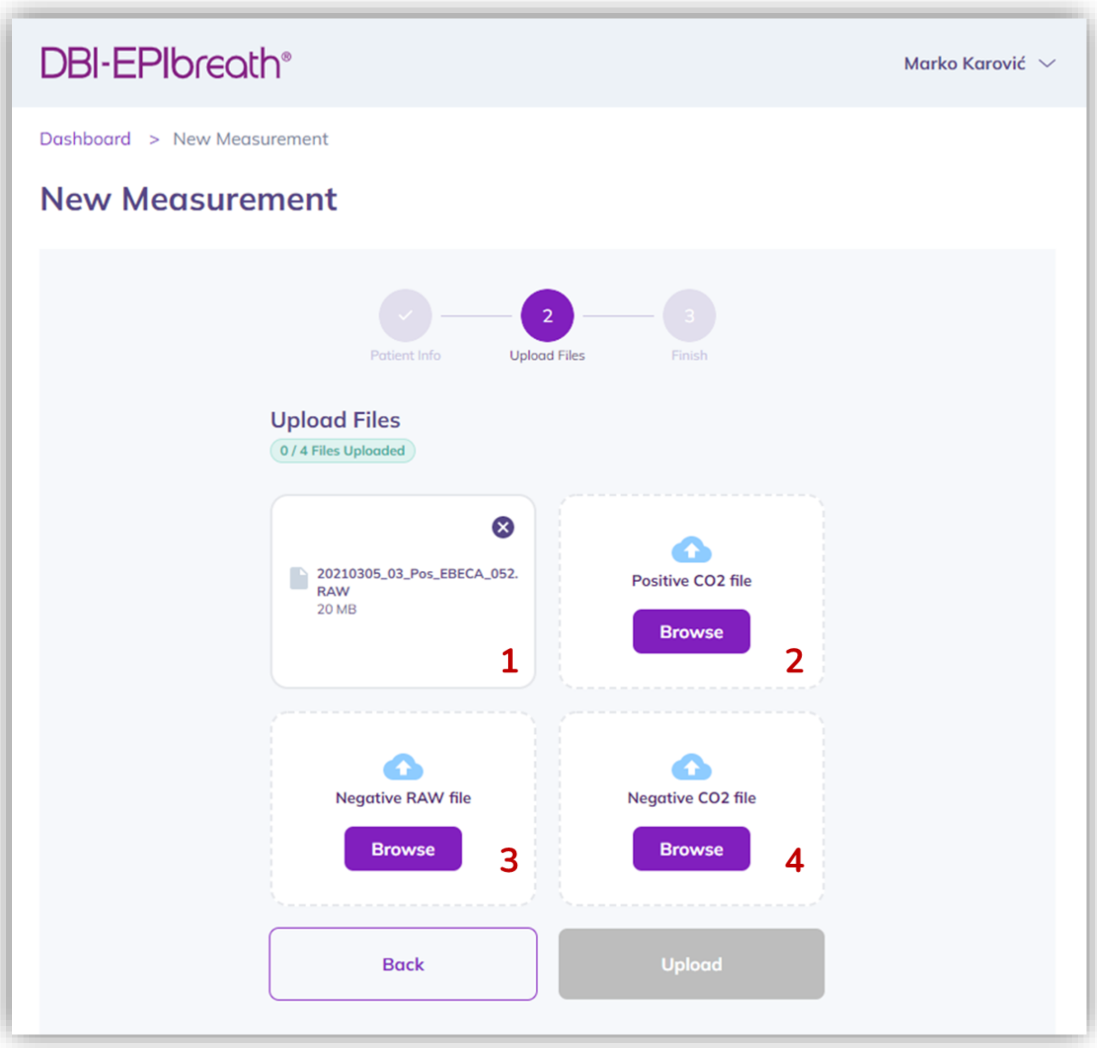


4.3.2. Upload files & generate report

As a next step you will be asked to upload the measurement files (see 1.5.3 Data files).

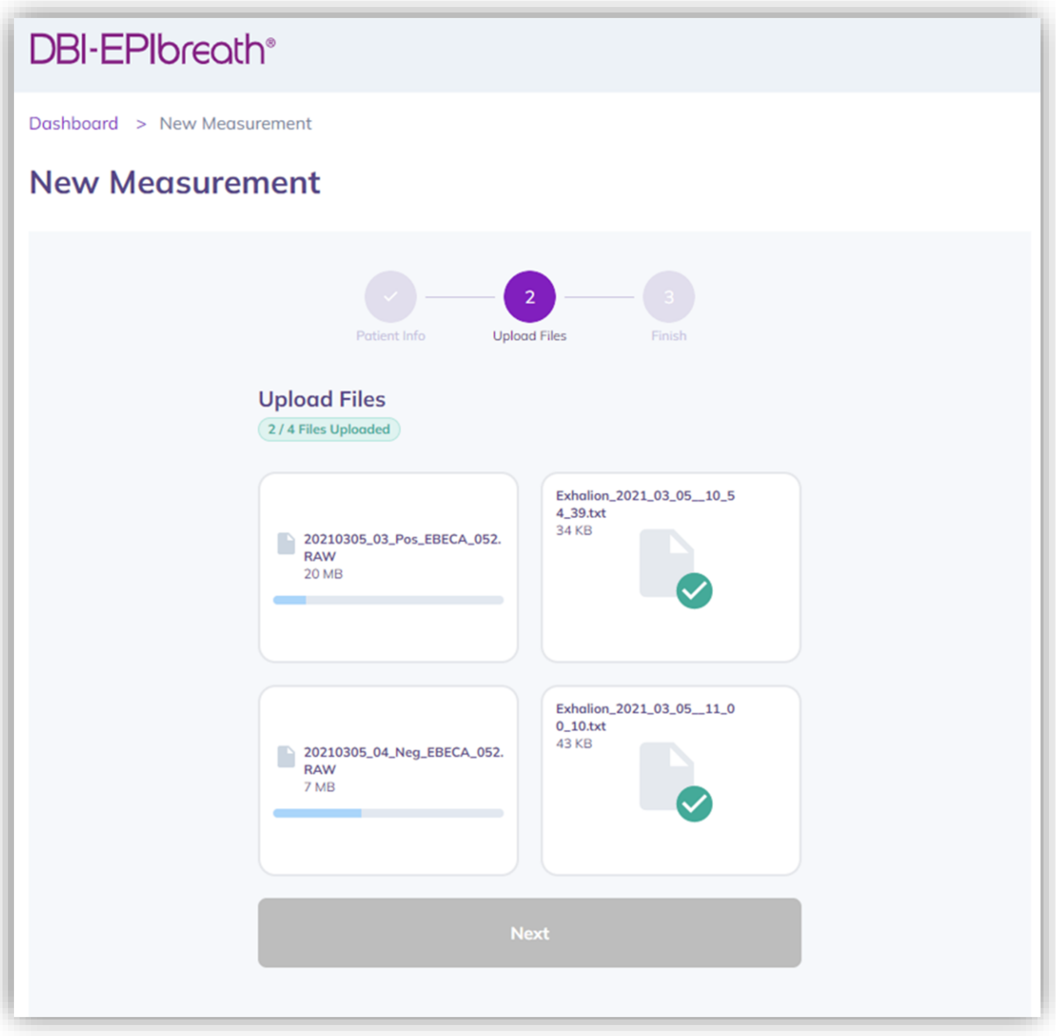
1. Upload **Positive Raw file (1)**
2. Upload **Positive CO_2 file (2)**
3. Upload **Negative Raw file (3)**

4. Upload **Negative CO_2 file (4)**
   You can either select files by clicking **Browse** or simply drag and drop them into the corresponding fields.
5. Click **Next** to calculate the results and generate a report.
   Please note: The **Next** button will only appear active once all four files have been uploaded.



20210305_03_Pos_EBECA_052.RAW
20 MB

6. Files uploading, if successfully uploaded the “tick” turns green.



7. Once all files are uploaded, the results are automatically calculated. Please be patient because it can take a couple of minutes.
   The system will flag a warning if the uploaded files do not match. If this happens, please repeat steps 1 to 4 and make sure that you upload the correct files.

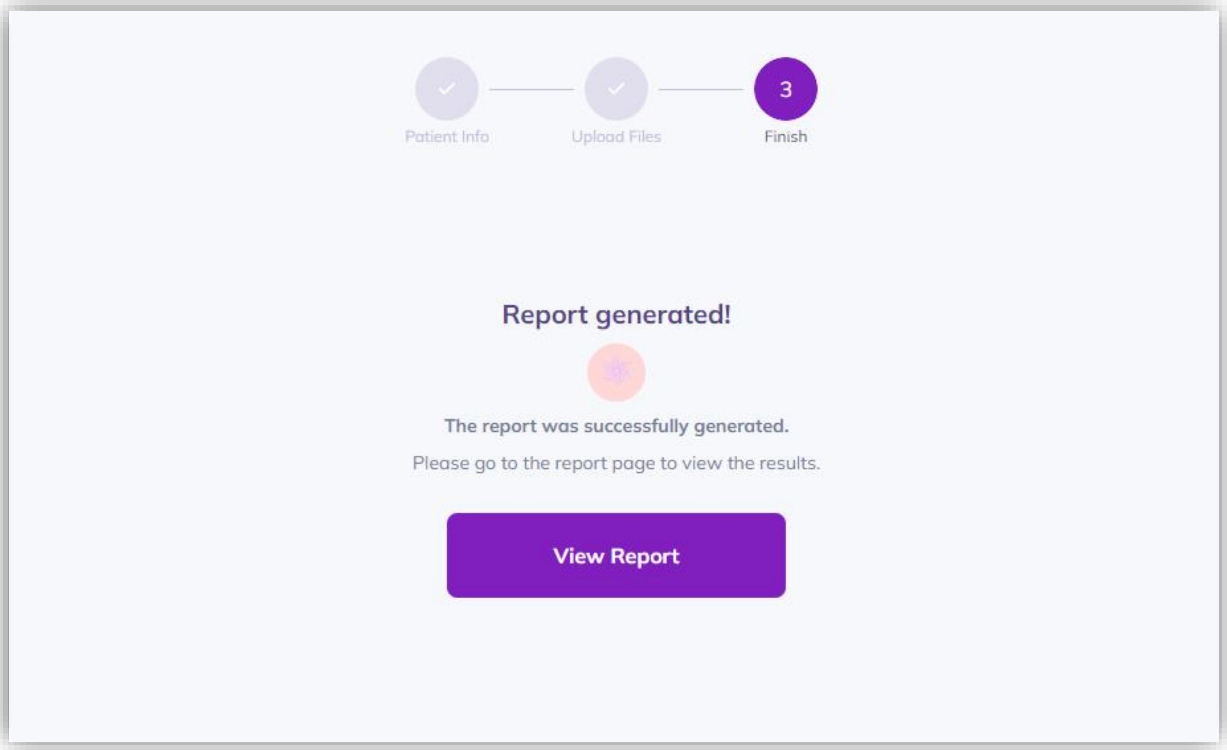
⚠ The software can recognize the patterns between positive and negative ion mode to minimize human error.

Click on **Run in Background** to continue with browsing data or starting a new measurement.
If you choose to run the calculation in the background, you will still see the progress **Running** in the main bar of the dashboard. Click on it to return to your running calculation.

4.3.3. Finish

You will automatically receive a success notification if the files have been successfully uploaded and processed.

Click on **View Report** to see the results of the new measurement.

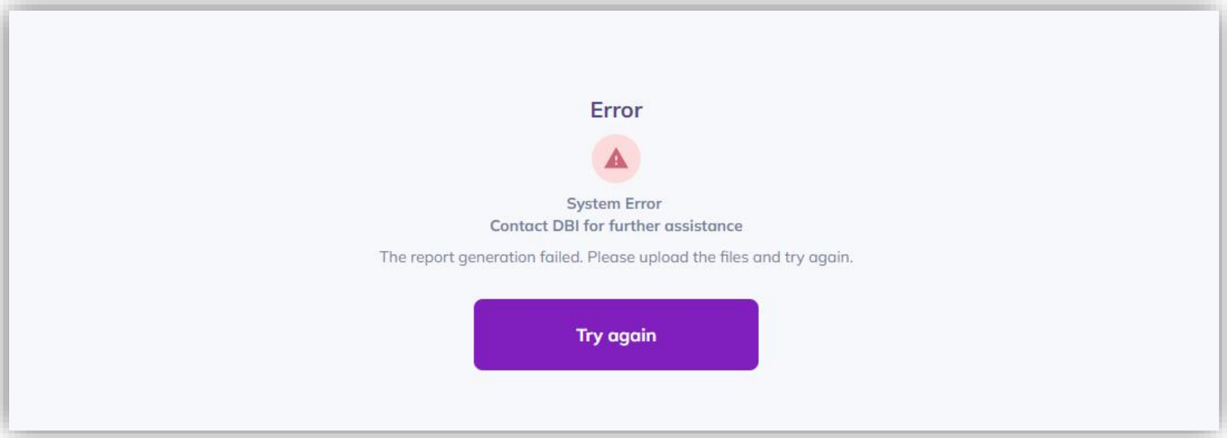


Report generated!

The report was successfully generated.

Please go to the report page to view the results.

For a failed measurement the following notification will appear



Error

System Error
Contact DBI for further assistance

The report generation failed. Please upload the files and try again.

4.4. Report

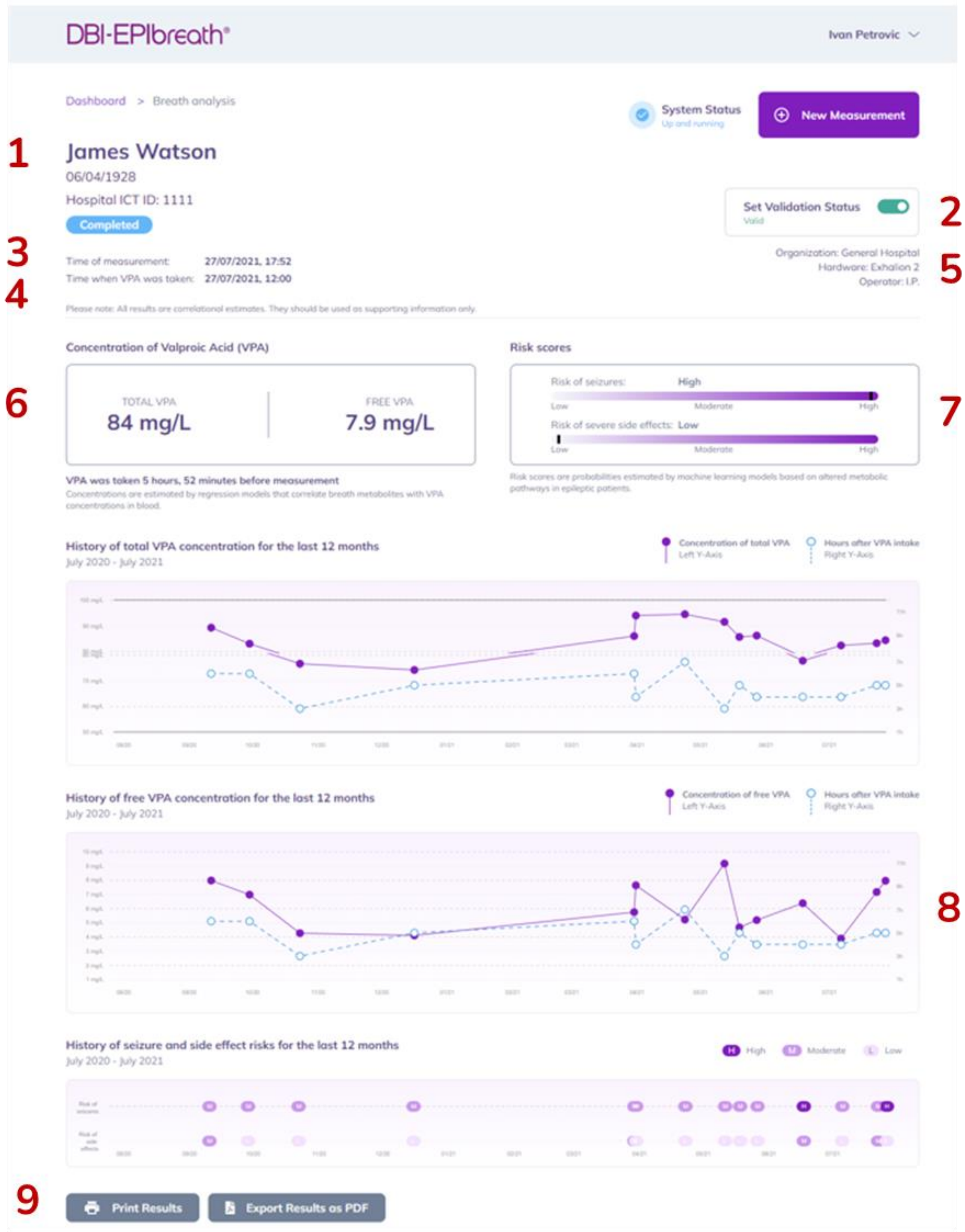
When the files are processed, a report is automatically generated. The report consists of the following elements:

1. Summary of **patient information (1)**

2. **Validation status** of current measurement **(2)**
   Based on your observations during the data acquisition and in case of reasonable doubts you can validate or invalidate the current measurement.
3. **Date** and **time** of current measurement **(3)**
4. Date and time of **last VPA intake (4)**
5. Summary of **operator information (5)**
6. Concentrations of **total** and **free VPA (6)**
7. **Risk of side effects and seizures (7)**
8. **History** of total and free VPA and risk scores from previous measurements over the last 12 months **(8)**
9. Options to save as **PDF** or **print report (9)**

⚠ The results only provide supporting information to the treatment monitoring and should be interpreted with care.

Report from a patient VPA taken:



James Watson
06/04/1928
Hospital ICT ID: 1111
Completed

Set Validation Status: Valid

Time of measurement: 27/07/2021, 17:52
Time when VPA was taken: 27/07/2021, 12:00

Organization: General Hospital
Hardware: Exhalion 2
Operator: I.P.

Please note: All results are correlational estimates. They should be used as supporting information only.

Concentration of Valproic Acid (VPA)

TOTAL VPA: 84 mg/L
FREE VPA: 7.9 mg/L

VPA was taken 5 hours, 52 minutes before measurement

Concentrations are estimated by regression models that correlate breath metabolites with VPA concentrations in blood.

Risk scores

Risk of seizures: High
Risk of severe side effects: Low

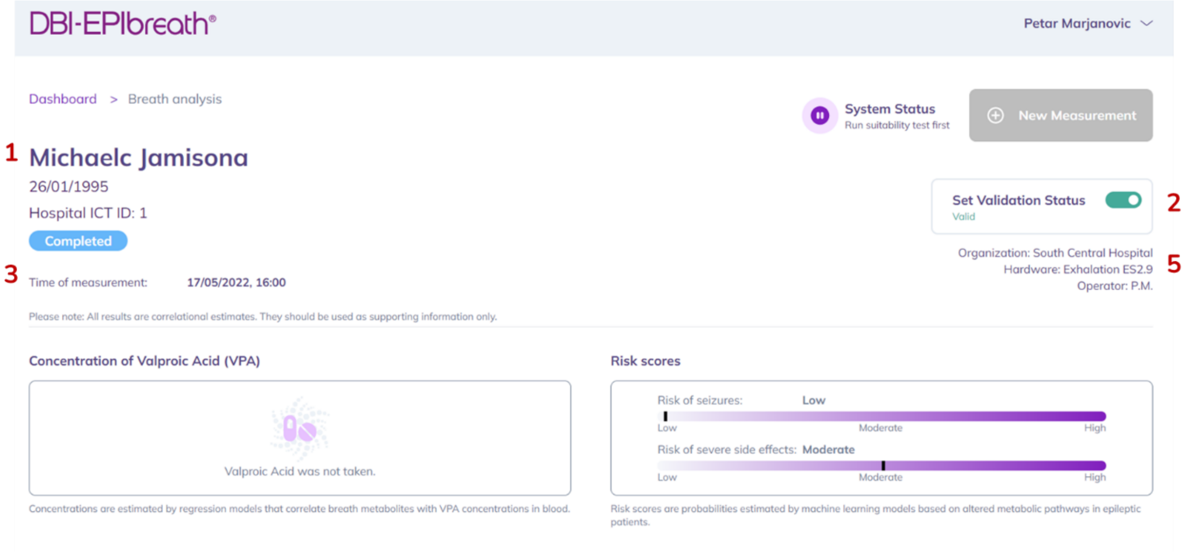
Risk scores are probabilities estimated by machine learning models based on altered metabolic pathways in epileptic patients.

History of total VPA concentration for the last 12 months
July 2020 - July 2021

History of free VPA concentration for the last 12 months
July 2020 - July 2021

History of seizure and side effect risks for the last 12 months
July 2020 - July 2021

Report from a patient without VPA intake: No VPA values are visible only risk scores in low, medium and high probability.



Michaelc Jamisona
26/01/1995
Hospital ICT ID: 1

Time of measurement: 17/05/2022, 16:00

Set Validation Status: Valid

Organization: South Central Hospital
Hardware: Exhalation ES2.9
Operator: P.M.

Please note: All results are correlational estimates. They should be used as supporting information only.

Concentration of Valproic Acid (VPA)

Valproic Acid was not taken.

Concentrations are estimated by regression models that correlate breath metabolites with VPA concentrations in blood.

Risk scores

Risk of seizures: Low

Risk of severe side effects: Moderate

Risk scores are probabilities estimated by machine learning models based on altered metabolic pathways in epileptic patients.

5. Support

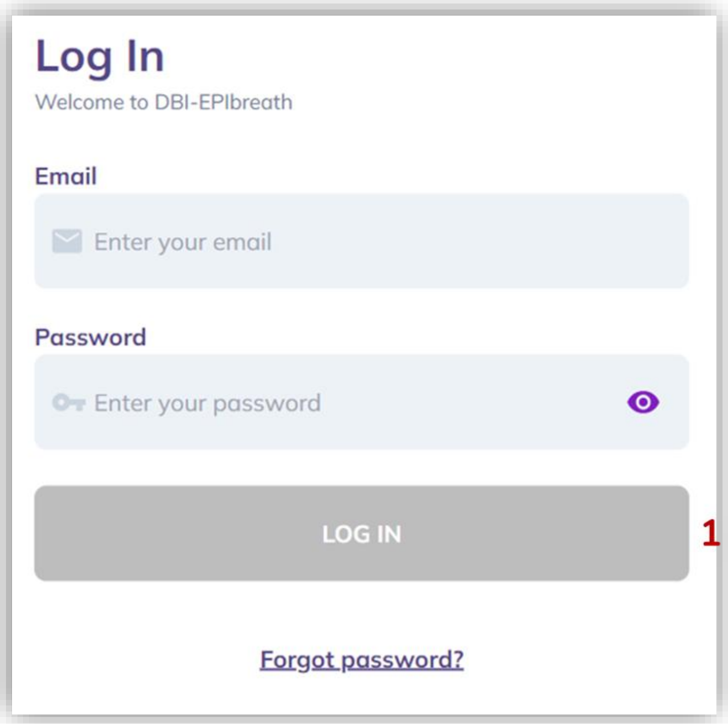
5.1. Add a new user

Please contact DBI technical support, if you need to add a new user to DBI-EPIbreath® (support@dbi.ch). They will set up a new account for them. Also refer to 3.2 Account set up.

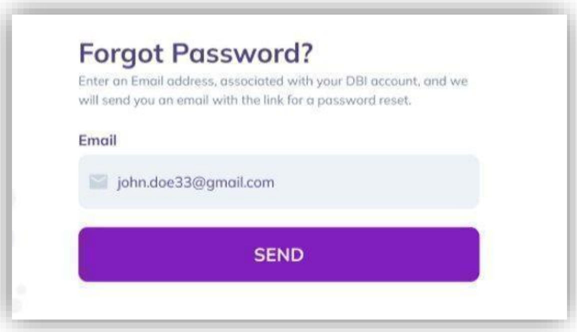
5.2. Reset password

If you want to change your password, please follow the steps below.

1. Open a web browser.
2. Type in the following web address: https://epibreath.dbi.ch
12. Click on **Forgot Password (1)**



13. Enter the **email address** that is associated with your DBI-EPIbreath® account.



Forgot Password?

Enter an Email address, associated with your DBI account, and we will send you an email with the link for a password reset.

Email: john.doe33@gmail.com

14. Click **SEND**. DBI will send you a reset link.
15. Check your email and **open the reset link**.
16. Type in your **new password**.

17. Click **RESET PASSWORD**. You should automatically see a confirmation that your password has been changed.
    Please note: The **RESET PASSWORD** button will only appear active once you have entered a password.

5.3. Troubleshooting

5.3.1. Error messages

Code	Error	Location	Reason

1	File update failed. Please refresh and try again.	Daily SST	Generic error: if upload of daily sst file for Daily SST fails due to network problems, frontend issues
2	File update failed. Please refresh and try again.	SST	Generic error: if upload of .raw files for sst fails due to network problems, frontend issues
3	File update failed. Please refresh and try again.	New Measurement	Generic error: if upload of .raw or co2 files fails due to network problems, frontend issues
4	Unable export as PDF. Please refresh and try again.	Report	Generic error: if generation of pdf fails due to network problems, frontend issues
5	Some error occurred. Validation status was not updated	Report	Generic error: if updating validation status fails due to network problems, frontend issues
6	The email address and/or password are not associated with an account.	Login	User entered wrong email or password
7	You have entered email or password too many times. Please check your credentials and try again later.	Login	User tried to login with wrong credentials too many times
8	Unknown error. Please try again later.	Login	Generic error: when an error occurred that is not one of the above (Error 7 and 8) or due to network connection issues, frontend issues
9	Unexpected error occurred. Please refresh and try again.	New Measurement	Generic error: after uploading files during new measurement, if there is some problem to start the analysis and that error is not covered by the backend error messages or happened due to network connection or frontend problem
10	Unexpected error occurred while uploading. Please refresh and try again.	New Measurement	Generic error: during file upload for new measurement, if there is some problem to upload the files and that error is not covered by the backend error messages or happened due to network connection or frontend problem
11	Unexpected error occurred. Please refresh and try again.	New Measurement	Generic error: if some error occurs that is not handled by backend error messages or happens due to network connection or frontend issues while updating patient information during new measurement flow
12	Unable to logout. Please refresh and try again.	All screens/ Logout functionality	Generic error: if logout fails due to network problems, fronted issues
400	Unsupported file extension	Daily and System SST	The uploading file (test) is not finishing with `.raw` extention
400	Unsupported file extension	Create Measurement - uploading files	The uploading RAW file is not finishing with `.raw` extention

400	Unsupported file extension	Create Measurement - uploading files	The uploading CO2 file is not finishing with `.txt` extention
400	Cannot upload test from the future.	System and Daily SST	When the file have filename date from the future
400	Please upload a file with expected filename format.	Create Measurement - uploading files	If one of the files does not have expected filename format (regarding date format, and `_pos` and `_neg` sufix for RAW)
400	Please upload a file with expected filename format.	Daily and System SST	If the file does not have expected filename format (regarding date format, and `_pos` and `_neg` sufix)
409	Please make sure there isn’t more than one file from the same day	System SST	When trying to upload System SST, if there is already file (test) with the same date in the filename uploaded
409	Conflicted state. 'ready' flag set when device isn't ready	Daily and System SST	When someone set "ready" flag to "True" of the device in the DB but there is less than 21 valid files uploaded for SST
422	Please make sure the file is from this day	Daily SST	When the uploading file (test) doesn't have the today's date in the filename
409	Item already exists	Daily SST	When trying to upload new Daily SST, but there is already uploaded valid (or processing) file (test)
404	Device does not exist	Create Measurement	If the user doesn't have a device linked to itself anymore through the organization (Should not happen, only if DB state is messed up)
404	Device does not exist	System and Daily SST	If the user doesn't have a device linked to itself anymore through the organization (Should not happen, only if DB state is messed up)
404	Device Suitability Test does not exist	Daily SST	If device suitability test doesn't exist for provided `uuid` when Matlab updating Daily SST result
404	Device Suitability Test does not exist	Daily and System SST	If device suitability test doesn't exist for provided `uuid` when confirming uploaded file (test)
400	Upload is already confirmed.	Daily and System SST	Trying to confirm already confirmed file (test) (unlikely to happen)
400	Drug Usage Time must be specified when Valproic Acid is taken.	Create Measurement - Filling Patient Info	When drug usage time is not specified but vpa was taken
400	Valproic Acid was not taken.	Create Measurement - Filling Patient Info	When vpa was taken but no drug usage time is specified
400	All files have to have same date in the filename	Create Measurement - uploading files	When files don't have the same date in their filenames
404	Patient does not exist	Download Patient (only admin)	When patient does not exist for provided `uuid` or is already deleted

404	Patient does not exist	Delete Patient (only admin)	When patient does not exist for provided `uuid` or is already deleted
404	Patient does not exist	Patient Info	When patient does not exist for provided `external_patient_id` within the organization
400	API Key must be specified	Donwload Patient and Delete Patinet (only admin)	When API key is not specified
403	The provided API key is not valid	Donwload Patient and Delete Patinet (only admin)	When provided API key is not valid
400	Measurement cannot be created	Create Measurement	If Measurement cannot be created (the state isn't suitable for measurement creation) (This should not happen because it is also secured on the FE)
404	Measurement does not exist	Matlab processing finished (for measurement)	When Matlab tries to update Measurement results for non existing measurement (for provided `uuid`) (the only case is when someone deletes measurement's patient while Matlab is processing)
400	Measurements process already started	Create Measurement - start measurement	When processing of the specific measurement is already started but tried to be started again
404	Patient does not exist	Create Measurement - start measurement	When uploading measurement files for the patient that is deleted in the meantime
404	Patient does not exist	Report Page	When patient of the measurement does not exist anymore
404	Measurement does not exist	Create Measurement - processing measurement	On progress bar page if measurement does not exist anymore (when someone deleted measurement's patient in the meantime)
404	Measurement does not exist	Create Measurement - start measurement	When trying to start measurement after files uplaod that does not exist anymore (when someone deleted measurement's patient in the meantime)
404	Measurement does not exist	Report Page	When Measurement does not exist
404	Measurement does not exist	Report Page	Updating a status of the measurement that does not exist anymore (when someone deleted measurement's patient in the meantime)
400	Not a valid UUID.	Download Patient (only admin)	When uuid from the endpoint path is not a valid uuid
400	Not a valid UUID.	Delete Patient (only admin)	When uuid from the endpoint path is not a valid uuid

400	Not a valid UUID.	Get single measurement (On checking measurement status while processing)	When uuid from the endpoint path is not a valid uuid
400	Not a valid UUID.	Report Page	When uuid from the endpoint path is not a valid uuid
400	External id not provided	Patient Info	If external patient id not provided
400	Missing data for required field.	Create Measurement - Filling Patient Info	One of first_name, last_name, external_patient_id, or date_of_birth is missing
400	Not a valid date.	Create Measurement - Filling Patient Info	date_of_birth is not a valid date.
400	Missing data for required field.	System and Daily SST	When uploading test (file), one of filename, file_created_at, or device_id is missing
400	Missing data for required field.	System and Daily SST	On upload confirm, \`uploaded\` is missing
400	Not a valid UUID.	System and Daily SST	On upload confirm, when uuid from the endpoint path is not a valid uuid
400	Missing data for required field.	Daily SST	When Matlab finish Daily SST processing and update it with result and one of result, or status is missing
400	Must be one of: error, ok, warning.	Daily SST	When Matlab finish Daily SST processing and result status is not one of error, ok, or warning
400	Not a valid mapping type	Daily SST	When Matlab finish Daily SST processing and result is mapping type.
400	Must be one of: external_patient_id, first_name, last_name, created_at, full_name.	Dashboard List Measurements	When sort query param is specified but not one in the list.
400	Must be one of: asc, desc.	Dashboard List Measurements	When sort query param is specified but not one in the list.
400	Not a valid UUID.	Create Measurement - uploading files	patient_uuid is not a valid uuid.
400	Missing data for required field.	Create Measurement - uploading files	One of patient_uuid, valproic_acid_taken, positive_raw_filename, negative_raw_filename, positive_co2_filename, or negative_co2_filename is missing
400	Missing data for required field.	Report Page - Update measurement status	validation_status is missing
400	Missing data for required field.	Create Measurement -	uploaded is missing

		start measurement	
400	Missing data for required field.	Matlab processing finished (for measurement)	status (validation_status) is missing

Raw Files 2VPA scores Errors

code	**Type**	**Message for user**	**Fixable**	**Actions**	**message**
-13	Error	System Error:	No	Contact DBI for further assistance	Unable to load TrainedModels (A struct with previously trained models for TotalVPA, FreeVPA, SideEffects and DrugResponse), Please check if path is correct.
-2	Error	System Error:	No	Contact DBI for further assistance	Unable to access RawFileReader C# functions, make sure C# functions are installed and paths are correctly set.
-21	Error	Raw File Error: Make sure the uploaded files are correct ones	Possible	Check if the correct files are provided	Error during 'GetBasicFileInfo'.
-26	Error	Raw File Error: Make sure the uploaded files are correct ones	Possible	Check if the correct files are provided	Error during 'GetScanFilter'.
-51	Error	Raw File Error: Mixed or unknown polarity	Possible	`	Some RAW fileshave either unknown or mixed polarity (Try to re-run after removing them and their paired files, if any).
-52	Error	Raw File Error: Wrong naming convention	Fixable	Check the file name	Some RAW files break RAW filename convention, please fix the issue and retry | correct convention is YYYYMMDD_SN_(pos|neg)_xx.RAW or see SOP.
-53	Error	Raw File Error: Inconsistent polarity in the filename and in the RAW file	Fixable	Check the file name, make sure the polarity in the file name is the same as in the RAW file	Some RAW files have different polarity than the polarity in the filename, please fix the issue and retry.
-54	Error	Raw File Error: More than one	Possible	Check the mass-spectrometer'	Some RAW files have more than 1 unique scan filter, please fix the

		scan filters detected		s setting of file and redo the measurement.	issue and retry | corresponding RAW file must be reoved.
-55	Error	Raw File Error: More than FT resolution detected	Possible	Check the mass-spectrometer's setting of file and redo the measurement.	Some RAW files have more than 1 FT Resolution, please fix the issue and retry | corresponding RAW file must be reoved.
-56	Error	Raw File Error: Measurement needs two RAW files	Fixable	Check if the correct files are provided	Some measurement do not have 2 RAW file, please fix the issue and retry.
-57	Error	Raw File Error: Measurement needs to have 1 positive RAW file and 1 negative RAW file	Fixable	Check if the correct files are provided	Some measurement do not have pos and neg files, please fix the issue and retry | Each measurement must have two RAW file one from pos and one from neg mode.
-58	Warning	Raw File Warning: Positive and Negative RAW files are more than 20 minutes apart	Fixable	Check if the correct files are provided	Some measurements have 20 minutes or more time difference between the acquisition of paired mode files.
-6	Error	System Error:	No	Contact DBI for further assistance	FOI in TotalVPA and FreeVPA trained modes are not same, they must be same.
-7	Error	System Error:	No	Contact DBI for further assistance	Error during ModeSpecific_Targated_Analysis in positive mode.
-8	Error	System Error:	No	Contact DBI for further assistance	Error during ModeSpecific_Targated_Analysis in negative mode.
-13	Error	System Error:	No	Contact DBI for further assistance	Unable to load TrainedModels (A struct with previously trained models for TotalVPA, FreeVPA, SideEffects and DrugResponse), Please check if path is correct.
-2	Error	System Error:	No	Contact DBI for further assistance	Unable to access RawFileReader C# functions, make sure C#

					functions are installed and paths are correctly set.
-21	Error	Raw File Error: Make sure the uploaded files are correct ones	Possible	Check if the correct files are provided	Error during 'GetBasicFileInfo'.
-26	Error	Raw File Error: Make sure the uploaded files are correct ones	Possible	Check if the correct files are provided	Error during 'GetScanFilter'.
-51	Error	Raw File Error: Mixed or unknown polarity	Possible	`	Some RAW fileshave either unknown or mixed polarity (Try to re-run after removing them and their paired files, if any).
-52	Error	Raw File Error: Wrong naming convention	Fixable	Check the file name	Some RAW files break RAW filename convention, please fix the issue and retry | correct convention is YYYYMMDD_SN_(pos|neg)_xx.RAW or see SOP.
-53	Error	Raw File Error: Inconsistent polarity in the filename and in the RAW file	Fixable	Check the file name, make sure the polarity in the file name is the same as in the RAW file	Some RAW files have different polarity than the polarity in the filename, please fix the issue and retry.
-54	Error	Raw File Error: More than one scan filters detected	Possible	Check the mass-spectrometer's setting of file and redo the measurement.	Some RAW files have more than 1 unique scan filter, please fix the issue and retry | corresponding RAW file must be reoved.
-55	Error	Raw File Error: More than FT resolution detected	Possible	Check the mass-spectrometer's setting of file and redo the measurement.	Some RAW files have more than 1 FT Resolution, please fix the issue and retry | corresponding RAW file must be reoved.
-56	Error	Raw File Error: Measurement needs two RAW files	Fixable	Check if the correct files are provided	Some measurement do not have 2 RAW file, please fix the issue and retry.

-57	Error	Raw File Error: Measurement needs to have 1 positive RAW file and 1 negative RAW file	Fixable	Check if the correct files are provided	Some measurement do not have pos and neg files, please fix the issue and retry | Each measurement must have two RAW file one from pos and one from neg mode.
-58	Warning	Raw File Warning: Positive and Negative RAW files are more than 20 minutes apart	Fixable	Check if the correct files are provided	Some measurements have 20 minutes or more time difference between the acquisition of paired mode files.
-6	Error	System Error:	No	Contact DBI for further assistance	FOI in TotalVPA and FreeVPA trained modes are not same, they must be same.
-7	Error	System Error:	No	Contact DBI for further assistance	Error during ModeSpecific_Targated_Analysis in positive mode.
-8	Error	System Error:	No	Contact DBI for further assistance	Error during ModeSpecific_Targated_Analysis in negative mode.

5.4. Bug reports

Please report any bug or issue to DBI technical support (support@dbi.ch).

6. Technical Specifications

6.1. Performance

The performance parameters for the total and free level of VPA rely on the concordance between the drug levels measured in the blood and in the breath. They are reported as Concordance Correlation Coefficient (Lin et al., 1989). This correlation coefficient measures the concordance between a new test and a gold standard test as a quantification of the agreement between these two measures of the same variable. Since the risk of seizures and risk of severe side effects can be measured as binary variables, they are quantified as classification parameters (sensitivity, specificity).

Performance parameter	**Performance characteristics**
Total VPA	Concordance correlation coefficient: 0.63
Free VPA	Concordance correlation coefficient: 0.66
Risk of seizures	Sensitivity: 0.78 Specificity: 0.58
Risk of severe side effects	Sensitivity: 0.91 Specificity: 0.42

6.2. Mathematical approach

VPA Concentrations are estimated by regression models that correlate breath metabolites with VPA concentrations in blood.

Risk scores are probabilities estimated by machine learning models based on altered metabolic pathways in epileptic patients.