Attachment 1 - FSN-RDS-CoreLab-2023-003
Description of mitigation measures for affiliate and/or customer

This attachment describes the mandatory actions that have to be implemented.
The actions can be performed by the customers themselves or, where required, with help of a Roche service representative.

The document structure describes first the measures for Situation 1 and Situation 2 and provides additional information as the last paragraph.

It is recommended that at least the action described for Situation 1 is done immediately by the customers themselves to avoid a potential delay if a Roche service representative shall be involved to perform the measures for Situation 2. This might include a software update for systems with SW 2.1.1 or earlier, if possible in the given timelines.

Situation 1: Principle of measure

The heated reagent probe (1x on **cobas t** 511 analyzer, 2x on **cobas t** 711 analyzer) has to be tightened properly.

⚠ Warning!

▼ **Contact with reagent probes**

Contact with reagent probes may result in injury and infection.
- Avoid touching the end of the reagent probes.
- Avoid contacting the reagent probes during maintenance.
- Wear appropriate personal protective equipment.

  Take extra care when working with lab gloves. They can easily be pierced or cut, leading to infection.

⚠ Warning!

▼ **Hot surfaces**

Risk of personal injury due to touching hot surfaces in the analyzer.
- Use caution near the heated reagent probe. If it is necessary to handle the heated reagent probe, allow time for it to cool down.
- Observe all safety labels on the analyzer.

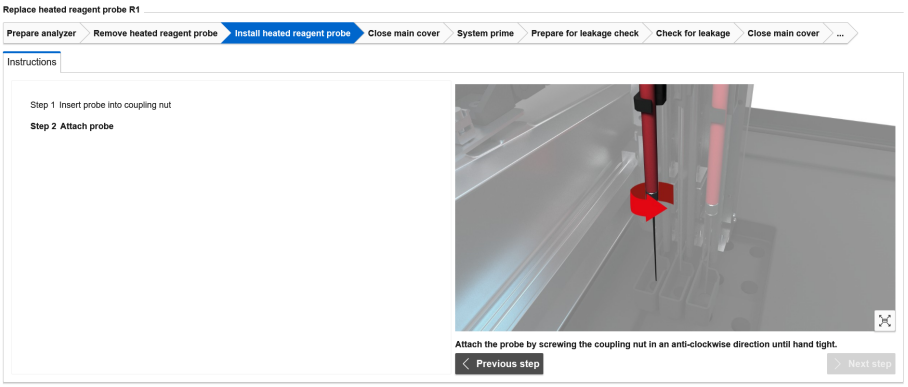
Notice!

▼ **Mechanical damage**

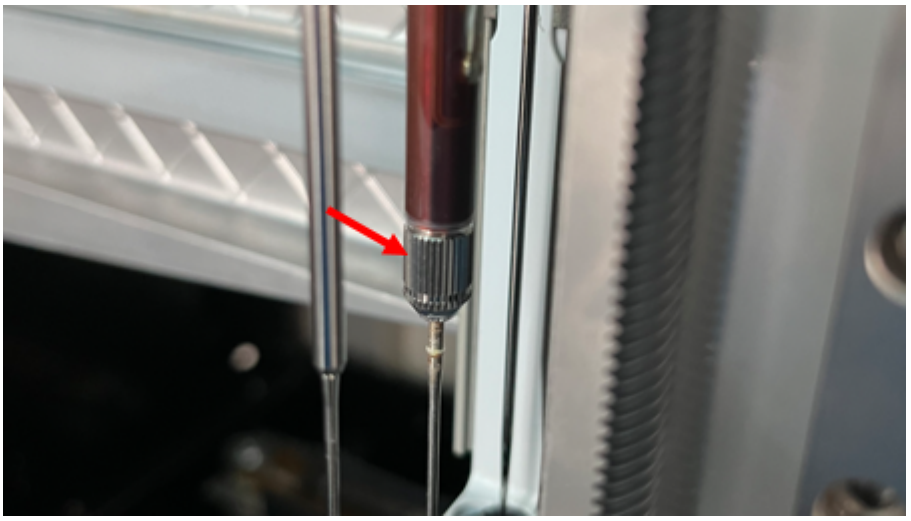
Moving the reagent transfer head to the furthest left-backwards position can lead to a tube or cable being bent when the main cover is closed.
- Do not move the reagent transfer head to the far left, backward position.

Situation 1: Measure to be taken for all systems

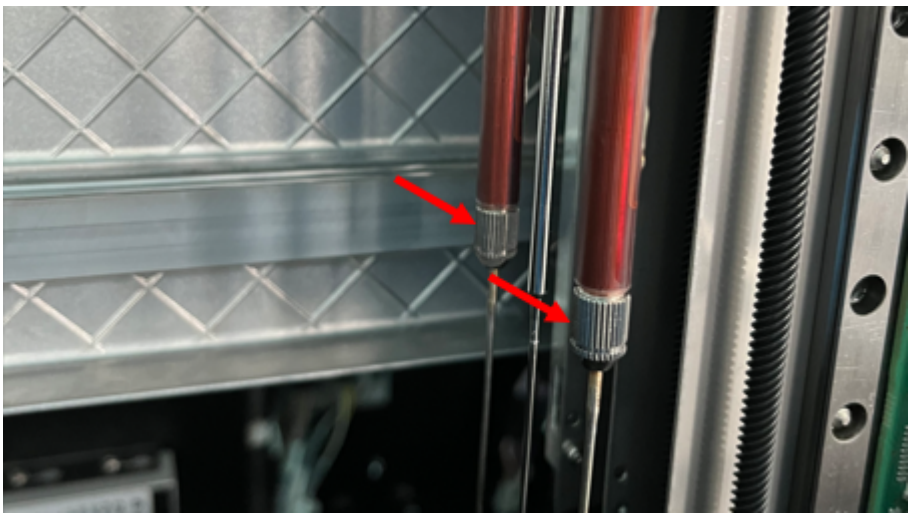
1) Start the maintenance workflow “Replace heated reagent probe R1”.
2) Do not execute the described actions in the wizard.
3) The only action that shall be performed is **to tighten the heated reagent probe**.
   For t 711 instruments, both heated probes must be tightened.
   This can be done during any step of the maintenance workflow. When tightening the probe please make sure that:
   - **a) You do not replace the probe**
   - b) Apply the maximum reasonable force the user can apply with the fingers (as tight as possible without e.g. causing pain in the finger).
   - c) Don’t worry about applying force, nothing will break.



Picture 1: Heated reagent probe as displayed in the software wizard



Picture 2: Heated reagent probe **cobas t** 511



Picture 3: Heated reagent probes **cobas t** 711

4) Future probe replacements are done as usual with a special focus on tightening the probes properly as described in steps 3b-c.

Currently, in the wizard of the maintenance workflow, the instructions say that the probe must be mounted “hand tight”. This part must be interpreted as described in the steps 3b-c above. The descriptions will be adapted in the user assistance and in the maintenance workflows.

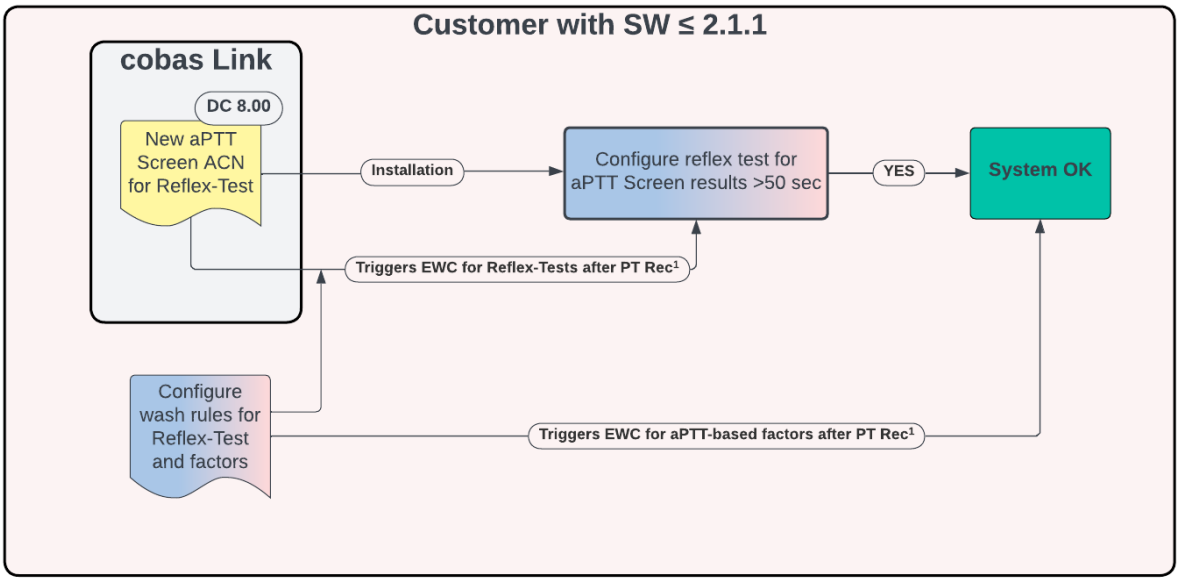
Situation 2: Principle of measure

The principle of the measure is to create a reflex test that is triggered in case an aPTT Screen result is 50s or higher. In this case a second aPTT Screen test (aPTT Screen Mod) is measured and in case there was a carryover condition, the instrument will first carry out an extra wash cycle.
Only the *aPTT Screen Mod* result must be interpreted if this occurs.
Optionally *aPTT Screen* can be defined in a way to suppress the original aPTT Screen result (see step 2 in instructions below). This might support result evaluation on LIS level too.

Example of result pair in this case:
aPTT Screen ****** > Val
aPTT Screen Mod 71s

Example of result pair without this configuration of the >Val Flag:
aPTT Screen 70s
aPTT Screen Mod 71s

SW versions 2.1.1 or earlier would require manual programming of extra wash cycles.
SW versions 2.1.2 or later, can use the new Reagent_COE e-Barcode V7 that contains all the new washrules. Wherever possible systems should be updated to SW versions 2.1.2 or higher, as this allows for a more convenient implementation of the required actions.

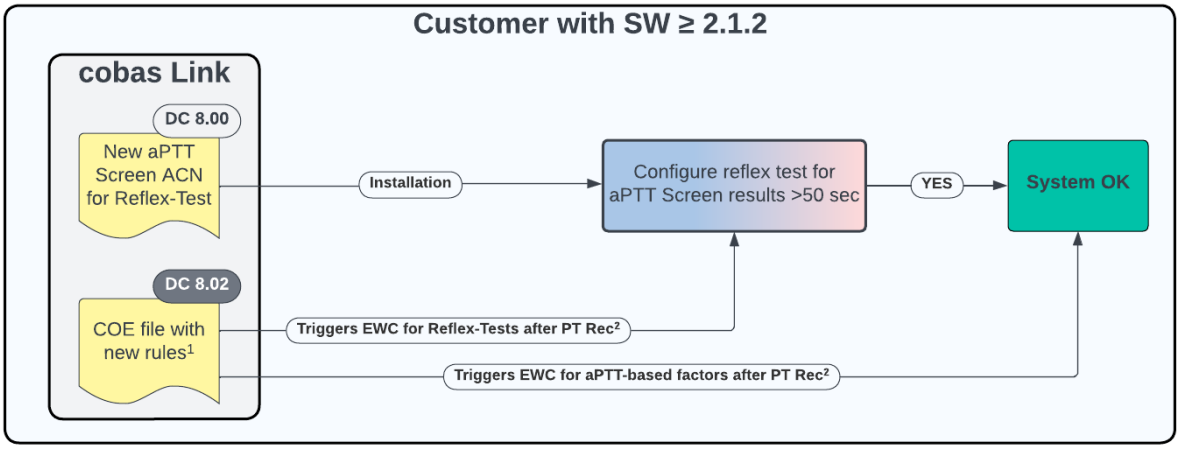


[1]PT Rec and PT-based factors

Picture 4: Illustration of measures for systems with SW 2.1.1. or before

Please note once the wash rules have been manually programmed:

- Once customers with SW 2.1.1 or earlier will update to SW 2.1.2 or 2.2.0, they will get the updated Reagent_COE e-Barcode V7.
  It is then required to delete all the manually programmed wash rules described in this attachment. This is done to avoid double wash rule definitions which the system can't handle, which would cause the instrument to go into error status.
- It is required to consider the information in this SBN if the customer is going to introduce any new factor assay in their lab. Programming an additional wash rule might be required, as also indicated in respective method sheets.



[1]New COE file will contain rules for aPTT Screen Reflex-Test and all aPTT-based factors
[2]PT Rec and PT-based factors

Picture 5: Illustration of measures for systems with SW 2.1.2 or newer

Summary of steps to implement in all SW Versions

1. Install the application aPTT Screen Mod (ACN28045).
2. Set up flagging of initial aPTT Screen result (for cases where *aPTT Screen Mod* is triggered)
3. Program the reflex rule on the system
4. Install the new Reagent_COE e-barcode file V7 (SW 2.1.2 or newer) or program the rules manually (SW 2.1.1 or before)
5. Result interpretation: As soon as there is an *aPTT Screen Mod* triggered by the system, the customers shall only use the *aPTT Screen Mod* result and not the aPTT Screen result, even in cases of marginal differences (Step 2 allows result suppressing)

Situation 2: Measures to be taken for all systems

1) Install and configure the new *aPTT Screen Mod* application with ACN 28045.
    a) Go to Administration > E-Library > Search and install e-barcodes
    b) Install aPTT Screen Mod (ACN 28045) Version 1

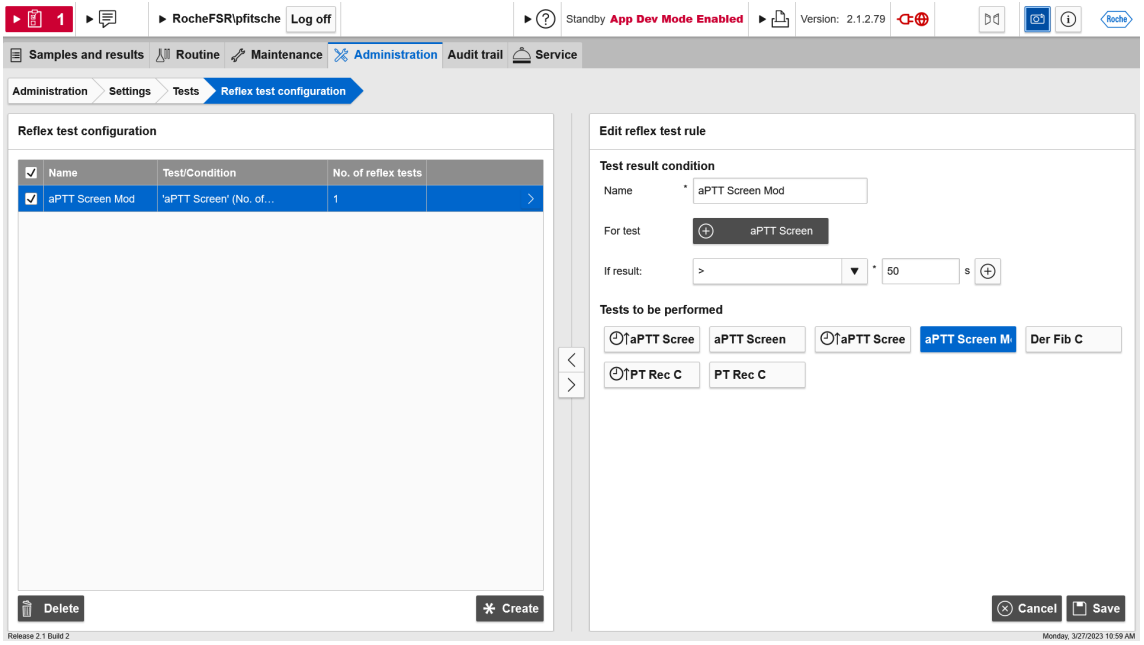
2) Optional step: Modify *aPTT Screen (not aPTT Screen Mod)* to suppress original aPTT Screen result
    a) Navigate to Administration > E-Library > View and edit installed e-barcodes
    b) Select the installed *aPTT Screen* (ACN 28040) and open the application parameter configuration by clicking on the arrow on the right hand side of the screen.
    c) Navigate to the second tab "Data alarms"
    d) Scroll down until you see the part "Result exceeds validation range upper limit [>Val]
    e) Click on "Edit"
    f) Tick the box to "Set active" enter the value 50 in the free text field. **Optionally**: do not tick the box to "Report result".
    g) By not ticking the box "Report result", the initial aPTT result will be suppressed (result will be shown as ******)

    Please note:
    Independent from passthrough mode the behaviour depends on the general setting for result suppression.
    Mode 1: Result would always be suppressed
    Mode 2: Result is suppressed dependent on setting (paragraph f and g above)
    Mode 3: Result is not suppressed, independent from setting in paragraph f and g above.

    The setting can be changed in Administration>Settings>Instrument settings>Process setting (requires Supervisor level).

3) Create a reflex test
    a) Go to Administration > Settings > Tests > Reflex test configuration
    b) Choose create
    c) Enter a name (Proposed name: *aPTT Screen Mod*)
    d) Choose the originally installed aPTT Screen application with ACN 28040
        i) IMPORTANT: Do not choose the newly installed aPTT Screen Mod application here
    e) Choose if result to be > 50 s

f) As test to be performed select the newly installed aPTT Screen Mod application, and then click “Save” to save this setting



Picture 6: Definition of the reflex test

4) Install *Reagent_COE e-Barcode Version 7 (displayed as 8.2.7*, only applicable for SW 2.1.2 or higher)
   a) Go to Administration > E-Library > Search and install e-barcodes
   b) Install *Reagent_COE e-Barcode Version 7 (displayed as 8.2.7)*. It is distributed with the new method sheet Version 7.0.

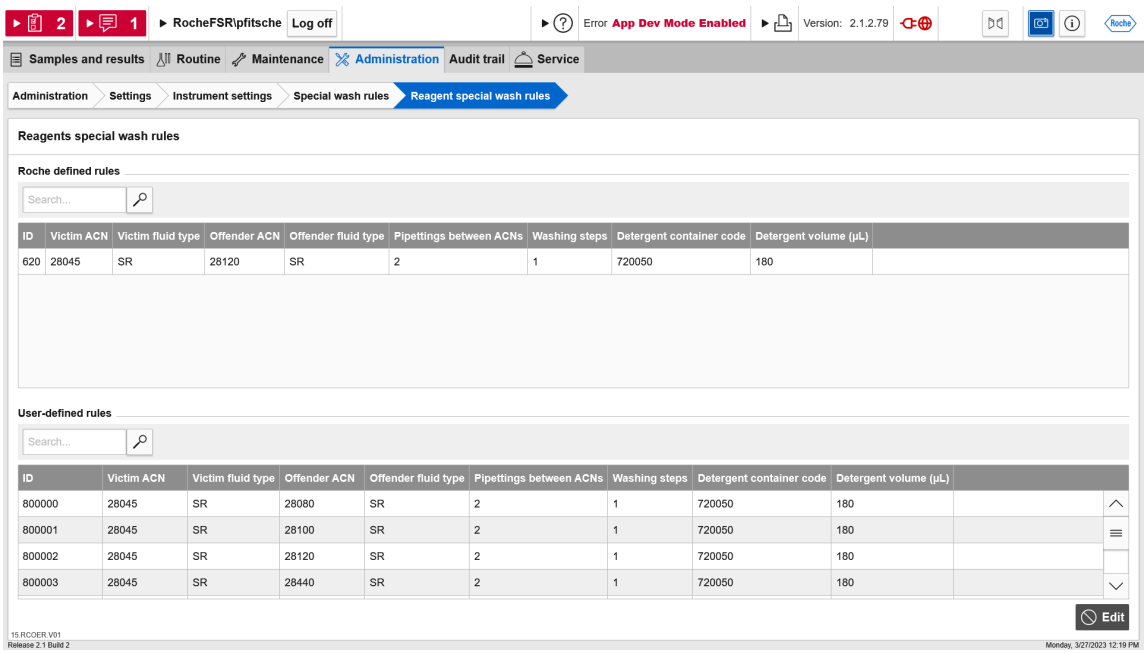
5) Configure wash rules (only applicable for 2.1.1 and lower)
   a) Please keep in mind that these wash rules can only be programmed after the tests (e.g. aPTT Screen Mod test (ACN 28045), FII (ACN 28440)) have been installed. But it is not necessary to install Factor tests that are not used by the customer.

      It is important to keep in mind that whenever a new test (e.g. Factor V) is installed in the future, to also program the associated wash rule. A respective disclaimer is in the method sheets of the affected assays.
   b) Log on as Supervisor or FSR
   c) Step 1 and 3 must be completed first
   d) Go to Administration > Settings > Instrument settings > Special wash rules > Reagent special wash rules
   e) The wash rules have to be entered as user defined wash rules

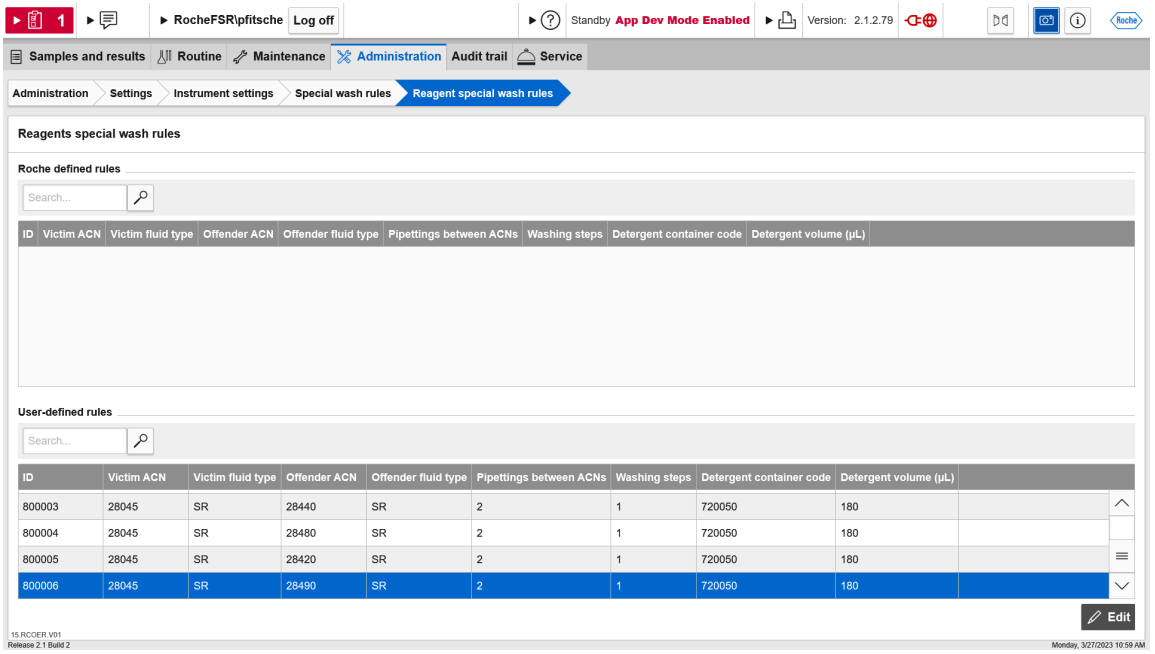
f) It is of utmost importance to work precisely and to enter each wash rule with the correct information. Risk of wrong results if not applied correctly!

g) Enter the wash rules as mentioned below one by one, refer also to the screenshots to see the final result. The used ID can be customer specific and is not relevant for the function.
Refer also to the screenshots below that show all 7 wash rules 1:1, in this example with IDs 800000 - 800006.

Victim ACN	Victim fluid type	Offender ACN	Offender fluid type	Pipettings between ACNs	Washing Steps	Detergent Container Code	Detergent volume [uL]
28045	SR	28080	SR	2	1	720050	180
28045	SR	28100	SR	2	1	720050	180
28045	SR	28120	SR	2	1	720050	180
28045	SR	28440	SR	2	1	720050	180
28045	SR	28480	SR	2	1	720050	180
28045	SR	28420	SR	2	1	720050	180
28045	SR	28490	SR	2	1	720050	180



Picture 7: New washrules (manual programming), Part I.



Picture 7: New washrules (manual programming), Part II.

Additional information

Check to verify if an instrument is affected by carryover

Not all instruments are affected to the same extent by this carryover.
Nevertheless it is not possible with reasonable effort to detect if a specific system is affected by carryover or not, therefore such a check is not offered.

Explanation about reflex test *aPTT Screen Mod*

Automatic reflex test for aPTT Screen results >=50 secs was provided to ensure detection of potential carry over effects while minimizing the laboratory workload and manual effort. 50 sec was chosen as the threshold in order to meet the maximum safety requirement in all foreseeable clinical situations. The aPTT Screen Mod repeats the aPTT Screen test, and automatically carries out extra wash only when a PT Rec reagent is pipetted before the aPTT Screen reagent. With this setup, we will achieve maximum safety while minimizing the amount of retest and extra wash. With this measure, the instrument throughput is also, if at all, only minimally impacted. Please note that aPTT Screen results <50 secs do not need to be retest because no significant carry over occurs

Result interpretation with *aPTT Screen Mod*

As soon as there is an *aPTT Screen Mod* result generated, the customer shall only interpret and report this result, even in cases of very small differences to the original result.

Refer to the instructions Step 2 to optionally set a flag to suppress the results of original aPTT Screen in case the reflex test rule is triggered.

Information about *aPTT Screen Mod*

aPTT Screen Mod is an exact copy of aPTT Screen. It will have exactly the same properties as the "normal" aPTT Screen assay. The only difference is that an extra wash cycle will be implemented between the PT Rec reagent pipetting and the *aPTT Screen Mod* assay.

Quality Controls for *aPTT Screen Mod*

It is technically not necessary to run Quality Controls for this assay, as this is already done for aPTT Screen.
Currently it is planned to provide target values for *aPTT Screen Mod* for Con 1, Con 2 and Con 4 with successive Quality Control lots.
It is then possible to either run the controls (set Controls to "mandatory" for the *aPTT Screen Mod* test in software) or to not run the controls (set to "optional") depending on the needs of the laboratory.

In case Quality Control results for *aPTT Screen Mod* are required/ requested by the customer prior to the availability of Con 1, Con 2 and Con 4, there is always the option to configure a 3rd party QC material which is assigned to the *aPTT Screen Mod*.
Please refer to the user assistance for detailed instructions on how to set up a 3rd party QC material.

Single use of aPTT Screen Mod:

The described measure was designed to ensure minimal impact of potential carryover while minimizing the amount of retest and extra wash, and to have minimal to no impact on the throughput of the system.
Implementation of an additional wash cycle independent of the initial aPTT Screen result would have a noticeable negative impact on the analyzer throughput. Depending on the test profiles the customer is using, throughput loss of up to 30-40% would take place.
If a customer intends to replace aPTT Screen with aPTT Screen Mod, and therefore to skip the reflex test solution and to accept more frequent extra wash cycles (incl. cleaner consumption) this can be done. We do not recommend this.
Consider also that until availability of next lots Con 1, Con 2 and Con 4 only 3rd party controls can be used.
Customers might use the aPTT Screen Mod also as occasional single test, in case an aPTT result >50s is already expected beforehand.