

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)	

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.

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

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

COBAS INTEGRA® 400 plus:

Customers have to install the following EWCs as described in detail in the below **attachment “Detailed workarounds”**

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

***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 THCI 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.

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]	x

	<i>OPI2S [0-409]</i> <i>OPI3Q [0-408]</i> <i>OP2QL [0-410]</i> <i>OP3QC [0-526]</i>	
	<i>THS22 [0-431]</i> <i>THS25 [0-531]</i> <i>THS21 [0-631]</i> <i>TH2QP [0-017]</i> <i>TH5QP [0-217]</i> <i>TH1QP [0-317]</i> <i>TH5QC [0-517]</i>	x
	<i>DIGM [0-283]</i>	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
<i>A1MG2 [0-291]</i>	<i>OPIS [0-406]</i> <i>OPIS6 [0-407]</i> <i>OPI2S [0-409]</i> <i>OPI3Q [0-408]</i> <i>OP2QL [0-410]</i> <i>OP3QC [0-526]</i>	x
	<i>THS22 [0-431]</i> <i>THS25 [0-531]</i> <i>THS21 [0-631]</i> <i>TH2QP [0-017]</i> <i>TH5QP [0-217]</i> <i>TH1QP [0-317]</i> <i>TH5QC [0-517]</i>	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

Test/Reagent combination in use		Extra wash cycle configuration				
Reagent carry-over (primary)		Type	Test	Component	with	Volume (µL)
offender	victim					
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

Test/Reagent combination in use		Extra wash cycle configuration				
Reagent carry-over (primary)		Type	Test	Component	with	Volume (µL)
offender	victim					
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

Test/Reagent combination in use		Extra wash cycle configuration				
Reagent carry-over (primary)		Type	Test	Component	with	Volume (µL)
offender	victim					
PCPQC	ALBS2	after	PCPQC	R1	CLEAN	150
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

Test/Reagent combination in use		Extra wash cycle configuration				
Reagent carry-over (primary)		Type	Test	Component	with	Volume (μL)
offender	victim					
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.

Local authorized distributor's Details:

Facility Name:
 Contact Name:
 Position:
 Phone:
 Date:
 Signature and Stamp:

Customer Details:

Facility Name:
 Contact Name:
 Position:
 Phone:
 Date:
 Signature and Stamp: