

## Customer Notification

### Viratrol (AT474543) QC Bias for HISCL HBsAg Assay

4 Aug 2022

Dear Sysmex Customer,

This letter contains important information pertaining to observed bias in assay values with specific lots of Viratrol when used in combination with the HISCL HBsAg Assay. As we improve the manufacturing quality of our products, we seek to inform our valued HISCL customers to understand potential changes in measurand recovery in their daily routine assay work as these reagents are released to the market over the coming months.

#### Background

As Sysmex recently improved the manufacturing quality and stability of our HISCL products, we would like to bring awareness to the potential increase in mean recovery levels of Viratrol control material with the following combinations of production LOTs of HISCL HBsAg Assay kit and HISCL HBsAg Calibrator (Table 1 below).

#### Affected Products

Product Code	Name of Product	Lot #
CH617178	HISCL HBsAg Assay Kit	ZS2104, ZS2105
05423111	HBsAg Calibrator	ZS2001, ZS2002
AT474543	Viratrol	VRAP-009, VRAP-010, VRAP-011, VRAP-012

**Table 1.**

Internal testing showed some specific Viratrol lots could exhibit higher recovery results when used with specific LOTs of HBsAg calibrators and HISCL HBsAg reagents, the data is shown in Table 2 is representative for the combinations, but not exhaustive to cover all permutations of reagents LOTs on-market. (Table 2). Sysmex wishes to assure all users the performance of the reagents remain within Sysmex's allowable manufacturing specification ranges. This letter serves to provide you information about each LOT differences when using HISCL HBsAg assay kits.

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### Internal Testing Results

Calibrator lot		ZS2001		Reference Target level value of the Viratrol control lot (IU/mL)
HBsAg Reagent lot		ZS2104	ZS2105	
Viratrol lot		IU/mL	IU/mL	
VRAP-012	VR-112	2.51	2.55	Target: 2.20 Range: 1.76-2.64
		2.60	2.61	
		2.60	2.60	
	Mean	<b>2.57</b>	<b>2.59</b>	
	CV (%)	2.00	1.20	
	VR-212	12.91	12.76	Target: 10.99 Range: 8.79-13.19
		13.02	12.51	
12.95		12.85		
Mean		<b>12.96</b>	<b>12.71</b>	
CV (%)	0.40	1.40		
VRAP-013	VR-113	2.17	2.13	Target: 2.21 Range: 1.77-2.65
		2.14	2.16	
		2.18	2.14	
	Mean	<b>2.16</b>	<b>2.14</b>	
	CV (%)	1.00	0.70	
	VR-213	11.10	10.90	Target: 10.98 Range: 8.78-13.18
		11.00	10.77	
11.11		10.98		
Mean		<b>11.07</b>	<b>10.88</b>	
CV (%)	0.50	1.00		

**Table 2.**

The reagent LOT combinations in Table 2 were applied to pre-characterised clinical samples and demonstrated 100% clinical specificity and sensitivity: 100 HBsAg non-reactive clinical samples remained below the HISCL HBsAg reactivity cutoff of 0.03 IU/mL; measurement of 50 HBsAg-reactive clinical samples showed good correlation with a mean positive bias within the acceptable performance limit. The evaluation data can be provided upon request.

### New Assigned Values for ZS2002 (calibrator), ZS2104 (reagent) and VRAP-010/011 (Viratrol)

Calibrator lot		ZS2002	Reference Target level values of the Viratrol control lot (IU/mL)
HBsAg Reagent lot		ZS2104	
Viratrol lot		IU/mL	
VRAP-010	VR-110	2.33	Target: 2.14 Range: 1.71-2.57
		2.40	
		2.30	
	Mean	<b>2.34</b>	
	CV (%)	2.10	

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	VR-210	12.15	Target: 10.69 Range: 8.48-12.72
		12.05	
		12.06	
	Mean	<b>12.09</b>	
	CV (%)	0.40	
VRAP-011	VR-111	2.41	Target: 2.12 Range: 1.70-2.54
		2.38	
		2.44	
	Mean	<b>2.41</b>	
	CV (%)	1.30	
VRAP-011	VR-211	12.26	Target: 10.93 Range: 8.74-13.12
		12.01	
		12.18	
	Mean	<b>12.15</b>	
	CV (%)	1.10	

**Table 3.**

Sysmex observed the specific combinations of ZS2002 (calibrator), ZS2104 (HBsAg reagent) and VRAP-010/011 (Viratrol controls) may experience mean recovery values close to or exceeding the upper limit of the target level value range. Sysmex internal testing has validated new assigned level values for specific Viratrol LOTS listed in Table 3 above which can be applied for routine use to reduce this over-recovery.

### **Recommendations for customer**

Please determine the change in recovery/ potential bias according to your own laboratory protocol for combinations of concerned reagent lots in Table 1:

1. Whenever there is a change to any of the HBsAg reagent, calibrator or Viratrol control LOTS as listed above in Table 1:
  - a. Verify any observations of increased recovery of Viratrol QC levels with pre-measured clinical specimens reactive for HBsAg.
2. Where significant increased % recovery of HBsAg is observed:
  - a. Inform clinical colleagues of the potential % increased bias for patient specimens
  - b. Where necessary, re-baseline HBsAg reactive patients with at least 2x HISCL HBsAg quantitative measurements 3-6 months apart to determine the true trend for clinical management decisions, together with other clinical assessments.

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We deeply appreciate your understanding and continued support.

Sincerely yours,



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Yoshiro Ueda

Sysmex Corporation Vice President of Regulatory Affairs and Quality Assurance Div.

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### Appendix 1. Measurement results of Viratrol lots

Calibrator lot HBsAg lot	Reagent lot	ZS2001		ZS2002		ZS2003		Reference Target level values of the Viratrol control lot (IU/mL)
		ZS2104 IU/mL	ZS2105 IU/mL	ZS2104 IU/mL	ZS2105 IU/mL	ZS2104 IU/mL	ZS2105 IU/mL	
VRAP-012	VR-112	2.51	2.55	2.66	2.66	2.67	2.70	Target: 2.20 Range: 1.76-2.64
		2.60	2.61	2.75	2.72	2.77	2.75	
		2.60	2.60	2.75	2.71	2.77	2.75	
	2.57	2.59	2.72	2.70	2.74	2.73		
	2.00%	1.20%	1.90%	1.20%	2.10%	1.10%		
Mean	CV	12.91	12.76	13.48	13.14	13.77	13.49	Target: 10.99 Range: 8.79-13.19
		13.02	12.51	13.60	12.89	13.88	13.23	
		12.95	12.85	13.52	13.23	13.80	13.59	
Mean	CV	12.96	12.71	13.53	13.09	13.82	13.44	Target: 2.21 Range: 1.77-2.65
		0.40%	1.40%	0.50%	1.30%	0.40%	1.40%	
		2.17	2.13	2.30	2.23	2.31	2.25	
VR-113	Mean	2.14	2.16	2.27	2.25	2.28	2.28	Target: 10.98 Range: 8.78-13.18
		2.18	2.14	2.32	2.24	2.33	2.26	
		2.16	2.14	2.30	2.24	2.31	2.26	
Mean	CV	1.00%	0.70%	1.10%	0.40%	1.10%	0.70%	Target: 10.98 Range: 8.78-13.18
		11.10	10.90	11.61	11.26	11.84	11.52	
		11.00	10.77	11.50	11.13	11.73	11.39	
VR-213	Mean	11.11	10.98	11.62	11.34	11.84	11.62	Target: 10.98 Range: 8.78-13.18
		11.07	10.88	11.58	11.24	11.80	11.51	
		0.50%	1.00%	0.60%	0.90%	0.50%	1.00%	

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Appendix2. Measurement result of HBV Immunoassay control lot

Calibrator lot HBsAg lot	Reagent lot	ZS2001			ZS2002			ZS2003			Reference Target level values of the Viratrol control lot (IU/mL)
		ZS2104	ZS2105	ZS2104	ZS2105	ZS2104	ZS2105	ZS2104	ZS2105		
HB-059	HBG-159	IU/mL		5.20	5.42	5.59	5.42	5.66	5.50	Target: 4.52 Range: 3.62-5.42	
		IU/mL		5.18	5.48	5.45	5.48	5.52	5.56		
	IU/mL		5.17	5.40	5.45	5.40	5.52	5.48			
	Mean		5.22	5.43	5.50	5.43	5.57	5.51			
	CV		1.50%	0.80%	1.50%	0.80%	1.50%	0.80%			
	HBG-259	IU/mL		32.70	34.83	33.95	34.83	34.68	36.31		
		IU/mL		33.62	33.44	34.91	33.44	35.66	34.86		
		IU/mL		33.14	34.01	34.41	34.01	35.15	35.46		
		Mean		33.15	34.09	34.42	34.09	35.16	35.54		
	CV		1.40%	2.00%	1.40%	2.00%	1.40%	2.10%	Target: 29.17 Range: 23.34-35.00		
HBG-160	IU/mL		5.94	6.12	6.25	6.12	6.34	6.22			
	IU/mL		5.88	6.07	6.18	6.07	6.27	6.16			
	IU/mL		5.92	6.11	6.23	6.11	6.32	6.21			
	Mean		5.91	6.10	6.22	6.10	6.31	6.20			
CV		0.50%	0.40%	0.60%	0.40%	0.60%	0.50%	Target: 5.29 Range: 4.23-6.35			
HBG-260	IU/mL		35.18	34.57	36.54	34.57	37.30			36.04	
	IU/mL		35.00	35.33	36.36	35.33	37.11			36.82	
	IU/mL		35.02	35.94	36.37	35.94	37.13			37.45	
	Mean		35.07	35.28	36.42	35.28	37.18			36.77	
CV		0.30%	1.90%	0.30%	1.90%	0.30%	1.90%		Target: 31.43 Range: 25.14-37.72		
HB-060	IU/mL		35.18	34.57	36.54	34.57	37.30			36.04	
	IU/mL		35.00	35.33	36.36	35.33	37.11			36.82	
	IU/mL		35.02	35.94	36.37	35.94	37.13			37.45	
	Mean		35.07	35.28	36.42	35.28	37.18			36.77	
CV		0.30%	1.90%	0.30%	1.90%	0.30%	1.90%				

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Calibrator lot HBsAg Reagent lot	ZS2001		ZS2002		ZS2003		Reference Target level values of the Viratrol control lot (IU/mL)
	ZS2104	ZS2105	ZS2104	ZS2105	ZS2104	ZS2105	
HBV Immunoassay control lot	IU/mL	IU/mL	IU/mL	IU/mL	IU/mL	IU/mL	
	5.90	5.84	6.20	6.07	6.29	6.17	
	6.07	5.75	6.38	5.99	6.48	6.08	
	5.88	5.87	6.18	6.11	6.27	6.21	Target: 5.21 Range: 4.17-6.25
	5.95	5.82	6.25	6.06	6.35	6.15	
HB-061	CV	1.80%	1.80%	1.00%	1.80%	1.10%	
	34.73	36.00	36.07	36.40	36.82	37.93	
	34.84	35.25	36.18	35.64	36.94	37.14	Target: 32.03 Range: 25.62-38.44
	34.58	34.74	35.91	35.12	36.66	36.60	
	34.72	35.33	36.05	35.72	36.81	37.22	
HB-062	CV	0.40%	0.40%	1.80%	0.40%	1.80%	
	4.71	4.79	4.96	5.00	5.02	5.07	
	4.77	4.81	5.02	5.01	5.09	5.09	Target: 5.33 Range: 4.26-6.40
	4.78	4.92	5.03	5.12	5.10	5.20	
	4.75	4.84	5.00	5.04	5.07	5.12	
HB-062	CV	0.80%	0.80%	1.30%	0.90%	1.40%	
	28.52	29.11	29.59	29.40	30.28	30.69	
	28.85	29.25	29.94	29.54	30.63	30.83	Target: 31.23 Range: 24.98-37.48
	29.23	29.68	30.33	29.98	31.03	31.29	
	28.87	29.35	29.95	29.64	30.65	30.94	
CV	1.20%	1.00%	1.20%	1.00%	1.20%	1.00%	