



Protocol Number 175151

**UK DEVICE MANUAL:****Effective Date: 08 August 2025****Randox Evidence MultiSTAT**

|                                     |                             |                              |
|-------------------------------------|-----------------------------|------------------------------|
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This document explains the different functionalities of the Randox Evidence MultiSTAT Device. This document will guide you through all the options from start to finish to ensure the optimum use of the device. Please read this manual carefully before using the device for the first time, and as a reference thereafter as needed.

## ABBREVIATIONS

|        |   |
|--------|---|
| IL-6   | Interleukin 6                             |
| sTNFR1 | soluble Tumour Necrosis Factor Receptor 1 |
| IFU    | Instructions for Use                      |
| RB     | Reconstitution Buffer                     |
| QC     | Quality Control                           |

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## 1. CONTACT DETAILS

### Technical Assistance

Contact Randox Laboratories Technical Services, Northern Ireland, telephone +44 (0) 28 9445 1070 or email [technical.services@randox.com](mailto:technical.services@randox.com)

## 2. EXPLANATION OF APPLICABLE SYMBOLS

Randox Laboratories uses the following symbols which may appear on the product labelling:

| Symbol  | Description   | Symbol  | Description   |
|---|---|---|---|
|    | Catalogue number                                    | <b>RxOnly</b>   | Prescription device (US only)                                     |
|    | Batch code  |    | Temperature limit   |
|    | Control   |    | Do not re-use   |
|    | Use-by date   | <b>YY/MM/DD</b>   | Date format (year/month/day)                                      |
|   | Manufacturer  | <b>UK CA</b>  | UK CA mark  |
|  | Authorized representative in the European Community |  | Keep away from sunlight   |
|  | Consult IFU   |  | Biological risks  |
|  | In vitro diagnostic medical device                  |  | This way up   |
|  | CE Marking  |  | Caution   |
|  | CE Marking with Notified Body                       |  | Do not use if package is damaged and consult instructions for use |

## 3. MULTISTAT DEVICE SPECIFICATIONS

|                |                                |
|----------------|--------------------------------|
| Dimensions     | 585 (H) x 535 (D) x 570 (W) mm |
| Weight         | 48kg (106lbs)                  |
| Sample Volume  | 250µl (0.25mL)                 |
| Time to Result | 36mins                         |

#### 4. RECEIPT OF THE DEVICE/KITS

Randox and the PANTHER study team will arrange for the order and delivery of your MultiSTAT device and separate kits:- an InflamiSTRAT kit and an accessory kit. Details of each kit is listed below:-

The **InflamiSTRAT kit** contains the following:-

- 12 x InflamiSTRAT Assay Test Cartridge
- 4 x 1mL InflamiSTRAT Adjuster 1
- 4 x 1mL InflamiSTRAT Adjuster 2
- 4 x 1mL InflamiSTRAT Control 1
- 4 x 1mL InflamiSTRAT Control 2
- 2 x 10ml Reconstitution buffer
- 1 x Barcode sheet
- 1 x Instructions For Use (IFU)

The **Accessory Kit** contains the following:-

- 12 x Tip Cartridges

A scanner is required (and will be delivered as part of the MultiSTAT device), pipettes are also required and will be either supplied by the site or the PANTHER study team.

The PANTHER team will arrange for the order and delivery of the separate kits. The entire InflamiSTRAT kit should be stored in a fridge 2-8°C upon delivery. Unreconstituted the contents are stable until the expiry of the kit. When reconstituted the vials are stable for 7 days when stored at 2-8°C.

#### 5. THE MULTISTAT DEVICE & INFLAMISTRAT ASSAY

The Evidence MultiSTAT InflamiSTRAT assay measures Interleukin 6 (IL-6), and soluble Tumour Necrosis Factor Receptor 1 (sTNFR-1) in plasma samples.

These values combined with sodium bicarbonate levels and an algorithm determine the subphenotypes of patients into hypo- and hyper-inflammatory subgroups.

Please ensure you have completed your Randox MultiSTAT device training before following these instructions.

Before the patient sample is collected the device should be prepared. Please ensure you have the following equipment available and ready:-

- 1 x Randox MultiSTAT device with accompanying barcode scanner
- 1 x InflamiSTRAT Assay Kit
- 1 x Accessory kit
- Pipettes/Syringes
- 1 x Barcode sheet

1 x USB will be provided to sites by the PANTHER study team

- a) Ensure the USB has been updated to match the assay kit batch – this step will be completed by the PANTHER team before despatch to site.
- b) Ensure the device has been calibrated – to be completed every month
- c) Ensure the QC process is complete – to be completed on each day of sample analysis

Before a patient sample can be analysed, the following steps are required to be completed on the device:-

## **6. OVERVIEW**

### **1. Batch Update**

Each time a new manufacture batch of kit is received an updated USB with the required batch software will be provided by the PANTHER study team . The PANTHER team will inform the site when a new manufacturer batch is available. The USB is updated from the Randox website. Please see section 7.1 for further details.

### **2. Device Calibration**

When the first InflamiSTRAT kit is first received a calibration on the device should be completed. Calibrations will then continue monthly or on receipt of a kit from a new batch. Adjuster materials (Adjuster 1 and Adjuster 2) are provided with each kit. These are required to complete the 3-step calibration process. This process will then be completed monthly; the device will provide a prompt when required. See section 6.3 for further detail.

### **3. Device Quality Control (QC) Check**

Once the calibration step is completed a QC check is required using the material provided with each kit (Control 1 and Control 2). Detailed instructions on these steps are provided below.

## 7. DEVICE INSTRUCTIONS

### 7.1 Batch update - USB

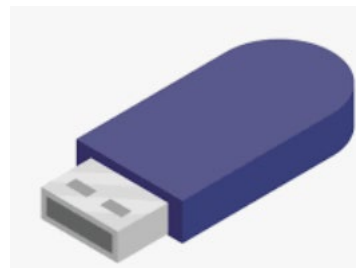
When a new manufacturer kit batch is received, the USB should be updated with the corresponding batch files. This will be completed by the site or the study team depending on restrictions. To do this follow the instructions below:-

1. On your computer enter [www.randox.com](http://www.randox.com) into a search engine

2. Select **Support & Documentation** —→ **Reagent Product Inserts**

Note:- an account is required at this point, to do this please select **Request Access** and complete the online form.

3. Once logged in enter the catalogue number EV4578 in the **Search** field. Plug the provided USB into the computer and copy these files on to the USB.

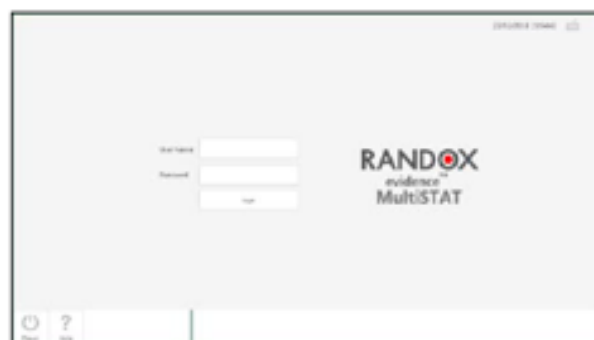


### 7.2 Getting the Device Ready

1. Switch the analyser on using Power Button located on right hand side of the device and insert USB.



2. Login with the user details you will have set up with Randox Technical Support during training



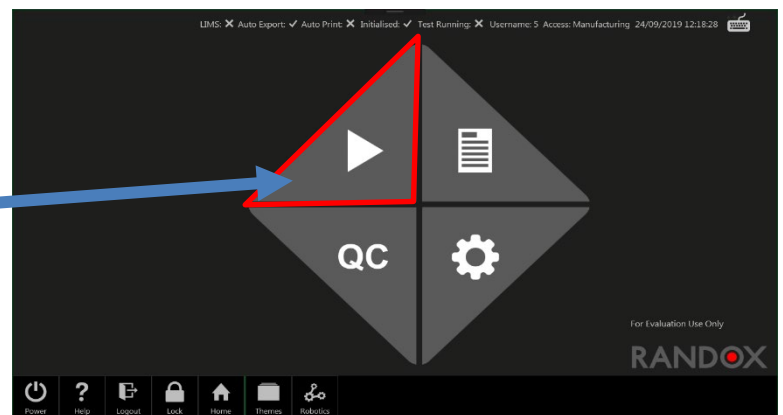
3. Following login select the 'With Robotics' option to bring the user to the Home Screen

**With Robotics**

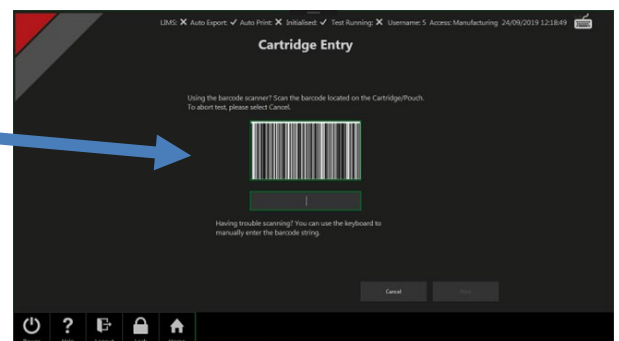
Tap this option to initialise the analysers robotics system

This is the mode used to perform analytical tests and view results

4. From the Home Screen select the **Run Test** (Play) Button– the Cartridge Entry Screen will be displayed



5. A prompt will appear to scan the barcode

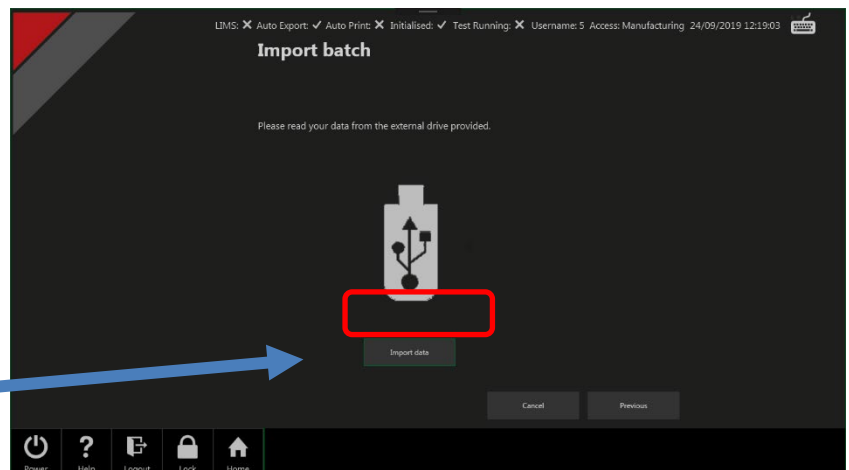


6. Scan the **Cartridge** Barcode from the Barcode sheet from the InflamiSTRAT kit.

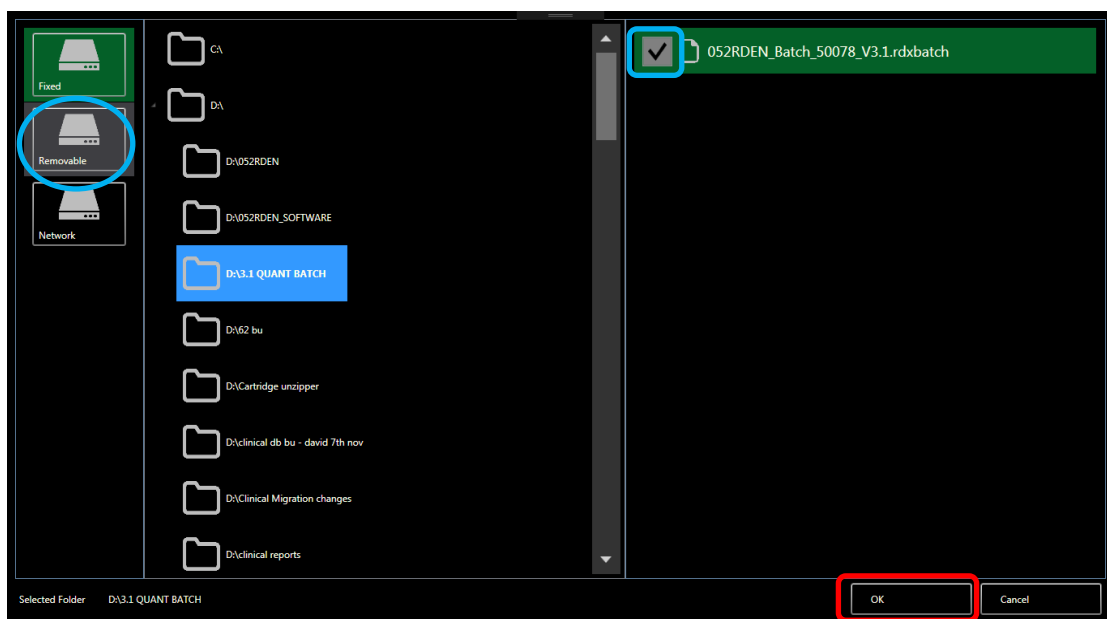


7. The system will automatically prompt you to install a new batch for the cartridge you have just scanned. Enter the USB and select the Import data button (highlighted in red)

Import data



8. Double tap **Removable**, followed by **E:\** and finally double tap the file you have downloaded on to the USB. Ensure the checkbox beside the filename is selected (highlighted in blue) Press the Ok button (highlighted in red)



### 7.3 Device Calibration

To be completed on the receipt of a new batch of kit and each month, the device will prompt when due.

#### Step 1 – Preparing the device



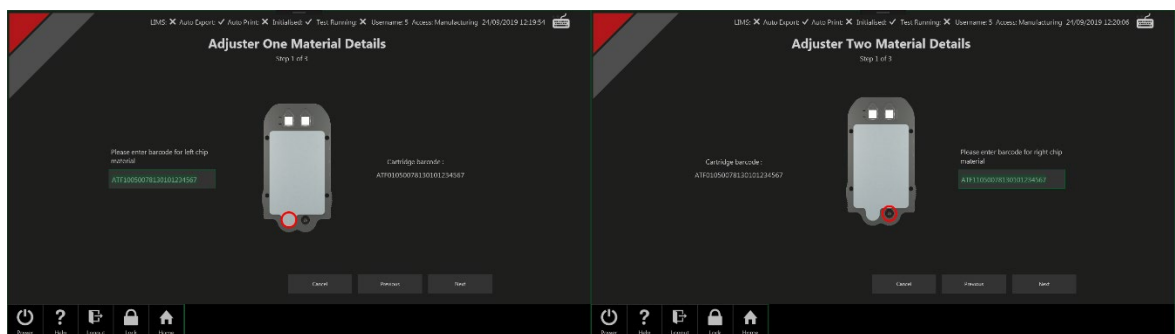


1. Remove the InflamiSTRAT Assay Cartridge from the kit but leave sealed in the foil bag for 30 minutes at +15°C to +25°C.

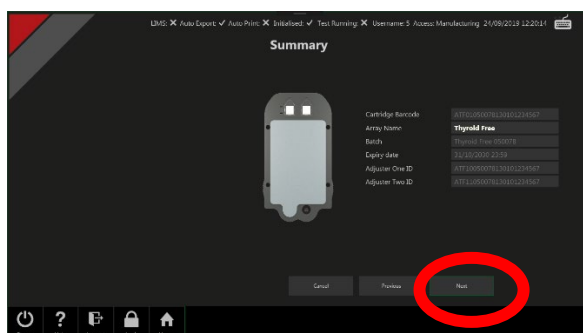
2. Scan the **Adjuster 1** Barcode from the Barcode sheet from the InflamiSTRAT kit. This will now become the barcode for the Adjusters. The system will then prompt to scan the **Adjuster 2** barcode.



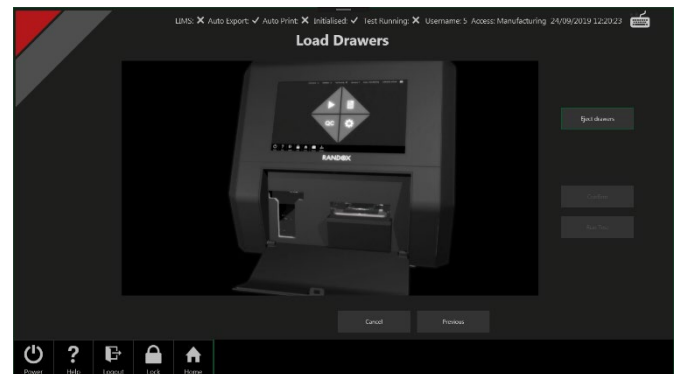
First scan adjuster 1 then adjuster 2 when prompted.



3. A summary screen will then appear, then click next

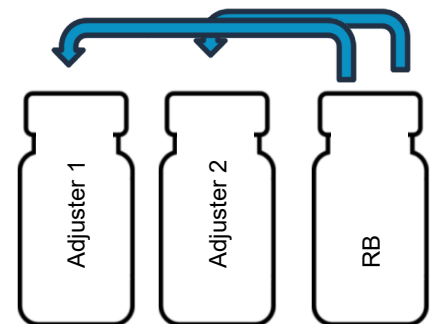


4. Select next and tap the screen when prompted to eject the drawers. The door will then open automatically followed by the cartridge and tip drawers.

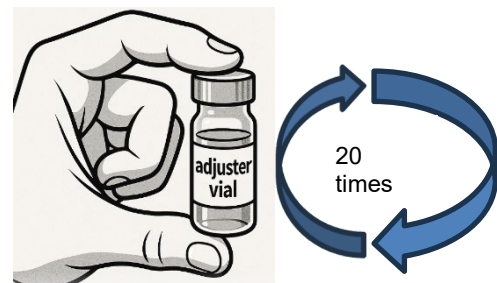


## Step 2 – Adjuster Run #1

1. From the InflamiSTRAT Assay Kit take one vial each of the freeze-dried Adjusters 1 & 2 and one vial each of Reconstitution Buffer (RB)
2. Transfer 1ml of RB into each of the Adjuster vials using a 1ml syringe or pipette.



3. Invert the Adjusters gently 20 times, allow to stand for 30min at room temperature and reinvert gently 20 times



4. Remove a pipette tip from the tip cartridge (accessory kit), pierce the sealed sample well on the left.
5. Using a pipette/syringe transfer 250µl of reconstituted adjuster 1 to the left well
6. Using a fresh pipette/syringe transfer 250µl of reconstituted adjuster 2 to the right well



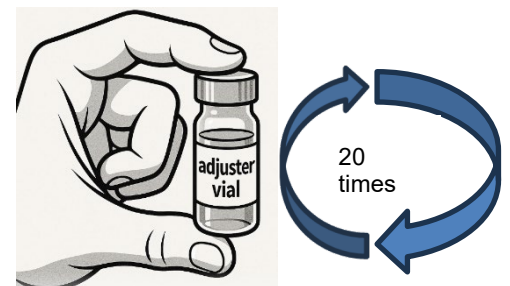
Load the InflamiSTRAT assay test cartridge (left hand drawer) and tip cartridge (right hand drawer) into the device. Push both drawers into place and close the door.



7. Select confirm, wait for the device to perform checks and select run test. The InflamiSTRAT Assay takes 36 minutes. In this time, you can remove the Test Cartridge from the kit but leave sealed in the foil bag for 30 minutes at +15°C to +25°C.
8. Once the run is complete, select Eject Drawers and remove the used cartridges and discard into biohazardous waste
9. Push empty drawers back into place, close the door and select confirm
10. The device will then prompt to perform 'Adjuster Run 2' see step below.

### Step 3 - Adjuster Run #2 – repeat steps from Step 2 above

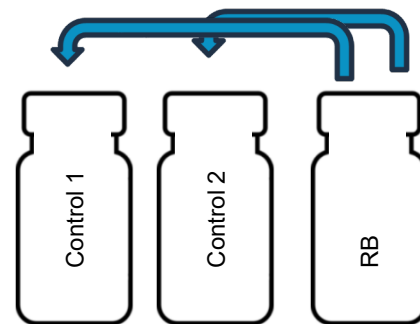
1. As the adjusters have already been prepared from Step 2 above these simply need to be added to the next cartridge for this run.
2. Scan the adjuster 1 and 2 barcodes from the sheet.
3. On the device check the summary, select next, then select eject drawers
4. Open the foil bag carefully remove the cartridge
5. Using a pipette tip, pierce the foil covering the left well
6. Using a syringe/pipette transfer 250µl of reconstituted adjuster 1 into the left well
7. Using a fresh syringe/pipette tip transfer 250µl of reconstituted adjuster 2 into the right well
8. Eject drawers and load analyser
9. Press confirm (wait for analyser to perform checks and select run test)
10. Once run is complete, select Eject Drawers, and remove the used cartridges to discard into biohazardous waste
11. The device will then generate a prompt to perform 'Control Run' see step below.



## 7.4 Device Quality Control (QC) Check

To be completed after the calibration (Adjuster Runs 1 and 2 as above) and each day that a sample is run (once per 24 hour period)

1. Transfer 1ml of reconstitution buffer into each control vial. Use a fresh syringe for reconstituting each control vial
2. Remove the InflamiSTRAT Assay Test Cartridge from the kit but leave sealed in the foil bag for 30 minutes at +15°C to +25°C
3. Invert vials 20x leave to stand with the cartridge at room temperature for 30 minutes, then invert 20x further times
4. Scan **Control 1** barcode from the sheet



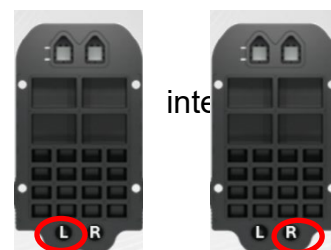
5. Import the batch details from the USB provided, select import data, navigate to the file and select ok  
*Note – if this step has already been completed for this batch, this step can be missed.*



6. Scan the **Control 2** barcode, check the summary and select next
7. Select eject drawers

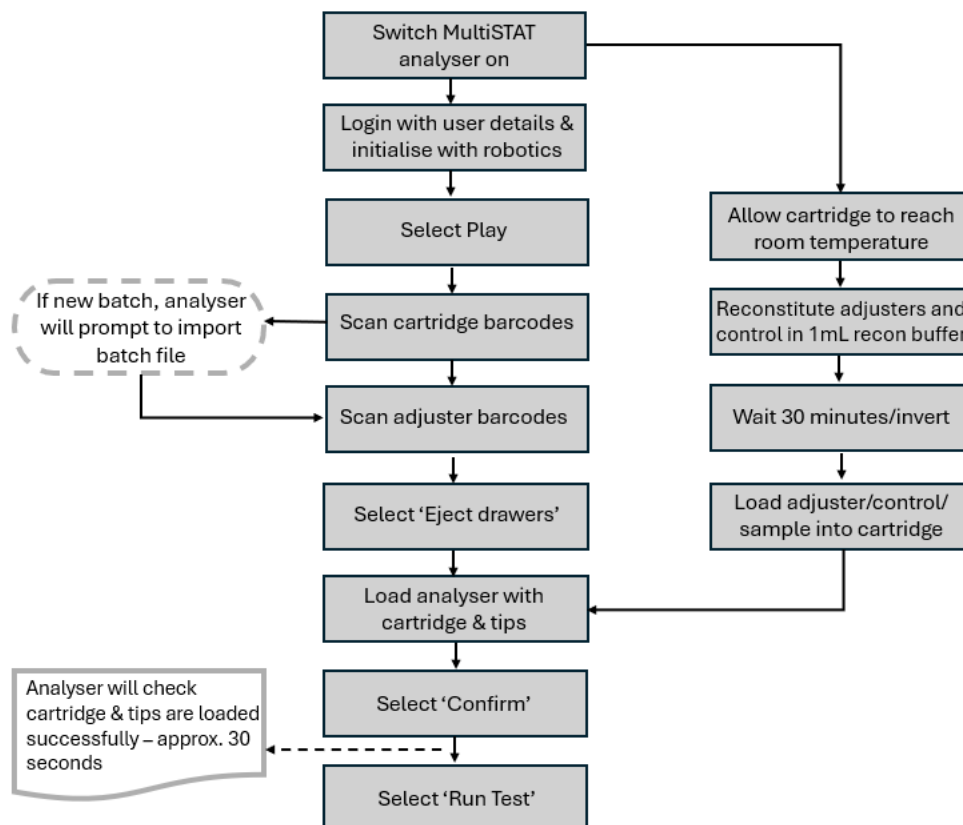
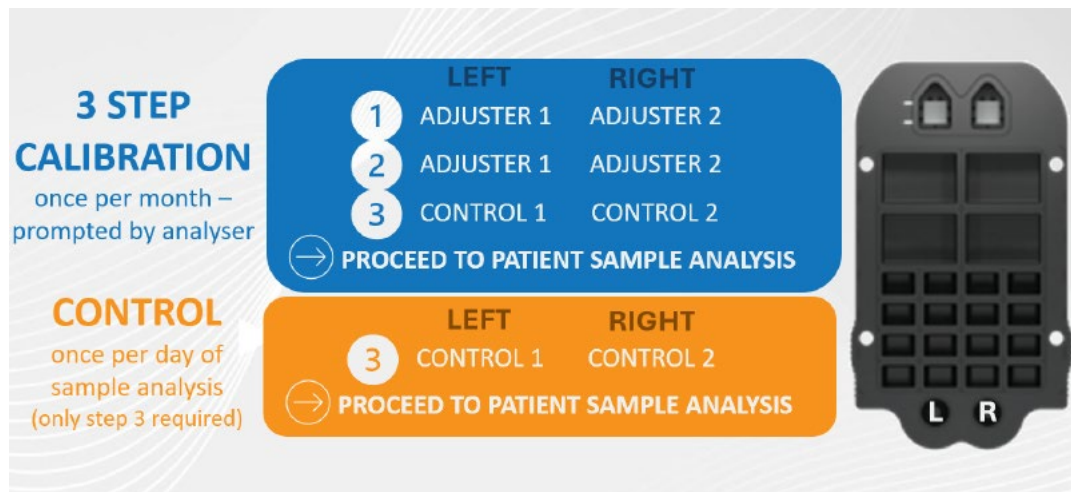
8. Using a pipette tip pierce the foil covering the left well
9. Using a syringe/pipette transfer 250µl of reconstituted Control 1 into the left well

10. Using a fresh syringe transfer 250µl of reconstituted Control 2 into the right well



11. Eject drawers and load analyser
12. Press confirm, wait for analyser to perform checks and select run test
13. Once run is complete, select Eject Drawers and remove the used cartridges and discard into biohazardous waste
14. Push empty drawers back into place, close the door and select confirm

## Summary of calibration and QC checks



## 8. COLLECTING THE SAMPLE FROM THE PATIENT

Personnel must follow 'Universal Precautions' when handling blood products as well as site-specific requirements for handling each type of specimen. Processing of blood specimens should be initiated as soon as possible (~ 30 minutes) following collection with all plasma and serum samples ideally processed and frozen within one hour.

## 8.1 Equipment preparation

Before the sample is collected, ensure you have the following equipment available and ready:-

- 1 x 4ml Lithium Heparin Tube
- Ice for temporary storage
- 1 x centrifuge
- 1 x Pasteur pipette
- 1 x 1ml cryovial tube
- 1 x red topped tube

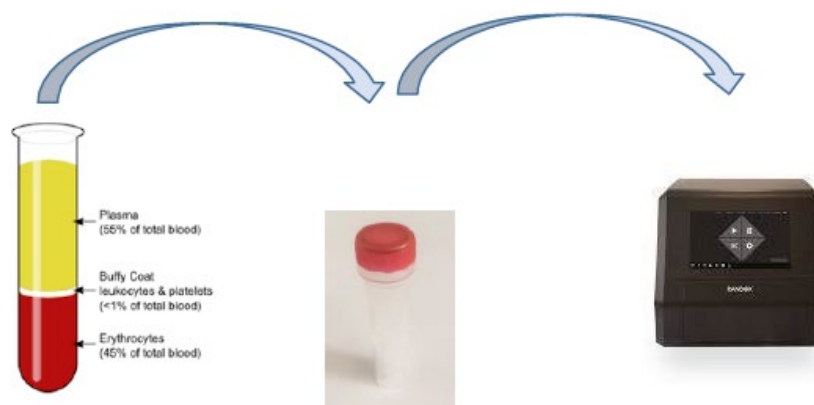
## 8.2 Collecting the sample for the subphenotype determination

Before the patient is randomised we need to determine the subphenotype, this sample will determine if the patient is hyper or hypo inflammatory.

- Collect 4ml of whole blood from the patient in a lithium heparin tube, invert the tube several times, then place on ice.

### 4ml Lithium Heparin Tube

- Centrifuge the blood at 2000g for 10 minutes.
- Pipette the plasma into the 1ml cryovial tube.
- Keep on ice until sample analysed in MultiSTAT. Keep any residual plasma in the red-topped tube on ice, until assay is complete (see below).
- Please refer to Step 5 below to run the samples. After sample has been successfully analysed by the MultiSTAT, discard this sample only.



*Note - please see Sample Manual for details on the other tiers.*

## Step 5 - Running samples on MultiSTAT

1. Scan the cartridge barcode and enter sample details
2. Select next and eject drawers
3. Using a pipette tip pierce the foil covering the left well
4. Using a syringe transfer 250µl of the patient sample into both cartridge wells
5. Load the analyser
6. Press confirm (wait for analyser to perform checks) and select run test
7. Once run is complete, select Eject Drawers, and remove the used cartridges to discard into biohazardous waste
8. Push empty drawers back into place, close the door and select confirm

Concentration values for IL-6 (pg/mL) and sTNFR1 (ng/mL) will be shown on the screen. Make a note of these to enter in the eCRF to allow the patient to be randomised.

### Example results

| Analyte | Concentration | Units |
|---------|---------------|-------|
| IL-6    | 253.09        | pg/mL |
| sTNFR1  | 7.18          | ng/mL |

**Note** - Only one patient sample can be run per cartridge.

## 8.3 Entering on the database

Once the MultiSTAT has provided the required concentration values (IL-6 and sTNFR1) these can now be entered into the CRF and the patient can be randomised.



### UA0-003: Phenotyping

|   |   |
|---|---|
| Device type?<br><input checked="" type="radio"/> Radox<br><input type="radio"/> Ella<br><input type="radio"/> Other |   |
| Date the subphenotyping was completed<br>2025-08-06   | Time the subphenotyping was completed<br><small>format (hh:mm [0-23] hrs [0-59] min)</small><br>13:00 |
| The lowest/worst bicarbonate in past 24h<br>25  |   |
| sTNFr1 Collected<br><input checked="" type="radio"/> Yes<br><input type="radio"/> No                                | sTNFr1 Value (ng/ml)<br>125   |
| IL-6 Collected<br><input checked="" type="radio"/> Yes<br><input type="radio"/> No                                  | IL-6 Value (pg/ml)<br>96  |

## 9. DEVICE TROUBLESHOOTING

- If a run should fail Randox will require the Support File in order to identify the issue
- If you experience a QC fail select the QC button on the Home Screen
  - Select InflamiSTRAT assay and at the top right select Display Calibration
  - Select the run file(s) corresponding to the failed QC run(s)
  - Select Support Files and navigate to the desired export location.
  - Select Ok
- If you experience a Sample fail select the Results button on the Home Screen
  - Select InflamiSTRAT assay and the run file corresponding to the failed sample run
  - Select Support Files and navigate to the desired export location
  - Select Ok

## 10. ON-SITE EQUIPMENT

All sites will be required to process the initial blood sample for centrifugation to separate plasma and be able to measure sTNFr-1 and IL-6 for stratification via the MultiSTAT device.

All participating centers must be equipped with the following minimum equipment:

- Centrifuge with 2000g force capability
- Evidence MultiSTAT point of-care analyzer (Randox laboratories Inc., Antrim, Northern Ireland)
- InflamiSTRAT assay kits

## 11. ORDERING ASSAY KITS

The MultiSTAT device uses specific kits for PANTHER, sites will first inform the PANTHER team when new kits are required, the team will then order the kits directly from RANDOX. These will be delivered to the site FAO the preferred contact and site address. The kits that are being used are:

- **InflamiSTRAT Assay Kit (EV4578)**
  - Kit contains 12 tests, Adjuster material, QC material, Instructions for Use (IFU), Barcode Sheet
  - Assay contained in a sealed cartridge
  - QC runs must be completed before patient samples can be assayed
  - Requires addition of a plasma sample separated by centrifugation from whole blood
- **Accessory Kit (EV4452)**

Please refer to the document InflamiSTRAT EV4578 IFU for full details on the following:



- Reagent Compositions
- Safety Precautions and Warnings
- Stability and Preparation of Reagents
- New Batch Updates
- Preparation of Tip Cartridge
- Preparation of Adjusters 1&2
- Preparation of Controls 1&2
- Cartridge Analysis
- Quality Control
- Instrument Settings
- Results Processing
- Quantitative Analysis
- Result Interpretation
- Interleukin-6 (IL-6)
- Soluble Tumour Necrosis Factor Receptor-I (sTNFRI)

## 12. REVISION HISTORY

| Version | Date        | Summary of changes |
|---------|-------------|--------------------|
| 1.0     | 08 AUG 2025 | First version      |