# Urgent Field Safety Notice
## *SBN-CPS-2018-012*

CPS / ClinChem fully automated Application
Version 1
Nov-2018

# Carryover on COBAS INTEGRA® 400 plus and cobas c 111 analyzer

| | | |
|---|---|---|
| **Product Name** | COBAS INTEGRA® 400 plus analyzer | |
| | **cobas c** 111 analyzer | |
| **GMMI / Device Identifier** | COBAS INTEGRA® 400 plus analyzer with ISE | 03245233001 |
| | COBAS INTEGRA® 400 plus analyzer without ISE | 04922859001 |
| | **cobas c** 111 with ISE | 04777433001 |
| | **cobas c** 111 without ISE | 04528778001 |
| | CLEAN (Cleaner Cassette, COBAS INTEGRA® 400 plus) | 20764337322 |
| | CLEAN (Cleaner- Special Wash Requirements, cobas c111 | 04774248190 |
| **Production Identifier (Lot No./Serial No.)** | n/a | |
| **SW Version** | n/a | |
| **Type of Action** | Field Safety Corrective Action (FSCA) | |

Dear Valued Customer,

## Description of Situation

Newly generated measurements at Roche Diagnostics revealed additional carryover for several tests on the COBAS INTEGRA® 400 plus and **cobas c** 111 analyzer. The internal findings for a number of tests show that the product specifications were not met. The recommended wash steps were either insufficient or missing altogether.

In case of carry over, it cannot be excluded that incorrect high results were generated. A medical risk cannot be excluded.

# Carryover on COBAS INTEGRA® 400 plus and cobas c111 analyzer

Affected test (also identified as victims) are listed in the following table:

| Material Number | Test | Instrument |
|---|---|---|
| 06 750 052 190 | A1MG<br>(Tina-quant α1-Microglobulin Gen.2) | COBAS INTEGRA® 400 plus |
| 03 032 566 122 | APOAT<br>(Tina-quant Apolipoprotein A-1 ver.2) | COBAS INTEGRA® 400 plus |
| 04 469 658 190 | ALBT2<br>(Tina-quant Albumin Gen.2) | COBAS INTEGRA® 400 plus |
| 03 263 991 190 | CREP2*<br>(Creatinine plus ver.2) | COBAS INTEGRA® 400 plus |
| 20 767 107 322 | TRIGL<br>(Triglycerides) | COBAS INTEGRA® 400 plus |
| 05 401 470 190 | CREP2*<br>(Creatinine plus ver.2) | **cobas c** 111 |
| 04 657 594 190 | TRIGL<br>(Triglycerides) | **cobas c** 111 |

*Serum/plasma application only. The urine application is not affected by carryover.

## Actions taken by Roche Diagnostics
The observed carryover will be averted by additional extra wash cycles. For some test combinations a needle assignment* is applicable (see table below victim/offender).
*Needle assignment* means, that dedicated tests will only be pipetted by a specific probe to exclude an interaction of a victim and offender combination and the resulting carryover. This assignment is part of the software (TAS = Test application software) and cannot be implemented manually.

For **COBAS INTEGRA® 400 plus** relevant changes are included in the upcoming TAS, solving the primary and secondary carry-overs; the update is planned for end of December 2018.
The updated extra wash cycle (EWC) List is part of the updated Instructions for Use (IFU) for the Cleaner Cassette (V 8.0), which will be available in Q1/2019.

**Please note:** The updated EWC list for **cobas c** 111 is part of the updated Instructions for Use (IFU) for the Cleaner (V 6.0), that will be published in Q1/2019.

## Actions to be taken by the customer/user
Customers running one or more offenders in combination with the affected victim applications (as described in the table below) need to install the required carryover evasions until the TAS and extra wash cycle lists are updated. For customers not running the affected tests no action is required.

# Carryover on COBAS INTEGRA® 400 plus and cobas c111 analyzer

**COBAS INTEGRA® 400 plus:**
Customers have to install the following EWCs as described in detail in **attachment "Detailed workarounds"**

| Affected test (Victim)<br>Application name [test ID] | Offender<br>Test name (Mat.Nr.) | Planned solution |
|---|---|---|
| A1MG2 [0-291] | **HDLC3** (04399803 190)<br>HDL-Cholesterol plus 3rd generation | Extra Wash Cycle |
| | **MDNII** (03046702 190)<br>ONLINE DAT Methadone II | Extra Wash Cycle |
| | **OPI** (20767158 122)<br>ONLINE DAT Opiates 300/2000 | Batch mode |
| | **THCII** (03046753 190)<br>ONLINE DAT Cannabinoids II | Batch mode |
| ALBS2 [0-172]<br>ALBU2 [0-171]<br>ALBC2 [0-170] | **HDLC3** (04399803 190)<br>HDL-Cholesterol plus 3rd generation | Extra Wash Cycle |
| | **FERR2** (03528995 190)<br>Ferritin Gen. 2 | Extra Wash Cycle |
| | **IGA** (20737755 322)<br>Immunoglobulin A | Extra Wash Cycle |
| | **RF–II** (20764574 322)<br>Rheumatoid Factors II | Extra Wash Cycle |
| | **MDNII** (03046702 190)<br>ONLINE DAT Methadone II | Extra Wash Cycle |
| | **OPI** (20767158 122)<br>ONLINE DAT Opiates 300/2000 | Extra Wash Cycle |
| | **PCP** (20738042 122)<br>Abuscreen OnLine Phencyclidine | Extra Wash Cycle |
| | **THCII** (03046753 190)<br>ONLINE DAT Cannabinoids II | Extra Wash Cycle |
| | **DIG** (20737836 322)<br>Digoxin | Needle assignment |
| APOAT [0-568] | **HDLC3** (04399803 190)<br>HDL-Cholesterol plus 3rd generation | Extra Wash Cycle |
| | **FERR2** (03528995 190)<br>Ferritin Gen. 2 | Extra Wash Cycle |
| | **RF–II** (20764574 322)<br>Rheumatoid Factors II | Extra Wash Cycle |
| | **DIG** (20737836 322)<br>Digoxin | Needle assignment |
| | **MDNII** (03046702 190)<br>ONLINE DAT Methadone II | Needle assignment |
| | **OPI** (20767158 122)<br>ONLINE DAT Opiates 300/2000 | Needle assignment |
| | **PCP** (20738042 122)<br>Abuscreen OnLine Phencyclidine | Extra Wash Cycle |
| | **THCII** (03046753 190)<br>ONLINE DAT Cannabinoids II | Needle assignment |
| CRE2 [0-612]** | **CHOL2** (03039773 190)<br>Cholesterol Gen.2 | Extra Wash Cycle |
| TRIGL [0-010]** | **CHOL2** (03039773 190) | Extra Wash Cycle |

# Carryover on COBAS INTEGRA® 400 plus and cobas c111 analyzer

| Affected test (Victim) Application name [test ID] | Offender Test name (Mat.Nr.) | Planned solution |
|---|---|---|
| | Cholesterol Gen.2 | |

** Secondary carry-over to TRIGL or CRE2 occurs only if a dextran sulfate containing assay is performed before CHOL2.
Hence these EWCs are only mandatory in case one of the following tests is also installed on the analyzer: HDLC4, HDLC3, LDLC3, PPXS, PPXQL, PPXQC, PCPS, PCPQL, PCPQC, MTQLS, MTQQL, MTQQC, HCYS, DIGM or any TDM test using SDR II.

For all carry-over evasions which require needle assignment the only possible workaround for the customers is running the applications in batches (batch mode) until the TAS is released.
==[COUNTRY ACTION: You are allowed to modify the local availability according to your local release schedules]==

*Please note:** The manual set-up of the EWCs as well as the batch mode are only required until the TAS is available. However, the observed carryover of the test combinations of A1MG with OPI or THCII cannot be overcome with EWCs or needle assignment. Therefore, these test combinations must not be measured at the same time (batch mode required) even after the TAS has been published.

**cobas c** 111:
Customers have to install the following EWCs as described in detail in **attachment 'Detailed overview about the required workarounds'**

| Affected test (Victim) Application name [ACN] | Offender Test name (Mat.Nr.) | Planned solution |
|---|---|---|
| CRE2 [652]** | **CHOL2** (04718917 190) Cholesterol Gen.2 | Extra Wash Cycle |
| TRIGL [781]** | **CHOL2** (04718917 190) Cholesterol Gen.2 | Extra Wash Cycle |

** Secondary carry-over to TRIGL or CRE2 occurs only if a dextran sulfate containing assay is performed before CHOL2.
Hence these EWCs are only mandatory in case one of the following tests is also installed on the analyzer: HDLC4, HDLC3 or LDLC3.

## Communication of this Field Safety Notice (if appropriate)
*<If the recipient needs to forward the FSN to additional organizations/individuals then one or more of the following statements may be included:*

This notice must be passed on to all those who need to be aware within your organization or to any organization/individual where the potentially affected devices have been distributed/supplied. (If appropriate).

Please transfer this notice to other organizations/individuals on which this action has an impact. (If appropriate).

Please maintain awareness of this notice and resulting action for an appropriate period to ensure the effectiveness of the corrective action. (If appropriate).

**The following statement is mandatory in FSNs for EEA countries but is not required for the rest of the World:**

# Carryover on COBAS INTEGRA® 400 plus and cobas c111 analyzer

*Include if applicable:* The undersigned confirms that this notice has been notified to the appropriate Regulatory Agency.

We apologize for any inconvenience this may cause and hope for your understanding and your support.

<closing salutations>,

**Contact Details**

*To be completed locally:*
Name
Title
Company Name
Address
Tel. +xx-xxx-xxxx xxxx
Email name@roche.com

## Attachment: Detailed overview about the required workarounds

### A) COBAS INTEGRA® 400 plus system

**Batch mode:**

Test combinations which require needle assignment and have to be run in batch mode until the TAS is available:

| Affected test (Victim) Application name [test ID] | Offender Application name [test ID] | Needle Assignment |
|---|---|---|
| ALBS2 [0-172] ALBU2 [0-171] ALBC2 [0-170] | DIGM [0-283] | x |
| APOAT [0-568] | MD3S2 [0-322] MD3Q2 [0-222] MD3QC [0-422] | x |
| | OPIS [0-406] OPIS6 [0-407] OPI2S [0-409] OPI3Q [0-408] OP2QL [0-410] OP3QC [0-526] | x |
| | THS22 [0-431] THS25 [0-531] THS21 [0-631] TH2QP [0-017] TH5QP [0-217] TH1QP [0-317] TH5QC [0-517] | x |
| | DIGM [0-283] | x |

Test combinations which must not be measured at the same time (batch mode required) even after publication of the TAS:

| Affected test (Victim) Application name [test ID] | Offender Application name [test ID] | Batch Mode |
|---|---|---|
| A1MG2 [0-291] | OPIS [0-406] OPIS6 [0-407] OPI2S [0-409] OPI3Q [0-408] OP2QL [0-410] OP3QC [0-526] | x |
| | THS22 [0-431] THS25 [0-531] THS21 [0-631] TH2QP [0-017] TH5QP [0-217] TH1QP [0-317] TH5QC [0-517] | x |

### Extra Wash Cycles (EWCs):

The following EWCs have to be set up for all affected customers manually until the TAS is available:

| Test/Reagent combination in use | | Extra wash cycle configuration | | | | |
|---|---|---|---|---|---|---|
| Reagent carry-over (primary) | | Type | Test | Component | with | Volume (µL) |
| offender | victim | | | | | |
| FER2P | ALBC2 | after | FER2P | R1 | CLEAN | 150 |
| FER2P | ALBS2 | after | FER2P | R1 | CLEAN | 150 |
| FER2P | ALBU2 | after | FER2P | R1 | CLEAN | 150 |
| FER2P | APOAT | after | FER2P | R1 | CLEAN | 150 |
| HDLC3 | A1MG2* | after | HDLC3 | R1 | CLEAN | 150 |
| HDLC3 | ALBC2 | after | HDLC3 | R1 | CLEAN | 150 |
| HDLC3 | ALBS2 | after | HDLC3 | R1 | CLEAN | 150 |
| HDLC3 | ALBU2 | after | HDLC3 | R1 | CLEAN | 150 |
| HDLC3 | APOAT | after | HDLC3 | R1 | CLEAN | 150 |
| HDLC3 | APOAT | after | HDLC3 | SR | CLEAN | 150 |
| IGA | ALBC2 | after | IGA | R1 | CLEAN | 150 |
| IGA | ALBS2 | after | IGA | R1 | CLEAN | 150 |
| IGA | ALBU2 | after | IGA | R1 | CLEAN | 150 |
| IGAP | ALBC2 | after | IGAP | R1 | CLEAN | 150 |
| IGAP | ALBS2 | after | IGAP | R1 | CLEAN | 150 |
| IGAP | ALBU2 | after | IGAP | R1 | CLEAN | 150 |
| MD3Q2 | A1MG2* | after | MD3Q2 | R1 | CLEAN | 150 |
| MD3Q2 | ALBC2 | after | MD3Q2 | R1 | CLEAN | 150 |
| MD3Q2 | ALBS2 | after | MD3Q2 | R1 | CLEAN | 150 |
| MD3Q2 | ALBU2 | after | MD3Q2 | R1 | CLEAN | 150 |
| MD3QC | A1MG2* | after | MD3QC | R1 | CLEAN | 150 |
| MD3QC | ALBC2 | after | MD3QC | R1 | CLEAN | 150 |
| MD3QC | ALBS2 | after | MD3QC | R1 | CLEAN | 150 |
| MD3QC | ALBU2 | after | MD3QC | R1 | CLEAN | 150 |
| MD3S2 | A1MG2* | after | MD3S2 | R1 | CLEAN | 150 |
| MD3S2 | ALBC2 | after | MD3S2 | R1 | CLEAN | 150 |
| MD3S2 | ALBS2 | after | MD3S2 | R1 | CLEAN | 150 |
| MD3S2 | ALBU2 | after | MD3S2 | R1 | CLEAN | 150 |
| OP2QL | ALBC2 | after | OP2QL | R1 | CLEAN | 150 |
| OP2QL | ALBS2 | after | OP2QL | R1 | CLEAN | 150 |
| OP2QL | ALBU2 | after | OP2QL | R1 | CLEAN | 150 |
| OP3QC | ALBC2 | after | OP3QC | R1 | CLEAN | 150 |
| OP3QC | ALBS2 | after | OP3QC | R1 | CLEAN | 150 |
| OP3QC | ALBU2 | after | OP3QC | R1 | CLEAN | 150 |
| OPI2S | ALBC2 | after | OPI2S | R1 | CLEAN | 150 |
| OPI2S | ALBS2 | after | OPI2S | R1 | CLEAN | 150 |
| OPI2S | ALBU2 | after | OPI2S | R1 | CLEAN | 150 |
| OPI3Q | ALBC2 | after | OPI3Q | R1 | CLEAN | 150 |
| OPI3Q | ALBS2 | after | OPI3Q | R1 | CLEAN | 150 |
| OPI3Q | ALBU2 | after | OPI3Q | R1 | CLEAN | 150 |
| OPIS | ALBC2 | after | OPIS | R1 | CLEAN | 150 |
| OPIS | ALBS2 | after | OPIS | R1 | CLEAN | 150 |
| OPIS | ALBU2 | after | OPIS | R1 | CLEAN | 150 |
| OPIS6 | ALBC2 | after | OPIS6 | R1 | CLEAN | 150 |
| OPIS6 | ALBS2 | after | OPIS6 | R1 | CLEAN | 150 |
| OPIS6 | ALBU2 | after | OPIS6 | R1 | CLEAN | 150 |
| PCPQC | ALBC2 | after | PCPQC | R1 | CLEAN | 150 |
| PCPQC | ALBS2 | after | PCPQC | R1 | CLEAN | 150 |

| Test/Reagent combination in use | | Extra wash cycle configuration | | | | |
|---|---|---|---|---|---|---|
| Reagent carry-over (primary) | | Type | Test | Component | with | Volume (µL) |
| offender | victim | | | | | |
| PCPQC | ALBU2 | after | PCPQC | R1 | CLEAN | 150 |
| PCPQC | APOAT | after | PCPQC | R1 | CLEAN | 150 |
| PCPQL | ALBC2 | after | PCPQL | R1 | CLEAN | 150 |
| PCPQL | ALBS2 | after | PCPQL | R1 | CLEAN | 150 |
| PCPQL | ALBU2 | after | PCPQL | R1 | CLEAN | 150 |
| PCPQL | APOAT | after | PCPQL | R1 | CLEAN | 150 |
| PCPS | ALBC2 | after | PCPS | R1 | CLEAN | 150 |
| PCPS | ALBS2 | after | PCPS | R1 | CLEAN | 150 |
| PCPS | ALBU2 | after | PCPS | R1 | CLEAN | 150 |
| PCPS | APOAT | after | PCPS | R1 | CLEAN | 150 |
| RF-II | ALBC2 | after | RF-II | R1 | CLEAN | 150 |
| RF-II | ALBS2 | after | RF-II | R1 | CLEAN | 150 |
| RF-II | ALBU2 | after | RF-II | R1 | CLEAN | 150 |
| RF-II | APOAT | after | RF-II | R1 | CLEAN | 150 |
| TH1QP | ALBC2 | after | TH1QP | R1 | CLEAN | 150 |
| TH1QP | ALBS2 | after | TH1QP | R1 | CLEAN | 150 |
| TH1QP | ALBU2 | after | TH1QP | R1 | CLEAN | 150 |
| TH2QP | ALBC2 | after | TH2QP | R1 | CLEAN | 150 |
| TH2QP | ALBS2 | after | TH2QP | R1 | CLEAN | 150 |
| TH2QP | ALBU2 | after | TH2QP | R1 | CLEAN | 150 |
| TH5QC | ALBC2 | after | TH5QC | R1 | CLEAN | 150 |
| TH5QC | ALBS2 | after | TH5QC | R1 | CLEAN | 150 |
| TH5QC | ALBU2 | after | TH5QC | R1 | CLEAN | 150 |
| TH5QP | ALBC2 | after | TH5QP | R1 | CLEAN | 150 |
| TH5QP | ALBS2 | after | TH5QP | R1 | CLEAN | 150 |
| TH5QP | ALBU2 | after | TH5QP | R1 | CLEAN | 150 |
| THS21 | ALBC2 | after | THS21 | R1 | CLEAN | 150 |
| THS21 | ALBS2 | after | THS21 | R1 | CLEAN | 150 |
| THS21 | ALBU2 | after | THS21 | R1 | CLEAN | 150 |
| THS22 | ALBC2 | after | THS22 | R1 | CLEAN | 150 |
| THS22 | ALBS2 | after | THS22 | R1 | CLEAN | 150 |
| THS22 | ALBU2 | after | THS22 | R1 | CLEAN | 150 |
| THS25 | ALBC2 | after | THS25 | R1 | CLEAN | 150 |
| THS25 | ALBS2 | after | THS25 | R1 | CLEAN | 150 |
| THS25 | ALBU2 | after | THS25 | R1 | CLEAN | 150 |
| CLEAN = COBAS INTEGRA Cleaner Cassette | | | | | | |

* not available in the US

**Reagent carry-over (secondary)**

| Test combination in use | | Extra wash cycle configuration | | | | |
|---|---|---|---|---|---|---|
| | | Type | Test | Component | With | Volume (µl) |
| CHOL2 | CRE2 | after | CHOL2 | R1 | CLEAN | 150 |
| CHOL2 | TRIGL | after | CHOL2 | R1 | CLEAN | 150 |

Secondary carry-over to TRIGL or CRE2 occurs only if a dextran sulfate containing assay is performed before CHOL2.
Hence these EWCs are only mandatory in case one of the following tests is also installed on the analyzer: HDLC4, HDLC3, LDLC3, PPXS, PPXQL, PPXQC, PCPS, PCPQL, PCPQC, MTQLS, MTQQL, MTQQC, HCYS, DIGM or any TDM test using SDR II.

## B) cobas c 111 analyzer

**Extra Wash Cycles (EWCs):**

The following EWCs have to be set up for all affected customers manually:

| Test combination in use | | Extra wash cycle configuration | | | | | |
|---|---|---|---|---|---|---|---|
| | | Action | Trigger Bottle Code | Pipetting type | Active | Cleaner Bottle Code | Volume [µL] |
| CHO2I | CRE2 | after | 798 | R1 | on | 947 | 150 |
| CHO2I | TRIGL | after | 798 | R1 | on | 947 | 150 |
| CHO2A | CRE2 | after | 798 | R1 | on | 947 | 150 |
| CHO2A | TRIGL | after | 798 | R1 | on | 947 | 150 |

Secondary carry-over to TRIGL or CRE2 occurs only if a dextran sulfate containing assay is performed before CHOL2.

Hence these EWCs are only mandatory in case one of the following tests is also installed on the analyzer: HDLC4, HDLC3 or LDLC3.