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Urgent Field Safety Notice:
ADVIA Centaur® XP /ADVIA Centaur® XPT /ADVIA Centaur® CP
Syphilis Assay Carryover with Multiple Assays

Dear Sirs,

Our records indicate that your facility may have received the following product:

Table 1. ADVIA Centaur Affected Product(s)

Assay	Test Code	Siemens Material Number (SMN)	Lot Number
ADVIA Centaur Syphilis Assay	SYPH	10492493	All Lots

Reason for Correction

The purpose of this communication is to inform you of an issue with the product indicated in Table 1 above and provide instructions on actions that your laboratory must take.

Siemens Healthcare Diagnostics Inc. has confirmed the potential for the ADVIA Centaur Syphilis assay to carryover into other commercial assays. This carryover effect only occurs when the impacted assays are used immediately following testing with the Syphilis assay on the ADVIA Centaur XP/XPT or ADVIA Centaur CP systems. Refer to Table 2 for the impacted assays, systems and a summary of the carryover effect.

Table 2. Assays with Observed Carryover Effect

Impacted System	Impacted Assay	Impact of Carryover
ADVIA Centaur XP/XPT	PRGE	Falsely depressed results
	T4	
ADVIA Centaur CP	AFP	Falsely elevated results
	COR	Falsely depressed results
	PHTN	
	VALP	

No assays are impacted on the Atellica IM analyzer.

The root cause of this issue is carryover from the Syphilis Lite Reagent. This issue affects all current and future lots until a solution is implemented.

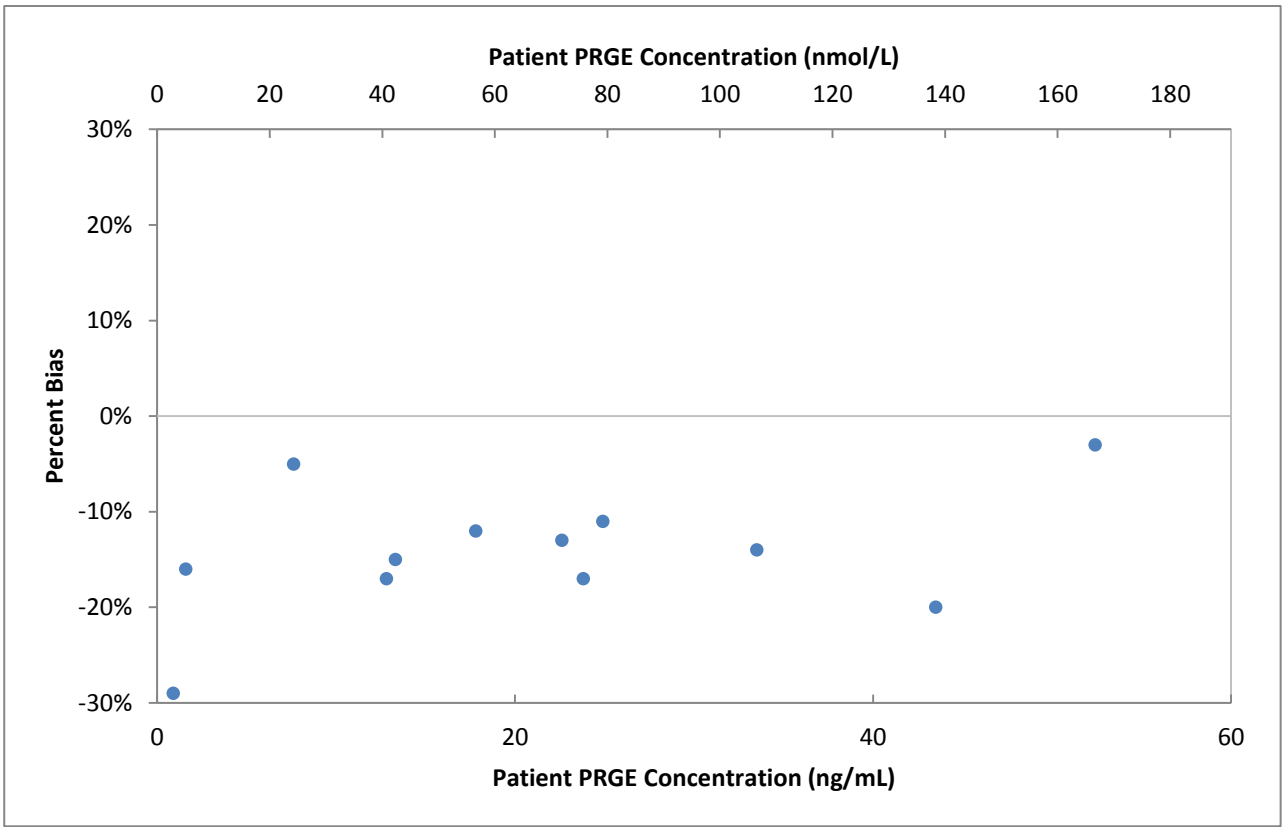
ADVIA Centaur XP/XPT Impacted Assays – PRGE and T4

Patient samples covering the Medical Decision Points for each assay were included in the investigation. Each patient sample was tested following ten Syphilis tests.

ADVIA Centaur Progesterone (PRGE) Assay

The analytical measuring range (AMR) of the ADVIA Centaur PRGE assay is 0.21 - 60 ng/mL (0.67 – 190.8 nmol/L). Patient samples ranging from <0.21 to >60 ng/mL (<0.67 to >190.8 nmol/L) were tested. The maximum bias observed was -29% at 0.89 ng/mL (2.83 nmol/L). Commercial controls tested recovered within published ranges.

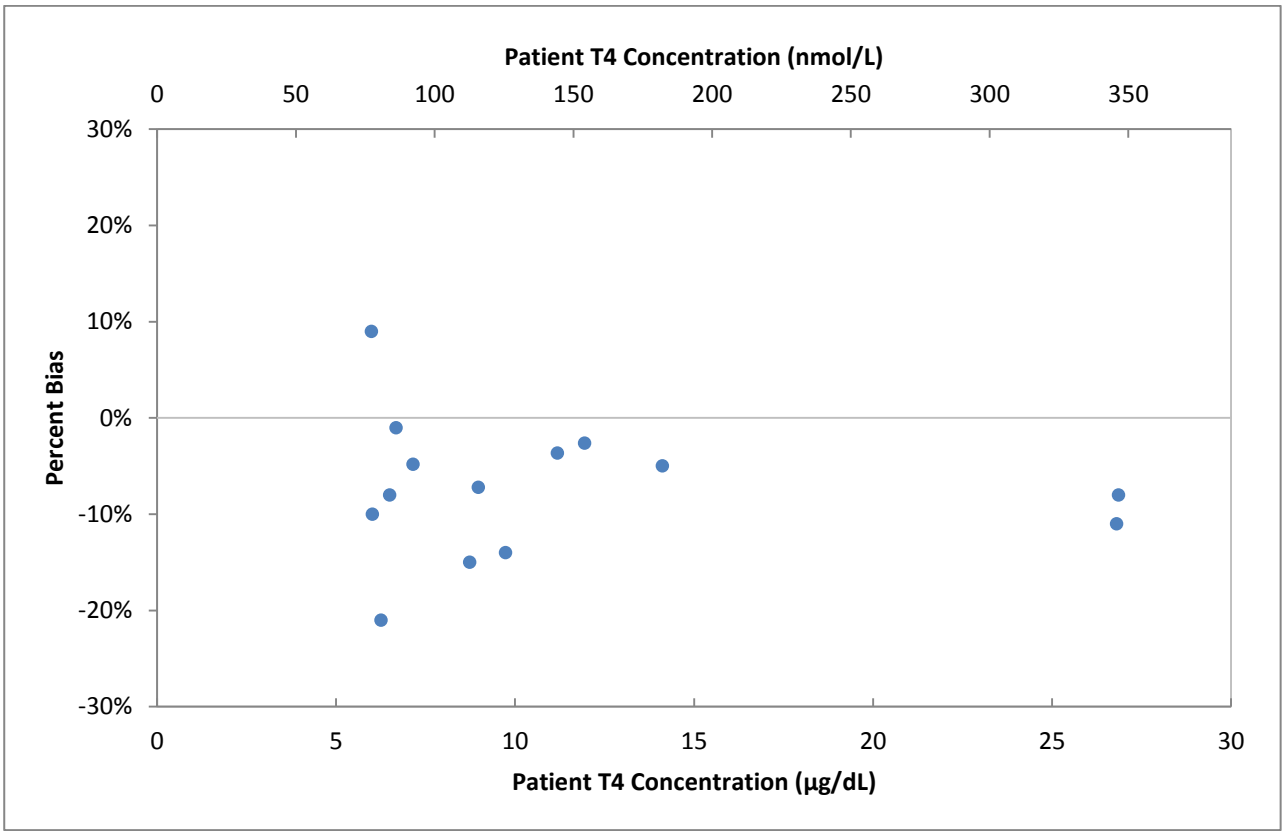
Figure 1. **Impact of Syphilis carryover on Progesterone (PRGE) on the ADVIA Centaur XP/XPT**



ADVIA Centaur T4 Assay

The analytical measuring range (AMR) of the ADVIA Centaur T4 assay is 0.3 - 30 µg/dL (3.9 – 387 nmol/L). Patient samples ranging from 5.98 to 26.9 µg/dL (77.1 to 347 nmol/L) were tested. The maximum bias observed was -21% at 6.25 µg/dL (80.6 nmol/L). Commercial controls tested recovered within published ranges.

Figure 2. **Impact of Syphilis carryover on T4 on the ADVIA Centaur XP/XPT**



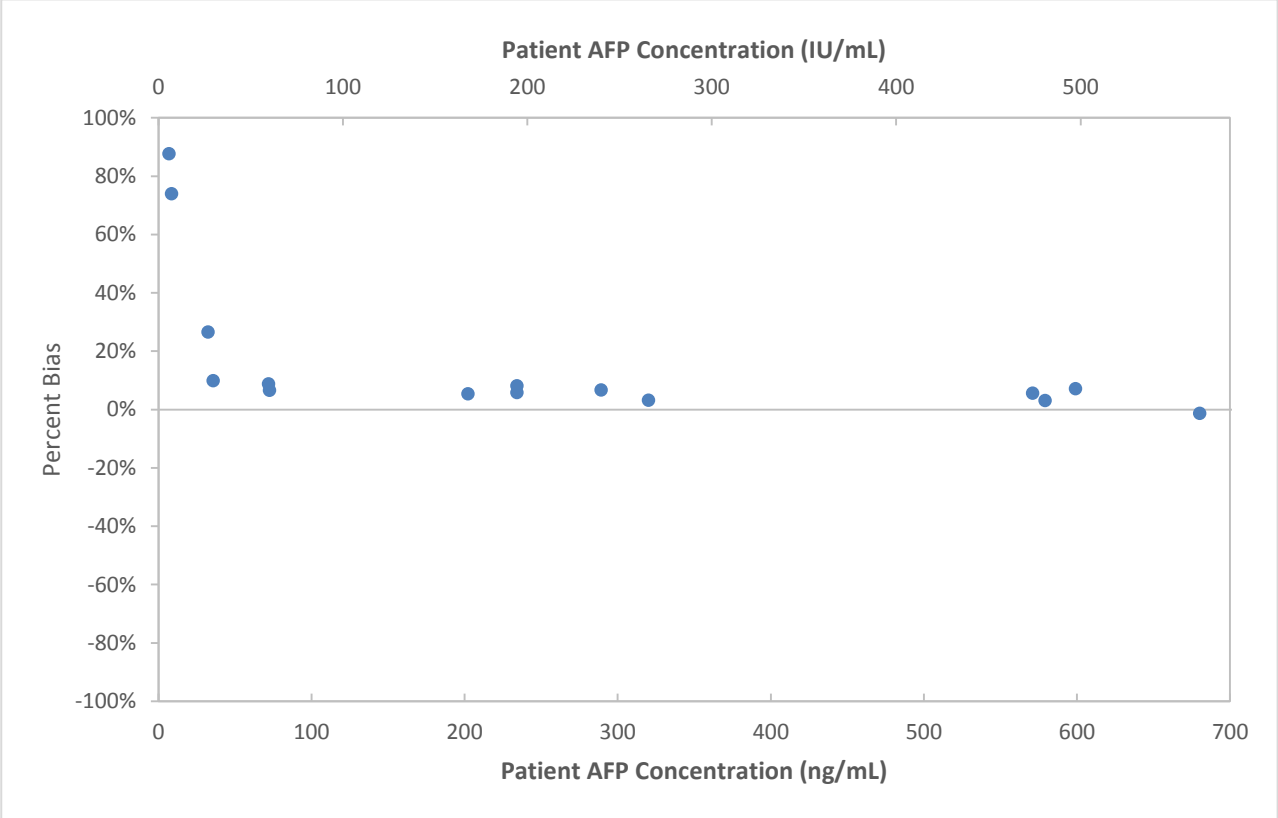
ADVIA Centaur CP Impacted Assays – AFP, COR, PHTN, VALP

Patient samples covering the Medical Decision Points for each assay were included in the investigation. Each patient sample was tested following ten Syphilis tests.

ADVIA Centaur AFP Assay

The analytical measuring range (AMR) of the ADVIA Centaur CP AFP assay is 1.7- 1000 ng/mL (1.4 – 830 IU/mL). Patient samples ranging from 6.76 to 680 ng/mL (5.61 to 564 IU/mL) were tested. The maximum bias observed was 87.8% at 6.76 ng/mL (5.61 IU/mL). Elevated results were sometimes observed with commercial controls tested.

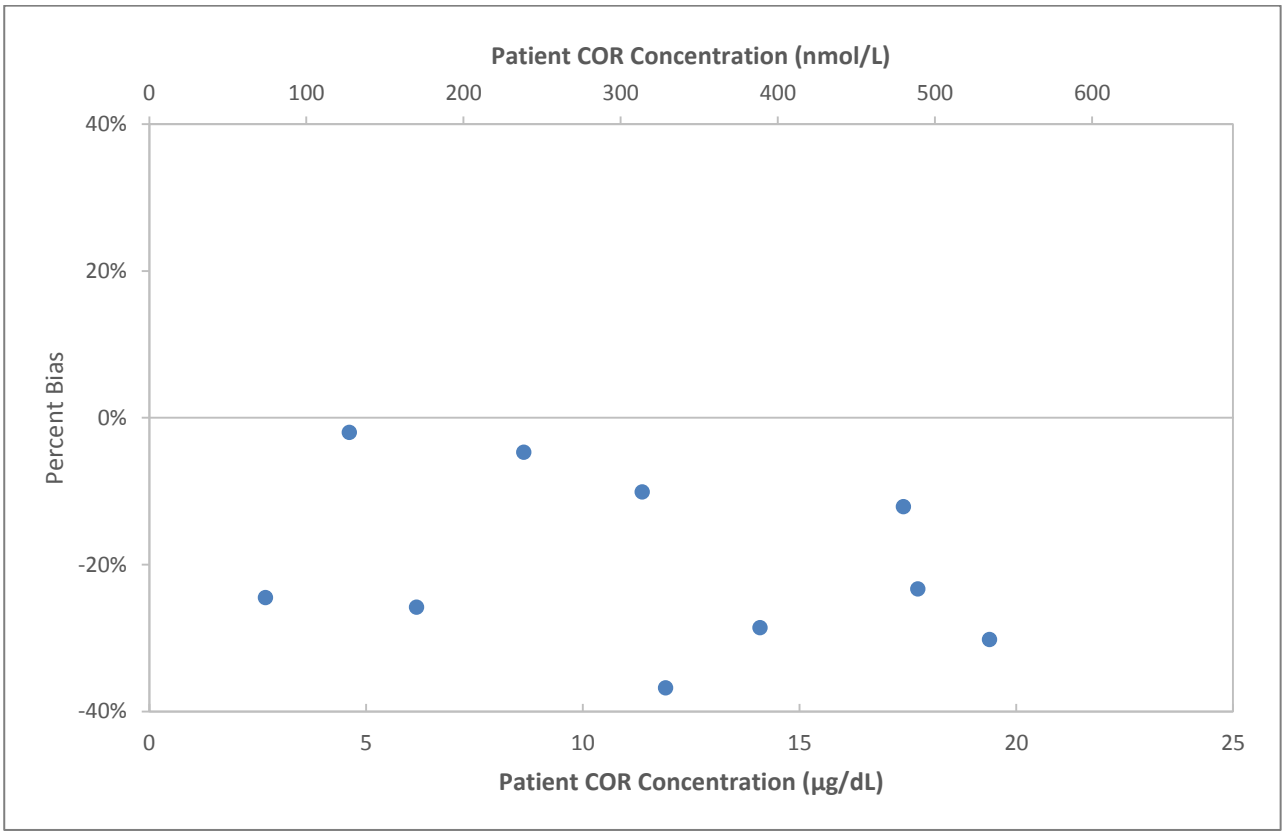
Figure 3. **Impact of Syphilis carryover on AFP on the ADVIA Centaur CP**



ADVIA Centaur Cortisol Assay

The analytical measuring range (AMR) of the ADVIA Centaur CP COR assay is 0.50 – 75 µg/dL (13.80 – 2069 nmol/L). Patient samples ranging from 2.68 to 19.4 µg/dL (73.9 to 535 nmol/L) were tested. The maximum bias observed was -36.8% at 11.9 µg/dL (328 nmol/L). Depressed results were sometimes observed with commercial controls tested.

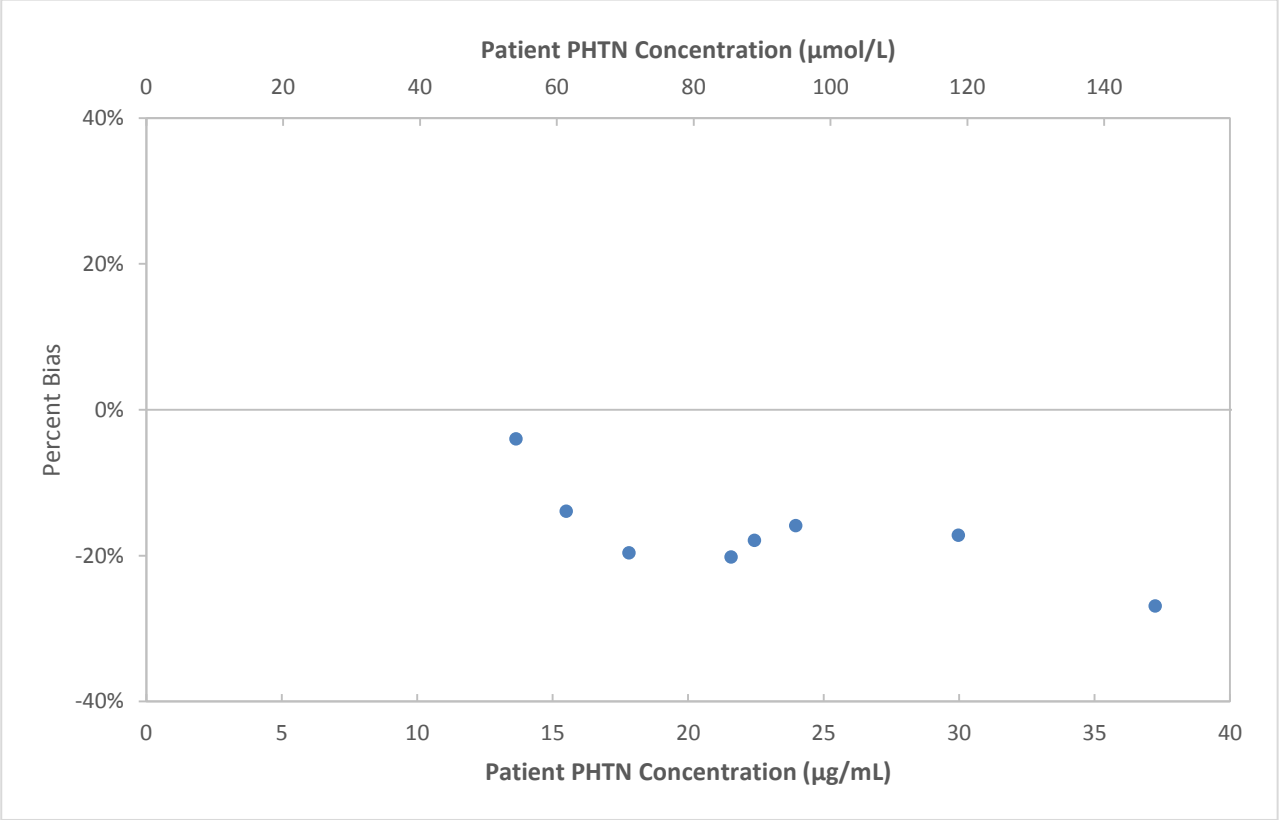
Figure 4. **Impact of Syphilis carryover on Cortisol (COR) on the ADVIA Centaur CP**



ADVIA Centaur Phenytoin Assay

The analytical measuring range (AMR) of the ADVIA Centaur CP PHTN assay is 0.5 – 40 µg/mL (1.98 – 158.4 µmol/L). Patient samples ranging from 13.6 to >40 µg/mL (54.0 to >158.4 µmol/L) were tested. The maximum bias observed was -26.9% at 37.2 µg/mL (147 µmol/L). Depressed results were sometimes observed with commercial controls tested.

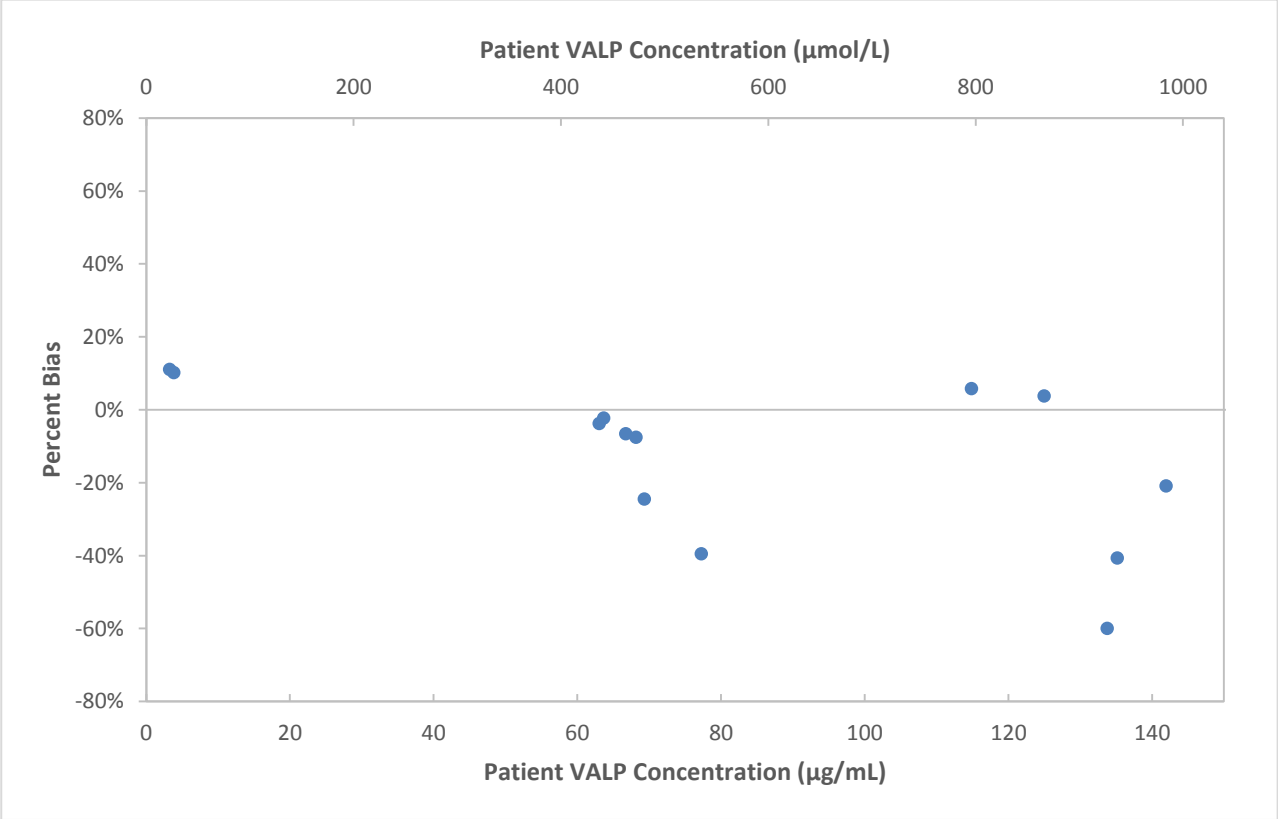
Figure 5. **Impact of Syphilis carryover on Phenytoin on the ADVIA Centaur CP**



ADVIA Centaur Valproic Acid Assay

The analytical measuring range (AMR) of the ADVIA Centaur CP VALP assay is 1 – 150 µg/mL (6.93 – 1039.5 µmol/L). Patient samples ranging from 3.24 µg/mL to >150 µg/mL (22.5 to >1039.5 umol/L) were tested. The maximum bias observed was -60.0% at 134 µg/mL (927 umol/L). Depressed results were sometimes observed with commercial controls tested.

Figure 6. **Impact of Syphilis carryover on Valproic Acid on the ADVIA Centaur CP**



Risk to Health

The probability of using an impacted assay immediately following multiple syphilis assays is low. If quality controls detect the issue, an apparent delay in testing on the affected instrument may occur. Due to the extremely unlikely probability of a clinical impact, Siemens is not recommending a review of previously generated results.

For PRGE, T4, PHTN and AFP, the biases observed at the medical decision limits would not be expected to cause a clinically significant difference in patient management. For AFP, additional imaging may occur as part of regular monitoring.

For COR, the differences observed may worst case lead to a truly elevated result to appear normal, which may confound the investigation of patients with potential hypercortisolism. The clinical impact would be mitigated by correlation with other clinical information such as symptomology and additional laboratory biomarkers.

For VALP, the differences observed may worst case lead to unnecessary dosing adjustment, resulting in higher and potentially toxic levels of valproic acid. Treatment of toxicity is generally supportive and would be based on

symptomology. The clinical impact would be mitigated by serial monitoring of VALP and additional laboratory biomarkers.

Actions to be Taken by the Customer

- Please review this letter with your Medical Director.
- If you have multiple ADVIA Centaur XP/XPT or ADVIA Centaur CP systems:
    - Siemens recommends testing the ADVIA Centaur Syphilis assay on a separate system from the impacted ADVIA Centaur assays (*ADVIA Centaur PRGE, T4 on the ADVIA Centaur XP/XPT and ADVIA Centaur AFP, COR, PHTN, VALP on the ADVIA Centaur CP*) to avoid the potential carryover effect.
- If you have a single ADVIA Centaur XP/XPT or ADVIA Centaur CP system:
    - It is important to prevent the impacted assays from being processed after the Syphilis assay without a Daily Cleaning Procedure (DCP) run in between. For example, this can be achieved by processing all Syphilis testing, running the DCP, and then proceeding with all other testing including the impacted assays.
- Complete and return the Field Correction Effectiveness Check Form attached to this letter within 30 days.
- If you have received any complaints of illness or adverse events associated with the products listed in Table 1, immediately contact your local Siemens Healthineers Customer Care Center or your local Siemens Healthineers technical support representative.

Please retain this letter with your laboratory records and forward this letter to those who may have received this product.

We apologize for the inconvenience this situation may cause. If you have any questions, please contact your Siemens Healthineers Customer Care Center or your local Siemens Healthineers technical support representative.

Sincerely yours,

Siemens Healthcare Diagnostics GmbH

Signature: *Electronically signed by: Roland Ertl*
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Signature: *Electronically signed by: Gernot Osterer*
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Date: Apr 30, 2021 09:51 GMT+2

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