



Center for Organ Recovery & Education

204 Sigma Drive  
RIDC Park  
Pittsburgh, PA 15238  
1-800-DONORS-7  
(1-800-366-6777)

May 23, 2001

6074 01 MAY 30 10:07

Center for Biologics Evaluation & Research (CBER)  
Food & Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

RE: Final Rule 21 CFR 1270.21 (d)

Subject: Genetic Systems Hepatitis B Surface Antigen Assay on Cadaver Blood Samples

Dear Sir/Madam:

Enclosed is a copy of a May 23, 2001 letter and data-tape results for two Hepatitis B surface antigen assays sent to Linda Miller, (Technical Support Rep, Bio-Rad Laboratories).

Two of the cadaver samples in question tested positive on initial screen and tested negative on duplicate repeat testing. This phenomenon occurs with frequency and Bio-Rad has not been able to explain why we are experiencing the problem. User technique has been ruled out as a potential cause of the problem. It has been suggested by Bio-Rad technical support staff to delay testing to allow the serum to age, thus avoiding what they are calling a "fresh serum effect". I cannot delay testing due to placement constraints of the corneal tissue. There is nothing stated in the manufacturers package insert regarding a "fresh serum effect".

I ask that you please review the continued problems that are being brought to the company's attention and continue to share our concern. Again, we want to provide the safest possible tissue and corneas to the recipients of these gifts; however, our deepest concern is the loss of these tissues due to either false positive results or delays in testing.

Thank you again for allowing me to share my concerns. I look forward to hearing from you.

Sincerely,



Karen A Brown, BA, MT(ASCP)  
Director of Regulatory Affairs & Laboratory Services

Cc: Anthony Gialamas, MD  
Medical Director, Laboratory

00D-1393

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Center for Organ Recovery & Education

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(1-800-366-6777)

May 23, 2001

Linda Miller  
Bio-Rad Laboratories  
6565 185<sup>th</sup> Avenue NE  
Redmond, Washington 98502  
425-881-8300

Dear Linda,

On April 25 and May 19 we tested cadaver blood in our lab for Hepatitis B surface Ag and the samples tested initially reactive and negative on duplicate repeat testing.

The data tapes **from** both runs are enclosed for your review.

Again, I appreciate any help you can give me in resolving these continued problems.

If you have any questions feel **free** to call me.

Sincerely,

A handwritten signature in cursive script that reads "Karen A. Brown". The signature is written in black ink and is positioned above the typed name.

Karen A Brown, B.A.,MT(ASCP)  
Director of Regulatory Affairs & Laboratory Services

SDP Microplate Assay Testing System V4.82 AVD V4.83 PRD V4.81 - Complete Results

Run # 1 Assay: User(HBsAg) Plate ID: 01U2-19MAY-0330 Master lot number: 059UM1 Exp. date: 30-NOV-01

5-19-01  
7c

Cutoff calculation:  $NC\bar{X} + 0.070 = 0.111$ ,  $NC\bar{X} = 0.041$ ,  $PC\bar{X} = 1.864$ ,  $PC1\bar{X} = 0.389$

Cutoff relationship: {Reactive is greater than or equal to cutoff} Validation protocol: GSC HBsAg EIA 2.0, Ver 1.00

Reader type: (SDP PR2100 V1.00) Dual wavelength reading: (Sample filter: 450 nm, Reference filter: 630 nm)

Load direction: A-H Loading method: MANUAL Curve fit method: NONE

Function	Tech Name	Start Time	End Time	Time Elapsed	(Assay date & time: 19-MAY-01 06:30)
enter info	MH				(Read date & time: 19-MAY-01 06:30)
load plate	MH				(Print date & time: 19-MAY-01 06:31)
inc 1	NH	03:45	04:45	1:01	
inc 2	a	04:53	05:53	1:00	
inc 3		05:59	06:29	0:31	(Total assay time: 2:46)

Key: - .. Nun-reactive      R+ .. Reactive      -- .. 2 of 3 tests Non-Reactive      \* .. Value Over Range  
 G- .. N&reactive Gray Zone      R2- .. Retest Non-reactive      +++ .. (2 or 3) of 3 tests Reactive      < .. Value Under Range  
 G+ .. Reactive Gray Zone      R2+ .. Retest Reactive      ??? .. Error      INV .. Assay Invalid

Well	Sample ID	O.D.	Result	Well	Sample ID	O.D.	Result	Well	Sample ID	O.D.	Result
A1	POS CTRL	1.853	R+ ok	E1	NEG CTRL	0.031	- ok	H1	010561861	0.028	-
B1	POS CTRL	1.874	R+ ok	F1	NEG CTRL	0.063	- ok	a 2	01051802	0.147	R+
C1	POS CTRL1	0.400	R+ ok	61	NE6 CTRL	0.028	- ok	B2	01051803	0.038	-
D1	POS CTRL1	0.378	R+ ok								

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END OF REPORT

SDP Microplate Assay Testing System V4.82 AVD V4.83 PRD V4.81 - Complete Results

5-19-01  
Z

Run # 2 (Assay: User(HBsAg)) Plate ID: 02U2-19MAY-0632 Master lot number: 059UM1 Exp. date: 30-NOV-01

Cutoff calculation:  $NC\bar{X} + 8.070 = 0.140$   $NC\bar{X} = 0.070$   $PC\bar{X} = 2.001$   $PC1\bar{X} = 0.495$   
 Cutoff relationship: [Reactive is greater than or equal to cutoff] Validation protocol: GSC HBsAg EIA 2.0, Ver 1.00

Reader type: (SDP PR2100 Vi.001 Dual wavelength reading: (Sample filter: 450 nm, Reference filter: 630 nm)

Load direction: A->H Loading method: MANUAL Curve fit method: NONE

Function	T e c h Name	Start Time	End Time	Tie Elapsed Time	(Assay date & time: 19-MAY-01 09:29)
enter info	JL				(Read date & time: 19-MAY-01 09:29)
load plate	JL				(Print date & time: 19-MAY-01 09:29)
inc 1	JL	06:46	07:46	1:00	
inc 2	a	07:52	08:52	1:00	
inc 3		08:58	09:29	0:31	(Total assay time: 2:43)

- . = Non-reactive R+ . . Reactive  
 G- . . Non-reactive Gray Zone R2- . . Retest Non-reactive  
 G+ . . Reactive Gray Zone I R2+ . . Retest Reactive  
 --- . . 2 of 3 tests Non-Reactive \* . . Value Over Range  
 +++ . . (2 or 3) of 3 tests Reactive ( . . Value Under Range  
 ??? . . Error I INV . . Assay Invalid

Well Sample ID	O.D.	Result	Well Sample ID	O.D.	Result	Well Sample ID	O.D.	Result
A1 POS CTRL	1.996	R+ ok	D1 POS CTRL1	0.485	R+ ok	G1 NEG CTRL	0.051	- ok
B1 POS CTRL	2.012	R+ ok	E1 NEG CTRL	0.077	- ok	H1 01051802	0.025	- -
C1 POS CTRL1	0.504	R+ ok	F1 NEG CTRL	0.001	- ok	a2 01051802	0.043	- -

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END OF REPORT

SDP Microplate Assay Testing System V4.P AVD V4.83 PRD V4.81 - Complete Results .

Run # 1 Assay: User(HBsAg) Plate ID: 01U2-24APR-2349 Master lot number: 010UM1 Exp. date: L2-OCT-01

Cutoff calculation:  $NC\bar{X} + 0.070 \cdot 0.1??$   $NC\bar{X} = 0.052$   $PC\bar{X} = 1.790$   $PC1\bar{X} = 0.388$

Cutoff relationship: (Reactive is greater than or equal to cutoff) Validation protocol: GSC HBsAg EIA 2.0, Ver 1.00

Reader type: (SDP PR2100 V1.00) Dual wavelength reading: (Sample filter: 450 nm, Reference filter: 630 nm)

Load direction: A->H Loading method: MANUAL Curve fit method: NONE

Function	Tech Name	Start Time	End Time	Elapsed Time	(Assay date & time: 25-APR-01 02:36)
enter info	MH				[Read date & time: 25-APR-01 02:36]
load	plate . 65				(Print date & time: 25-APR-01 02:37)
inc 1	MH	23:52	00:53	1:00	
inc 2	MH	00:58	01:59	1:00	
inc 3		02:05	02:35	0:30	(Total assay time: 2:44)

Key: - .. Non-reactive R+ . . . Reactive  
 G- .. Non-reactive Gray Zone R2- .. Retest Non-reactive  
 G+ .. Reactive Gray Zone R2+ .. Retest Reactive  
 --- .. 2 of 3 tests Non-Reactive  
 +++ .. (2 or 3) of 3 tests Reactive  
 ??? .. Error  
 • .. Value Over Range  
 { .. Value Under Range  
 INV .. Assay Invalid

Well	Sample ID	O.D.	Result	Well	Sample ID	O.D.	Result	Well	Sample ID	O.D.	Result
A1	POS CTRL	1.866	R+ ok	D1	POS CTRL1	0.368	R+ ok	61	NEG CTRL	0.055	- ok
B1	POS CTRL	1.714	R+ ok	E1	NEG CTRL	0.102	- High	H1	01042402	0.185	Rt
C1	POS CTRL1	0.407	R+ ok	F1	NEG CTRL	0.049	- ok				

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END OF REPORT

SD-P Microplate Assay Testing System V4.02 AVD V4. 83 PRD V4.81 - Complete Results

Run # 2 Assay: User (HBsAg) Plate ID: 0212-25APR-0241 Blaster lotnumber: 010UM1 Exp. date: 12-OCT-01

Cutoff calculation:  $NC\bar{X} + 0.070 = 0.158$   $NC\bar{X} = 0.088$   $PC\bar{X} = 1.630$   $PC1\bar{X} = 0.383$   
 Cutoff relationship: (Reactive is greater than or equal to cutoff) Validation protocol: GSC HBsAg EIA 2.0, Ver 1.00

Reader type: (SDP PR2100 VI.001 Dual wavelength reading: (Sample filter: 450 nm, Reference filter: 630 nm)  
 Load direction: A->H Loading method: MANUAL Curve fit Method: NONE

Function	Tech Name	Start Time	End Time	Elapsed Time	(Assay date & time: 25-APR-01 05:19)
enter info	NH				(Read date & time: 25-APR-01 05:19)
load plate	NH				(Print date & time: 25-APR-01 05:20)
inc 1	NH	02:42	03:42	1:00	
inc 2	NH	03:46	04:46	1:00	
inc 3		04:48	05:19	0:30	(Total assay time: 2:37)

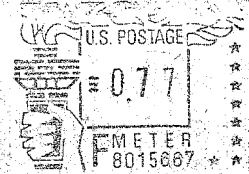
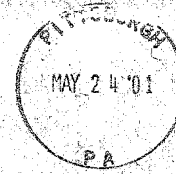
Key: - . . Non-reactive      R+ . . . Reactive      -- . . 2 of 3 tests Non-Reactive      \* . . Value Over Range  
 G- . . Non-reactive Gray Zone      R2- . . Retest Non-reactive      +++ . . (2 or 3) of 3 tests Reactive      ( . . Value Under Range  
 G+ . . Reactive Gray Zone      R2+ . . Retest Reactive      ??? . . . Error      INV . . Assay Invalid

Well	Sample ID	O.D.	Result	Well	Sample/ID	O.D.	Result	Well	Sample ID	O.D.	Result
A1	POS GTRL	1.717	R+ ok	D1	POS CTRL1	0.361	R+ ok	61	NE6 CTRL	0.081	- ok
B1	POS CTRL	1.542	R+ ok	E1	NEG CTRL	0.096	- ok	H1	01042402	0.095	-
C1	POS CTRL1	0.404	R+ ok	F1	NE6 CTRL	0.086	- ok	A2	01042402	0.062	-

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