

**Atellica® Solution**

**Atellica IM HER-2/neu (H2n) Positive Bias versus Internal Standardization**

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

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

Product Name	Siemens Material Number (SMN)	Kit Lot Number	1 <sup>st</sup> Distribution Date (YYYY-MM-DD)	Expiration Date (YYYY-MM-DD)
Atellica IM HER-2/neu Assay 50 Test Kit	10995591	98034139 32478139	2020-03-30 2020-05-29	2021-01-30
Atellica IM HER-2/neu Calibrator (2 pack)	10995592	22695A49	2020-05-19	2020-12-11

**Reason for Urgent Field Safety Notice**

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 has confirmed an average positive bias of 49.5% with current in date lots listed in Table 1 as compared to Siemens internal standardization. The bias is proportional across the assay measuring interval. In addition, Siemens confirmed that Upper Limit of Normal (ULN) as claimed in the Instructions for Use (IFU) was no longer achieved. See Additional Information section below for details of the observed bias.

Alignment to the internal standardization has been restored with Atellica IM H2n reagent kit lots ending in 141 and higher, when calibrating with Atellica IM H2n calibrator lots ending in 54 and higher (available in August 2020). Moving forward, this alignment will be maintained through enhancements to the control system.

Customers will observe a negative shift when transitioning from current to new Atellica IM H2n reagent and calibrator lots. See Additional Information section below for details on the expected shift.

The Atellica IM H2n assay and associated materials are not “lot-locked”. However, the specified mandatory lot combinations must be used as noted in Table 2.

**Table 2. Mandatory Lot Combinations**

Component	Current Lot Combinations	New Lot Combinations
Atellica IM H2n Assay 50 Test Kit (lots ending in)	139	141 and above
Atellica IM H2n Calibrator (2 pack) (lots ending in)	49	54 and above
Atellica IM H2n Quality Control (QC) lots	4225901/4225902, 4230501/4230502 and 4202211/4202212	4202111/4202112 and future lots
Atellica IM H2n Master Curve Material (MCM) lots	62270 and 81622	46523 and future lots

Siemens is currently investigating the root cause of this issue.

### Risk to Health

The issue described causes a positive proportional bias across the entire analytical measuring range. Erroneously elevated H2n results may lead to additional investigations that are clinically well tolerated. The slow rate of increase in bias across different reagent lots does not impact treatment decisions or the ability to monitor treatment efficacy. The test results are not used in isolation, rather in conjunction with the overall clinical picture and history and other results such as imaging. Siemens is not recommending a review of previously generated patient results.

### Actions to be Taken by the Customer

- Please review this letter with your Medical Director.
- You may continue use of Atellica IM H2n lots in Table 1 until you receive replacement product in your laboratory. Refer to Table 3 for Atellica IM H2n bias information.
- If you are currently using Atellica IM H2n Assay kit lots and calibrator lots in Table 1, review your inventory of these products, as well as the associated Atellica IM H2n QC and MCM, and order replacement products by completing the Field Correction Effectiveness Check Form attached to this letter.
- Upon acceptance of the replacement lots in Table 2 New Lot Combinations column, discontinue use of and discard the products listed in Table 2 Current Lot Combinations column. Refer to Figures 1 through 4 for expected results with replacement lots.

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.

## Additional Information

### Current Lot Combination Performance Compared to Internal Standardization

Current lot performance compared to internal standardization was evaluated with 46 serum samples covering the assay measuring interval (0.5 – 350 ng/mL). Table 3 summarizes the biases observed when comparing Atellica IM H2n reagent kit lot ending in 139 with H2n calibrator lot ending in 49, to the internal standardization.

**Table 3. Atellica IM H2n Reagent Lot 139 Bias vs. Internal Standardization**

H2n Dose	Atellica IM	
	Average Bias	Range of Bias
<15.0 ng/mL	54.2%	49.6% to 68.5%
15.0 ng/mL to 50.0 ng/mL	47.7%	47.2% to 49.3%
>50.0 ng/mL	47.5%	47.2% to 47.8%
Overall Bias Across Assay Measuring Interval	49.5%	

In addition, Siemens' investigation included a review of historical H2n assay performance and determined the current bias versus the internal standard developed slowly over multiple lots (~4%/year (~2 lots/year)).

### Current Lot Combination Upper Limit of Normal

Testing was performed following CLSI Guidance EP28-A3c "Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory" using 132 patient samples (premenopausal and postmenopausal, without a history of cancer) to evaluate the Upper Limit of Normal (ULN) stated in the IFU (15.2 ng/mL, defined as the 95<sup>th</sup> percentile of the observed results). The results, 53 out of 132 samples or 40% of apparently healthy females had values below 15.2 ng/mL, demonstrating the reference interval was not achieved with Atellica IM H2n reagent lot ending in 139 with Atellica IM H2n calibrator lot ending in 49.

### Restoration with New Lot Combination

The reference interval in the IFU was restored and the bias throughout the assay measuring interval was eliminated. In addition, Siemens Commercial Controls and Master Curve Material targets were reset starting with the new lot combinations in Table 2 to ensure acceptable performance. IFU performance claims were verified including the Atellica IM H2n result alignment compared to ADVIA Centaur XP/XPT and Upper Limit of Normal.

### New Lot Combination Comparison to Current Lot Combination

After restoring alignment to the internal standardization as claimed in the IFU with the new lot combinations in Table 2, Siemens completed internal testing to evaluate the performance of Atellica IM H2n reagent kit lot ending in 141 (new) compared to Atellica IM H2n reagent kit lot ending in 139 (current). Method comparison studies included n=100 samples across the assay measuring interval (0.5 – 350 ng/mL) to evaluate the performance of Atellica IM H2n reagent kit lot ending in 141 (new) with Atellica IM H2n calibrator lot ending in 54 (new) compared to Atellica IM H2n reagent kit lot ending in 139 (current) with Atellica IM H2n calibrator lot ending in 49 (current).

Figures 1 and 2 show the approximate negative 42% shift that is expected when transitioning to the new reagent and calibrator lots.

Figure 1. Atellica IM H2n Reagent Lot 141 (new) vs. Reagent Lot 139 (current) Graph

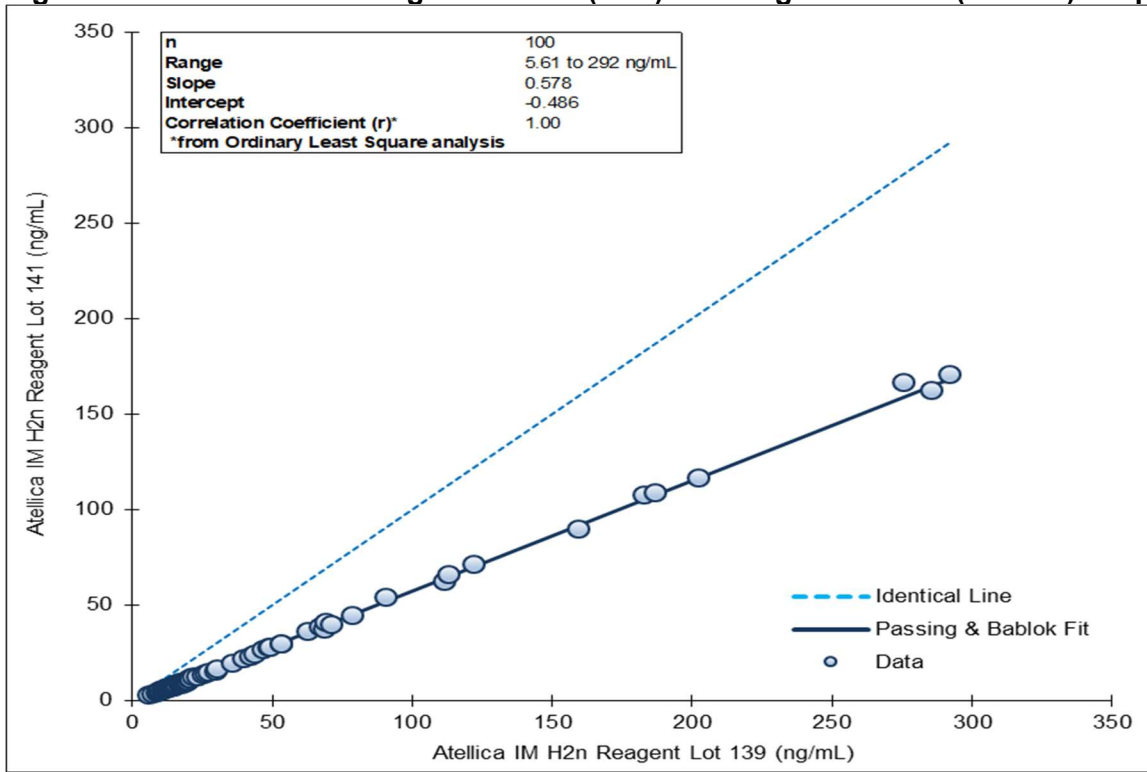
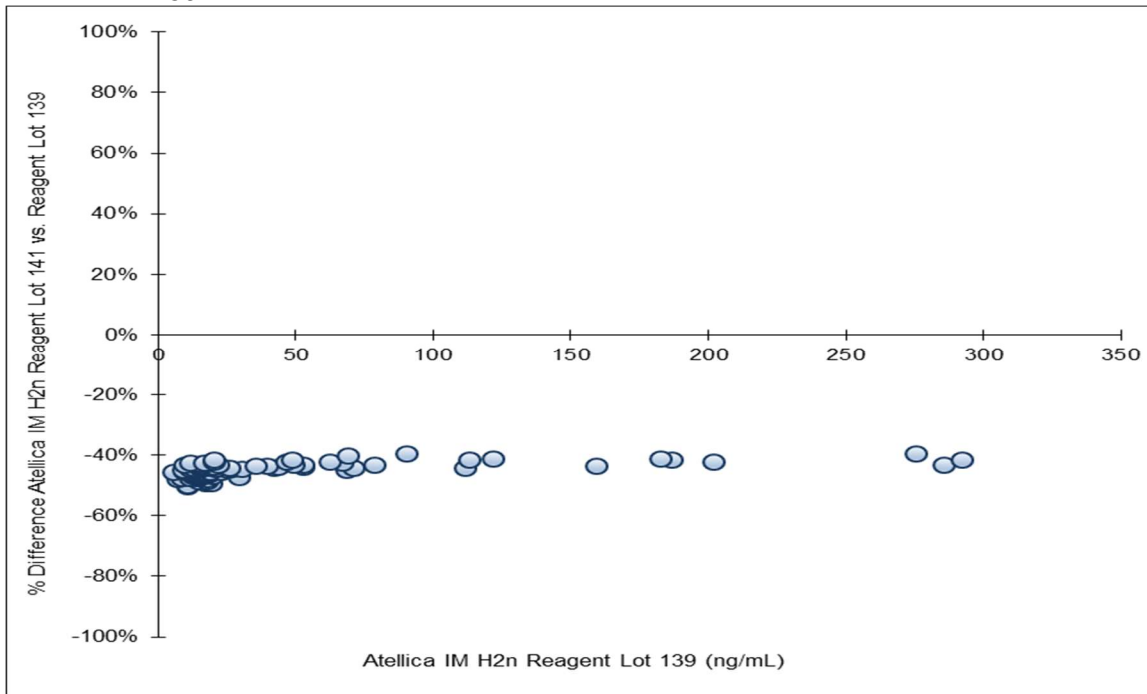


Figure 2. Atellica IM H2n Reagent Lot 141 (new) vs. Reagent Lot 139 (current) % Difference Plot



### New Lot Combination Upper Limit of Normal

The same testing protocol using the same patient samples noted above was completed with Atellica IM H2n reagent kit lot ending in 141 (new). The results demonstrate the Upper Limit of Normal has been restored with Atellica IM H2n reagent kit lot ending in 141 (130 out of 132 samples or 98% of apparently health females had values below 15.2 ng/mL).

### New Lot Combination Bias between Atellica IM and ADVIA Centaur XP/XPT

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

Evaluation of Atellica IM H2n result recovery compared to ADVIA Centaur XP/XPT utilized the same method comparison samples and study format as noted above for Figures 1 and 2, with Atellica IM H2n reagent lot ending in 141 with Atellica IM H2n calibrator lot ending in 54.

Figures 3 and 4 demonstrate H2n result alignment between the Atellica IM analyzer and ADVIA Centaur XP/ADVIA Centaur XPT systems has been maintained.

**Figure 3. Atellica IM H2n Recovery vs. ADVIA Centaur XP/XPT Graph**

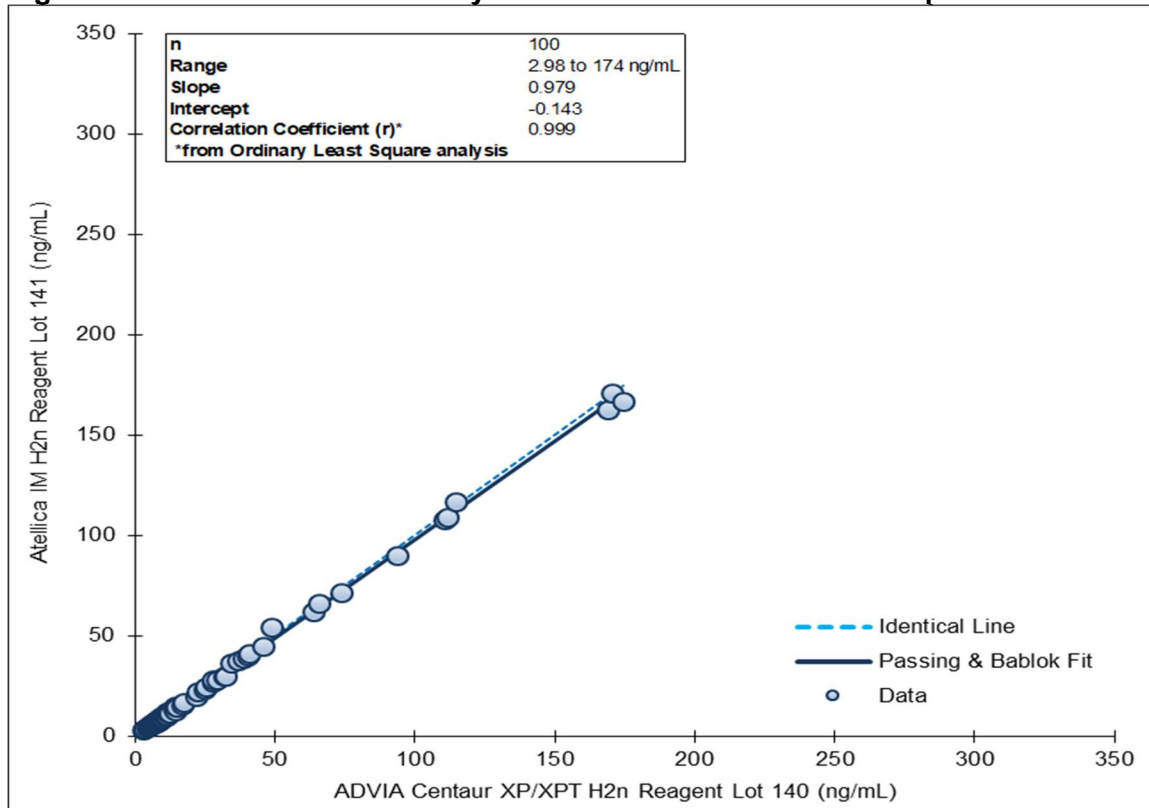
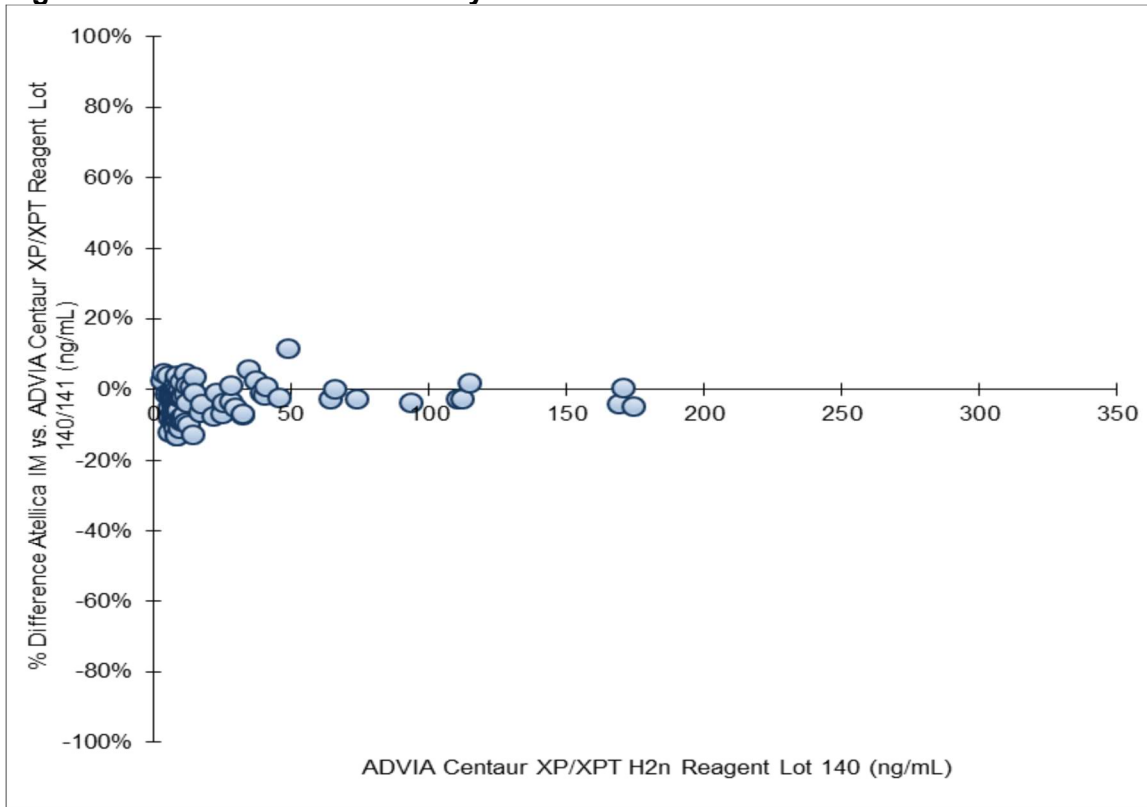


Figure 4. Atellica IM H2n Recovery vs. ADVIA Centaur XP/XPT % Difference Plot



Atellica is a trademark of Siemens Healthcare Diagnostics Inc.

**FIELD CORRECTION EFFECTIVENESS CHECK**

Atellica IM HER-2/neu (H2n) Positive Bias versus Internal Standardization

This response form is to confirm receipt of the enclosed Siemens Healthcare Diagnostics Urgent Field Safety Notice AIMC 20-05.A-1.OUS dated August 2020 regarding Atellica IM HER-2/neu (H2n) Positive Bias versus Internal Standardization. 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 SMN and Lot #	Quantity Discarded/ Replacement Quantity Required
Atellica IM H2n Assay (50 test kit) SMN:10995591 Kit Lots ending in 139	
Atellica IM H2n Calibrator (2 pack) SMN: 10995592 Kit Lot ending in 49	
Atellica IM H2n QC SMN: 10995594 (Lots 4225901/4225902, 4230501/4230502 and 4202211/4202212)	
Atellica IM H2n Master Curve Material SMN: 10995593 (Lots 62270 and 81622)	

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.