SIEMENS Healthineers
Siemens Healthcare Diagnostics Inc.

Urgent Field Safety Notice

CC 19-04.A-1.OUS

December, 2018

ADVIA Centaur®
ADVIA Centaur® XP
ADVIA Centaur® XPT
ADVIA Centaur® CP

ADVIA Centaur Anti-Thyroglobulin (aTG) Positive Bias

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

Table 1. ADVIA Centaur Affected Product(s)

Assay	Siemens Material Number (SMN)	Lot Number	Expiration Date (YYYY-MM-DD)	1st Distribution Date (YYYY-MM-DD)
ADVIA Centaur aTG (100 test kit)	10492398	68748302 68749302 83577304 88637304 05610306 96436306 19097308 31866310 45386310 55627312 69208316 73000316	2018/12/13 2018/12/13 2019/01/12 2019/01/12 2019/02/11 2019/02/11 2019/03/14 2019/04/27 2019/04/27 2019/05/27 2019/06/29 2019/06/29	2018-02-20 2018-02-21 2018-03-29 2018-04-04 2018-05-22 2018-05-03 2018-06-18 2018-07-17 2018-08-08 2018-09-04 2018-10-03 2018-10-17
ADVIA Centaur aTG (500 test kit)	10492399	68750302 68751302 83578304 91382304 04642306 08116306 19098308 22635308 33640310 39133310 55625312 55626312 56285312 69206316 73001316	2018/12/13 2018/12/13 2019/01/12 2019/01/12 2019/02/11 2019/02/11 2019/03/14 2019/03/14 2019/04/27 2019/04/27 2019/05/27 2019/05/27 2019/05/27 2019/06/29 2019/06/29	2018-02-23 2018-03-01 2018-04-03 2018-04-18 2018-05-15 2018-06-05 2018-06-21 2018-06-28 2018-07-24 2018-08-02 2018-09-11 2018-09-11 2018-09-13 2018-10-02 2018-10-22

Reason for Urgent Field Safety Notice

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

511 Benedict Avenue
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Siemens identified a positive bias with ADVIA Centaur aTG kit lots ending in 316 and lower when compared to the standardization to World Health Organization (WHO) Reference Preparation MRC 65/93 stated in the Instructions for Use (IFU). See Additional Information below, Traceability to WHO MRC 65/93.

Traceability to WHO Reference Preparation MRC 65/93 is restored with the release of ADVIA Centaur aTG kit lots ending in 318 and higher (available in December 2018). As stated in the IFU, the theoretical WHO International units (IU/mL) is on average 3-fold higher than Siemens Healthcare Diagnostics standardization. Moving forward, this traceability will be maintained through enhancements to the control system.

Customers will observe a negative shift in patient results when transitioning from ADVIA Centaur aTG reagent kit lots 316 and lower to ADVIA Centaur aTG reagent kit lots 318 and higher. See Additional Information, Method Comparison.

The ADVIA Centaur aTG assay remains “lot-locked”. Reagent lots must be used with specific lots of ADVIA Centaur Calibrator 1, ADVIA Centaur aTG 1, 2 Quality Control Material, and ADVIA Centaur aTG Master Curve Material as noted on the notecard contained in each reagent kit.

Risk to Health

Use of lots affected by this issue may cause misinterpretation of antibody status for patients whose results are truly below but approaching the cut-off (60 U/mL per the IFU). Anti-thyroglobulin results would not be used in isolation, but rather would be used in conjunction with results of other thyroid tests. Therefore, Siemens is not recommending a review of previously generated results.

Actions to be Taken by the Customer

- Please review this letter with your Medical Director.
- You may continue use of ADVIA Centaur aTG kit lots in Table 1 until you receive replacement product in your laboratory. Refer to Figure 1 through Figure 4 for ADVIA Centaur aTG bias information.
- If you are currently using ADVIA Centaur aTG kit lots in Table 1, review your inventory of these products as well as the associated Calibrator 1, aTG QC and aTG Master Curve Material and order replacement products by completing the Field Correction Effectiveness Check Form attached to this letter.
- Upon receipt of replacement product in your laboratory, discontinue use of and discard the ADVIA Centaur aTG kit lots listed in Table 1. Refer to Figures 5 through 8 for expected results with replacement lots.
- 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 Customer Care Center or your local Siemens technical support representative.

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

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

Additional Information

(Note: Data and plots below that reference ADVIA Centaur XP are representative of the performance seen on the ADVIA Centaur, ADVIA Centaur XP and ADVIA Centaur XPT systems.)

Traceability to WHO MRC 65/93

Figures 1 through 4 show the results obtained ("Observed") as compared to the internal standards traceable to WHO MRC 65/93 ("Expected") for ADVIA Centaur aTG reagent kit lots ending in 310 and 316. Kit Lots ending in 310 are included to demonstrate the largest differences observed as compared to kit lots ending in 318. Kit lots ending in 316 are included as the most recently released lots.

Figure 1: ADVIA Centaur XP- Reagent Lot 310 Observed vs Expected

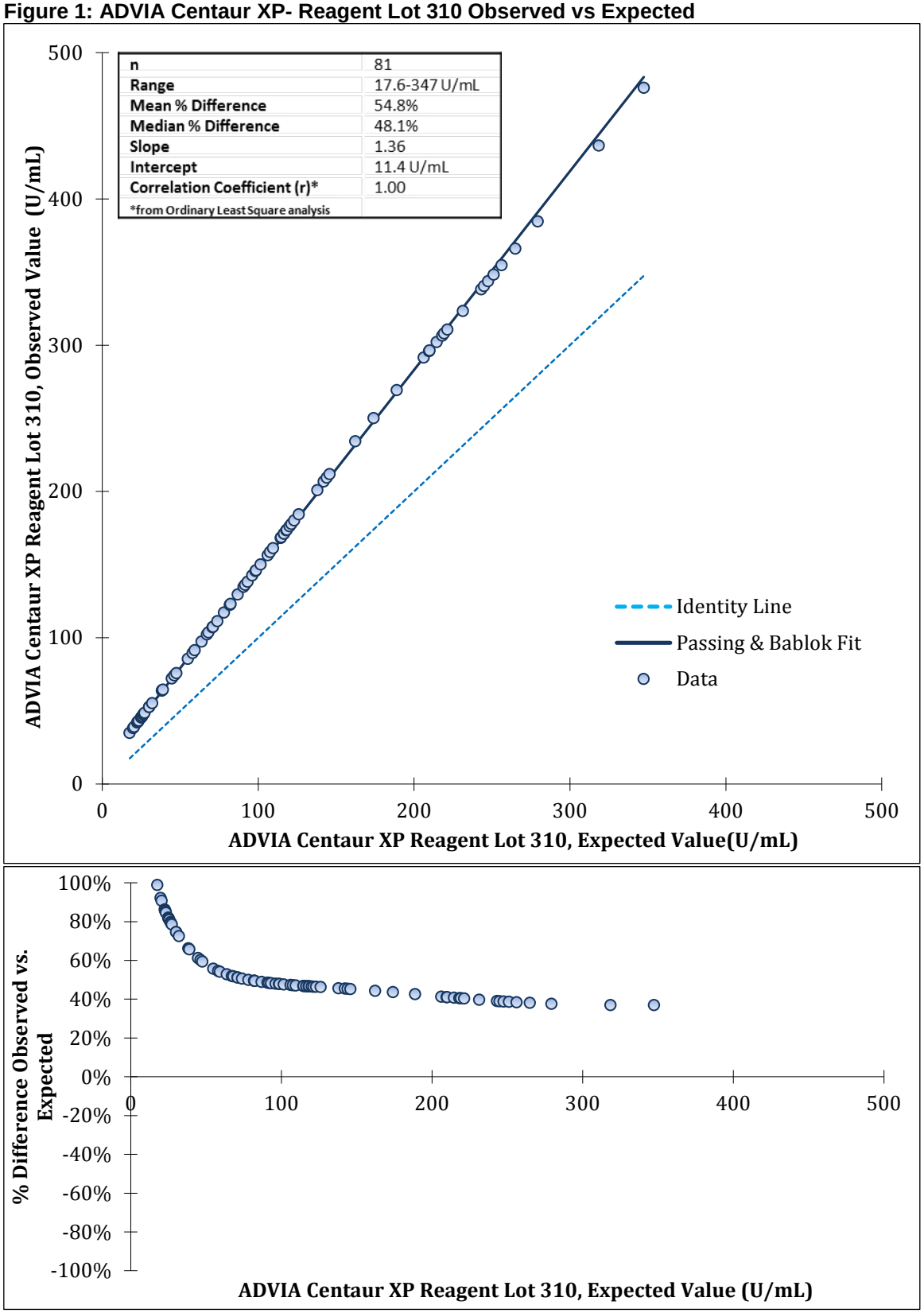


Figure 2: ADVIA Centaur XP- Reagent Lot 316 Observed vs Expected

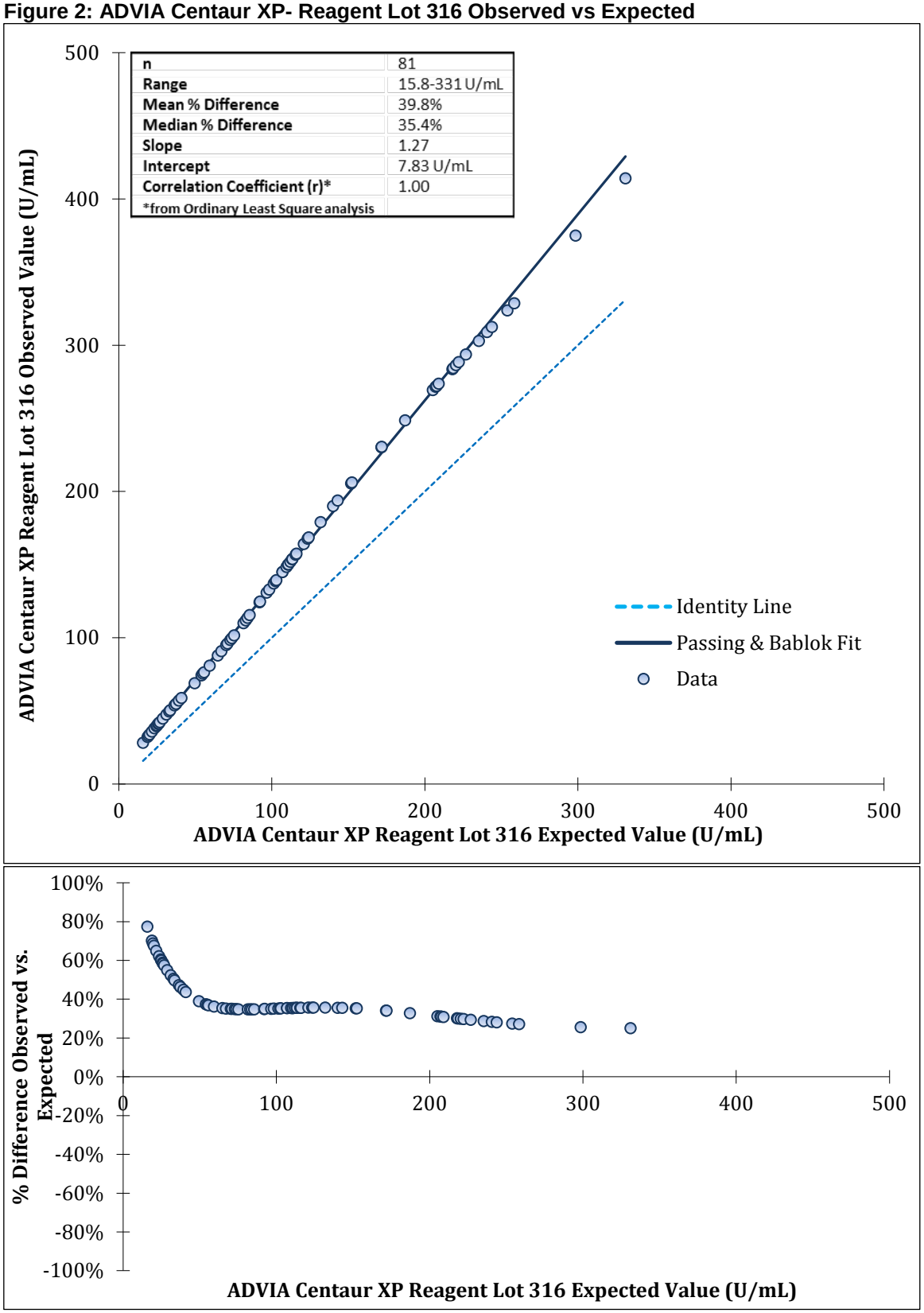


Figure 3: ADVIA Centaur CP- Reagent Lot 310 Observed vs Expected

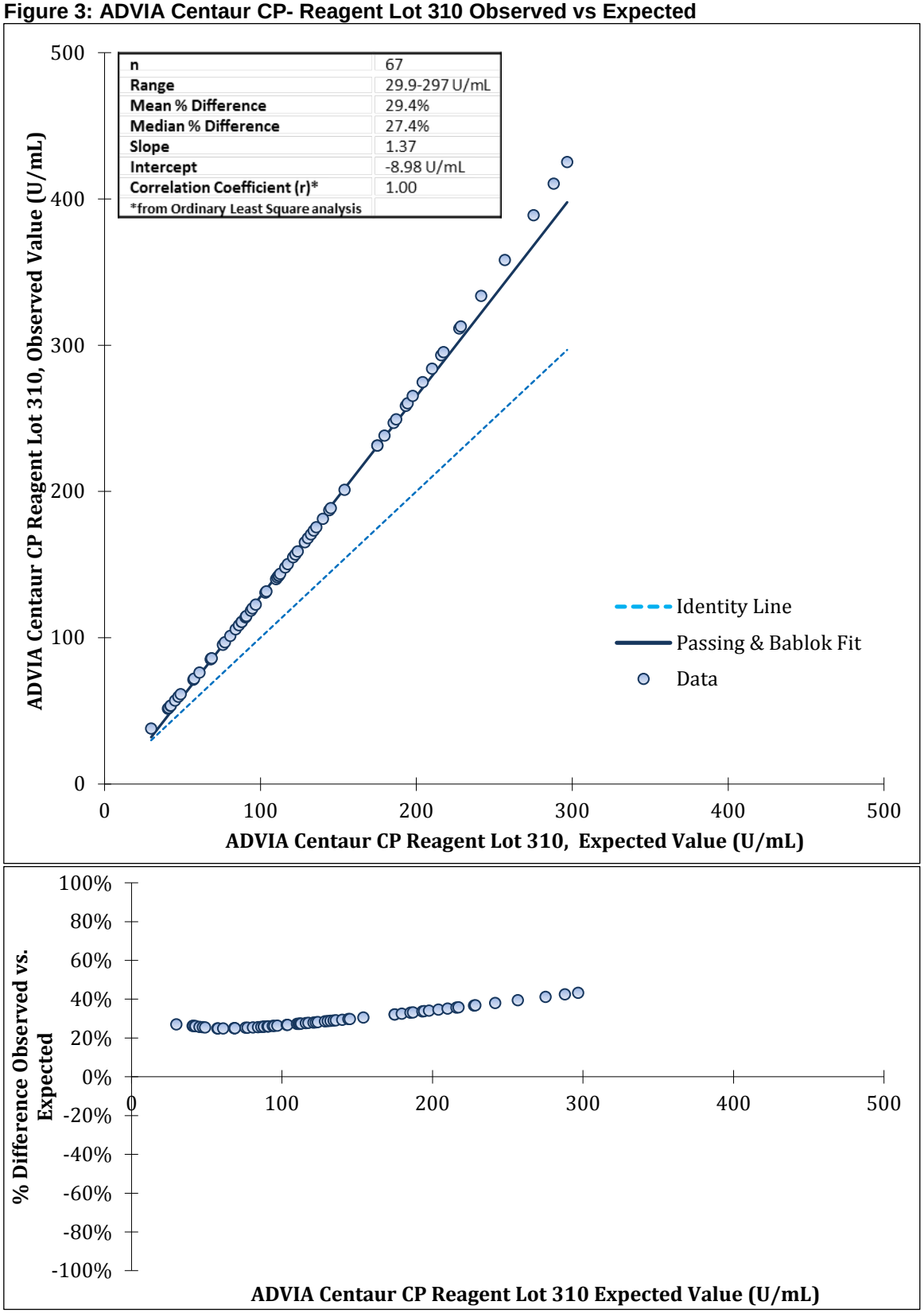
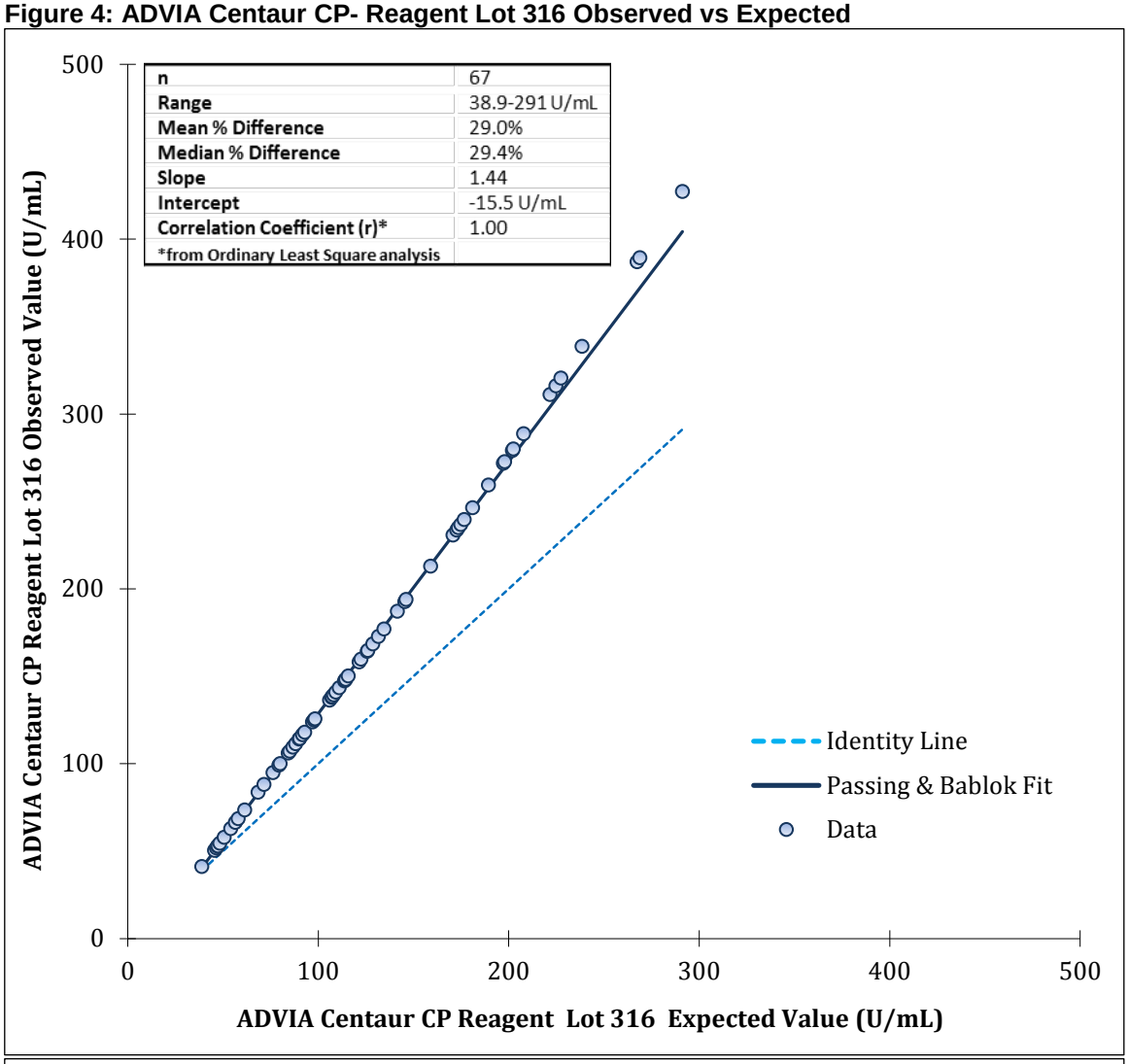
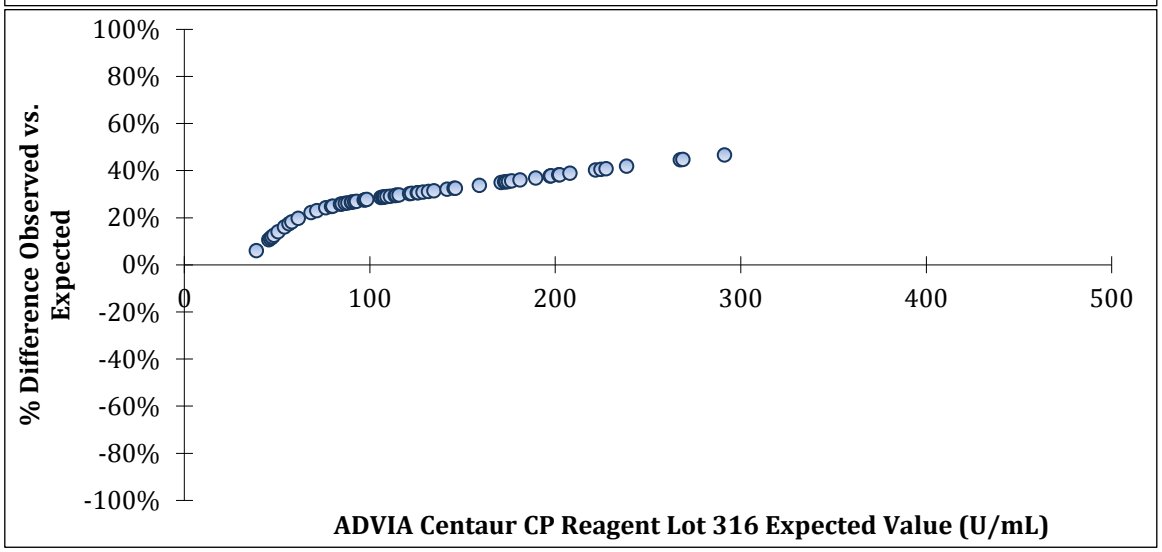


Figure 4: ADVIA Centaur CP- Reagent Lot 316 Observed vs Expected





Performance Characteristics

Siemens completed internal testing to evaluate the performance of ADVIA Centaur aTG reagent kit lots ending in 310 and 316 when compared to ADVIA Centaur aTG kit lots ending in 318. Kit Lots ending in 310 are included to demonstrate the largest differences observed as compared to kit lots ending in 318. Kit lots ending in 316 are included as the most recently released lots.

Limit of Detection (LoD)

LoD studies were performed on ADVIA Centaur aTG kit lots ending in 310, 316 and 318 following Clinical and Laboratory Standards Institute (CLSI) Guidance EP17-A2 "Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures". Data from the LoD studies verified that the assay performs as described in the Instructions for Use.

Expected Values

Testing was performed following CLSI Guidance EP28-A3c "Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory", using 198 euthyroid patient samples to verify the cut-off stated in the IFU (60 U/mL). All samples included in this study had normal Thyroid-stimulating Hormone (TSH) values. The results in Table 2 demonstrate equivalent performance across lots. As with all in vitro diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.

Table 2. Verification of Euthyroid Cut-off

	Kit Lots Ending in		
	310	**316**	**318**
ADVIA Centaur XP/XPT %< 60 U/mL (n < 60 U/mL)	94% (186)	94% (186)	94% (186)
ADVIA Centaur CP %< 60 U/mL (n < 60 U/mL)	94% (186)	93% (184)	94% (186)

Method Comparison

Siemens completed internal testing to evaluate the performance of ADVIA Centaur aTG kit lots ending in 318 compared to earlier reagent lots. Figure 5 through Figure 9 provide the performance data assessments listed in Table 3 comparing kit lots ending in 318 to kit lots ending in 310 and 316. The graphs show the shift that is expected when transitioning to the new reagent lots.

Table 3. Method Comparison Assessments

Figure	Assessment	System	Reagent Lots
5	Method Comparison	ADVIA Centaur XP	Lot 318 (y) vs. Reference Lot 310 (x)
	Difference Plot		
6	Method Comparison	ADVIA Centaur XP	Lot 318 (y) vs. Reference Lot 316 (x)
	Difference Plot		
7	Method Comparison	ADVIA Centaur CP	Lot 318 (y) vs. Reference Lot 310 (x)
	Difference Plot		
8	Method Comparison	ADVIA Centaur CP	Lot 318 (y) vs. Reference Lot 316 (x)
	Difference Plot		
9	Method Comparison	ADVIA Centaur XP vs ADVIA Centaur CP	ADVIA Centaur CP Lot 318 (y) vs. ADVIA Centaur XP Lot 318 (x)
	Difference Plot		

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Figure 5: ADVIA Centaur XP- Reagent Lot 318 vs. Reagent Lot 310

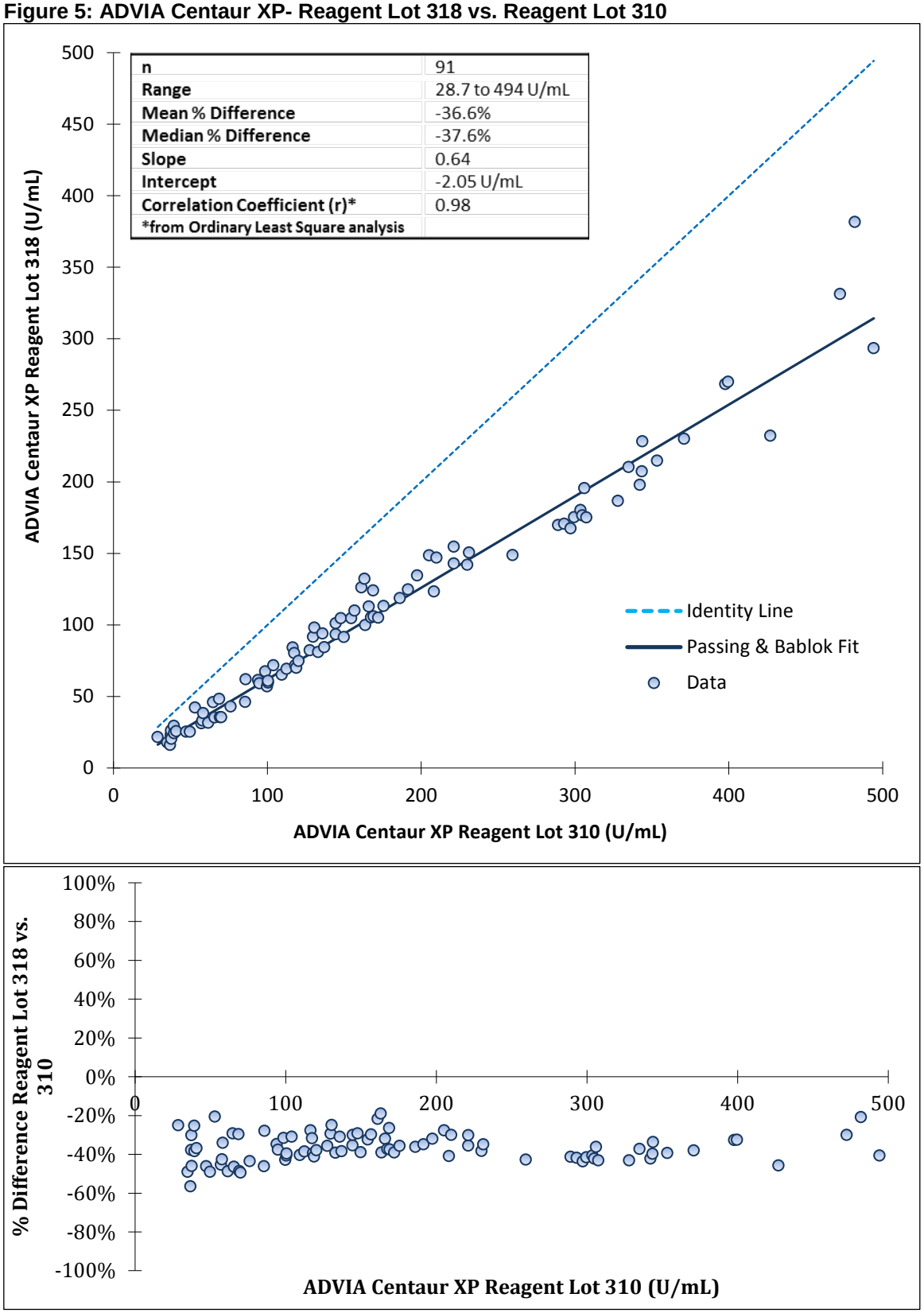
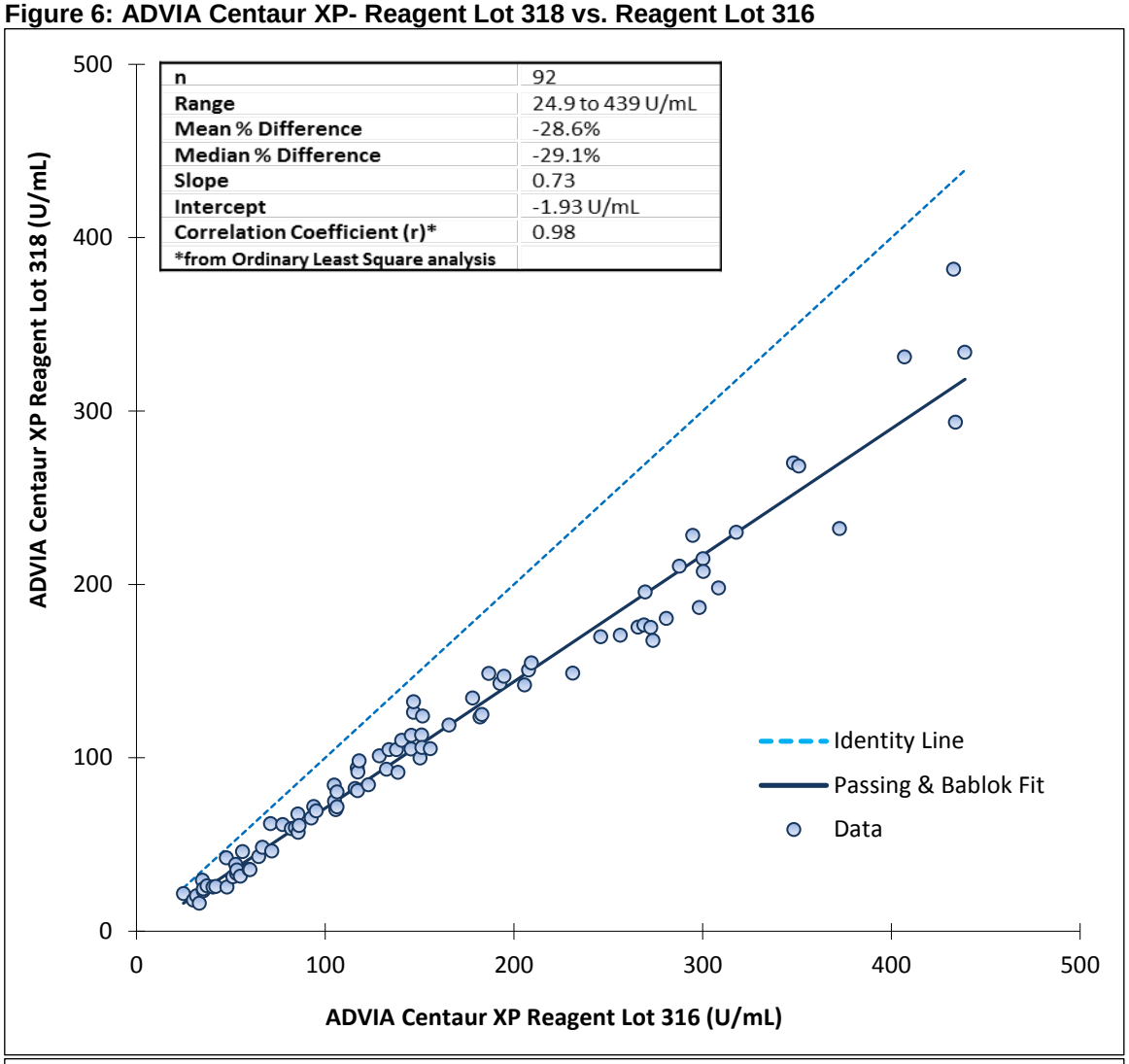


Figure 6: ADVIA Centaur XP- Reagent Lot 318 vs. Reagent Lot 316



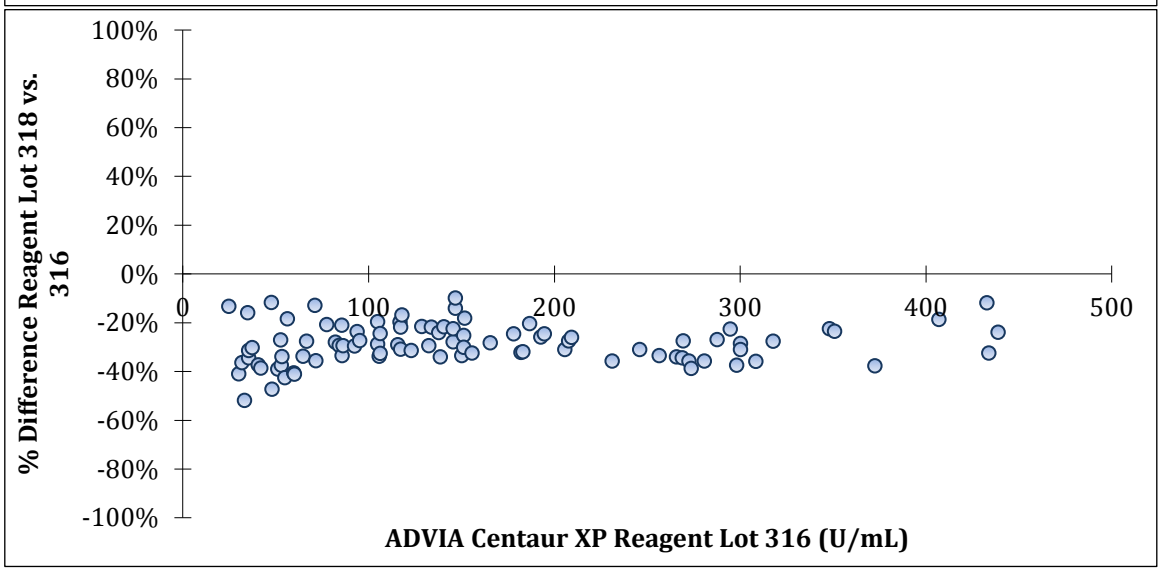
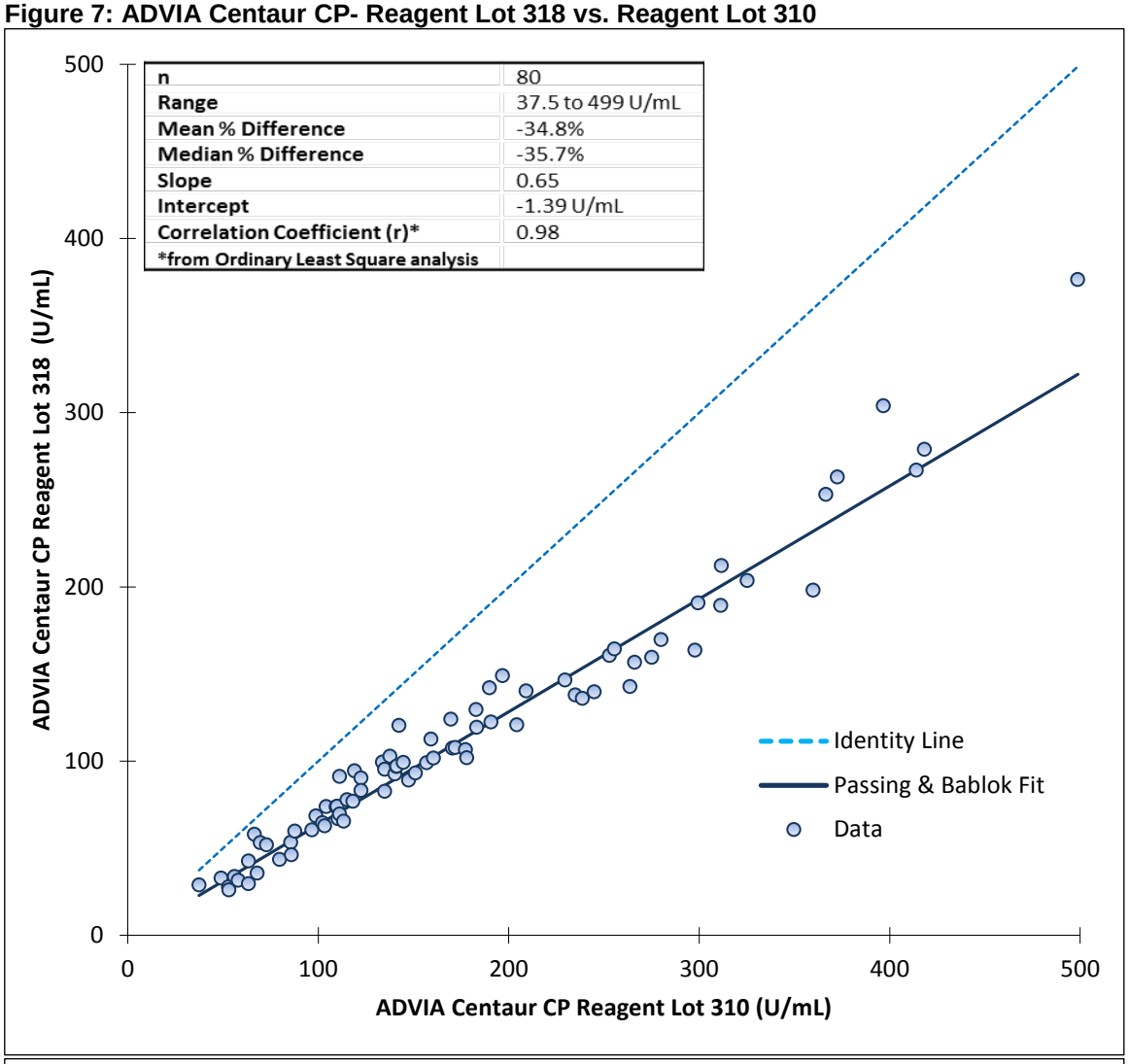


Figure 7: ADVIA Centaur CP- Reagent Lot 318 vs. Reagent Lot 310



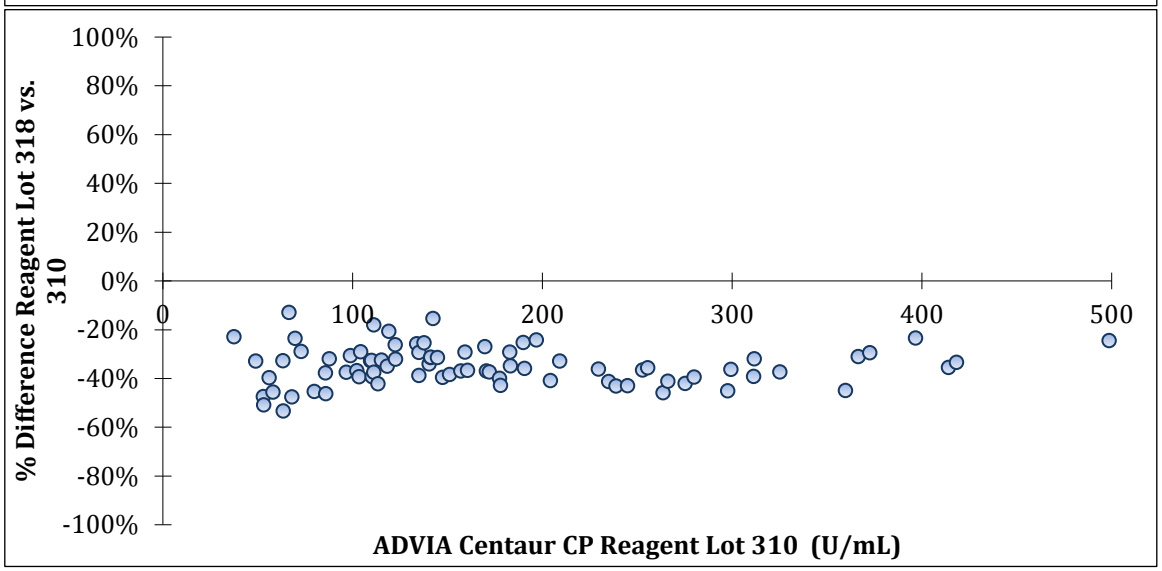
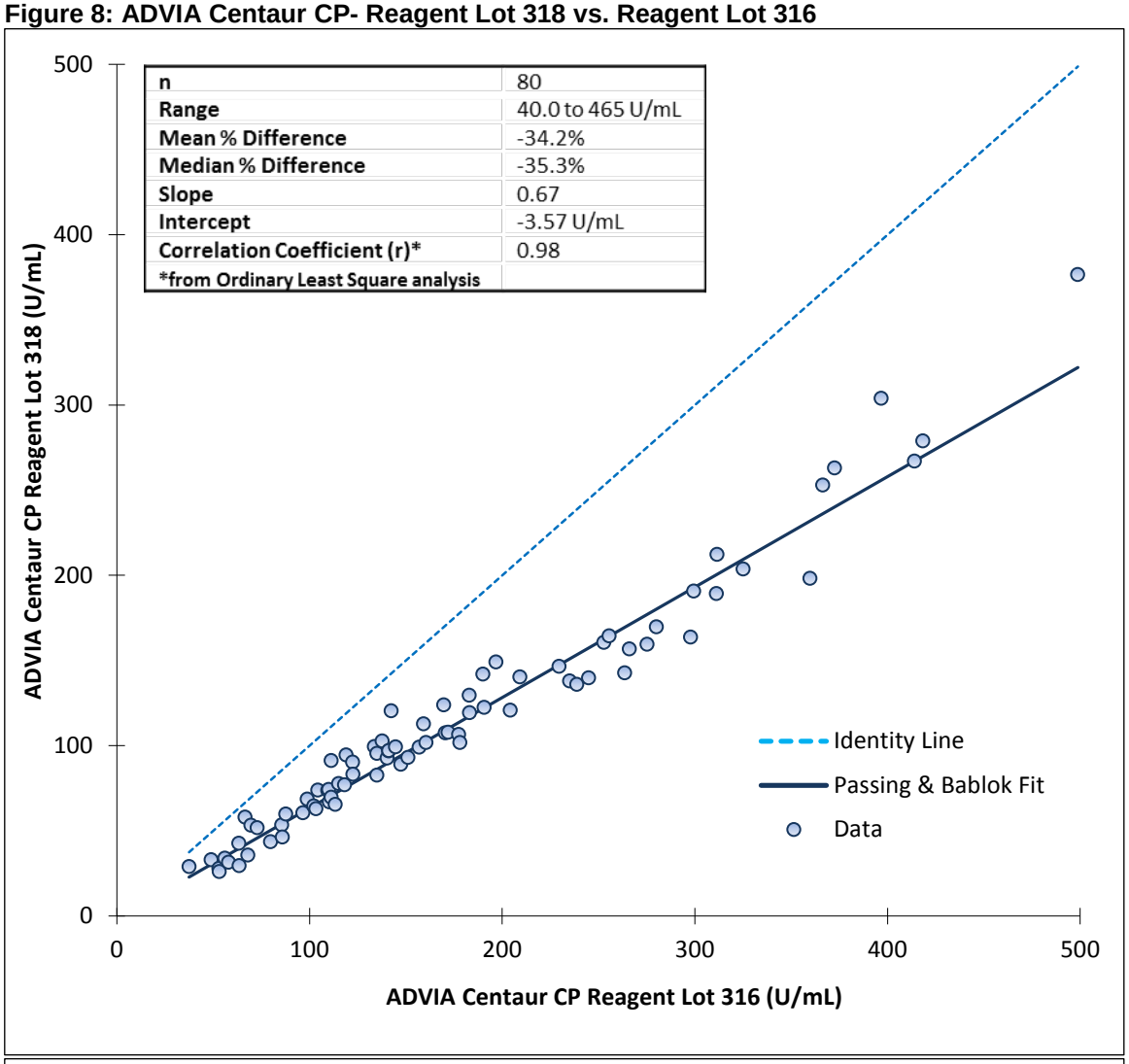


Figure 8: ADVIA Centaur CP- Reagent Lot 318 vs. Reagent Lot 316



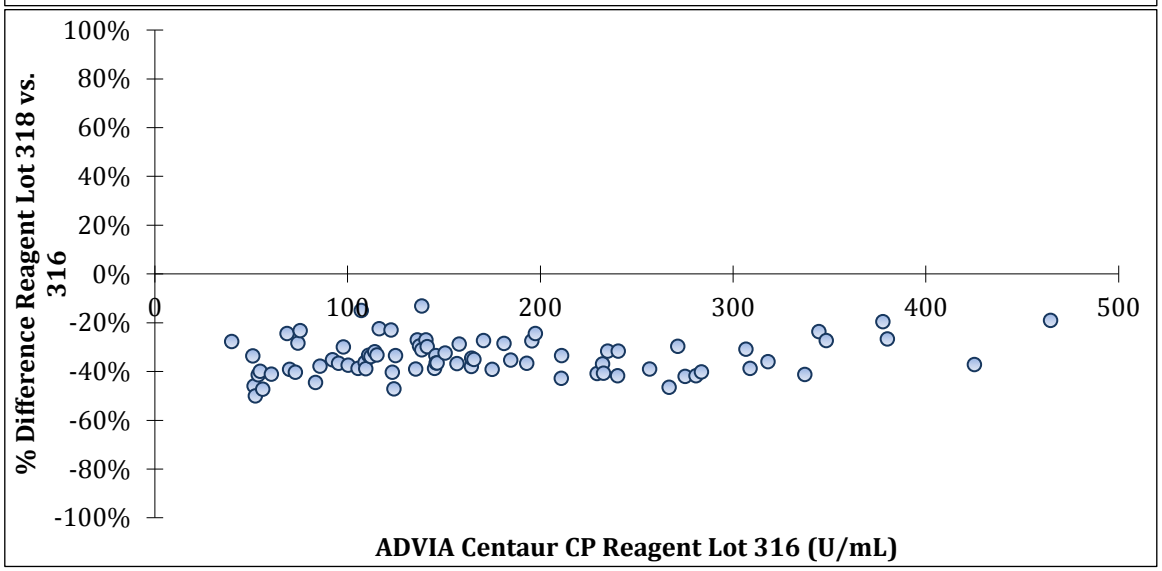
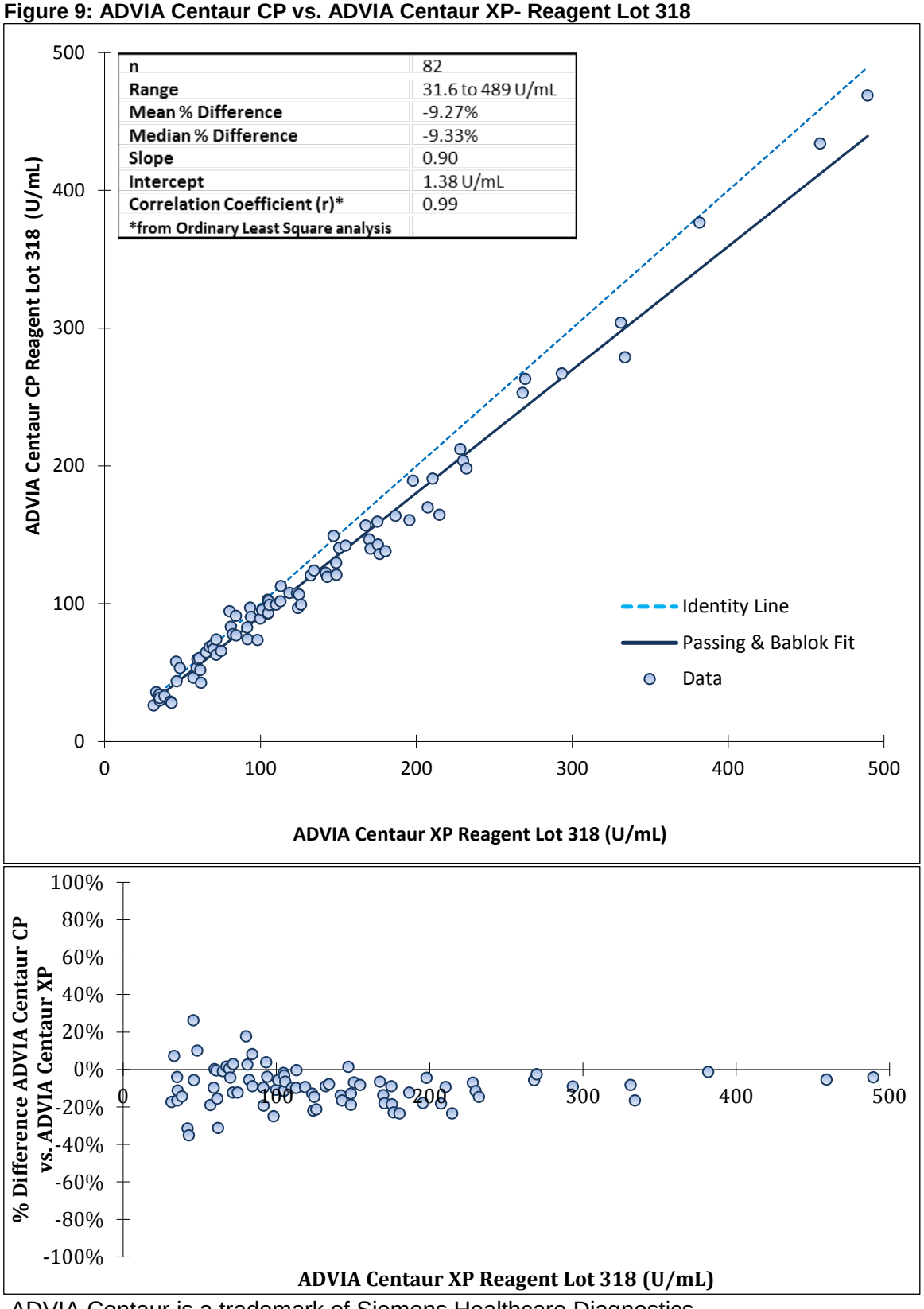


Figure 9: ADVIA Centaur CP vs. ADVIA Centaur XP- Reagent Lot 318



ADVIA Centaur is a trademark of Siemens Healthcare Diagnostics

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FIELD CORRECTION EFFECTIVENESS CHECK

ADVIA Centaur Anti-Thyroglobulin (aTG) Positive Bias

This response form is to confirm receipt of the enclosed Siemens Healthcare Diagnostics Urgent Field Safety Notice CC 19-04.A-1.OUS dated December, 2018 regarding ADVIA Centaur Anti-Thyroglobulin (aTG) Positive Bias. Please read each question and indicate the appropriate answer.

Return this completed form to Siemens Healthcare Diagnostics as per the instructions provided at the bottom of this page.

1. I have read and understood the Urgent Field Safety Notice instructions provided in this letter. Yes ☐ No ☐

2. Do you now have any of the noted product(s) on hand? Please check inventories before answering. Yes ☐ No ☐

   If the answer to the question above is yes, please complete the table below to indicate the quantity of affected product in your laboratory and replacement product required.

Product Description **REF# and Lot #**	**Quantity Discarded/** **Replacement Quantity Required**
ADVIA Centaur aTG (100 test kit) REF 10492398 Kit Lots ending in 316 or lower	
ADVIA Centaur aTG (500 test kit) REF 10492399 Kit Lots ending in 316 or lower	
ADVIA Centaur Calibrator 1 REF 10630915 Kit Lots ending in 116 or lower	
ADVIA Centaur aTG QC REF 10630917 (Lots 8507691/8507692; 8510391/8510392; 8514691/8514692; 8517391/8517392; 8522591/8522592; 8524691/8524692; 8534091/8534092)	
ADVIA Centaur aTG Master Curve Material REF 10492692 Lot 44594; 54245; 57375; 68887; 04648; 04649; 31777)	

Name of person completing questionnaire: _____

Title: _____

Institution: _____ Instrument Serial Number: _____

Street: _____

City: _____ State: _____

Phone: _____ Country: _____

Customer Sold To #: _____ Customer Ship To #: _____

Please send a scanned copy of the completed form via email to XXXX@XXXX.

Or to fax this completed form to the Customer Care Center at XXXXXX.
If you have any questions, contact your local Siemens technical support representative.

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