

Cc to Chairman Medical Board and relevant Head of Departments

**Atellica® IM**

**Atellica IM Anti-Thyroglobulin (aTG) Positive Bias**

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

**Table 1. Atellica IM Affected Product(s)**

Assay	Siemens Material Number (SMN)	Lot Number	Expiration Date (YYYY-MM-DD)	1 <sup>st</sup> Distribution Date (YYYY-MM-DD)
Atellica IM aTG (100 test kit)	10995461	72259303	2018-12-13	2018-04-03
		87903305	2019-01-12	2018-04-23
		94908307	2019-02-11	2018-05-03
		96439307	2019-02-11	2018-05-21
		16824309	2019-03-14	2018-06-21
		25822309	2019-03-14	2018-08-16
		28942311	2019-04-27	2018-07-25
		55978313	2019-05-27	2018-09-13
		70389317	2019-06-29	2018-10-11
Atellica IM aTG (500 test kit)	10995462	56683313	2019-05-27	2018-10-16
		70390317	2019-06-29	2018-10-24

**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.

Siemens identified a positive bias with Atellica IM aTG kit lots ending in 317 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, "Traceability to WHO MRC 65/93".

Traceability to WHO Reference Preparation MRC 65/93 is restored with the release of Atellica IM aTG kit lots ending in 319 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 Atellica IM aTG reagent kit lots 317 and lower to Atellica IM aTG reagent kit lots 319 and higher. See Additional Information, Method Comparison.

The Atellica IM aTG assay remains “lot-locked”. Reagent lots must be used with specific lots of Atellica IM Calibrator 1, Atellica IM aTG 1, 2 Quality Control Material, and Atellica IM 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 Atellica IM aTG kit lots in Table 1 until you receive replacement product in your laboratory. Refer to Figure 1 and Figure 2 for Atellica IM aTG bias information.
- If you are currently using Atellica IM 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 product 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 Atellica IM aTG kit lots listed in Table 1. Refer to Figures 3 through 5 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.

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**

#### **Traceability to WHO MRC 65/93**

Figures 1 and 2 show the results obtained (“Observed”) as compared to the internal standards traceable to WHO MRC 65/93 (“Expected”) for Atellica IM aTG reagent kit lots ending in 311 and 317. Kit Lots ending in 311 are included to demonstrate the largest differences observed as compared to kit lots ending in 319. Kit lots ending in 317 are included as the most recently released lots.

Figure 1: Atellica IM- Reagent Lot 311 Observed vs Expected

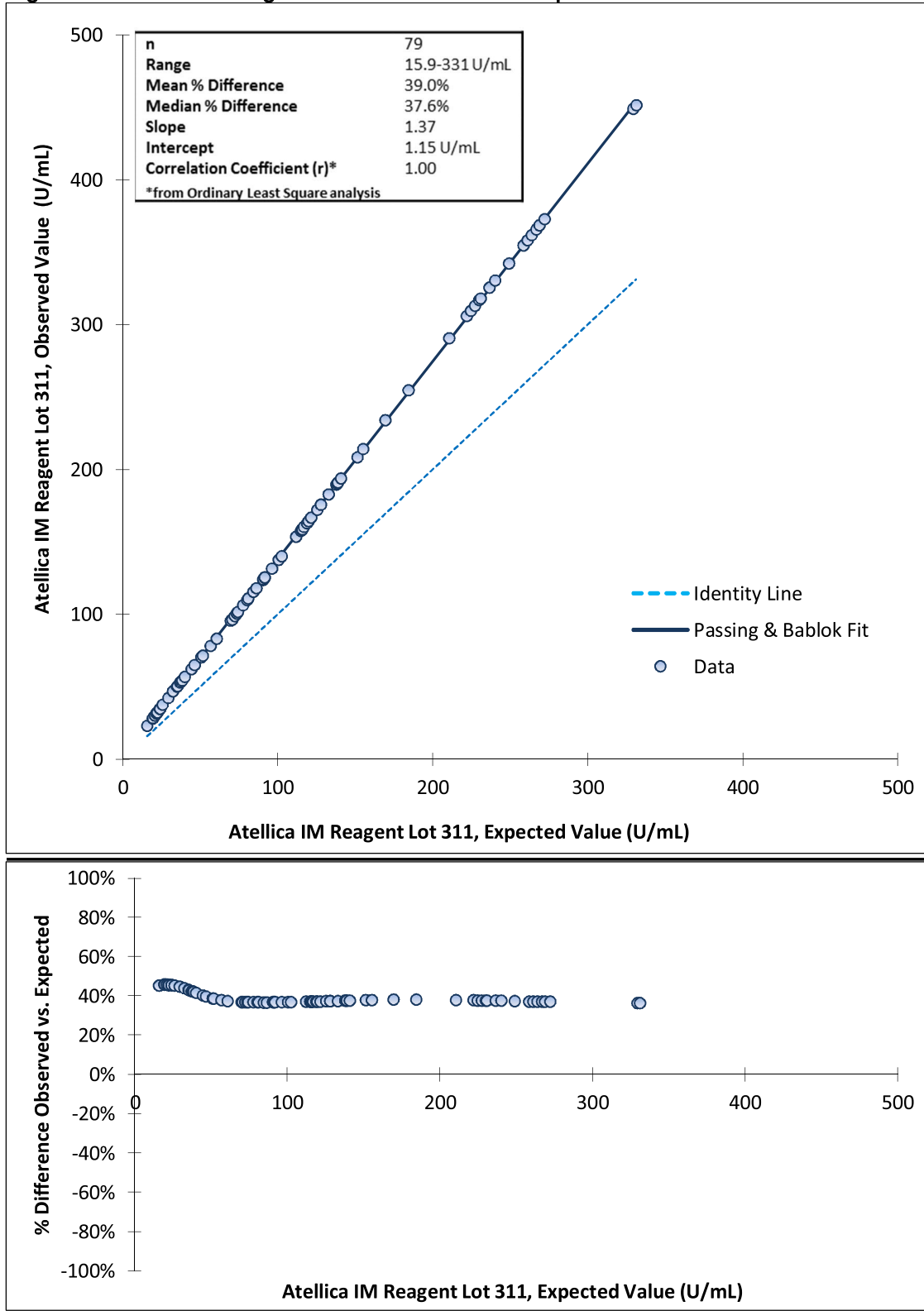
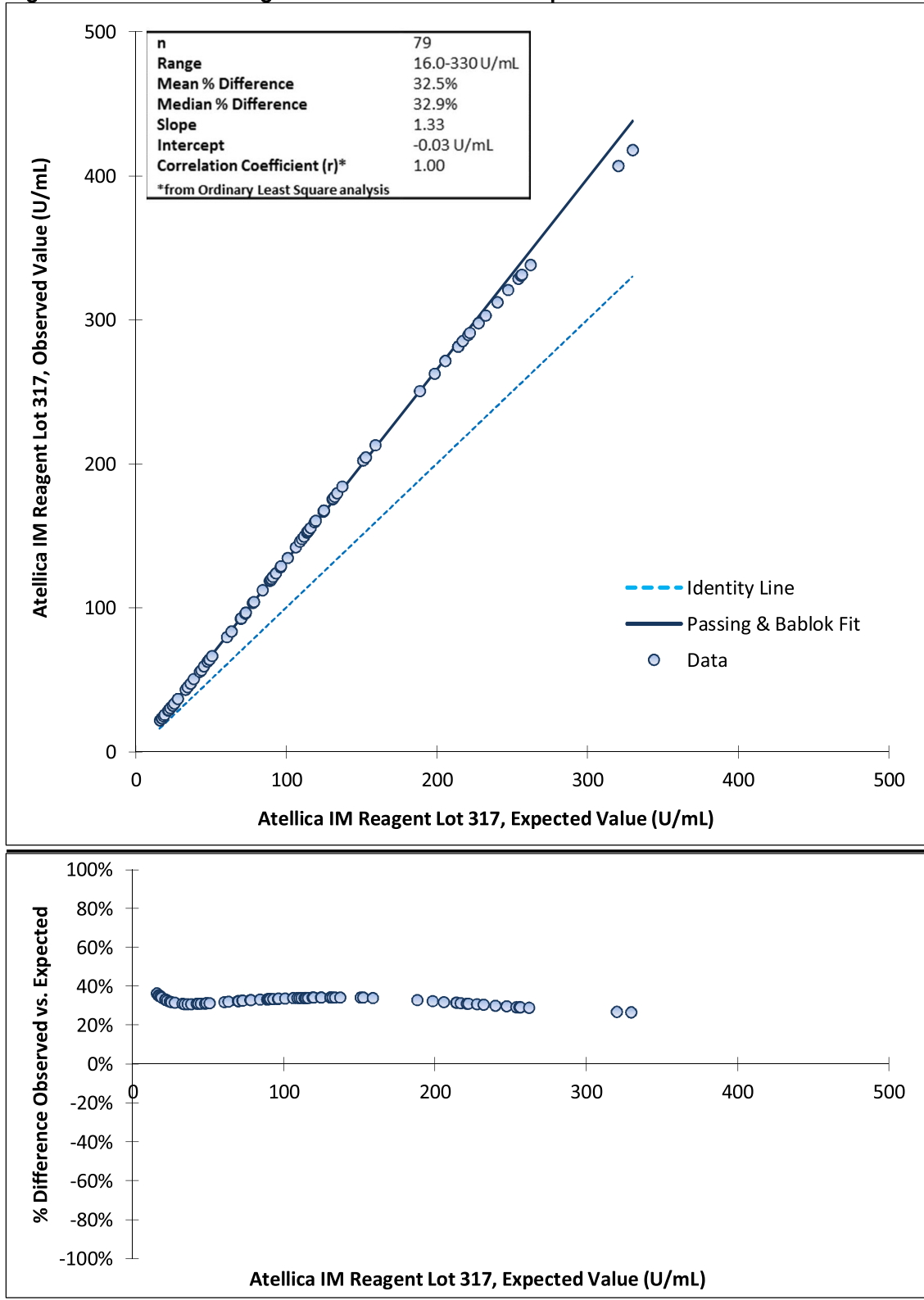


Figure 2: Atellica IM- Reagent Lot 317 Observed vs Expected



## Performance Characteristics

Siemens completed internal testing to evaluate the performance of Atellica IM aTG reagent kit lots ending in 311 and 317 when compared to Atellica IM aTG kit lots ending in 319. Kit Lots ending in 311 are included to demonstrate the largest differences observed as compared to kit lots ending in 319. Kit lots ending in 317 are included as the most recently released lots.

### Limit of Detection (LoD)

LoD studies were performed on Atellica IM aTG kit lots ending in 311, 317 and 319 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		
	311	317	319
Atellica IM %< 60 U/mL (n < 60 U/mL)	94% (186)	94% (186)	94% (187)

### Method Comparison

Siemens completed internal testing to evaluate the performance of Atellica IM aTG kit lots ending in 319 compared to earlier reagent lots. Figure 3 through Figure 5 provide the performance data assessments listed in Table 3 comparing kit lots ending in 318 to kit lots ending in 311 and 317. The graphs show the shift that is expected when transitioning to the new reagent lots.

**Table 3. Atellica IM Method Comparison Assessments**

Figure	Assessment	Reagent Lots
3	Method Comparison	Lot 319 (y) vs. Reference Lot 311 (x)
	Difference Plot	
4	Method Comparison	Lot 319 (y) vs. Reference Lot 317 (x)
	Difference Plot	
5	Method Comparison	Atellica IM Lot 319 (y) vs. ADVIA Centaur XP Lot 318 (x) The ADVIA Centaur XP data is representative of the performance seen on the ADVIA Centaur, ADVIA Centaur XP and ADVIA Centaur XPT systems.
	Difference Plot	

Figure 3: Atellica IM- Reagent Lot 319 vs. Reagent Lot 311

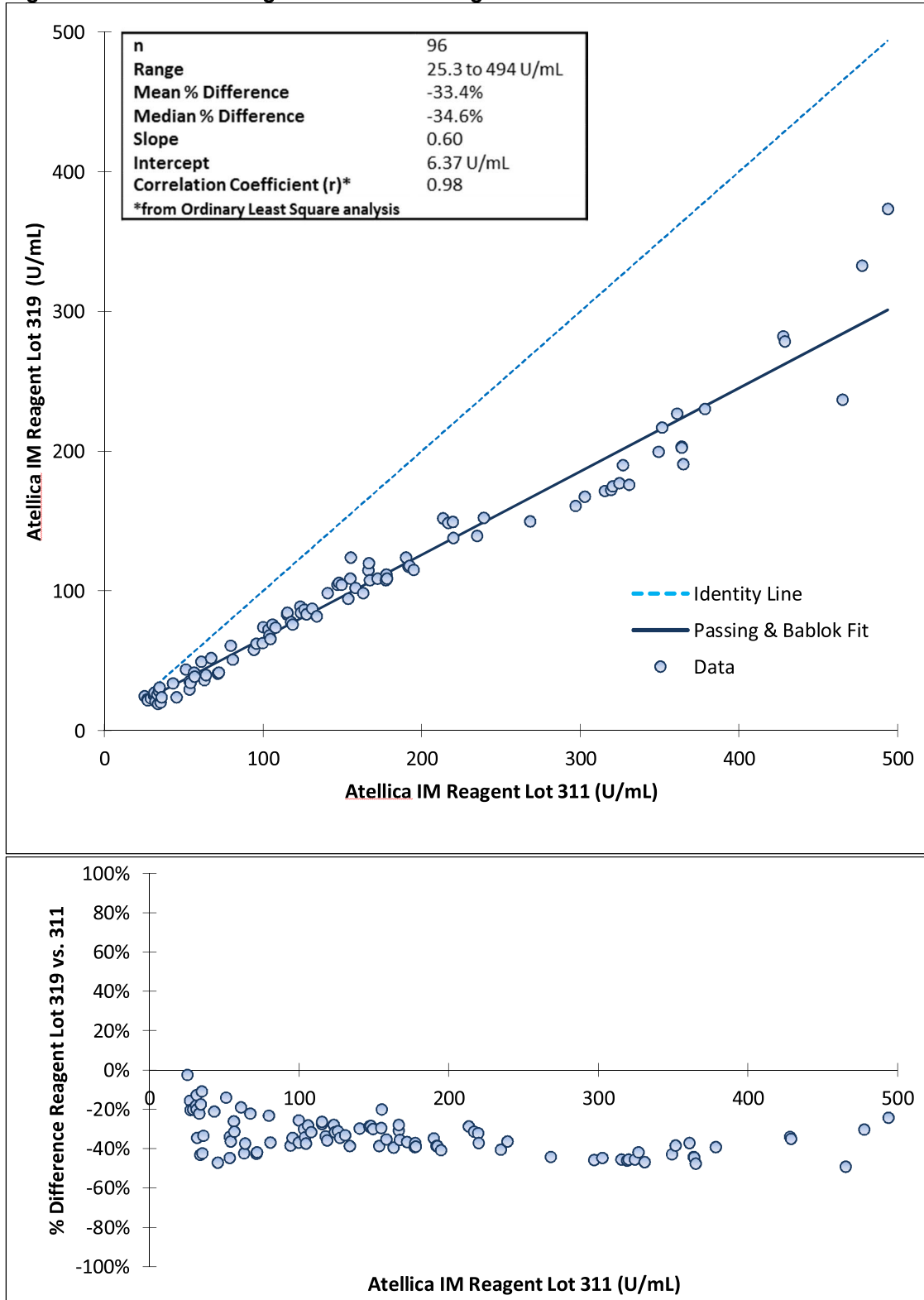


Figure 4: Atellica IM- Reagent Lot 319 vs. Reagent Lot 317

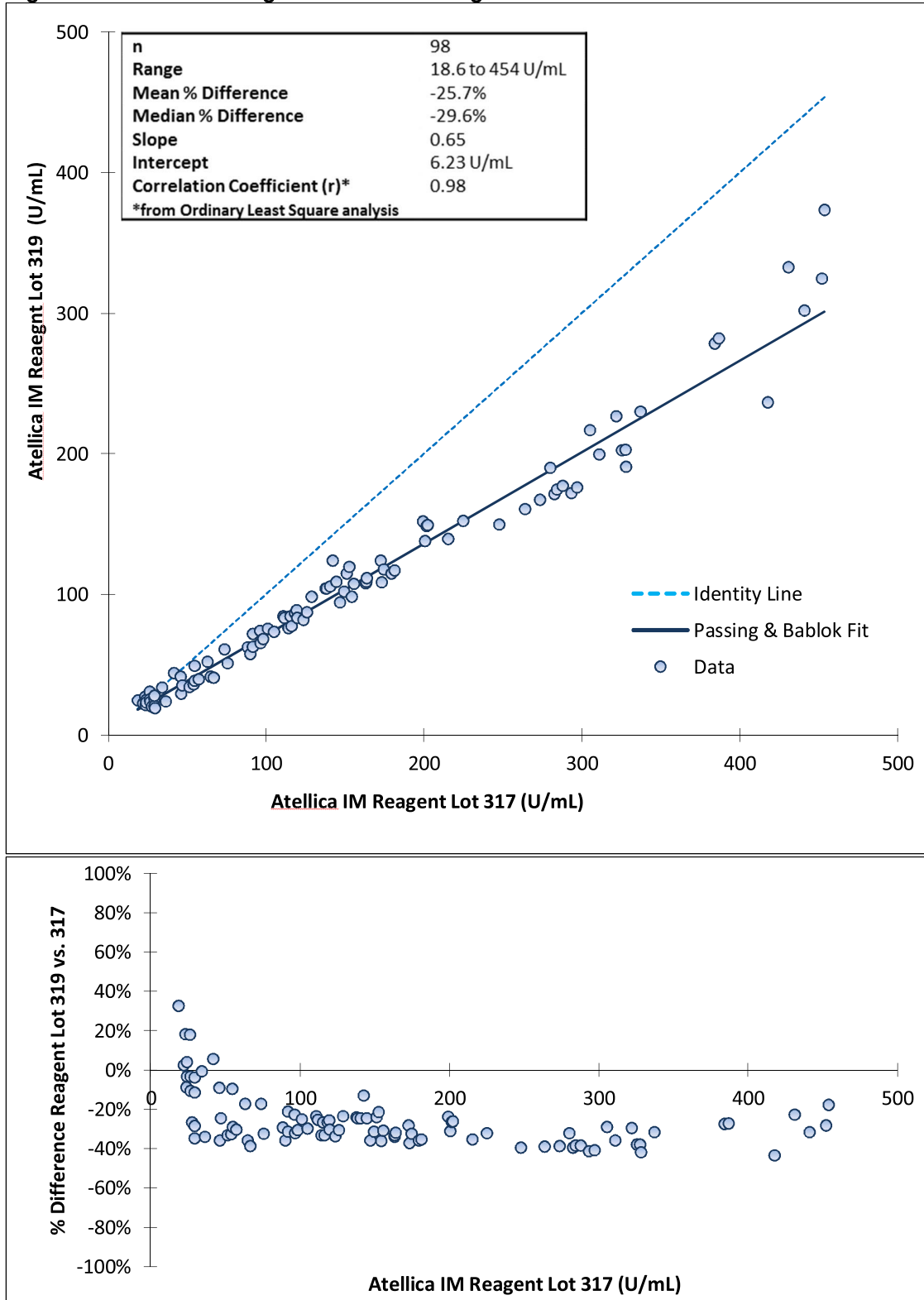
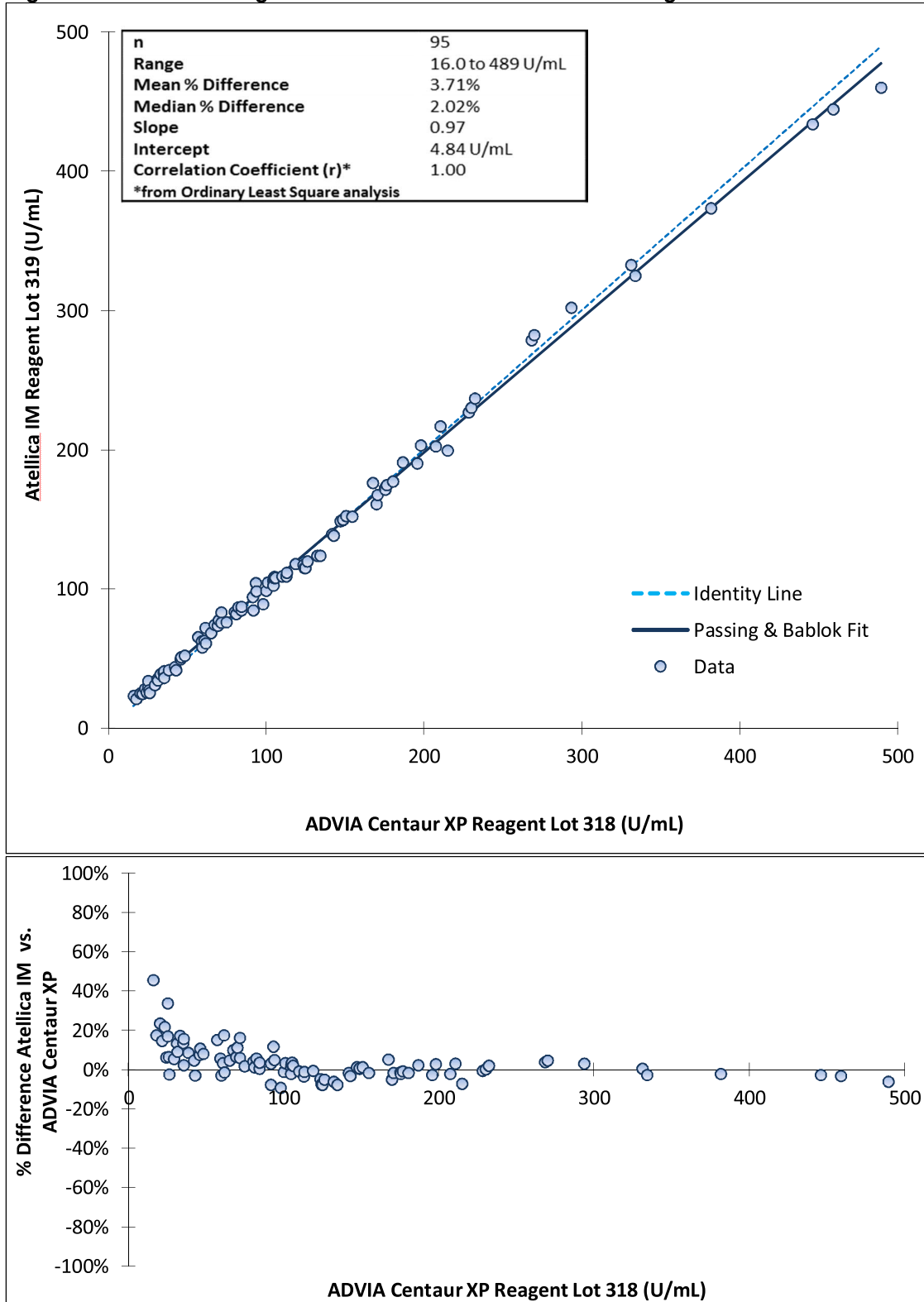


Figure 5: Atellica IM Reagent Lot 319 vs. ADVIA Centaur XP Reagent Lot 318



Atellica IM is a trademark of Siemens Healthcare Diagnostics

**FIELD CORRECTION EFFECTIVENESS CHECK**

Atellica IM 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-2.OUS dated December, 2018 regarding Atellica IM 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
Atellica IM aTG (100 test kit) REF 10995461 Kit Lots ending in 317 or lower	
Atellica IM aTG (500 test kit) REF 10995462 Kit Lots ending in 317 or lower	
Atellica IM Calibrator 1 REF 10995493 Kit Lots ending in 117 or lower	
Atellica IM aTG QC REF 10995465 Lots 8507591/8507592; 8510291/8510292; 8514591/8514592; 8517291/8517292; 8522491/8522492; 8524591/8524592; 8533991/8533992	
Atellica IM aTG Master Curve Material REF10995464 Lot 12789; 54247; 67408; 68888; 04650; 04652; 31778	

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  
If you have any questions, contact your local Siemens technical support representative.

Cc to Chairman Medical Board and relevant Head of Departments

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

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.

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.

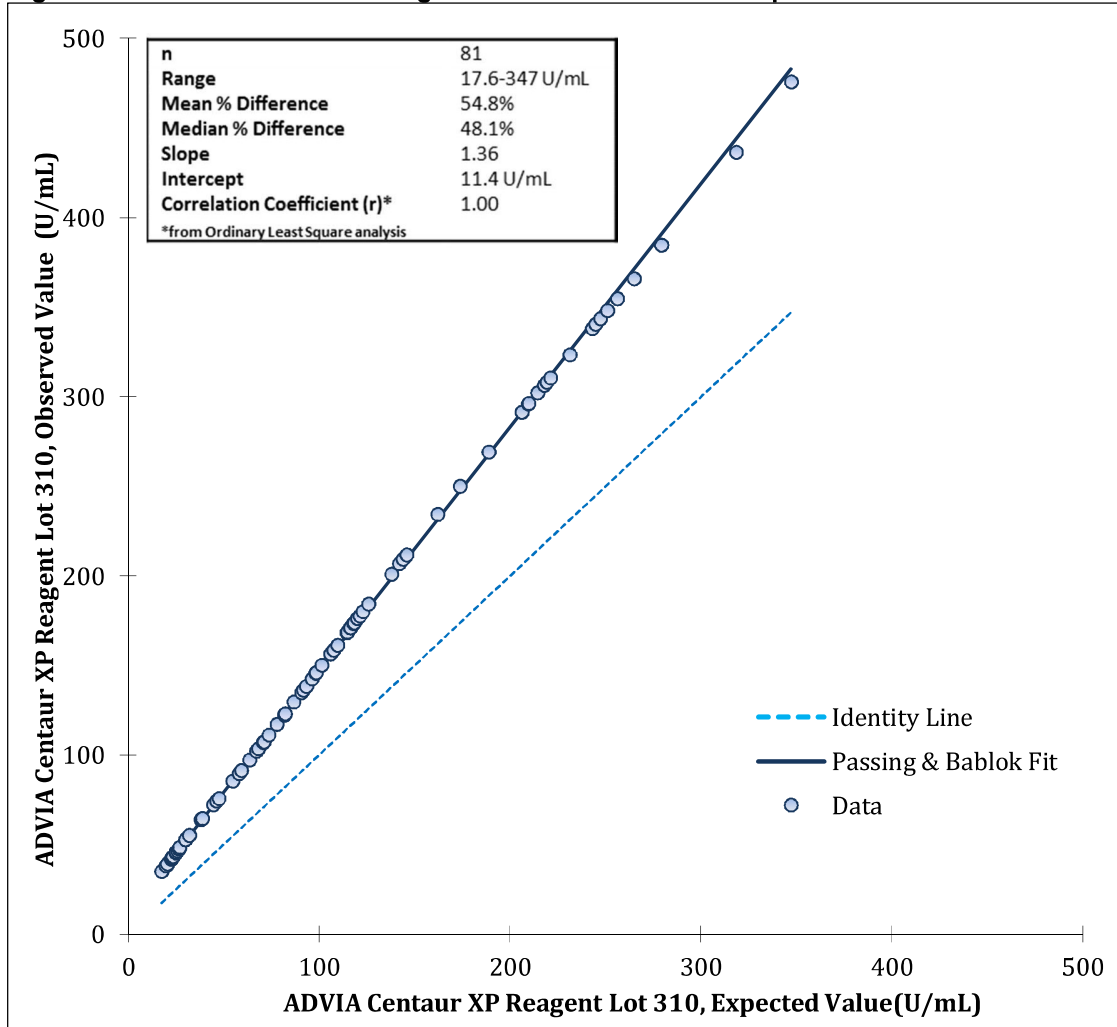
### **Additional Information**

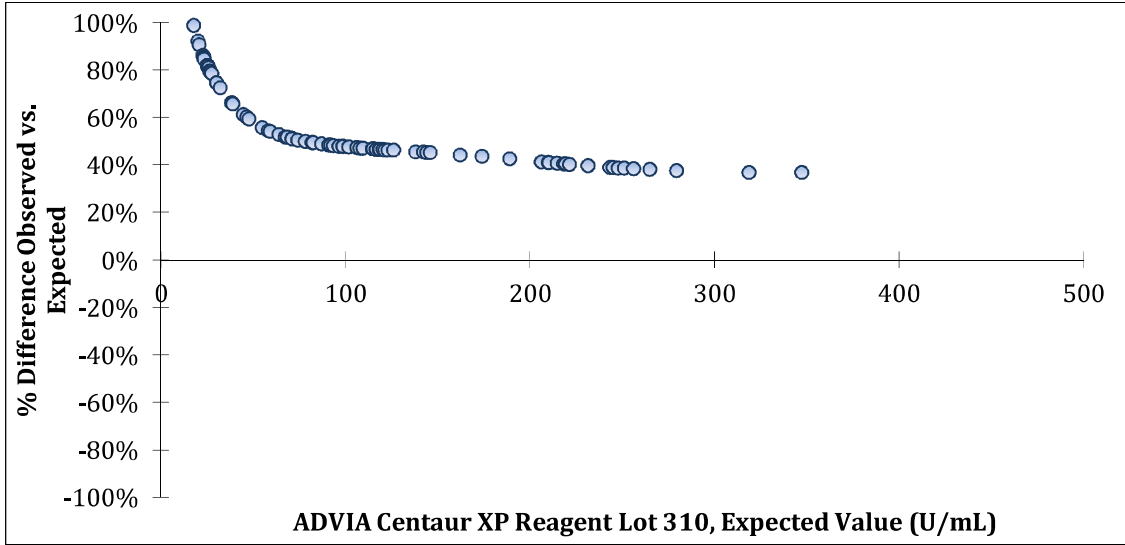
(Note: Data and plots below that reference ADVIA Centaur XP are representative of the performance seen on the ADVIA Centaur, ADVIA Centaur XP and ADVIA Centaur XPT systems.)

### **Traceability to WHO MRC 65/93**

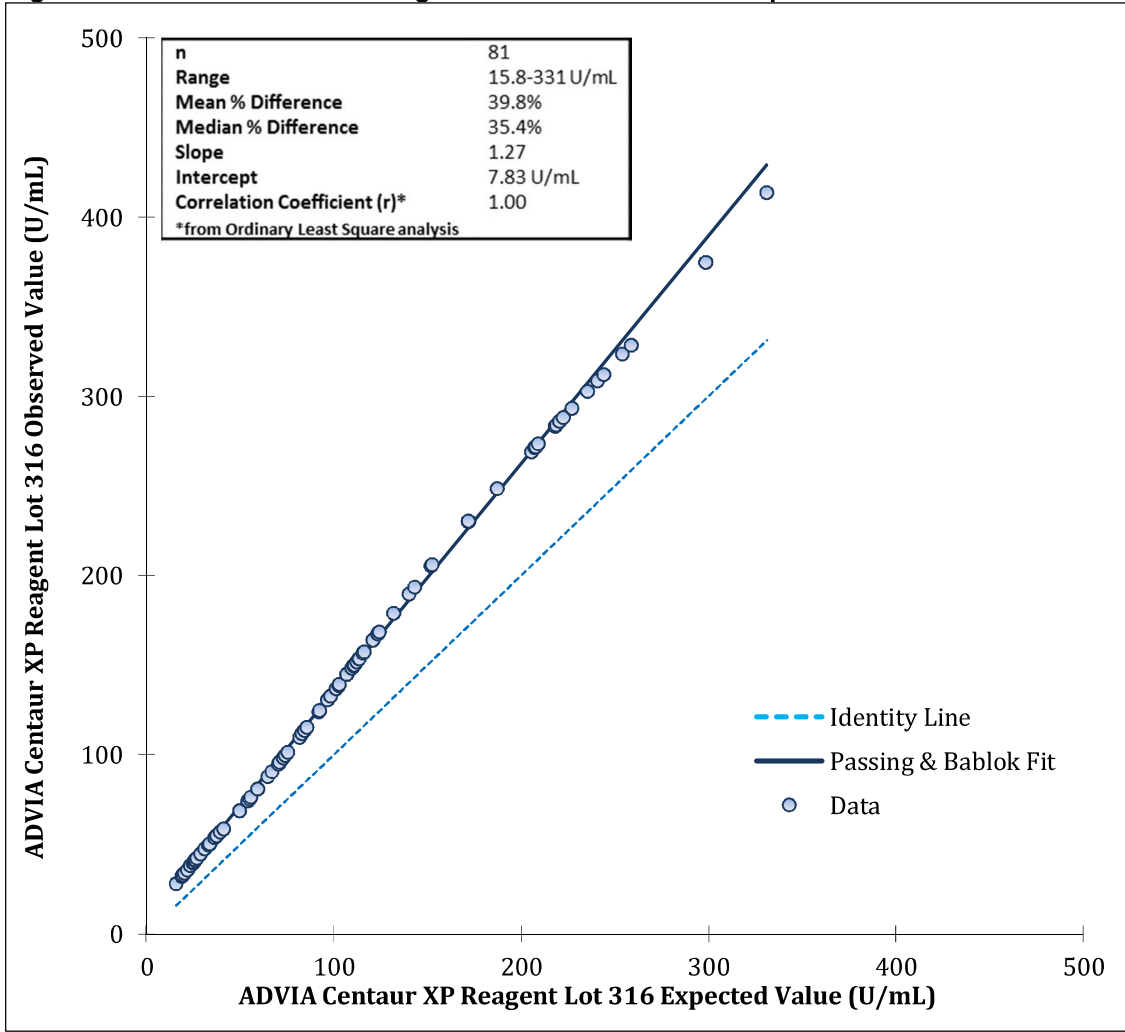
Figures 1 through 4 show the results obtained (“Observed”) as compared to the internal standards traceable to WHO MRC 65/93 (“Expected”) for ADVIA Centaur aTG reagent kit lots ending in 310 and 316. Kit Lots ending in 310 are included to demonstrate the largest differences observed as compared to kit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



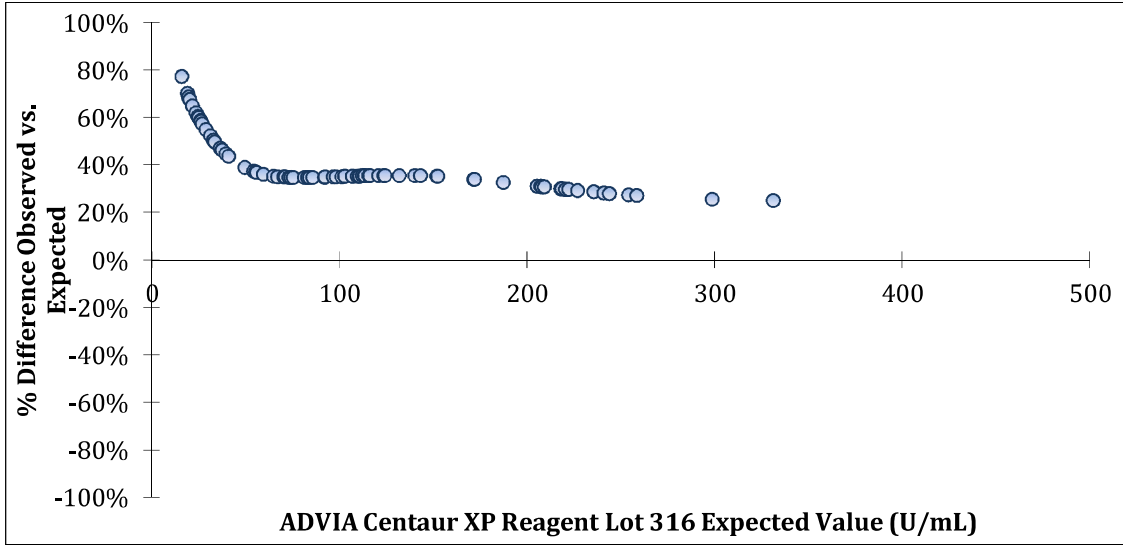
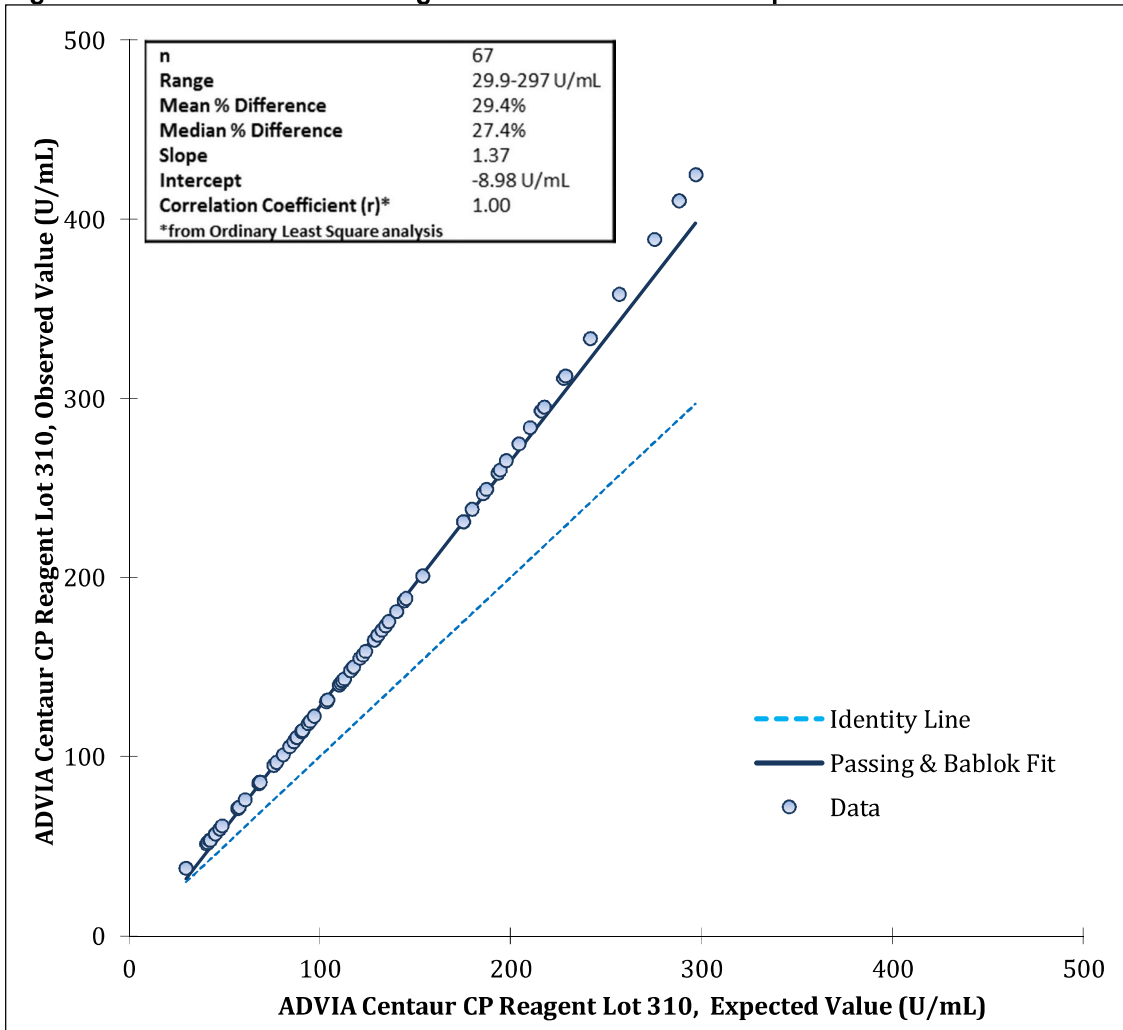


Figure 3: ADVIA Centaur CP- Reagent Lot 310 Observed vs Expected



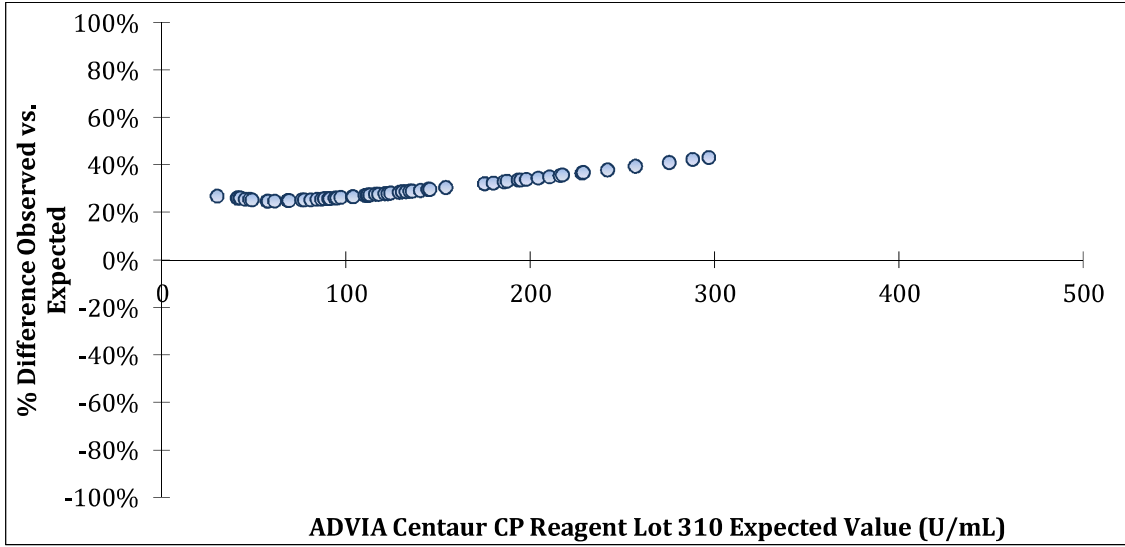
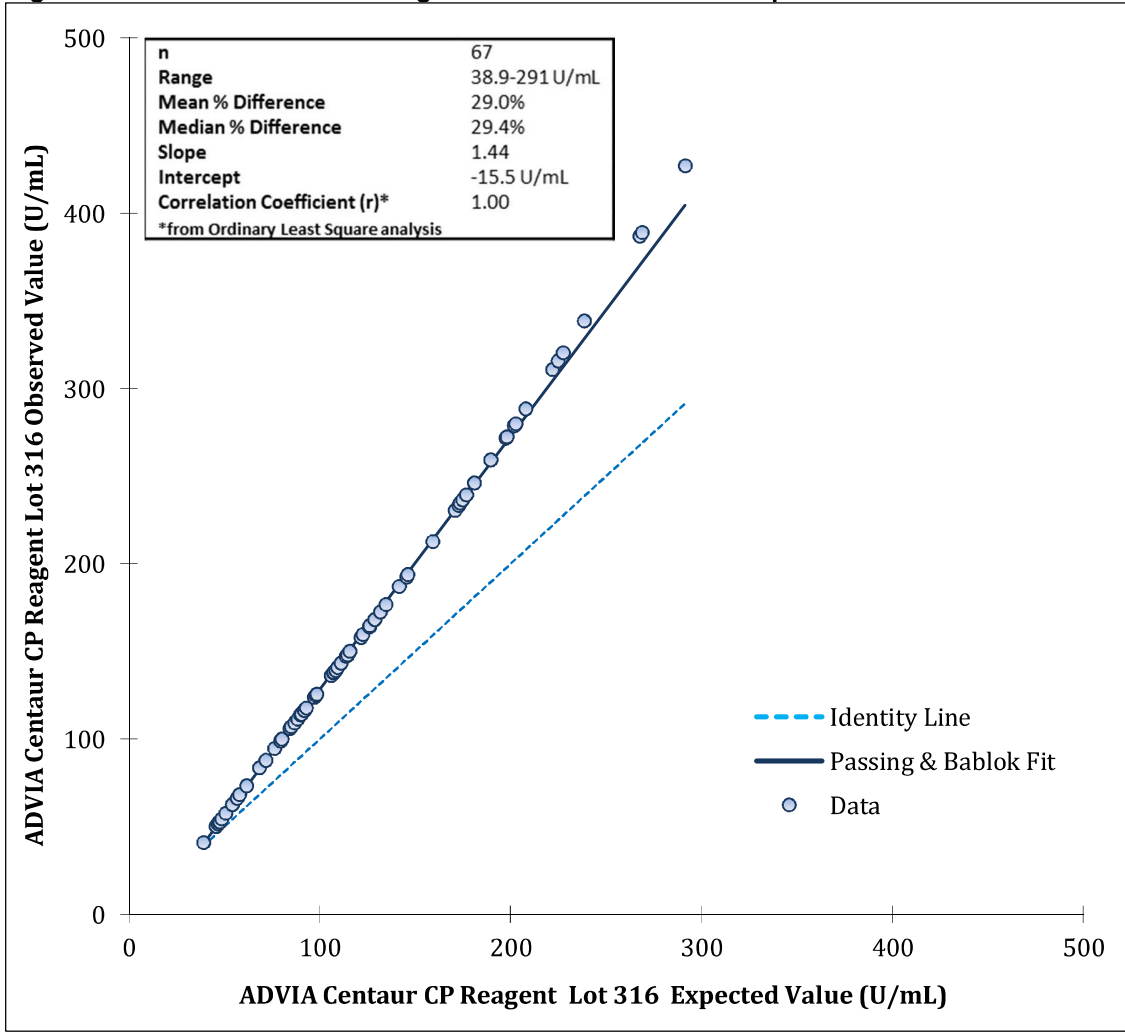
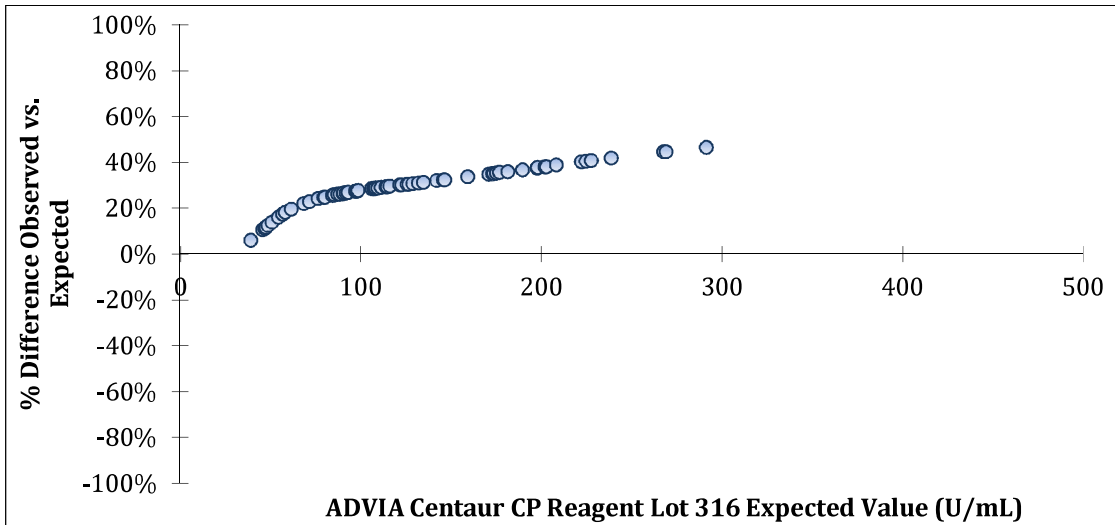


Figure 4: ADVIA Centaur CP- Reagent Lot 316 Observed vs Expected





**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		

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

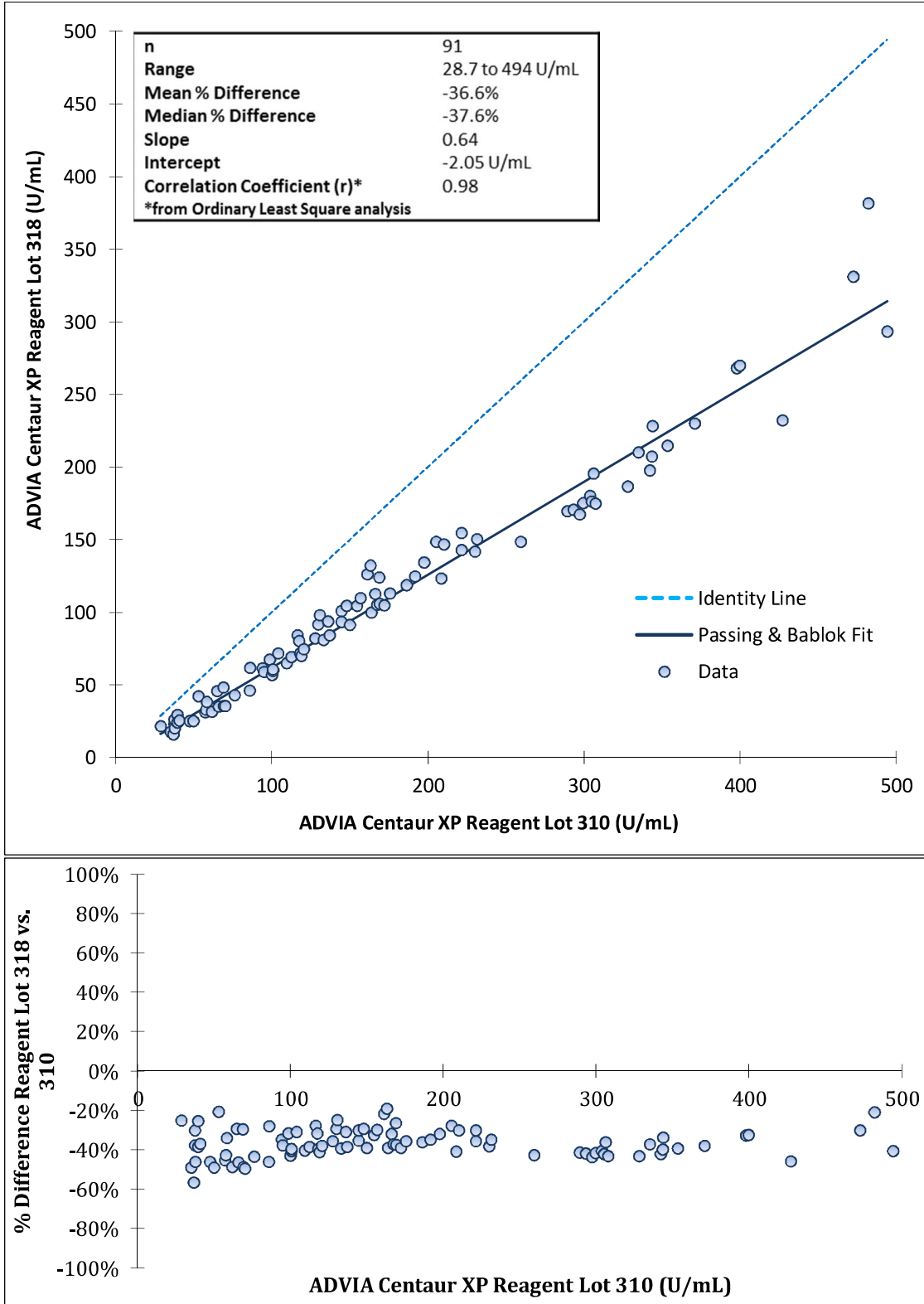


Figure 6: ADVIA Centaur XP- Reagent Lot 318 vs. Reagent Lot 316

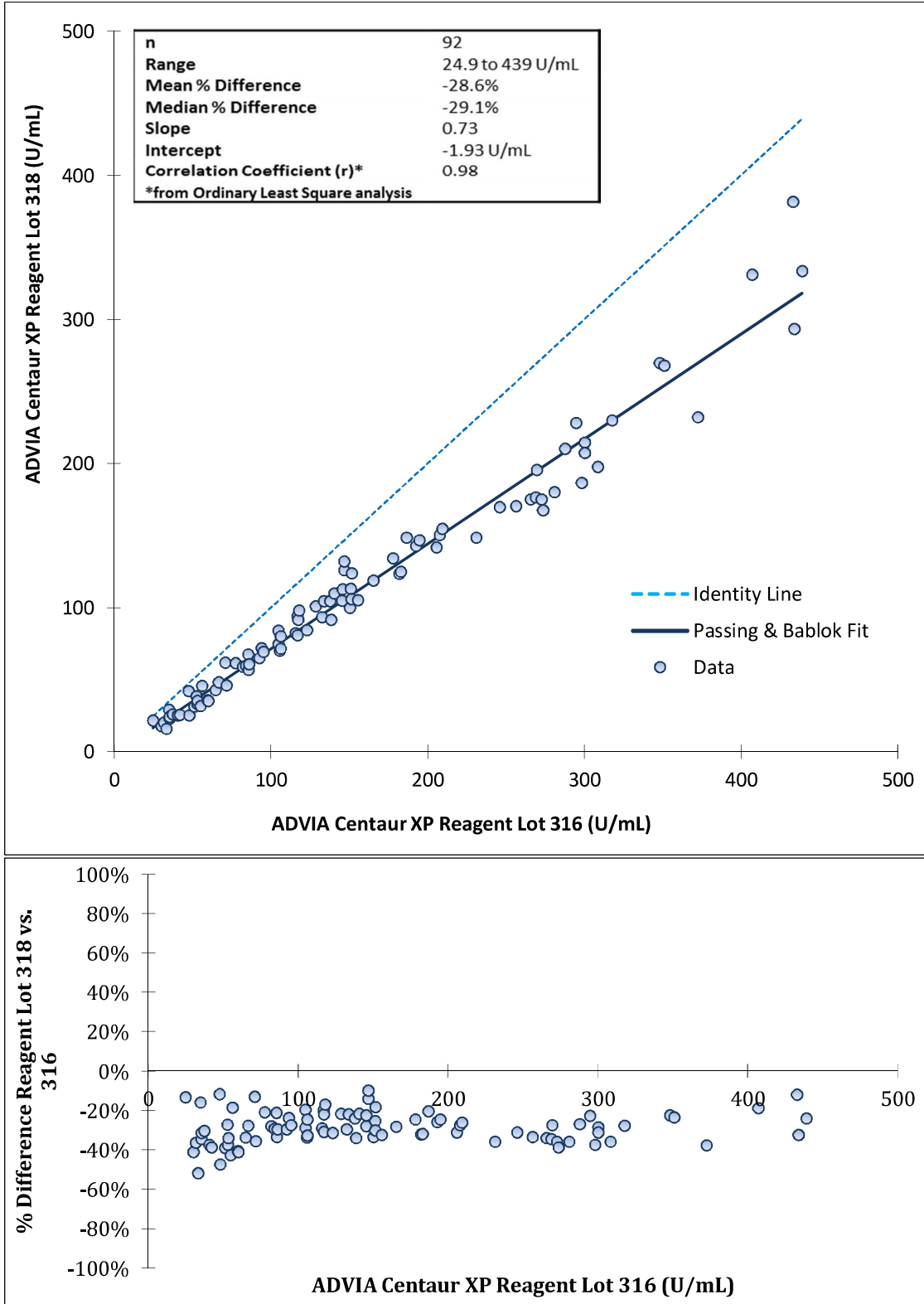


Figure 7: ADVIA Centaur CP- Reagent Lot 318 vs. Reagent Lot 310

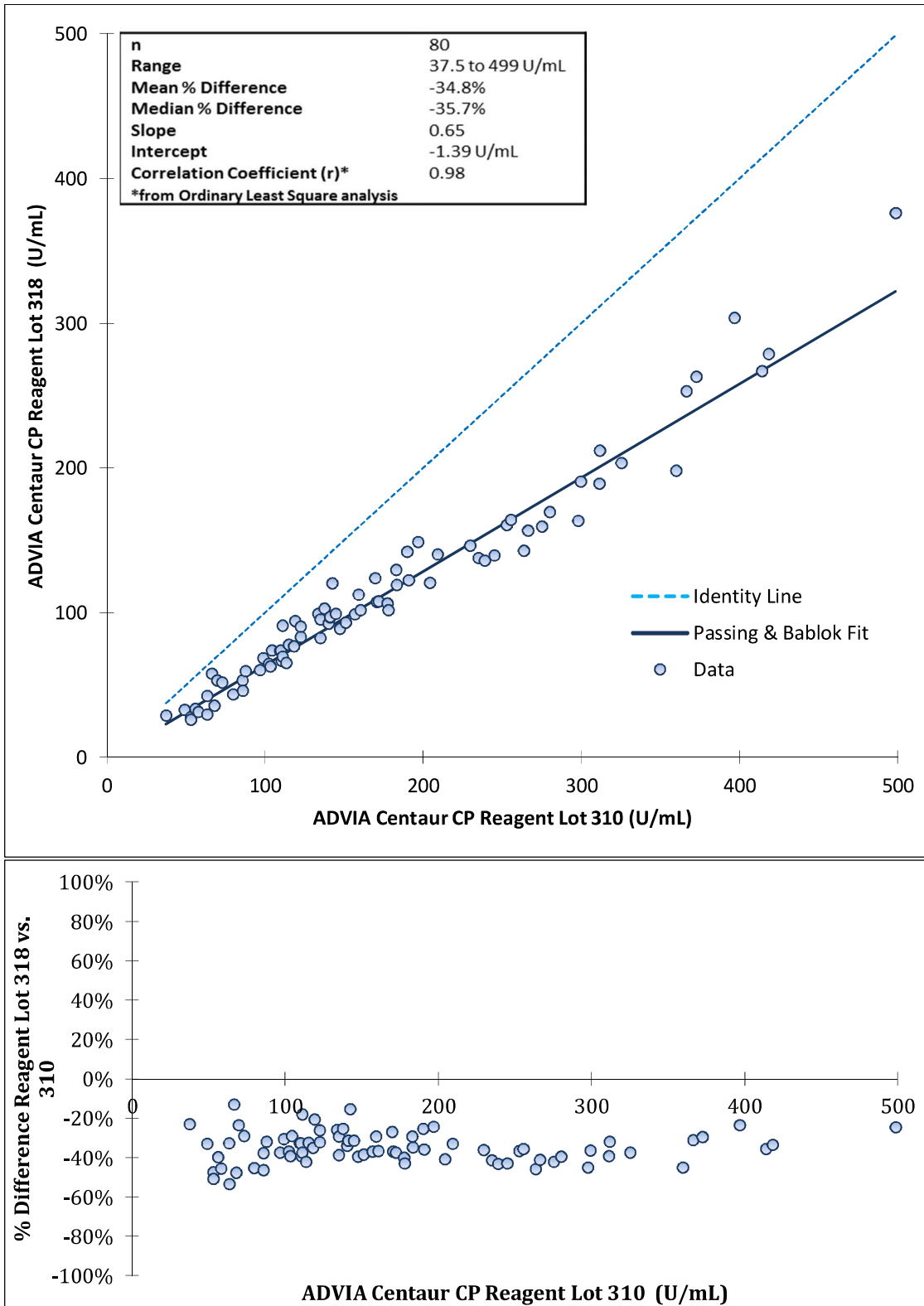


Figure 8: ADVIA Centaur CP- Reagent Lot 318 vs. Reagent Lot 316

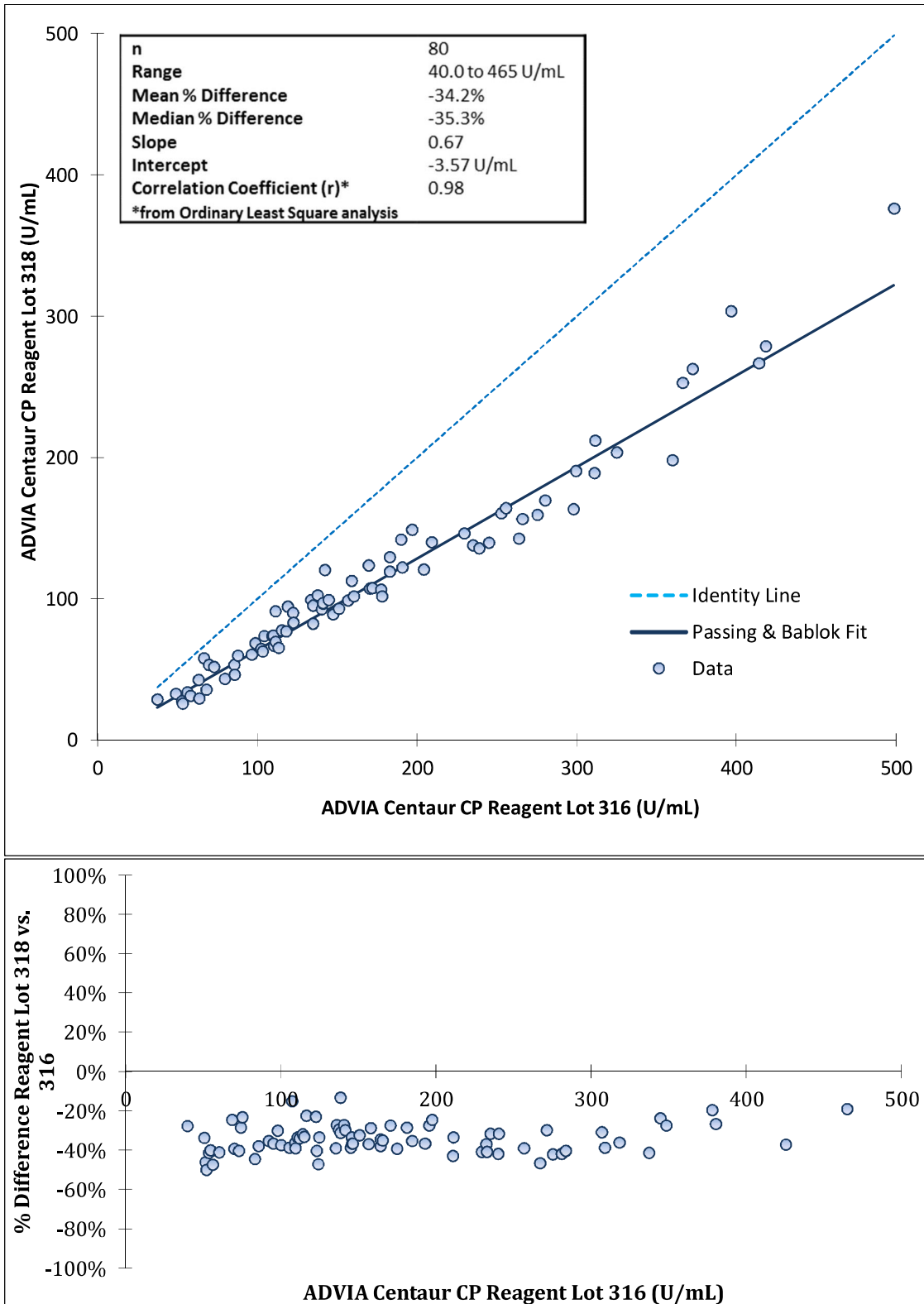
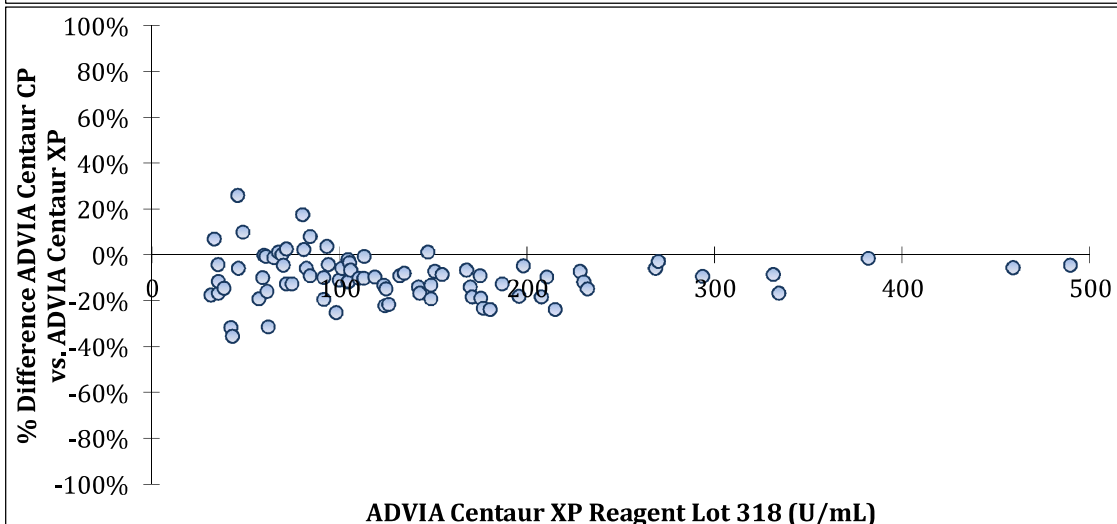
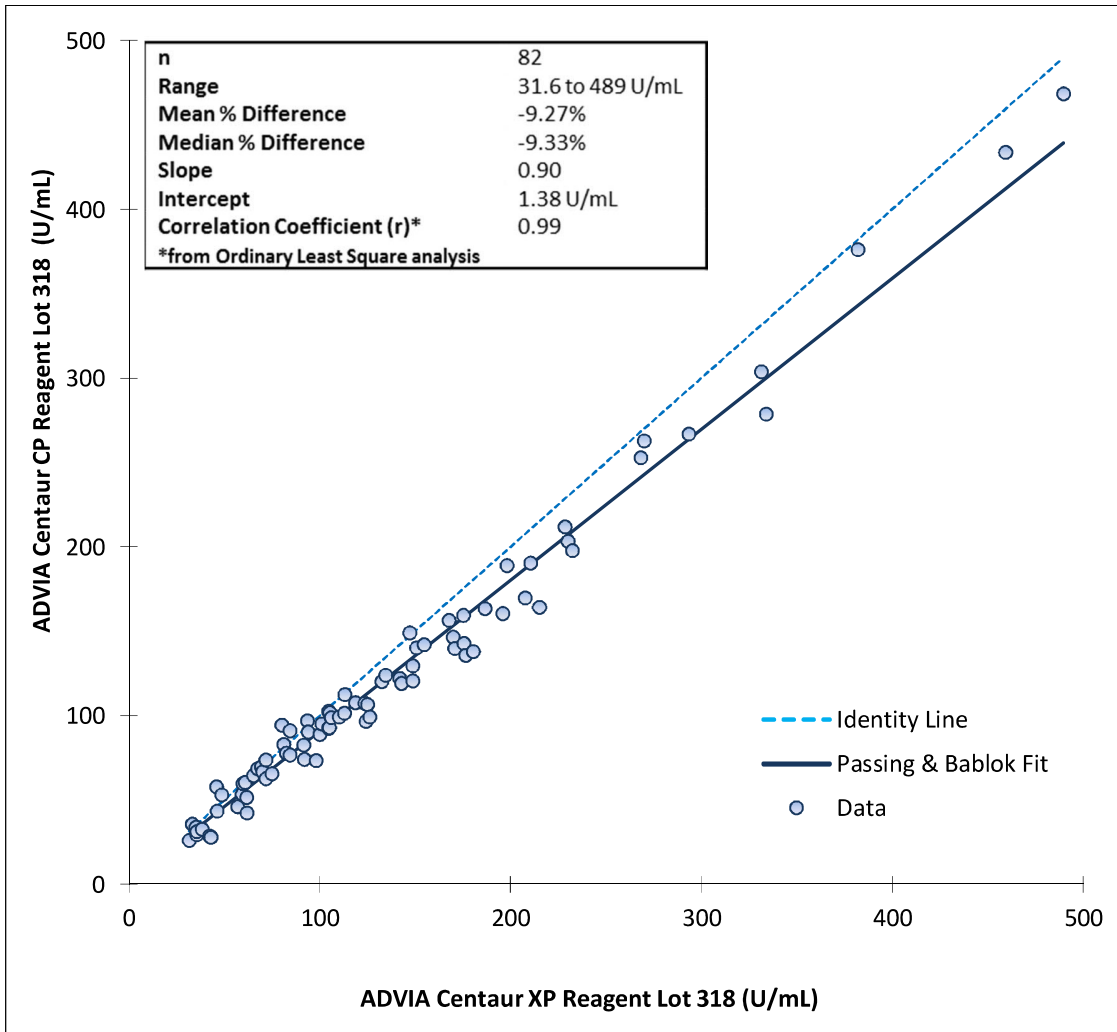


Figure 9: ADVIA Centaur CP vs. ADVIA Centaur XP- Reagent Lot 318

ADVIA Centaur Anti-Thyroglobulin (aTG) Positive Bias



ADVIA Centaur is a trademark of Siemens Healthcare Diagnostics

**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  
If you have any questions, contact your local Siemens technical support representative.