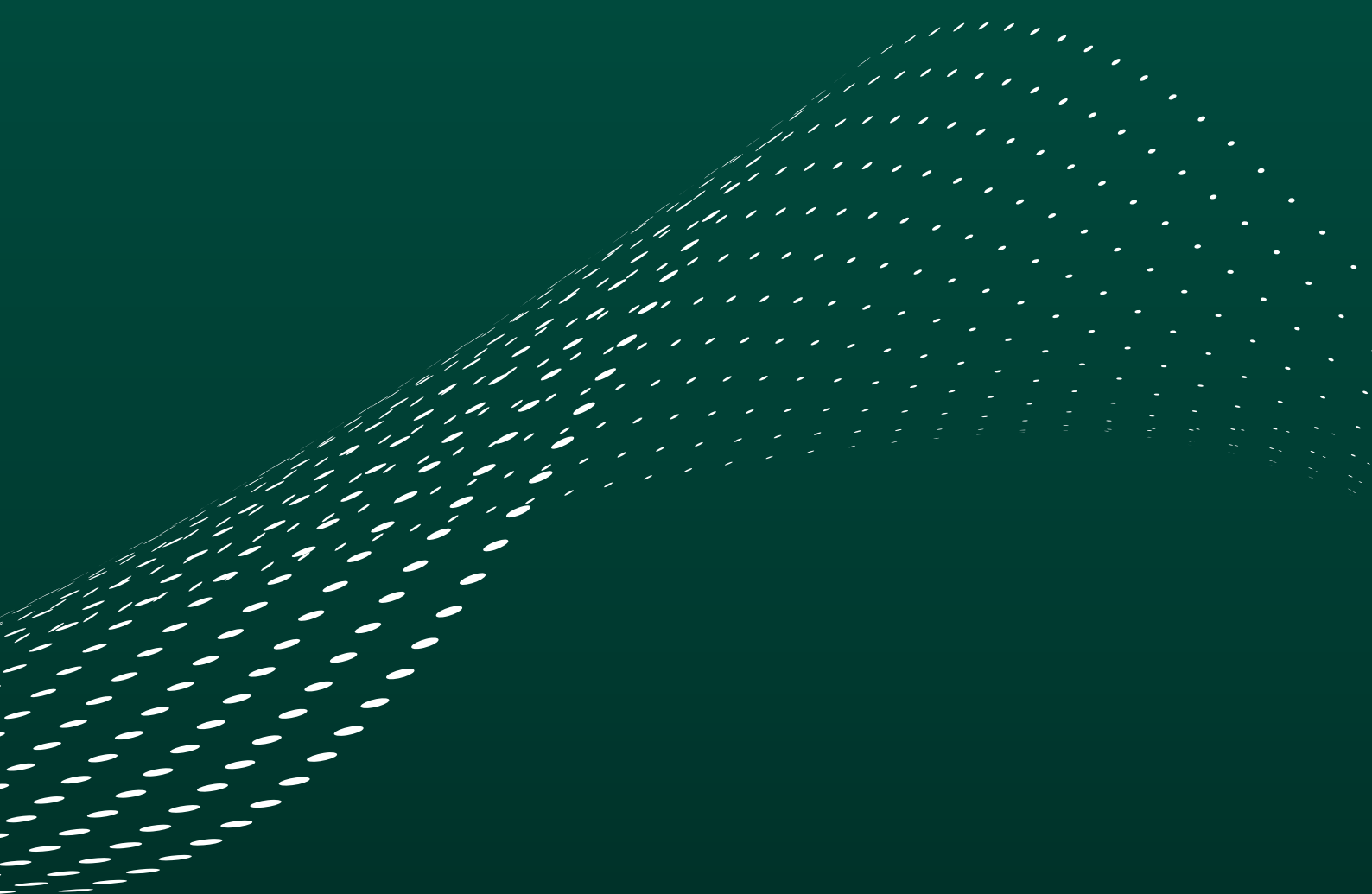




ConcizuTrace™ ELISA

Protocol Guide for Running ConcizuTrace™ ELISA
and Sample Handling



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WELCOME TO THE RANDOX LAB NETWORK

We value your support in joining our ConcizuTrace™ laboratory network to provide certainty to patients, enabling them to achieve greater confidence in consistent daily steady-state protection, with the benefit of a simplified administration, sample collection and effective patient reporting process.

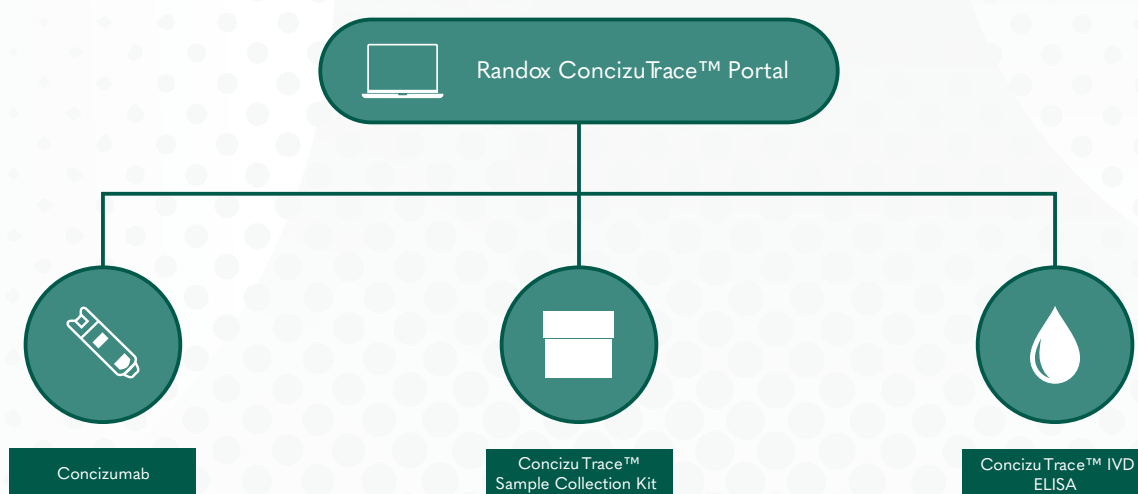
Randox Laboratories are proud to support Novo Nordisk to allow Haemophilia Treatment Centers (HTCs) provide their patients with a novel, first-in-class treatment with rapid, simplified drug administration.

Concizumab is a monoclonal antibody for subcutaneous prophylaxis (PPX) across all haemophilia subtypes (haemophilia A or B, with or without inhibitors). Haemophilia is a rare, chronic, serious, life-threatening bleeding disorder significantly affecting the lifestyle and health-related quality of life of patients and their caregivers.

Every patient receiving Novo Nordisk Concizumab drug will be assessed at week 4 to allow for personalised dose optimisation in accordance with the drug label.

The Randox ConcizuTrace™ service solution comprises:

- Randox ConcizuTrace™ Sample Collection Kit, a kit to provide physicians and healthcare staff with all needed materials for compliant blood sample collection and citrated plasma preparation.
- We provide comprehensive logistical support for transporting blood samples to analytical laboratories, managed seamlessly through a fully global, unique solution, entrusted to a single partner courier.
- Randox ConcizuTrace™ ELISA Kit, an IVD kit for laboratories to perform the measurement of Concizumab concentration in plasma.
- Randox ConcizuTrace™ Portal to acknowledge sample reception at Labs and report results to the prescribing physician.



SECTION 1: SAMPLE COLLECTION PREPARATION AND LOGISTICS USING THE CONCIZUTRACE™ SAMPLE COLLECTION KIT

1.1. ConcizuTrace™ Sample Collection Kit

To facilitate and standardize the measurement of Concizumab, Randox blood sample collection kits are manufactured and made available to HTCs at the time of sampling. The pre-labelled transfer tube, together with the Test Order Form, are shipped together in a Pathoseal bag, on dry ice, to the assigned laboratory for testing using the Randox ConcizuTrace™ assay.

The assay is validated for human 3.2% citrate plasma. Kits are supplied separately to HTCs and arrive at your laboratory on dry ice for testing. Each patient sample is tracked, monitored, and reported using the Randox portal.

1.2. Delivery of the Sample to the Lab

The selected courier company for this transportation is Marken

The Courier will deliver the samples on dry ice to the Lab in charge of performing the test (based on the HTC location), within the contractual timelines (variable by country).



1.2.1. What should you expect to receive into your laboratory for Concizumab assessment?

Marken will arrive at your laboratory with the Biosystem shipper containing the following items:

- 1x pre-labelled frozen cryotube containing patient plasma sample
- The sister aliquot will be stored at HTC site as back up



In the case that the HTC does not have suitable freezing capabilities for sample storage, the lab will receive two aliquots, one to be processed and reported, the second to be stored at -80°C as back up until the result is reported.

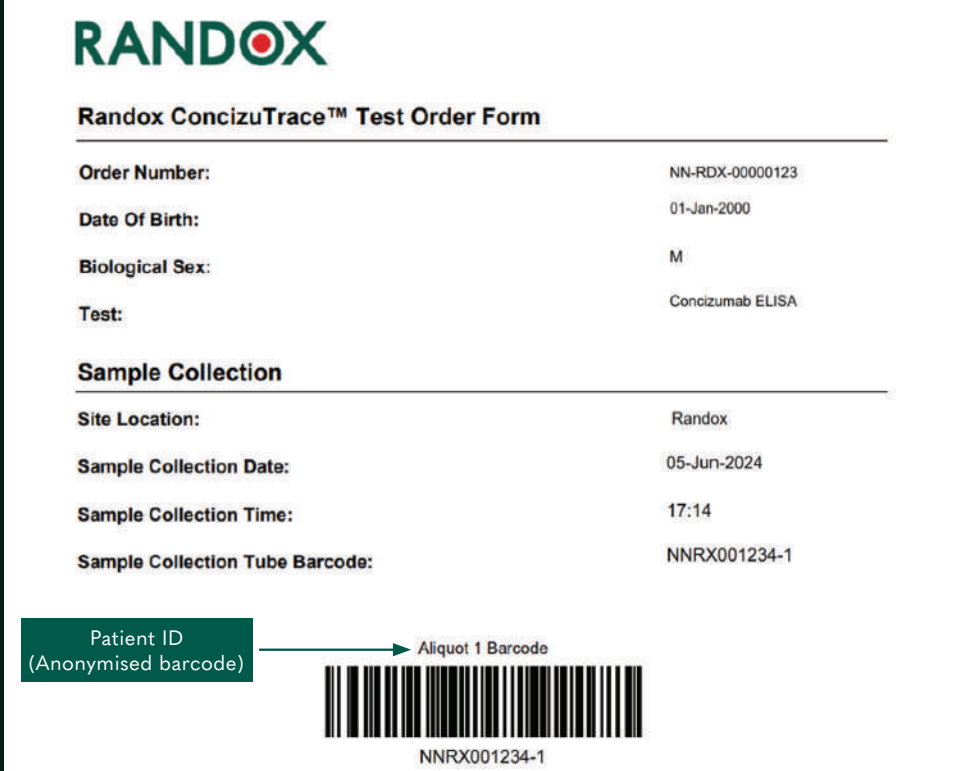
Shipped frozen on dry ice

- 1x temperature logger with every shipment which will have been started by Marken upon collection

SECTION 1: SAMPLE COLLECTION PREPARATION AND LOGISTICS USING THE CONCIZUTRACE™ SAMPLE COLLECTION KIT (CONTINUED)

Shipment Packaging includes a paper Test Order Form with:

- Date of Birth
- Biological Sex
- Test
- HTC Identification
- Sample Collection Date
- Sample Collection Time
- Patient ID (Anonymised Barcode)



The image shows a 'Randox ConcizuTrace™ Test Order Form'. At the top left is the Randox logo. Below it is the title 'Randox ConcizuTrace™ Test Order Form'. The form is divided into two main sections by horizontal lines. The first section contains fields for 'Order Number' (NN-RDX-00000123), 'Date Of Birth' (01-Jan-2000), 'Biological Sex' (M), and 'Test' (Concizumab ELISA). The second section, titled 'Sample Collection', contains fields for 'Site Location' (Randox), 'Sample Collection Date' (05-Jun-2024), 'Sample Collection Time' (17:14), and 'Sample Collection Tube Barcode' (NNRX001234-1). At the bottom, there is a green box labeled 'Patient ID (Anonymised barcode)' with an arrow pointing to a barcode labeled 'Aliquot 1 Barcode'. Below the barcode is the text 'NNRX001234-1'.

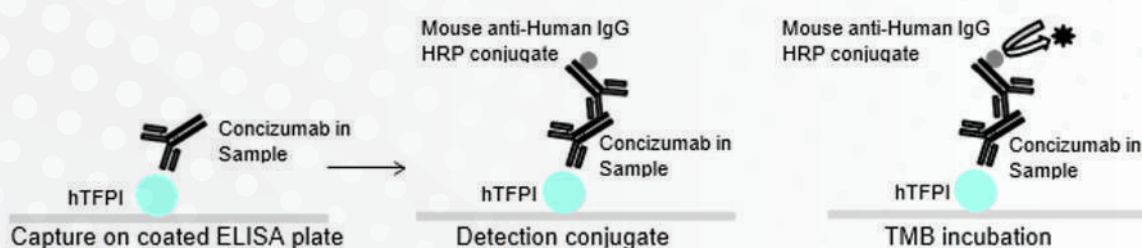
Randox	
Randox ConcizuTrace™ Test Order Form	
Order Number:	NN-RDX-00000123
Date Of Birth:	01-Jan-2000
Biological Sex:	M
Test:	Concizumab ELISA
Sample Collection	
Site Location:	Randox
Sample Collection Date:	05-Jun-2024
Sample Collection Time:	17:14
Sample Collection Tube Barcode:	NNRX001234-1
Patient ID (Anonymised barcode)	Aliquot 1 Barcode
	
NNRX001234-1	

If the delivery package does not arrive as expected- for example, if an item is damaged or missing- please email Randox Laboratories Technical services by contacting concizutracessupport@randox.com.

SECTION 2: SAMPLE TESTING USING THE RANDOX CONCIZUTRACE™ ELISA KIT

2.1. ConcizuTrace™ ELISA Format

The ConcizuTrace™ ELISA is an in vitro diagnostic (IVD) used for the quantification of total Concizumab (drug compound as analyte) present in 3.2% citrated human plasma samples. The ConcizuTrace™ ELISA is a direct sandwich ELISA in which recombinant human Tissue Factor Pathway Inhibitor (TFPI) is used as capture antigen and a monoclonal mouse anti-human IgG4Fc antibody as a detection antibody. The assay is conducted in a classic 96-well microtiter plate format.



2.2. Randox ConcizuTrace™ Elisa Kit Contents

COMPONENT	VOLUME/AMOUNT SUPPLIED
Microtitre Plate	12 x 8 well
ELISA Diluent/Wash Buffer Conc	4 x 30 mL
Assay Buffer	1 x 30 mL
Acidification/ Neutralisation Plate	6
Acetic Acid	1 x 20 mL
Neutralising Solution	1 x 25 mL
Conjugate	1 x 70 µL
TMB Substrate	1 x 25 mL
ELISA Stop Solution	1 x 25 mL
ConcizuTrace™ Calibrators 1-8	8 x 0.5 mL
ConcizuTrace™ QC Low, Medium, and High	3 x 0.5 mL
Sample Dilution Matrix	3 x 5 mL

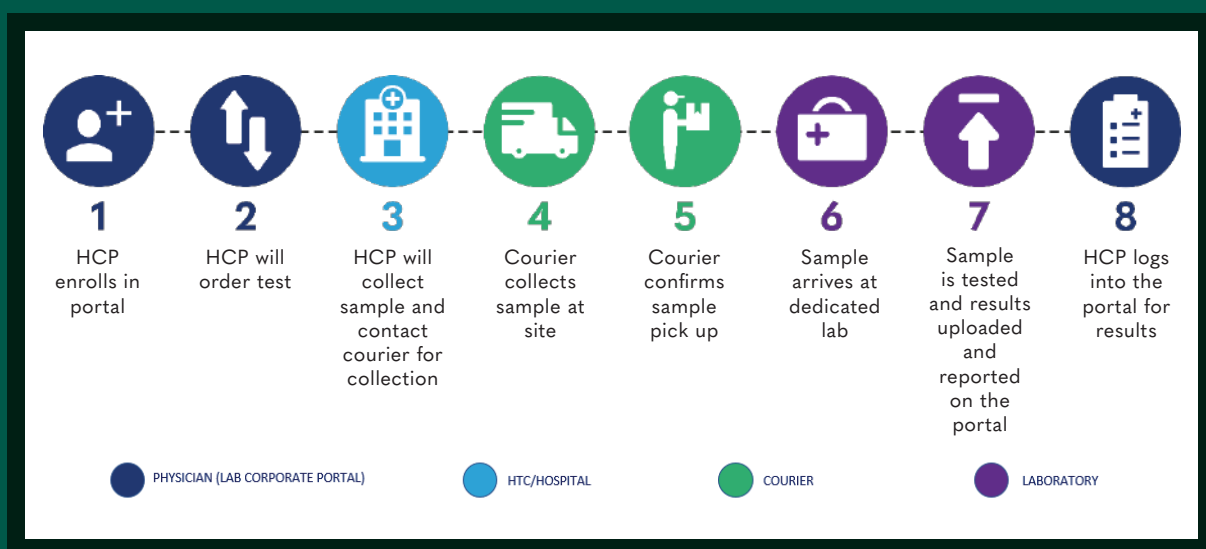
Please refer to the **ConcizuTrace™ ELISA IFU (CZM10591)** for more information.

SECTION 3: SAMPLE REPORTING USING THE RANDOX CONCIZUTRACE™ PORTAL

The Radox ConcizuTrace™ Portal is a dedicated web portal, that has been developed to enable test ordering, sample collection and shipment, laboratory analysis and result reporting under a unique web platform.

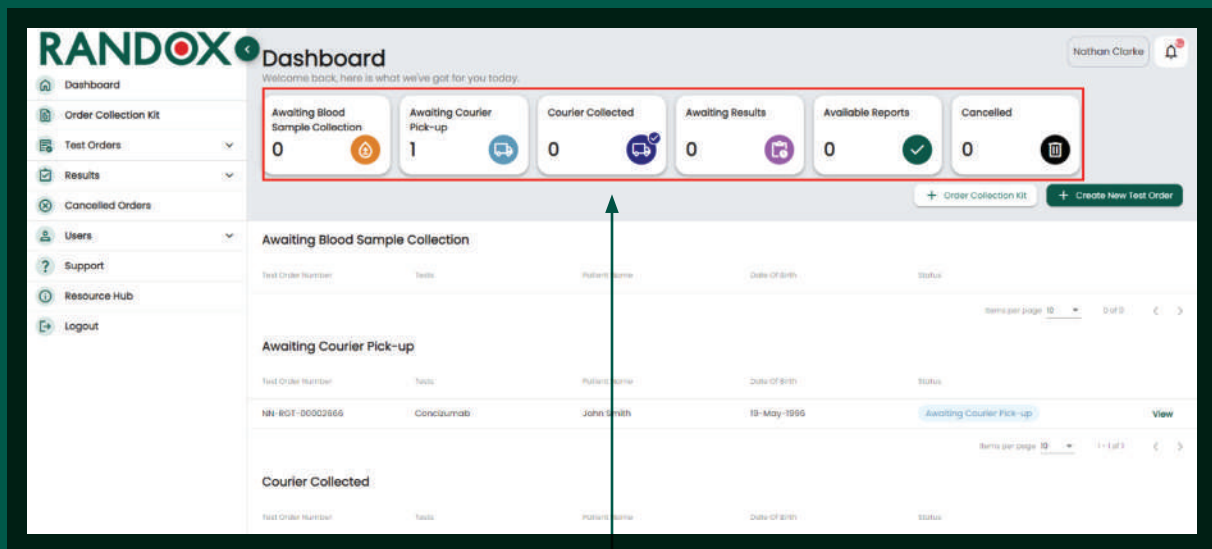
To secure the highest levels of privacy for patients, only authorized personnel can access the Radox ConcizuTrace™ Portal.

3.1. Process Overview



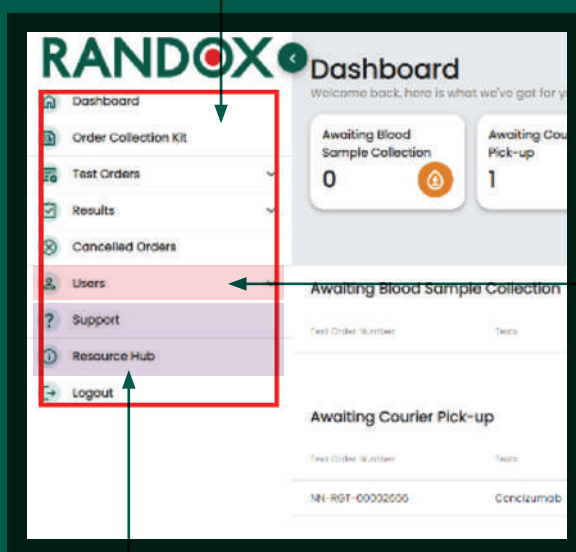
SECTION 3: SAMPLE REPORTING USING THE RANDOX CONCIZUTRACE™ PORTAL (CONTINUED)

3.2. Features at a glance



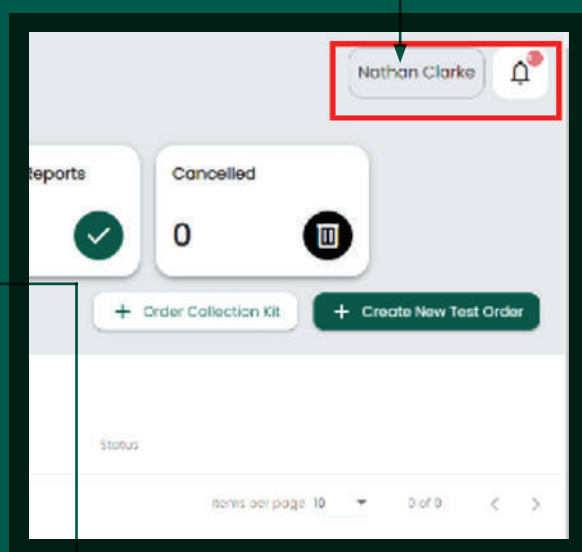
The icon-based dashboard provides an intuitive overview of the status of all samples logged by a HTC!

The Navigation Menu also directs the end users to the different stages of their samples and to access their results



Links to support and additional resources

Active alerts inform the end user



New End users can be invited or created

SECTION 4: NAVIGATING THE RANDOX CONCIZUTRACE™ PORTAL

Laboratory Level access users have a more streamlined version of the portal with access being provided for each end user role on a need-to-know basis. This version of the portal has been tailored to only allow access to the necessary information required by the Lab. This includes the status of all samples coming from health care facilities that are associated with your laboratory.

The screenshot shows the RANDOX Dashboard for user Niamh Admin O'Connor. The dashboard includes a sidebar with navigation links: Dashboard, Test Orders, Results, Cancelled Orders, Support, Resource Hub, and Logout. The main content area features a 'Welcome back, here is what we've got for you today' message and a summary of order statuses: Awaiting Courier Pick-up (38), Courier Collected (6), Orders in Lab (6), Available Reports (19), and Cancelled Orders (20). Below this, the 'Awaiting Courier Pick-up' section displays a table of orders.

Aliquot Number	Test Order Number	Tests	Date Of Birth	Collection Date	Courier	Status	Action
RD1-025-A	NH-H01-00000028	Concisaumab	24-Aug-2000	24-Aug-2023 09:30	Not Scheduled	Awaiting Courier Pick-up	View
123456	NH-NMT-00000030	Concisaumab	01-Jan-2021	27-Nov-2023 09:32	Not Scheduled	Awaiting Courier Pick-up	View
12345	NH-NMT-00000031	Concisaumab	01-Jan-2000	28-Nov-2023 03:38	Not Scheduled	Awaiting Courier Pick-up	View
12345	NH-NMT-00000032	Concisaumab	29-Nov-2008	29-Nov-2023 08:35	Not Scheduled	Awaiting Courier Pick-up	View
12345	NH-NMT-00000034	Concisaumab	01-Dec-2000	01-Dec-2023 07:48	Pickup Confirmed	Awaiting Courier Pick-up	View
adefg	NH-IPS-00000045	Concisaumab	01-Jan-1995	06-Dec-2023 02:00	Not Scheduled	Awaiting Courier Pick-up	View

When a lab receives a shipment with a sample, there will be a unique barcode on the cryotube, and the test order form will also be in the shipment that will contain the unique order number.

The screenshot shows the RANDOX Test Orders page for user Niamh Admin O'Connor. The page title is 'Test Orders' with a subtitle 'On this page you can view awaiting courier pick-up, courier collected and in-lab test orders.' The 'Courier collected' tab is selected in the sidebar. The main content area shows a search bar and a table of collected orders.

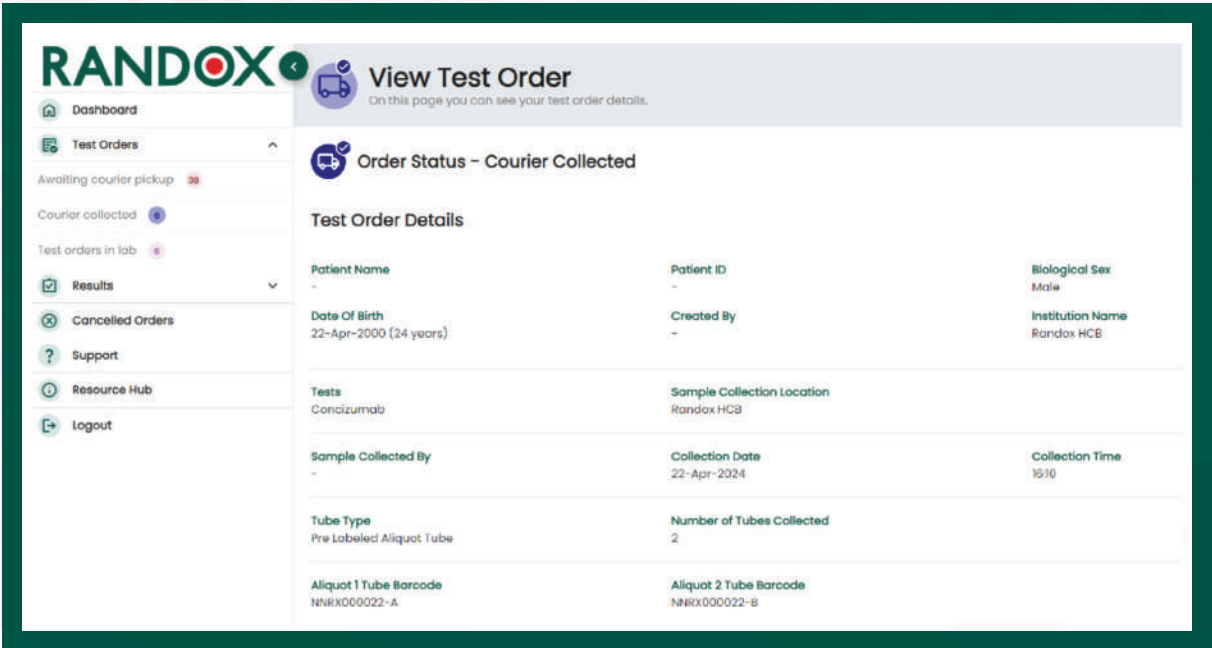
Aliquot Number	Test Order Number	Tests	Date Of Birth	Collection Date	Courier	Status	Action
NH-X0000022-A	NH-HCB-00000064	Concisaumab	22-Apr-2000		In Transit	Courier Collected	View
RD1-025-A	NH-H01-00000029	Concisaumab	27-Sep-2000	28-Sep-2023 15:00	Not Scheduled	Courier Collected	View
123456	NH-IPS-00000035	Concisaumab	13-Dec-1988	06-Dec-2023 09:24	Not Scheduled	Courier Collected	View

Once the Test Order Form (TOF) and patient sample have been collected by the courier- this order will appear under the **"Courier Collected"** tab on the dashboard. The Lab technician can then find the test order number that relates to the test order form provided in the shipment. Click 'view' on the right-hand side.

SECTION 4: NAVIGATING THE RANDOX CONCIZUTRACE™ PORTAL (CONTINUED)

4.1. Accessioning the Samples

Having selected the order of interest, the lab technician will be able to see all the relevant details, including the aliquot tube barcodes which can be matched up to the tubes you have received.



You can then choose to accession the order once it has been received by selecting “**Order Accession**,” at the bottom of the page. Doing so will confirm to the end user that their sample has been successfully delivered to the laboratory.

The lab can also choose to ‘**Cancel Order**’ if required.



SECTION 4: NAVIGATING THE RANDOX CONCIZUTRACE™ PORTAL (CONTINUED)

RANDOX Update Accessioning Details

Update the accessioning details for this test order.

Niamh Admin O'Connor

Aliquot Number: NNRX000022-A

NN-HCB-00000064

Test Order Details

Biological Sex: Male

Date Of Birth: 22-Apr-2000 (24 years)

Accessioning Laboratory: Randox RCLS

Accessioning Date *: 19 Nov 2024

Accessioning Time *: 12:05

Back Update

You will be prompted to confirm the accessioning details are correct before selecting “update”

There will be a further prompt to confirm this action. Select ‘Yes, accession order’ to proceed.

Confirmation

This order will now be accessioned. This action cannot be reversed. Are you sure you wish to proceed?

Go back Yes, accession order

The order will progress into the “Test orders in lab” tab, where the lab technician will be provided with a full overview of the test order details.

RANDOX Test Orders

On this page you can view awaiting courier pick-up, courier collected and in-lab test orders.

Test orders in lab for processing

Search here

Aliquot Number	Test Order Number	Tests	Date Of Birth	Order Date	Status
NNRX000054-I	NN-8DX-0000018	Concizumab	12-Jun-2002	24-Jul-2024 12:37	Order in lab
NNRX000047-I	NN-HCB-0000083	Concizumab	05-Jan-2004	30-Apr-2024 12:09	Order in lab
NNRX000015-I	NN-HCB-0000067	Concizumab	01-Jan-2001	23-Apr-2024 13:36	Order in lab

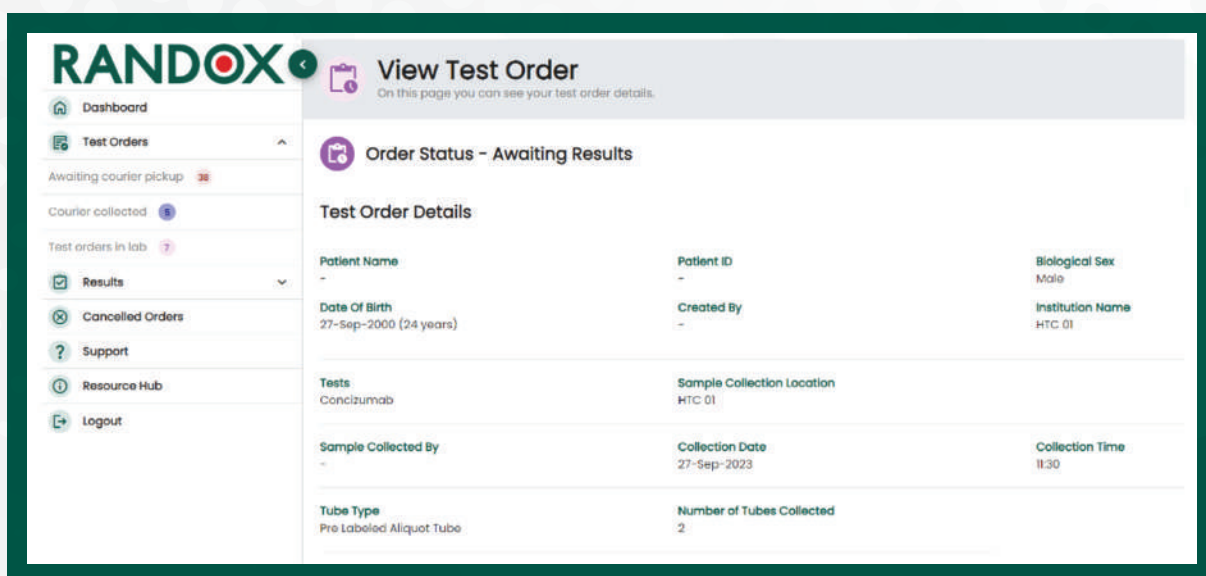
View View View

Within the “Test Orders in Lab tab” find the test order number that relates to the test order form provided in the shipment. Once you have selected the order of interest, click on the view button.

SECTION 4: NAVIGATING THE RANDOX CONCIZUTRACE™ PORTAL (CONTINUED)

4.2. Uploading a Report

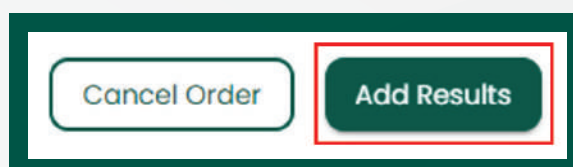
Once the testing of the sample has been completed, it is **mandatory** that the lab technician uploads a PDF version of the Lab report to the portal as soon as it's available, for the health care practitioner to access and/or download.



The screenshot displays the RANDOX portal interface. On the left is a sidebar menu with options: Dashboard, Test Orders (selected), Results, Cancelled Orders, Support, Resource Hub, and Logout. The main content area is titled 'View Test Order' with a sub-header 'Order Status - Awaiting Results'. Below this, 'Test Order Details' are listed in a table format:

Patient Name	Patient ID	Biological Sex
-	-	Male
Date Of Birth	Created By	Institution Name
27-Sep-2000 (24 years)	-	HTC 01
Tests	Sample Collection Location	
Concizumab	HTC 01	
Sample Collected By	Collection Date	Collection Time
-	27-Sep-2023	11:30
Tube Type	Number of Tubes Collected	
Pre Labeled Aliquot Tube	2	

By clicking on “Add Results” at the bottom of the page, it will bring you to a new page where it will allow you to upload a PDF report- Simply drag and drop the PDF file directly into the portal or browse your PC to upload the appropriate file.



Two buttons are shown side-by-side. The 'Cancel Order' button is light blue with a dark blue border. The 'Add Results' button is dark blue with white text and is highlighted with a red rectangular border.

SECTION 4: NAVIGATING THE RANDOX CONCIZUTRACE™ PORTAL (CONTINUED)

RANDEX Add Results to Test Order
On this page you can upload result for the specified test order.

Drag and drop file here
or
Browse files
Accepts: pdf files only

Other Relevant Details
Please add any comments that you feel are relevant to the results for the physician to view i.e. suspected reasons for anomalies etc.

Comments

← Back **Save Results**

You can also add any additional details if required.

Other Relevant Details
Please add any comments that you feel are relevant to the results for the physician to view i.e. suspected reasons for anomalies etc.

Comments

← Back **Save Results**

Once ready, select **“Save Results”** to finalise the Test Order.

The Test Order will now be available under the **“Available Reports”** tab.

RANDEX Results
On this page you can view available test orders.

Available reports
Search here

Report Number	Test Order Number	Tests	Date Of Birth	Order Date	Status
NH&K00052-1	NH-401-0000103	Concisaumab	01-Feb-2001	25-Jun-2024 15:46	Available Reports
NH&K00052-1	NH-401-0000102	Concisaumab	01-Feb-2001	25-Jun-2024 16:55	Available Reports

View

Select **“View”** on the right-hand side to review the test order details.

SECTION 5: EQA SCHEME

As part of a proficiency scheme specifically dedicated to the ConcizuTrace™ assay, the laboratory must run Precision materials supplied by Randox. A challenge of 3 samples will need to be reported back to Randox within a specified time window at the end of each quarter.

Proficiency testing program

- 1. Report Format:** Samples will be reported on qc.randox.com
- 2. No. of cycles:** 4 cycles per year
- 3. No. of samples per cycle:** 3 samples per cycle
- 4. Sample Matrix:** 3.2% citrated plasma

Participation to the Proficiency testing program is required to keep the assay certified as per ISO15189.

Results will be reported back to each laboratory individually, together with data reported by the peer group, consisting in all the sites (n=8) contributing to the ConcizuTrace™ Laboratory network. The result of each challenge will be delivered prior to the submission date of the next challenge. Any unexpected results will be investigated through the support of Randox Technical Services.

5.3. Monthly KPI Reporting

Country	Number of samples analysed	Number of samples cancelled	Result ≤200	Result >200 & ≤4000	Result >4000	Samples Delayed	Reasons for cancellation: (Select one option from the below) 1. Sample integrity compromised 2. Incomplete sample ID 3. Run fail 4. Others (please specify)
Total							

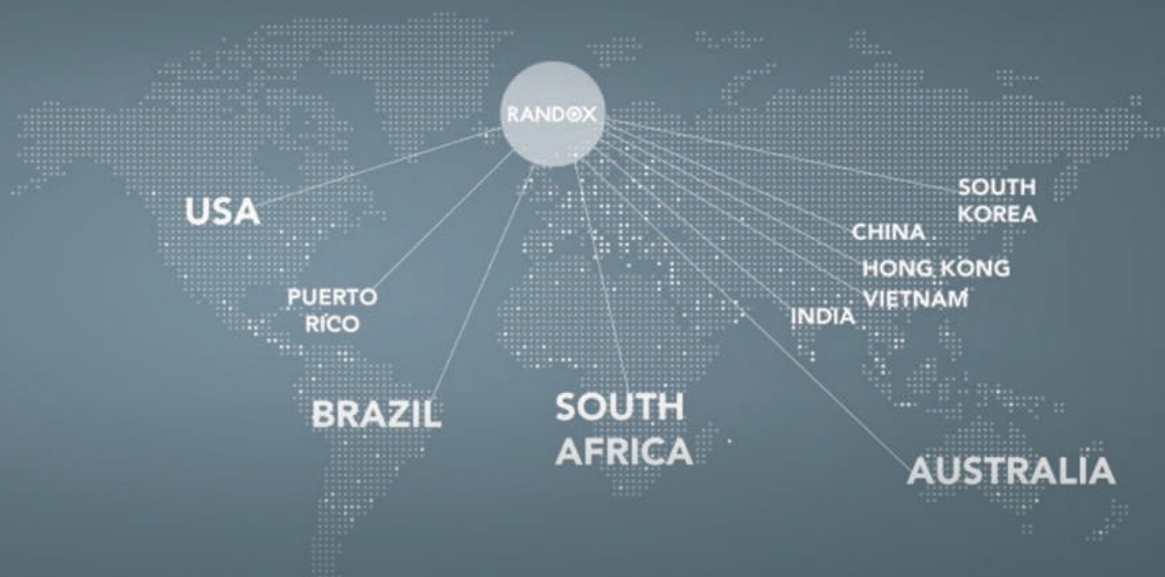
- A 10-working day turnaround time is required from sample pick-up to result reporting. Samples are considered delayed, if reported beyond the 10-day TAT limit.
- Reporting of sample numerical values as displayed above, is expected monthly. Please make sure the results are expressed in ng/ml and strictly anonymized (no indication of sample number).
- When samples are received from several countries, please report the KPIs by country.

RANDOX SUPPORT NETWORK

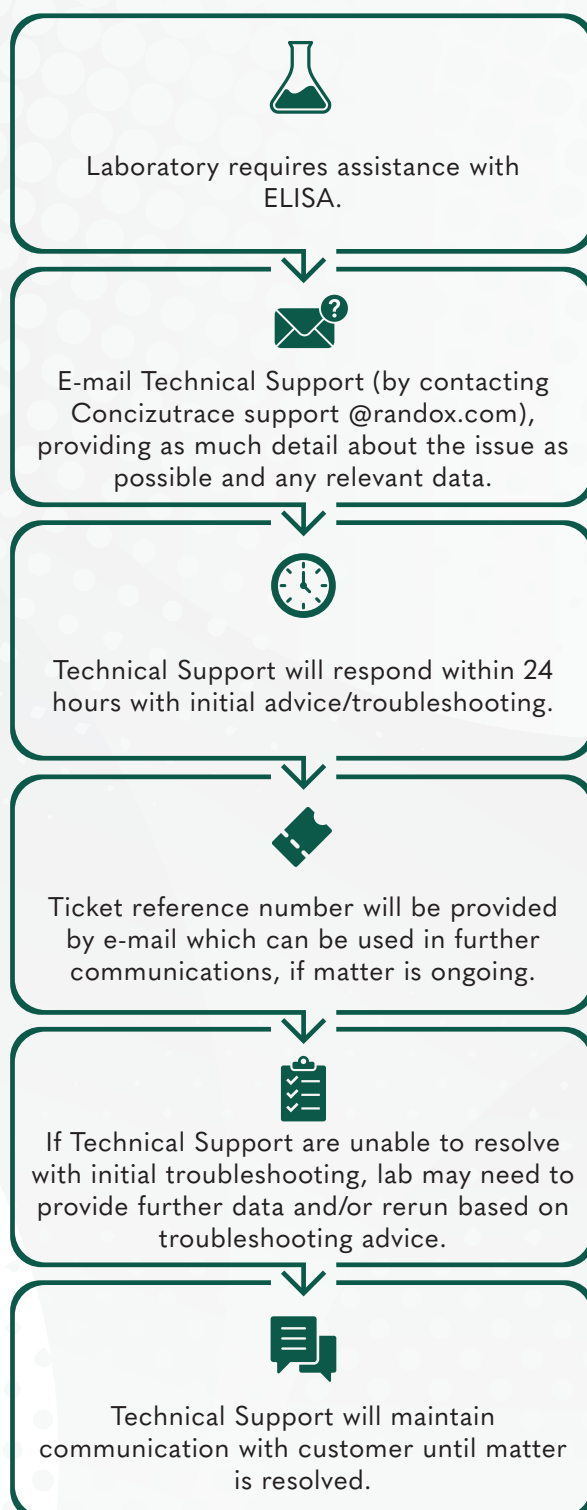
How to reach out?

All support queries in regards to our ConcizuTrace™ ELISA and the Randox platform are to be directed to **concizutracesupport@randox.com** where a member of our global team will support. Please see below process flow and response times for all internal queries.

- Randox has a global and experienced Technical Support Team of over 40 Technical Support Staff, providing best in class customer support.
- Specialists are located in HQ in N.Ireland, France, Portugal, Italy, Poland, China, India, Puerto Rico, USA, Brazil, Australia & Japan.



LAB TECHNICAL SUPPORT



VIDEO GUIDES

We are pleased to provide you with additional visual support tools to assist with the operation of the ConcizuTrace™ ELISA. Video guides are also included for navigation on the Randox Portal for reporting of patient samples back to HTC's.



SCAN HERE TO
VISIT OUR SUPPORT HUB

TECHNICAL TIPS

- T1: All reagents must be equilibrated to room temperature prior to running the assay (+15°C to +25°C).
- T2: Always check storage conditions on the kit/component label.
- T3: Always check expiration dates of all components prior to use.
- T4: After the stop solution has been added to the plate, shaking the plate for 5 seconds prior to reading is recommended to ensure thorough mixing.

FREQUENTLY ASKED QUESTIONS (FAQS)

How can I order ConcizuTrace™ ELISA Kits?

- ELISA kit orders should be placed directly through Randox by contacting **orderentry@randox.com**

** Labs located in Argentina or Japan will be required to order ELISA kits through local distributors.*

- **Argentina** - Cromoion - alicia.gelabert@cromoion.com
- **Japan** - Kohjin Bio Co., Ltd

What can we do when a sample has been physically delivered to the Lab, with either no TOF or discrepant information between TOF and tube label?

- Please contact Technical Services, who will contact the HTC from which the sample originated. Technical Services will clarify discrepancies and obtain the TOF, as needed.

What do I do when I receive the two aliquots in the same delivery?

- One aliquot should be used for testing and the second one stored at -20°C or below up until the report has been released. If any issue happens with Aliquot 1 preventing the result from being reported, then Aliquot 2 should be reported.

IN NO CASE SHOULD THE TWO ALIQUOTS BE USED SIMULTANEOUSLY.

Can I release the test result if I haven't received the temperature logger information?

- The temperature logger information should be made available to you within the 24h of sample delivery. If not available by then, please contact Technical Services who will reach out to Marken and deliver the data to you.

What do I do when a sample has been received, but the sample status in the portal still reads "awaiting courier" in the portal?

- Please contact Randox Technical Services who will progress the sample status to "Courier Collected".

[illegible]

RANDOX

LTXXX DEC24