

QC Services Investigation: PMM-QC-1661

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and distributed in the week beginning 2023/DEC/20

INTRODUCTION

NRL was notified by Bio-Rad Laboratories, of an urgent product defect correction (TGA number: RC-2023-RN-01051-1) for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay. The notification discusses an observation in the decrease of HCV sensitivity for specimens that are near the limit of detection. Due to this decrease in HCV antigen sensitivity, a recent HCV infection may not be detected in patient samples as early as prior batches of the Monolisa HCV Ag-Ab ULTRA V2 assay. There is no impact to seroconversion observed for these batches through HCV antibody detection.

This report will review data reported to EDCNet for reagent lot numbers affected by the notice to establish if trends or variation are observed across the peer group.

FINDINGS

Below are the full listing of charts included in the investigation:

- Figure 1 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Blue DM21187, by reagent lot.
- Figure 2 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Blue DM22009, by reagent lot.
- Figure 3 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Blue DM22121, by reagent lot.
- Figure 4 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Green DM21254, by reagent lot.
- Figure 5 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Antigen Positive Kit Control, by reagent lot.
- Table 1 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Blue DM21187, by reagent lot.
- Table 2 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Blue DM22009, by reagent lot.
- Table 3 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Blue DM22121, by reagent lot.
- Table 4 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Green DM21254, by reagent lot.
- Table 5 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Antigen Positive Kit Control, by reagent lot.
- Appendix 1: Bio-Rad AU Customer letter notification.

DISCUSSION

All participant data reported to EDCNet for the Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay were investigated to establish whether there was any evidence of trends or patterns.

Figures and Tables 1 – 3 show peer group data for Optitrol Blue DM22187, DM22009 and DM22121 when tested on the Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay. Several affected reagent lot numbers (lots 2J0063, 2L0064 and 3B0066) were in use across the peer group. All laboratories in the peer group testing with Optitrol Blue are within Australia. No significant changes were observed between affected and non-affected reagent lots.

Figure and Table 4 show peer group data for Optitrol Green DM21254 when tested on the Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay. Affected reagent lot number, 2L0580, was reported for all participants in the peer group, with one laboratory additionally reporting data for 3B0582, and 3D0583. All laboratories in the peer group testing with Optitrol Green are located outside of Australia. No significant changes were observed between affected and non-affected reagent lots.

Figure and Table 5 show data for Antigen Positive kit control when tested on the Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay. The kit control data includes both the Optitrol Blue and Optitrol Green peer groups. No significant changes were observed between affected and non-affected reagent lot numbers.

On review of the peer groups for the Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay no shifts or trends were observed for either Optitrol products (Optitrol Blue and Green) in use. S/Co values for both Optitrol Blue and Optitrol Green remained consistent across all reagent lots in use.

RECOMMENDATIONS

NRL recommends participants using these reagent lots should monitor any trends with peer group data.

Actions proposed by Bio-Rad can be found in Appendix 1: *Bio-Rad AU Customer letter notification – Urgent Product Defect Correction*.

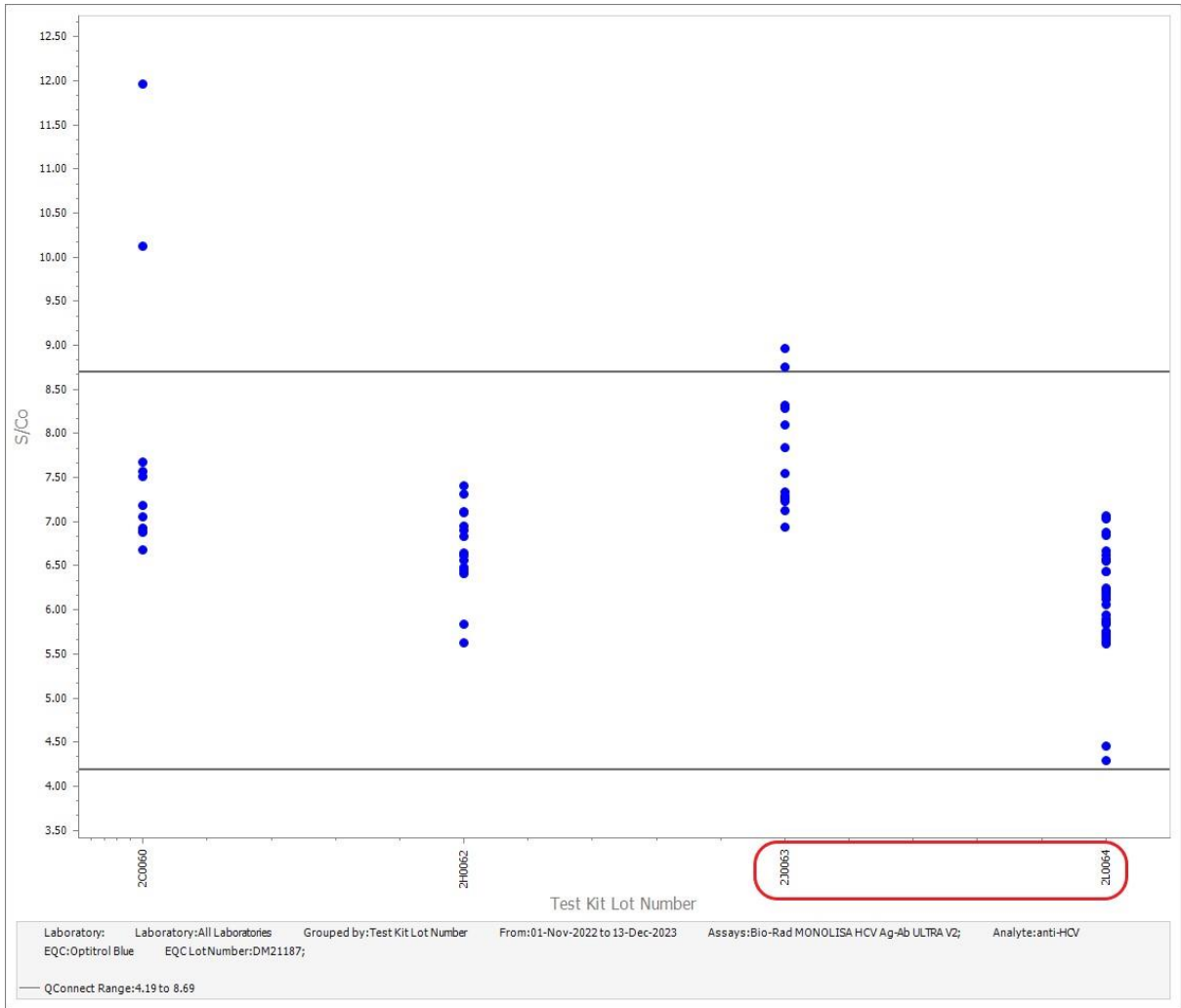


Figure 1 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Blue DM21187, by reagent lot.

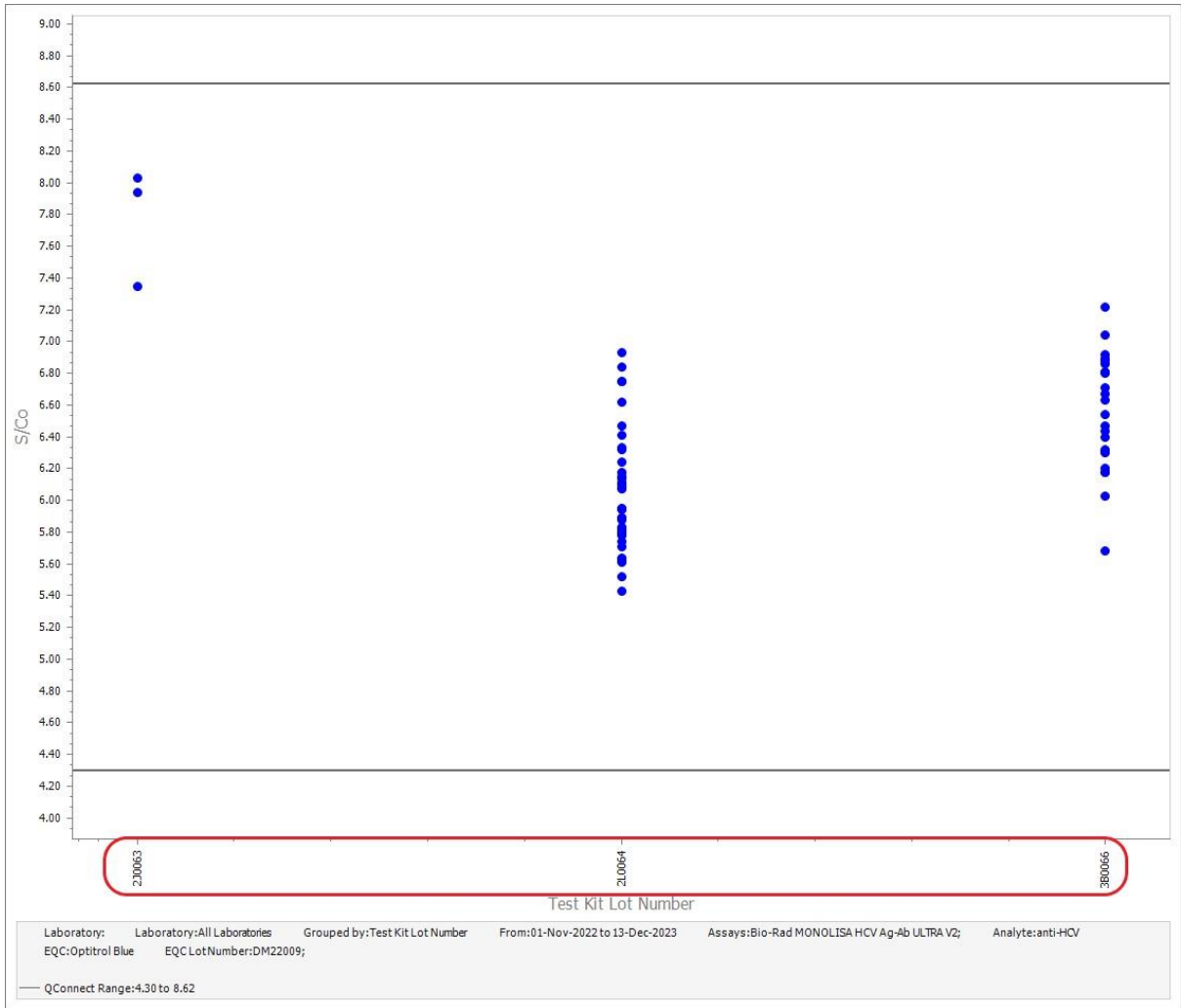


Figure 2 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Blue DM22009, by reagent lot.



Figure 3 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Blue DM22121, by reagent lot.

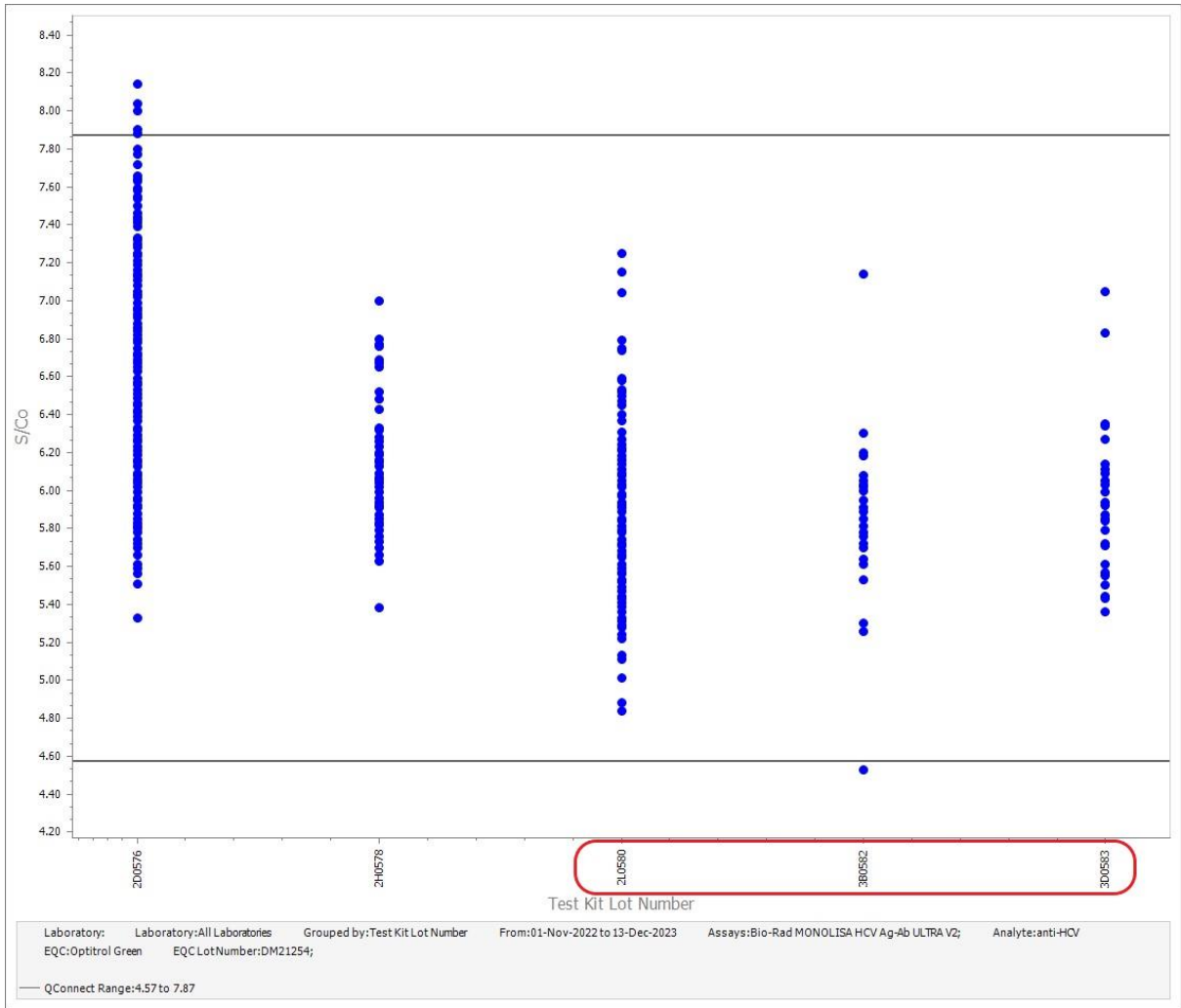


Figure 4 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Green DM21254, by reagent lot.

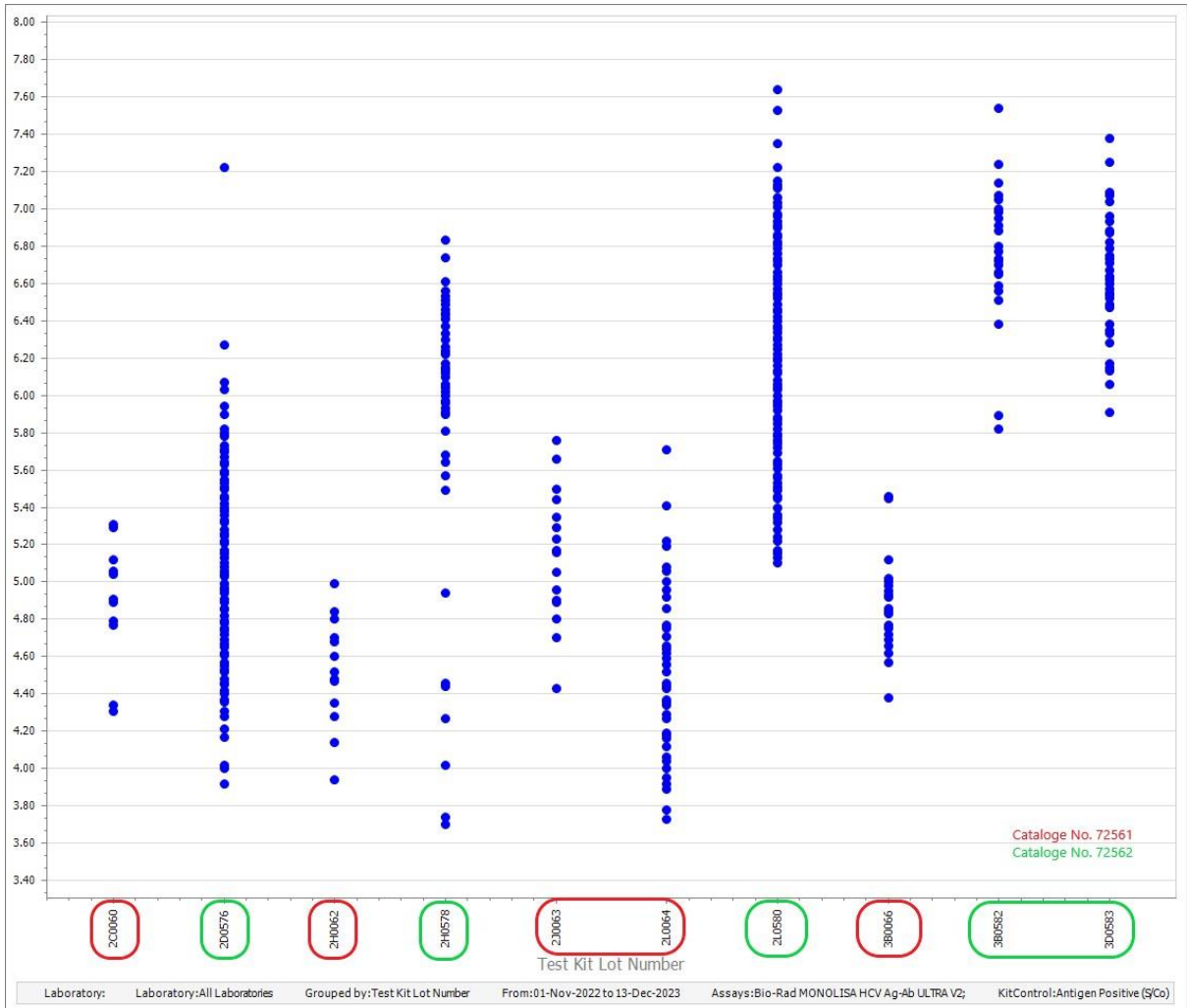


Figure 5 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Antigen Positive Kit Control, by reagent lot.

Test Kit Lot Number	n	Mean	SD	x-2SD	x+2SD	Min	Max	CV(%)
2C0060	9	7.15	NA	NA	NA	6.68	7.68	NA
2H0062	16	6.68	0.48	5.72	7.64	5.63	7.41	7.17
2J0063	14	7.74	0.65	6.44	9.03	6.94	8.96	8.35
2L0064	33	6.13	0.63	4.87	7.39	4.29	7.07	10.29
Totals	72	6.69	0.84	5.01	8.37	4.29	8.96	12.59

Legend:

Laboratory:

Laboratory: All Laboratories

Grouped by: Test Kit Lot Number

From: 01-Nov-2022 to 13-Dec-2023

Assays: Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2;

Analyte: anti-HCV

EQC: Optitrol Blue

EQC Lot Number: DM21187;

NA = Not enough data to compute standard deviation

Table 1 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Blue DM21187, by reagent lot.

Test Kit Lot Number	n	Mean	SD	x-2SD	x+2SD	Min	Max	CV(%)
2J0063	3	7.77	NA	NA	NA	7.35	8.03	NA
2L0064	37	6.05	0.38	5.28	6.81	5.43	6.93	6.35
3B0066	24	6.55	0.36	5.83	7.28	5.68	7.22	5.54
Totals	64	6.32	0.55	5.22	7.42	5.43	8.03	8.71

Legend:

Laboratory:

Laboratory: All Laboratories

Grouped by: Test Kit Lot Number

From: 01-Nov-2022 to 13-Dec-2023

Assays: Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2;

Analyte: anti-HCV

EQC: Optitrol Blue

EQC Lot Number: DM22009;

NA = Not enough data to compute standard deviation

Table 2 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Blue DM22009, by reagent lot.

Test Kit Lot Number	n	Mean	SD	x-2SD	x+2SD	Min	Max	CV(%)
2L0064	2	6.36	NA	NA	NA	6.06	6.66	NA
3B0066	2	6.85	NA	NA	NA	6.70	6.99	NA
Totals	4	6.60	NA	NA	NA	6.06	6.99	NA

Legend:

Laboratory:

Laboratory: All Laboratories

Grouped by: Test Kit Lot Number

From: 01-Nov-2022 to 13-Dec-2023

Assays: Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2;

Analyte: anti-HCV

EQC: Optitrol Blue

EQC Lot Number: DM22121;

NA = Not enough data to compute standard deviation

Table 3 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Blue DM22121, by reagent lot.

Test Kit Lot Number	n	Mean	SD	x-2SD	x+2SD	Min	Max	CV(%)
2D0576	458	6.60	0.51	5.59	7.61	5.33	8.14	7.66
2H0578	84	6.11	0.31	5.50	6.73	5.38	7.00	5.04
2L0580	591	5.81	0.30	5.21	6.40	4.84	7.25	5.12
3B0582	30	5.86	0.42	5.03	6.70	4.53	7.14	7.11
3D0583	44	5.94	0.32	5.30	6.58	5.36	7.05	5.39
Totals	1207	6.13	0.54	5.05	7.21	4.53	8.14	8.80

Legend:

Laboratory:

Laboratory: All Laboratories

Grouped by: Test Kit Lot Number

From: 01-Nov-2022 to 13-Dec-2023

Assays: Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2;

Analyte: anti-HCV

EQC: Optitrol Green

EQC Lot Number: DM21254;

Table 4 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Optitrol Green DM21254, by reagent lot.

Test Kit Lot Number	n	Mean	SD	x-2SD	x+2SD	Min	Max	CV(%)
2C0060	11	4.89	0.33	4.23	5.56	4.31	5.31	6.78
2D0576	462	5.05	0.36	4.33	5.77	3.90	7.22	7.15
2H0062	15	4.56	0.29	3.98	5.14	3.94	4.99	6.36
2H0578	84	5.99	0.66	4.66	7.32	3.70	6.83	11.08
2J0063	17	5.14	0.35	4.45	5.84	4.43	5.76	6.75
2L0064	62	4.50	0.39	3.72	5.28	3.73	5.71	8.68
2L0580	593	6.24	0.40	5.43	7.05	5.10	7.64	6.48
3B0066	25	4.86	0.25	4.37	5.35	4.38	5.46	5.05
3B0582	30	6.77	0.35	6.07	7.46	5.82	7.54	5.14
3D0583	44	6.62	0.33	5.96	7.27	5.91	7.38	4.96
Totals	1343	5.69	0.77	4.14	7.23	3.70	7.64	13.59

Legend:

Laboratory:

Laboratory: All Laboratories

Grouped by: Test Kit Lot Number

From: 01-Nov-2022 to 13-Dec-2023

Assays: Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2;

KitControl: Antigen Positive (S/Co)

Table 5 – Peer group data for Bio-Rad MONOLISA HCV Ag-Ab ULTRA V2 assay, Antigen Positive Kit Control, by reagent lot.



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Freecall 1800 224 354
Facsimile (+61 2) 9914 2888

11/12/2023

Urgent Product Defect Correction

TGA Reference Number: RC-2023-RN-01051-1

ARTG Number: 231015

Affected product details:

Product UDI	Product Name	Catalog No	Serial/ Lot No	Expiry Date
03610520013762	Monalisa HCV Ag/Ab ULTRA V2	72561	2J0063	2024-01-28
			2L0064	2024-03-24
			3A0065	2024-06-09
			3B0066	2024-07-14
			3B1066	2024-07-14
			3C0067	2024-08-11
			3H0068	2024-12-22
			3K0069	2025-02-25
03610520013779	Monalisa HCV Ag/Ab ULTRA V2	72562	2J0579	2024-01-28
			2L0580	2024-03-24
			3A0581	2024-06-09
			3B0582	2024-07-14
			3D0583	2024-09-01
			3F0584	2024-10-13
			3H0585	2024-12-22
			3K0586	2025-02-25

Bio-Rad Laboratories, after consultation with Therapeutic Goods Administration (TGA), is conducting an Urgent Product Defect Correction of the above products. We are contacting you as the potentially affected product may have been supplied to your organisation.

There has been an observation in the decrease of HCV antigen sensitivity for specimens that are near the limit of detection. Due to this decrease in HCV antigen sensitivity, a recent HCV infection may not be detected in patient samples as early as prior batches of the Monalisa HCV Ag-Ab ULTRA V2 assay. There is no impact to seroconversion observed for these batches through HCV antibody detection.

All batches of Monalisa HCV Ag-Ab ULTRA V2 assay currently on the market have been tested on 12 HCV seroconversion panels. A few additional days of delay (≤ 7 days on average) for HCV Antigen positivity are observed in seroconversion sample testing when compared to HCV NAT testing and predicate combined Ag-Ab HCV assay testing results in the original performance studies provided in the IFU.

TGA Reference Number: RC-2023-RN-01051-1

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Early HCV infections are still detectable with positive HCV Antigen prior to HCV antibody assays (>12 days on average).

Actions proposed by Bio-Rad:

The Monolisa HCV Ag-Ab ULTRA V2 assay batches currently on the market can continue to be used as intended for detection of infection by HCV based on the detection of anti-HCV antibodies and capsid antigen in serum or human plasma, considering the decrease in HCV antigen sensitivity.

In case of suspected early HCV infection, customers must perform HCV NAT testing in addition to testing on the Monolisa HCV Ag-Ab ULTRA V2 assay as per the current IFU.

We request you to transfer this information to all persons impacted in your institution and/or forward it to all locations where products may have been transferred/used and/or notify Bio-Rad.

Please sign and return the attached Customer Acknowledgement form and return it to the Bio-Rad RA department via email RAQA_Pacific@bio-rad.com.

We apologise for any inconvenience that may have been caused by this action and we appreciate your prompt cooperation in this matter. For further information, please contact Bio-Rad Laboratories Technical Support Department at 1800224-354, or techSupport.ANZCDG@bio-rad.com.

Sincerely,

DocuSigned by:

168E4A33380F48E...

Anna Yang

RA Specialist

Bio-Rad Laboratories Pty Ltd



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Customer Acknowledgement Form

Please complete this form and return *even if you do not have any affected stock*.

TGA Reference Number: RC-2023-RN-01051-1

Product UDI	Product Name	Catalog No	Serial/ Lot No	Expiry Date
03610520013762	Monalisa HCV Ag/Ab ULTRA V2	72561	2J0063	2024-01-28
			2L0064	2024-03-24
			3A0065	2024-06-09
			3B0066	2024-07-14
			3B1066	2024-07-14
			3C0067	2024-08-11
			3H0068	2024-12-22
3K0069	2025-02-25			
03610520013779	Monalisa HCV Ag/Ab ULTRA V2	72562	2J0579	2024-01-28
			2L0580	2024-03-24
			3A0581	2024-06-09
			3B0582	2024-07-14
			3D0583	2024-09-01
			3F0584	2024-10-13
			3H0585	2024-12-22
			3K0586	2025-02-25

On behalf of this organisation I acknowledge receipt of the notice date _____
relating to the above product, and have proceeded according to the instructions issued by Bio-Rad.

If you have no affected stock, tick this box:

Organisation		
Name		
Position		
Email		
Telephone no.		
Catalogue No.	Lot/Batch/Serial No.	No. Affected Items
Signed	Date	

Other organisations

Has your organisation supplied potentially affected product to any other organisation?

No

Yes, I/we will forward all the above information to the other organisation/affiliate.

Return completed forms by fax or email to:

Email: RAQA_Pacific@bio-rad.com

FAX: (02) 9914 2888

TGA Reference Number: RC-2023-RN-01051-1

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Appendix 1: Bio-Rad Au Customer letter notification.