

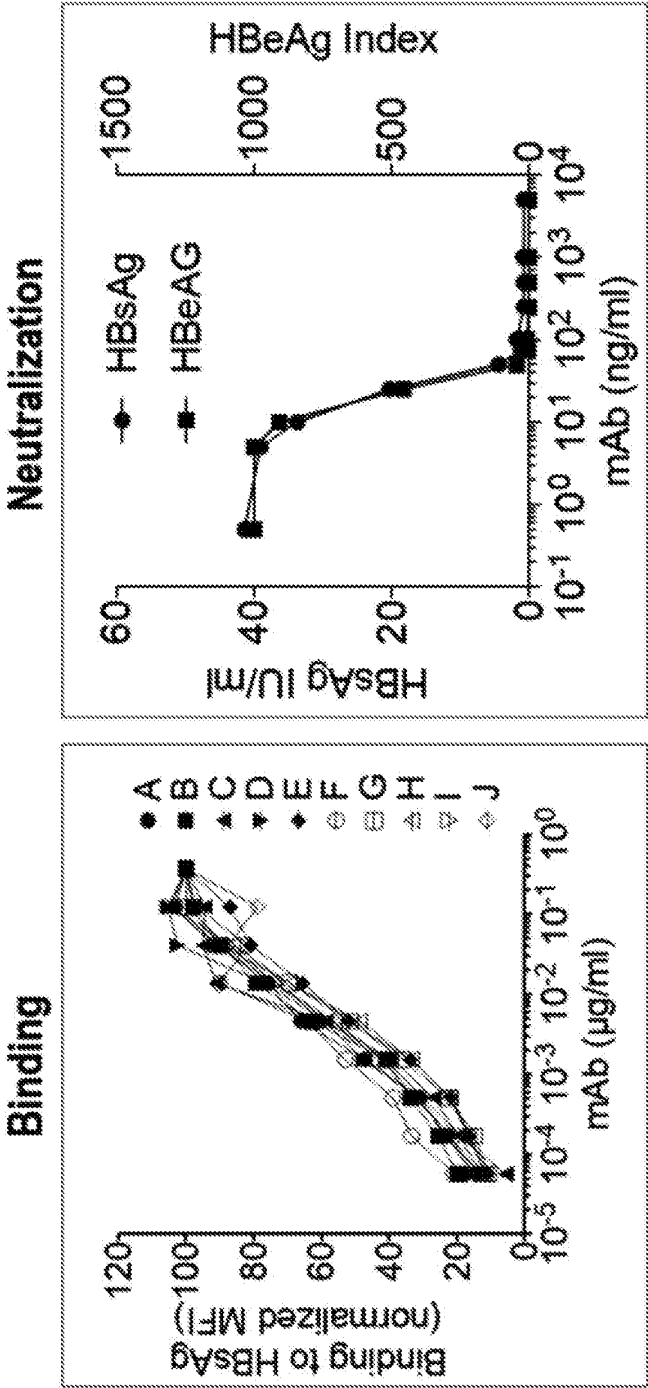


FIG. 1

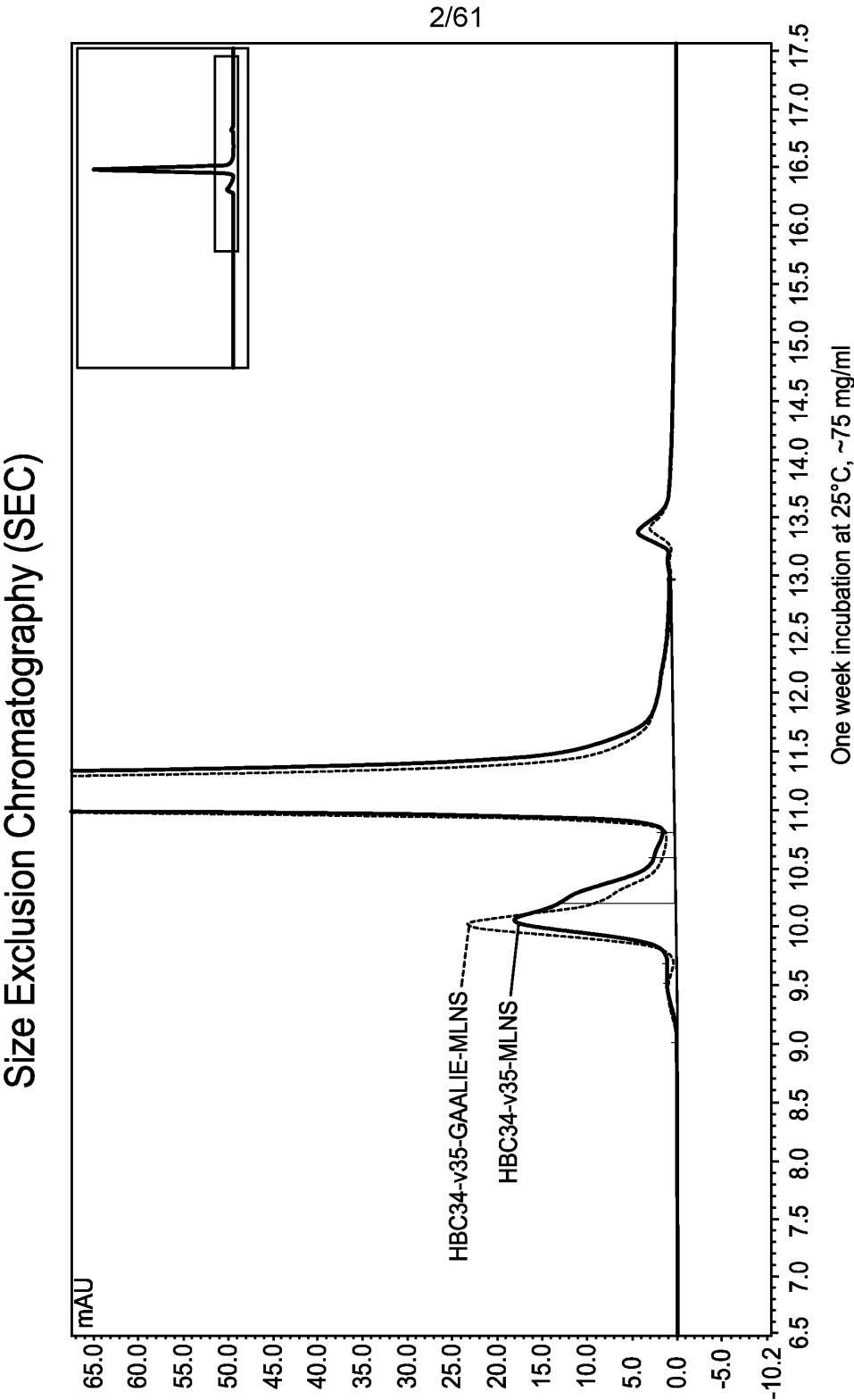


FIG. 2

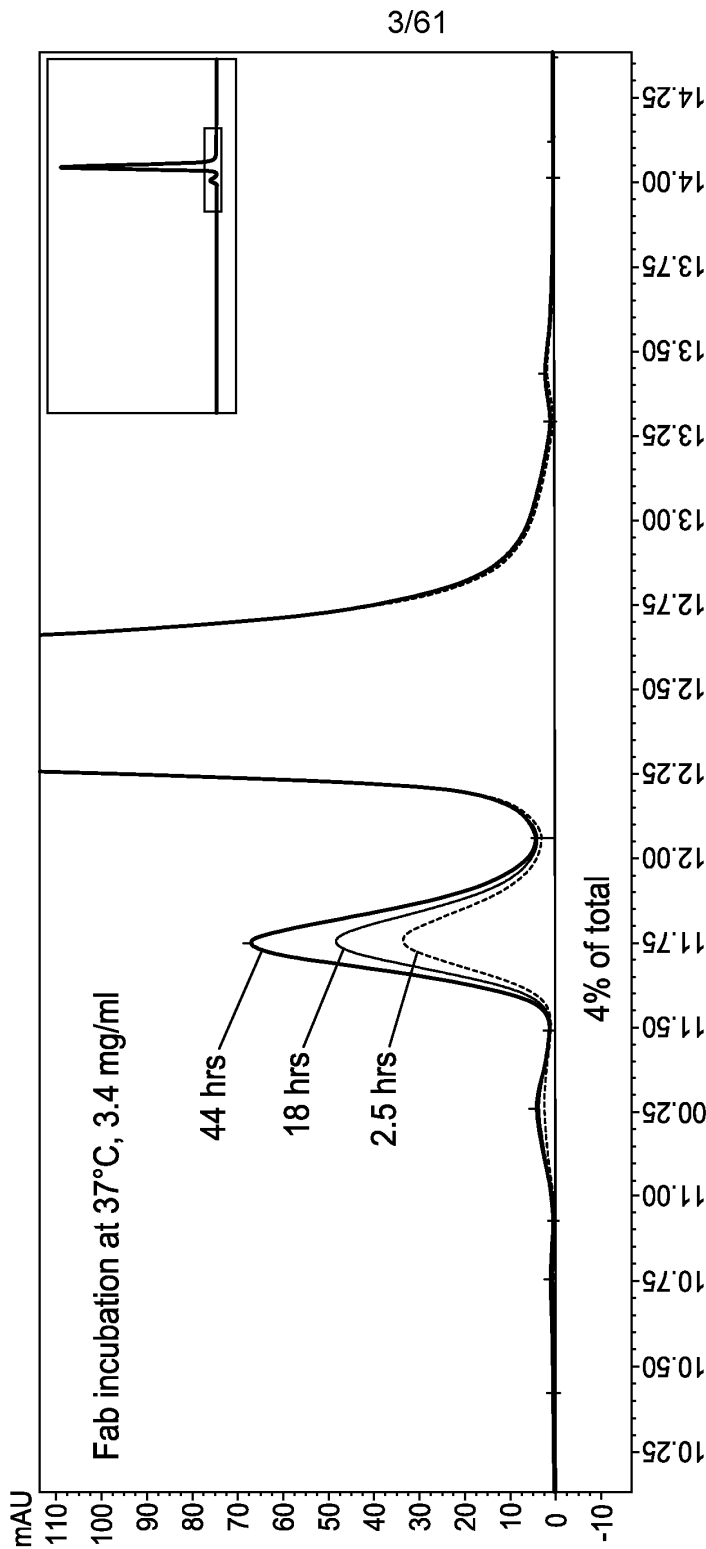


FIG. 3

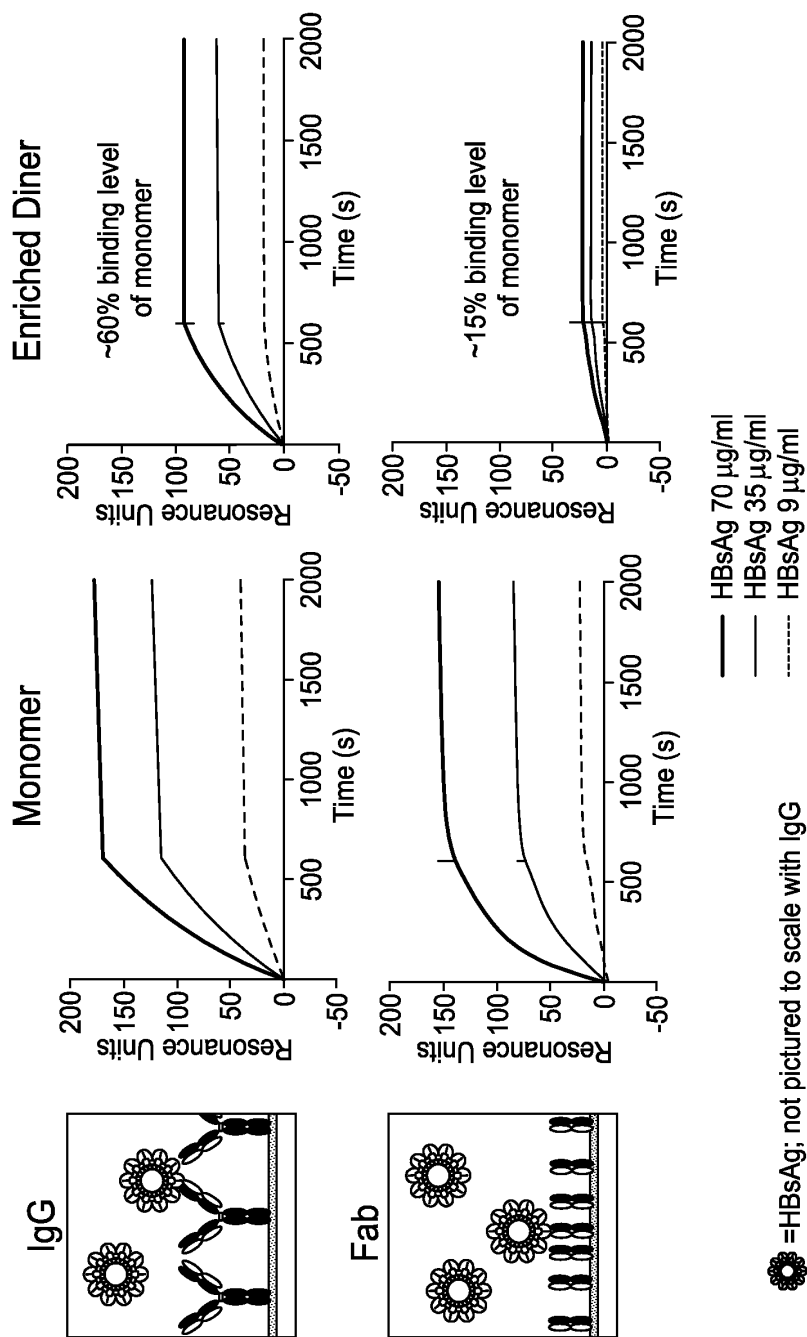


FIG. 4

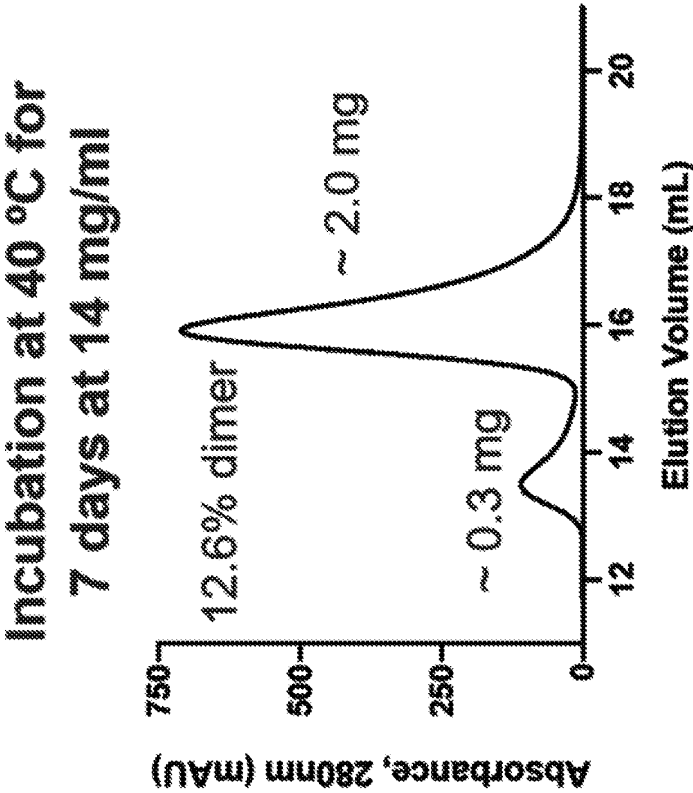


FIG. 5A

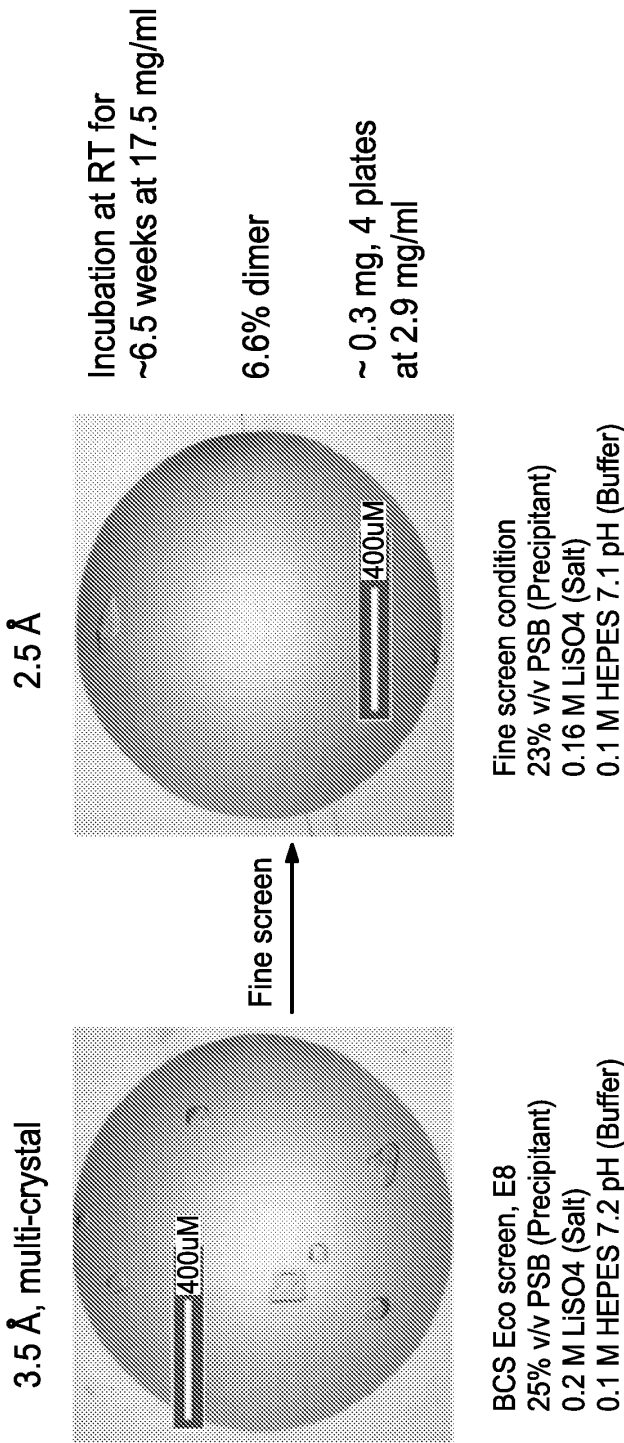


FIG. 5B

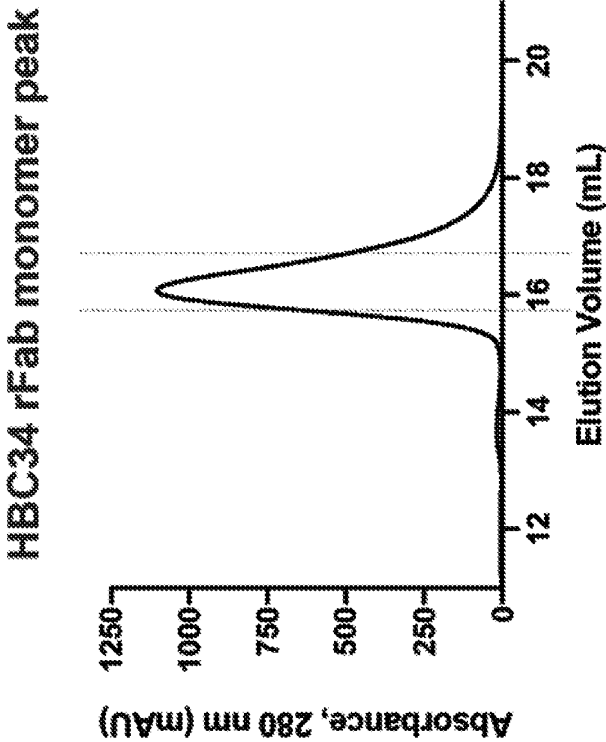


FIG. 6A

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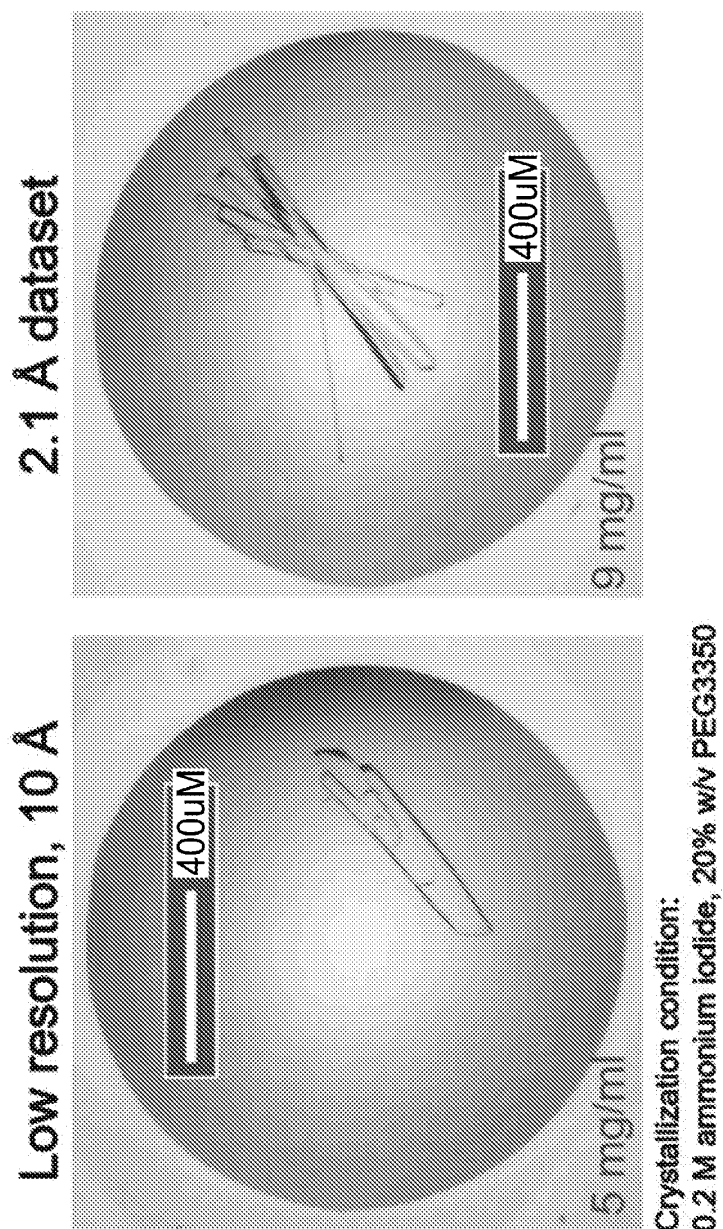


FIG. 6B

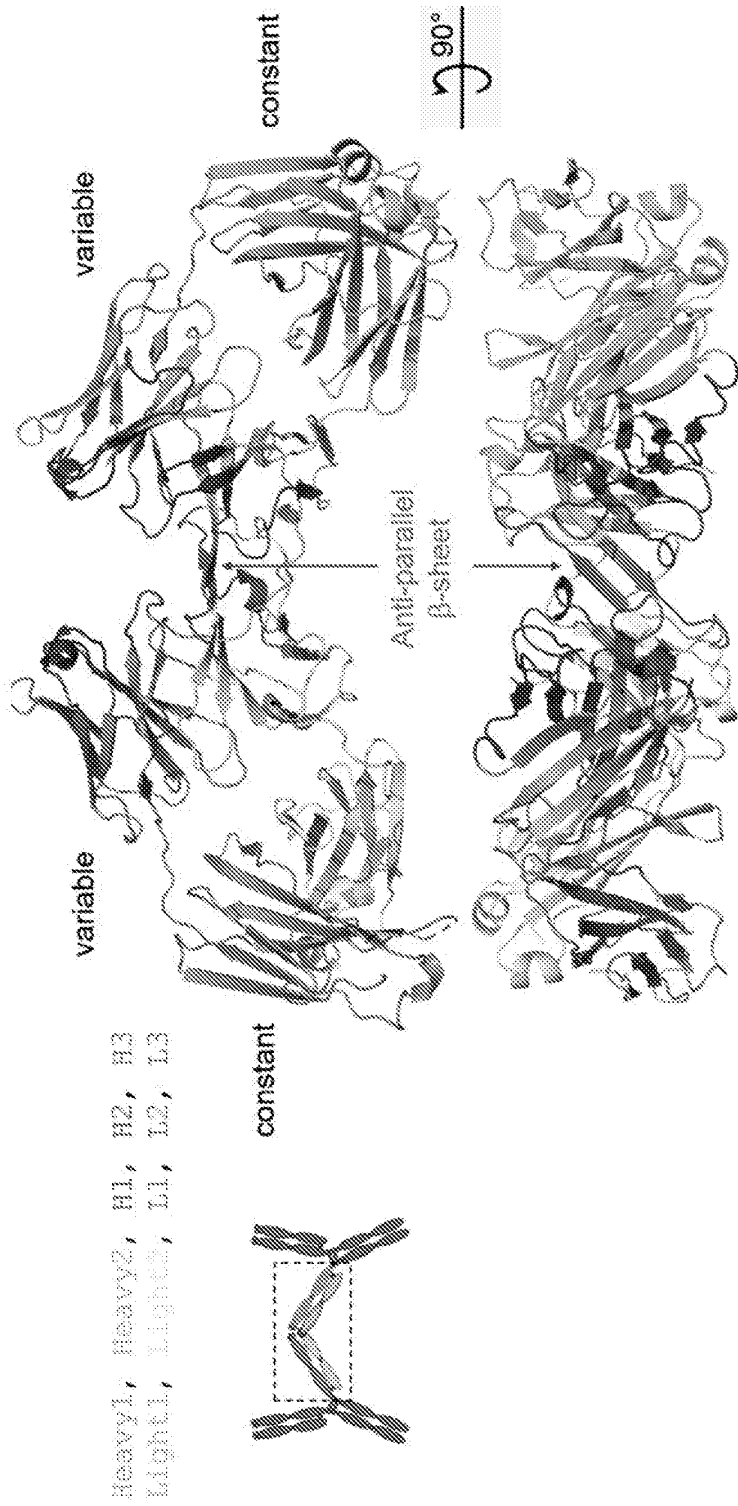


FIG. 7

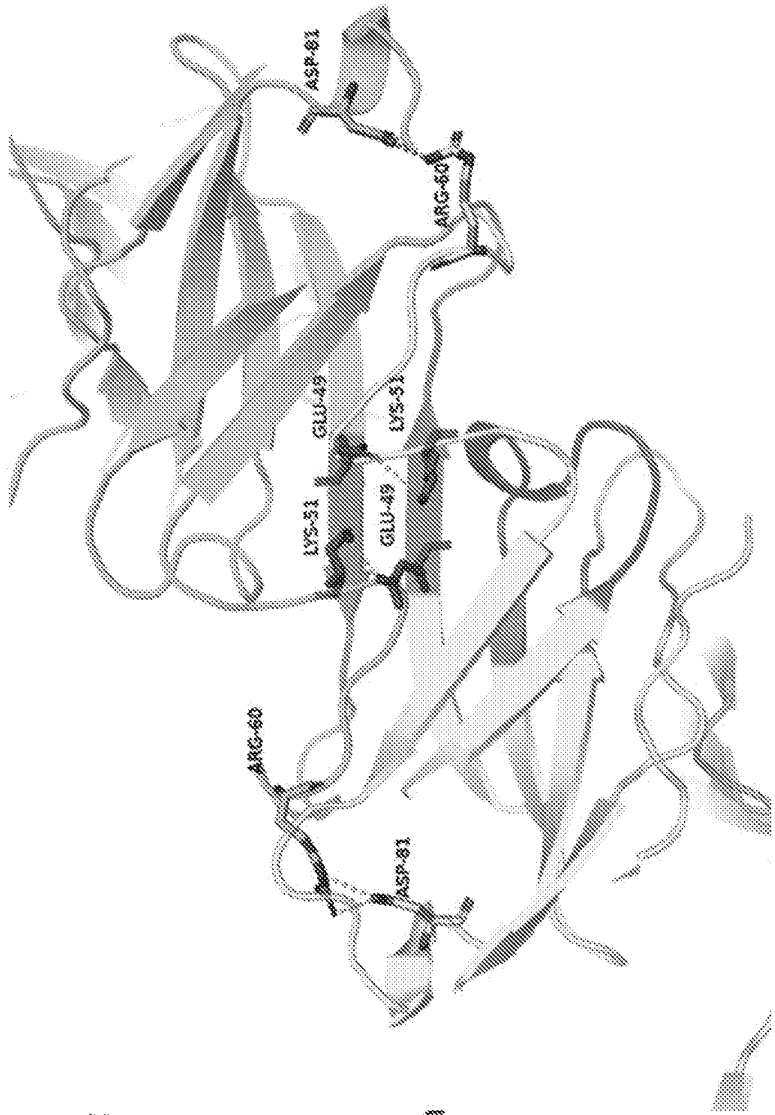


FIG. 8

Heavy1, Heavy2
Light1, Light2, L2

C- ...Lys-Val-Glu...-N
| | | |
N- ...Glu-Val-Lys...-C

--- = salt bridge
--- = hydrophobic intxn

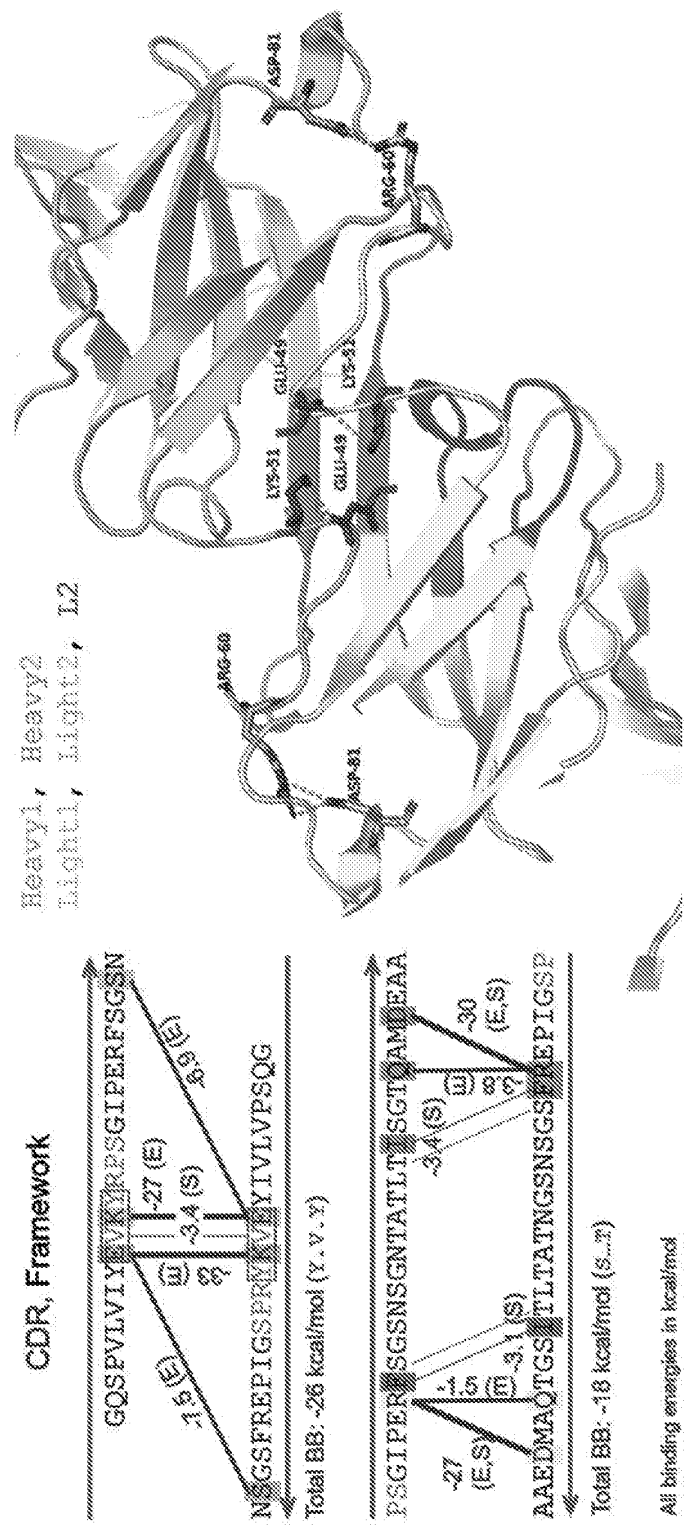
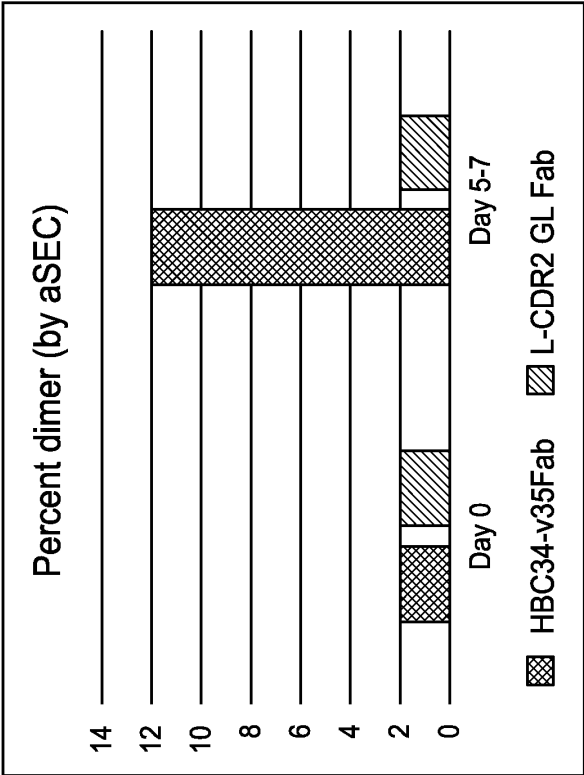


FIG. 9



FIG. 10



Fab	Temperature	Conc	Duration
HBC34-v35	40°C	14 mg/ml	7 days
L-CDR2 GL	40°C	26 mg/ml	5 days

FIG. 11A

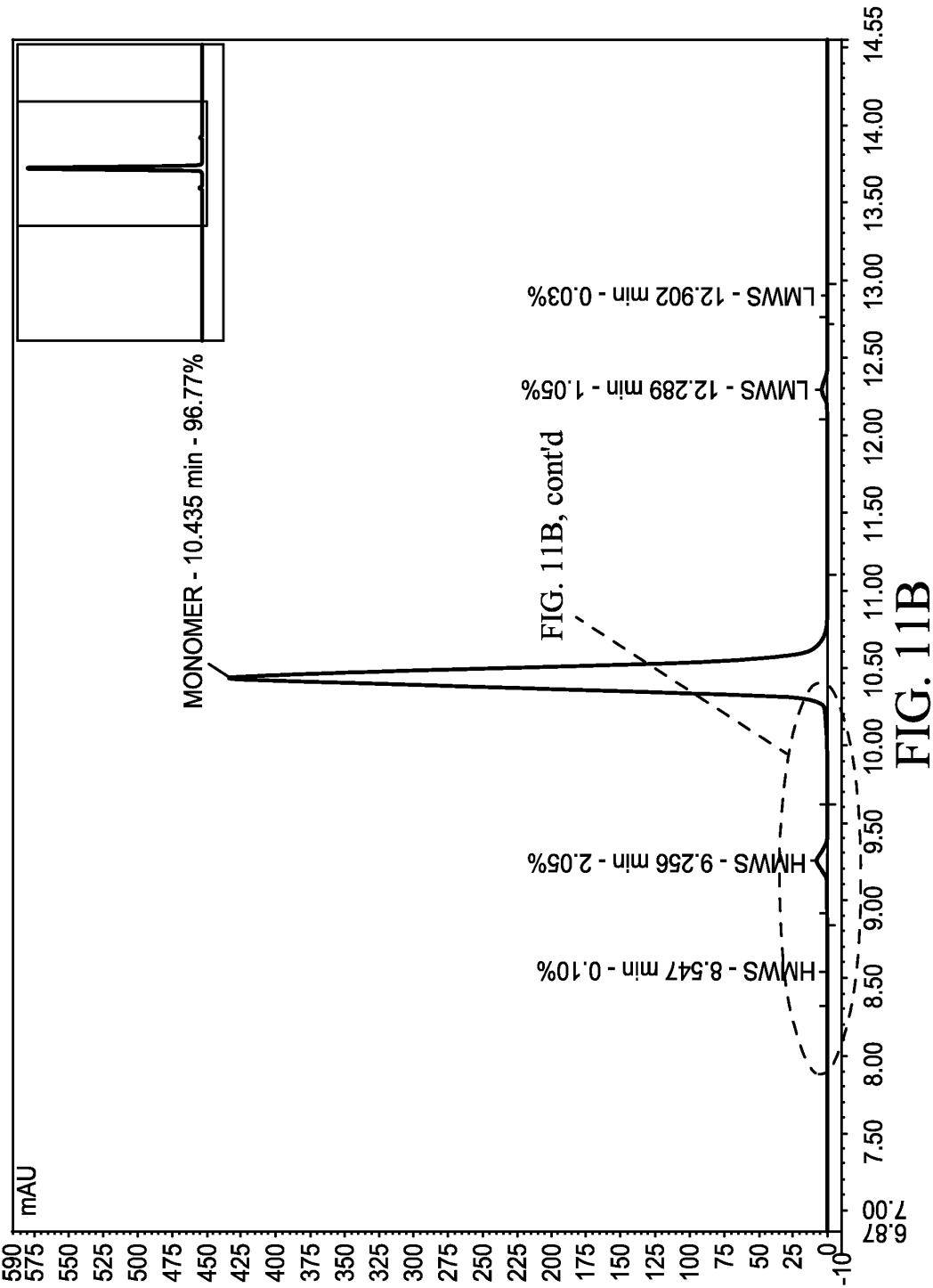


FIG. 11B

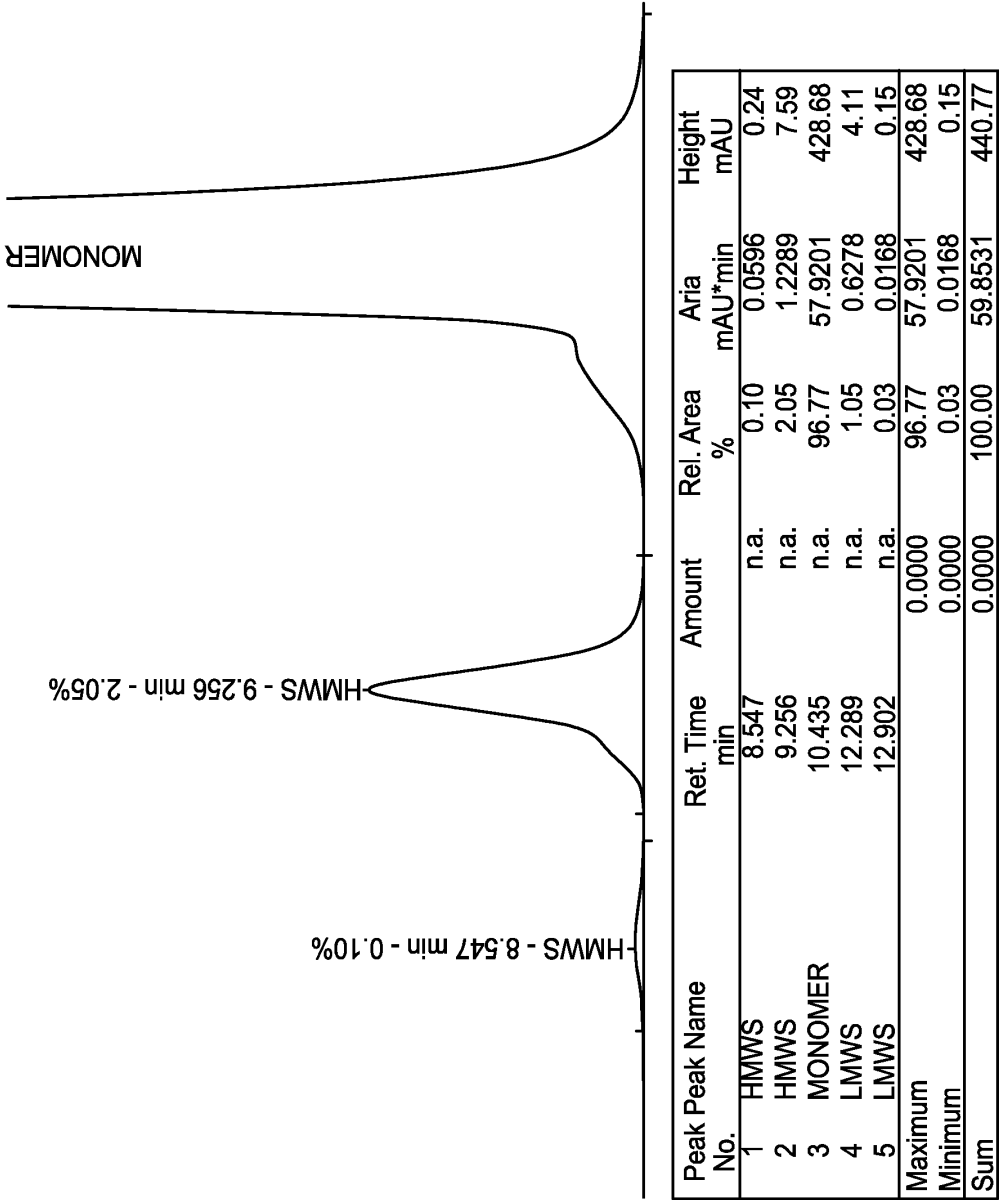
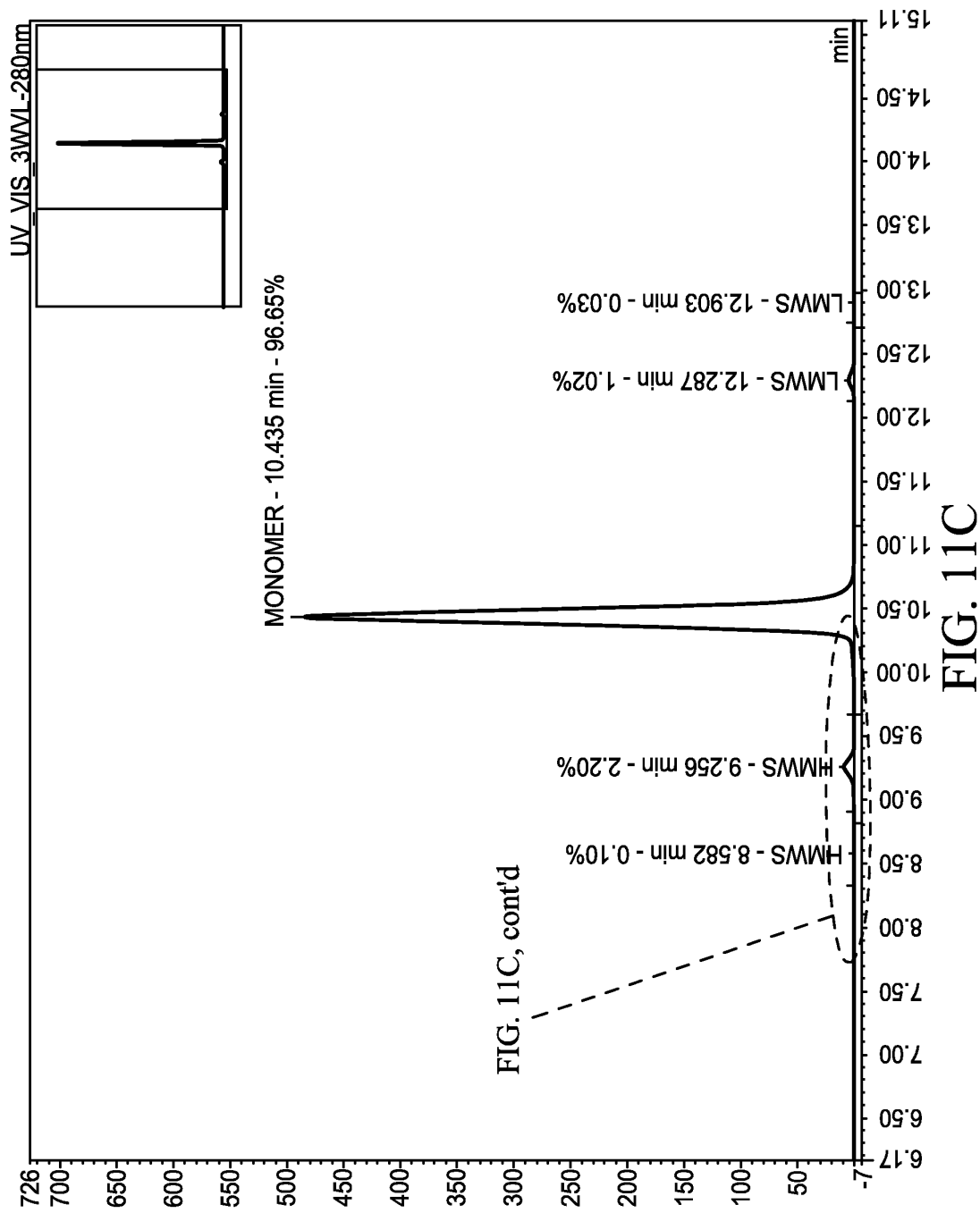


FIG. 11B, cont'd



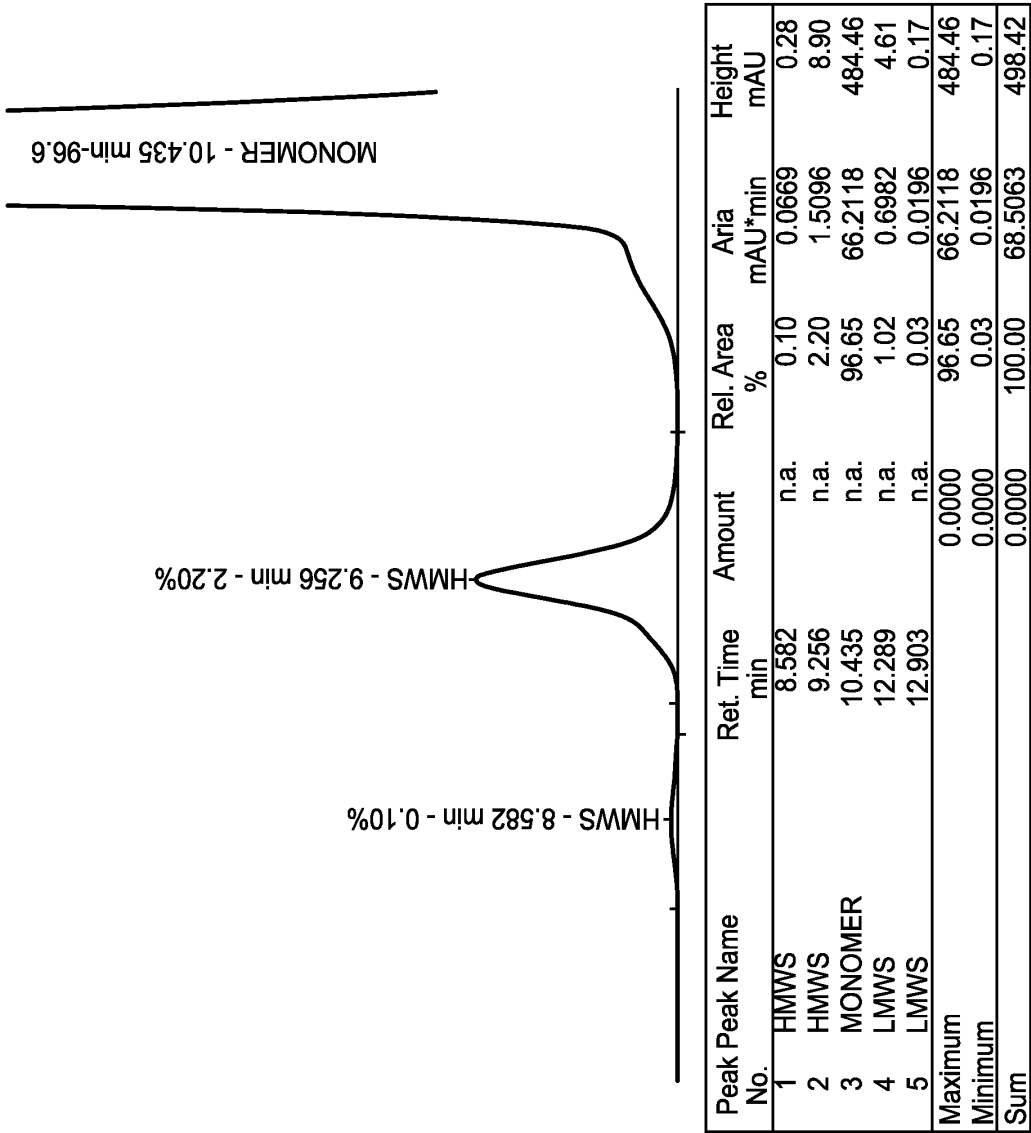


FIG. 11C, cont'd

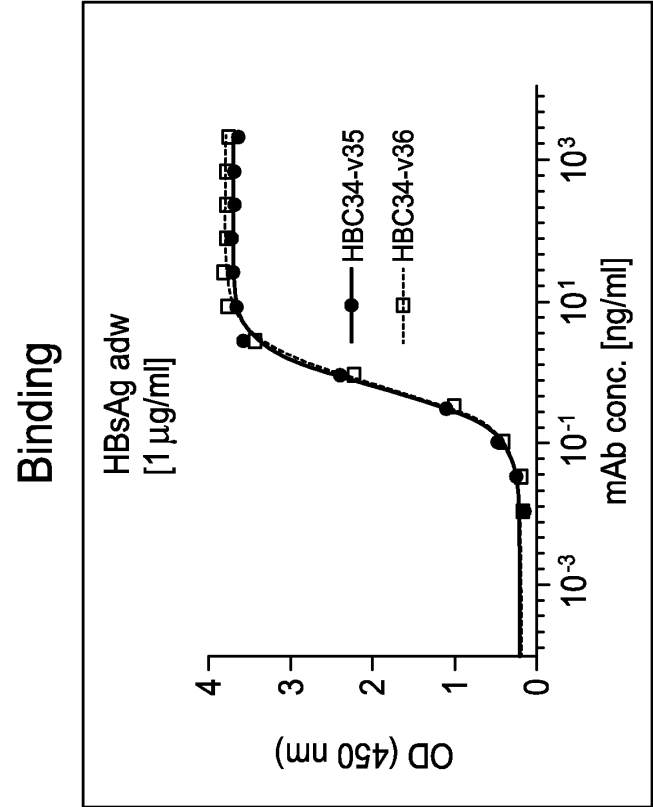


FIG. 12

Neutralization

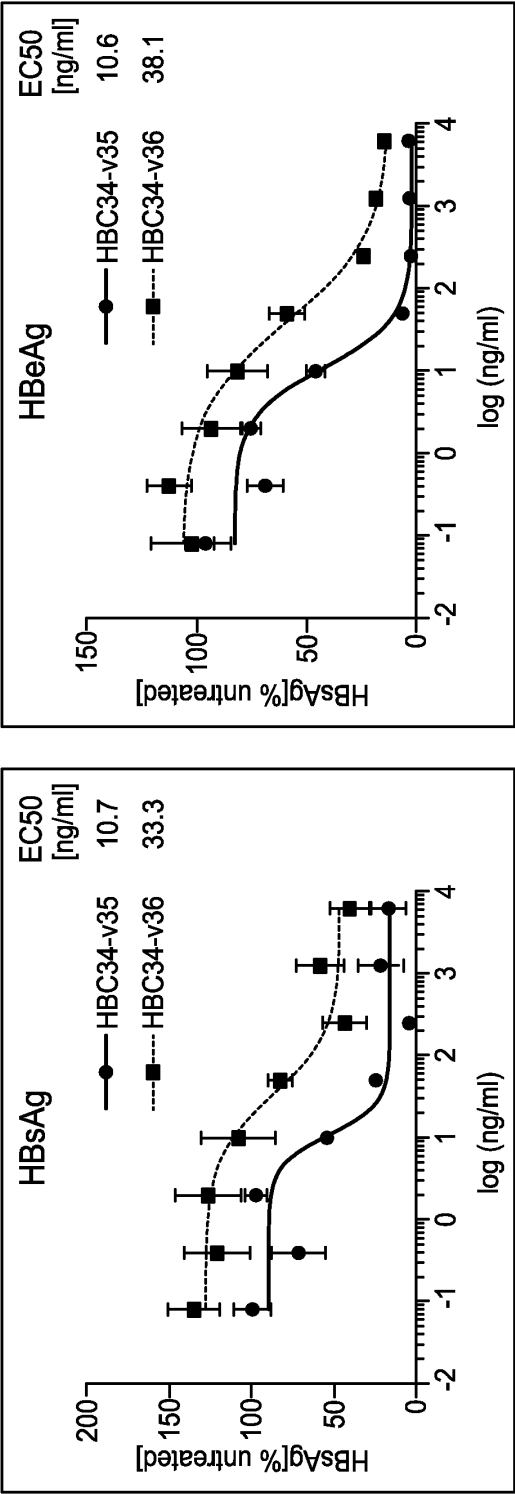


FIG. 13

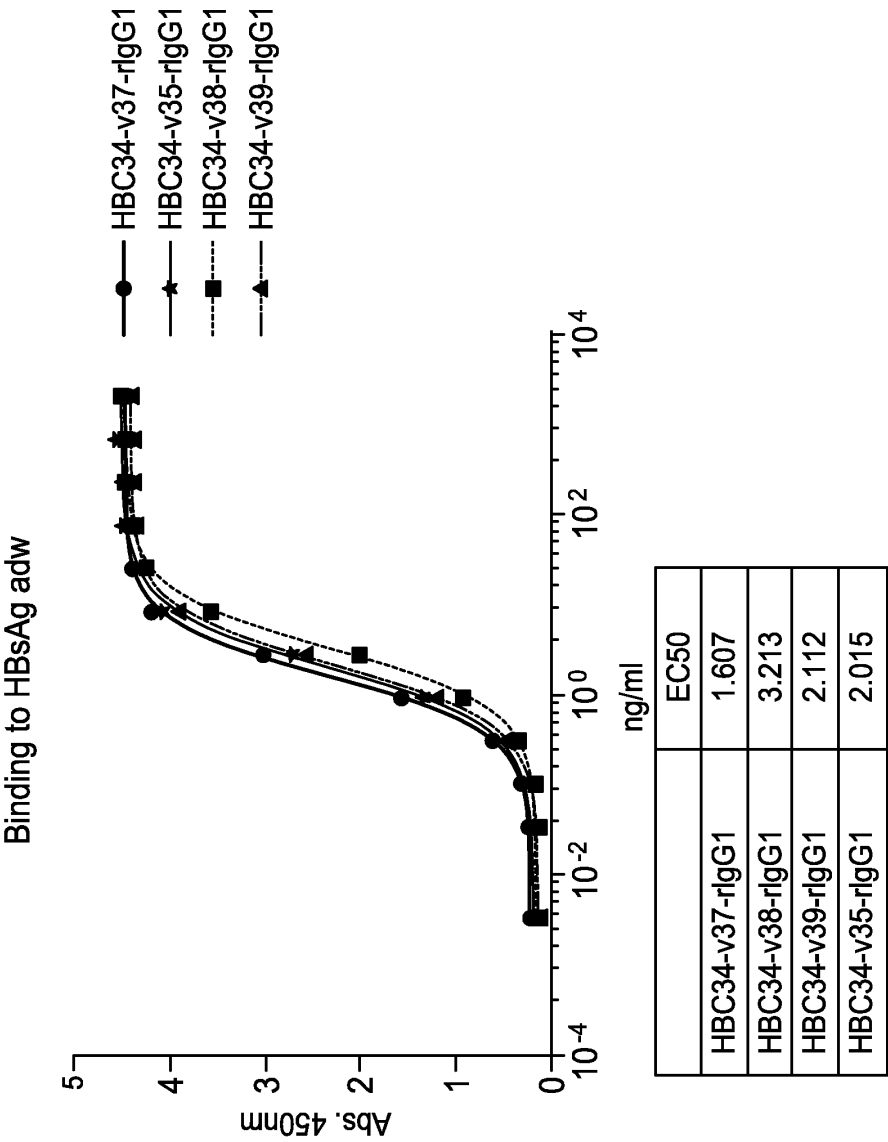


FIG. 14A

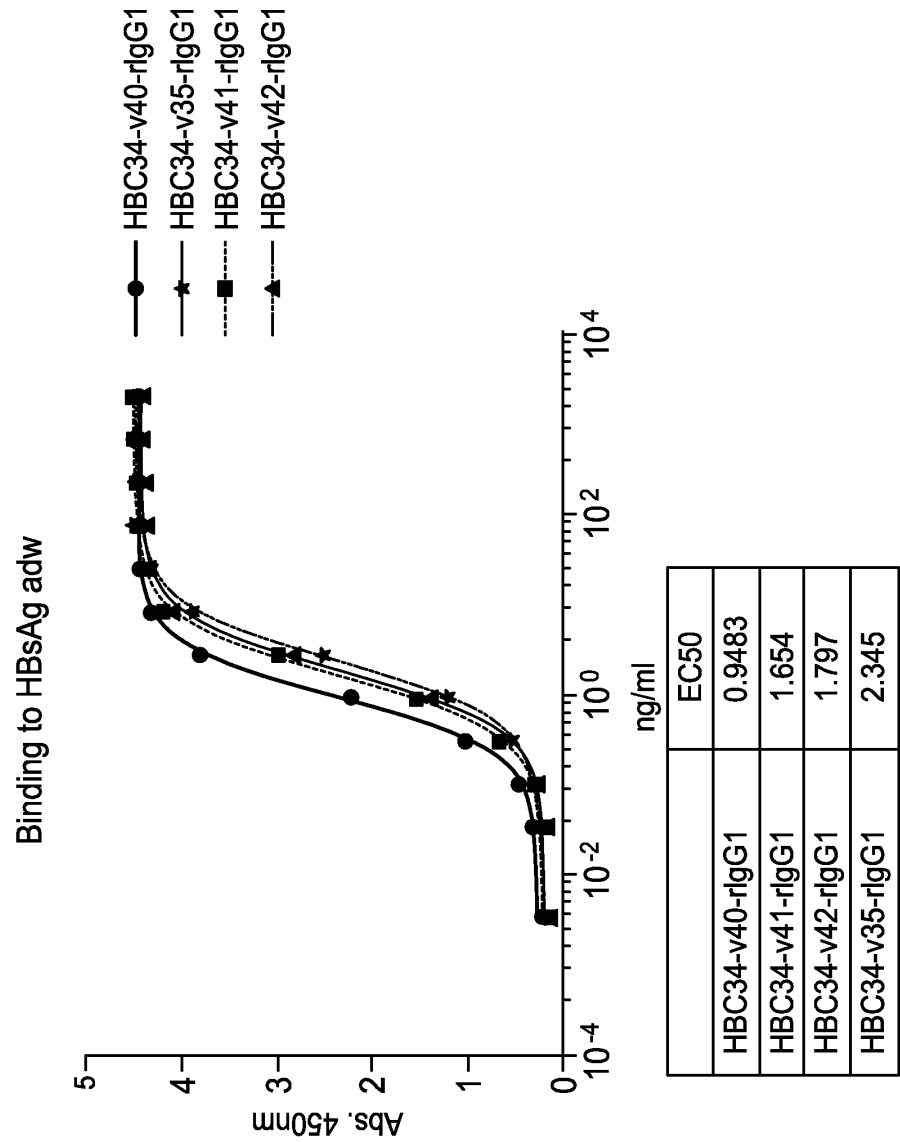


FIG. 14B

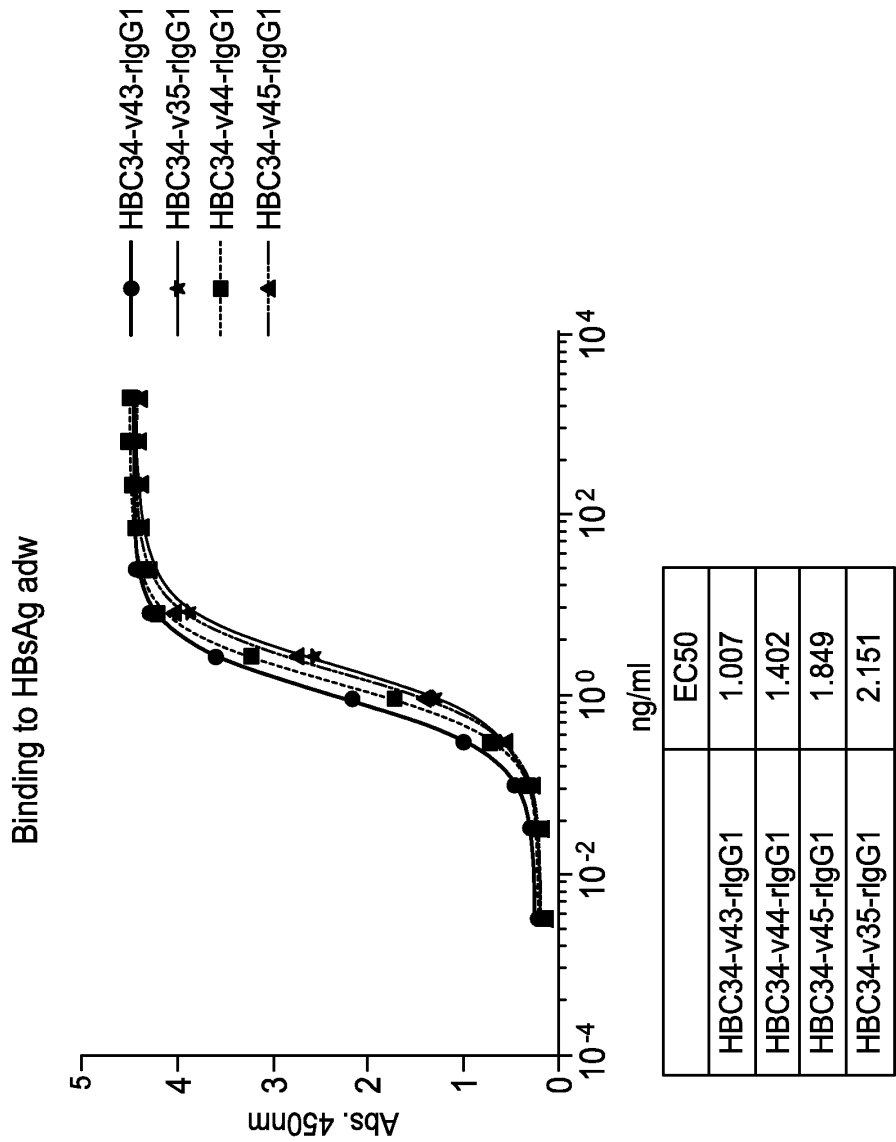


FIG. 14C

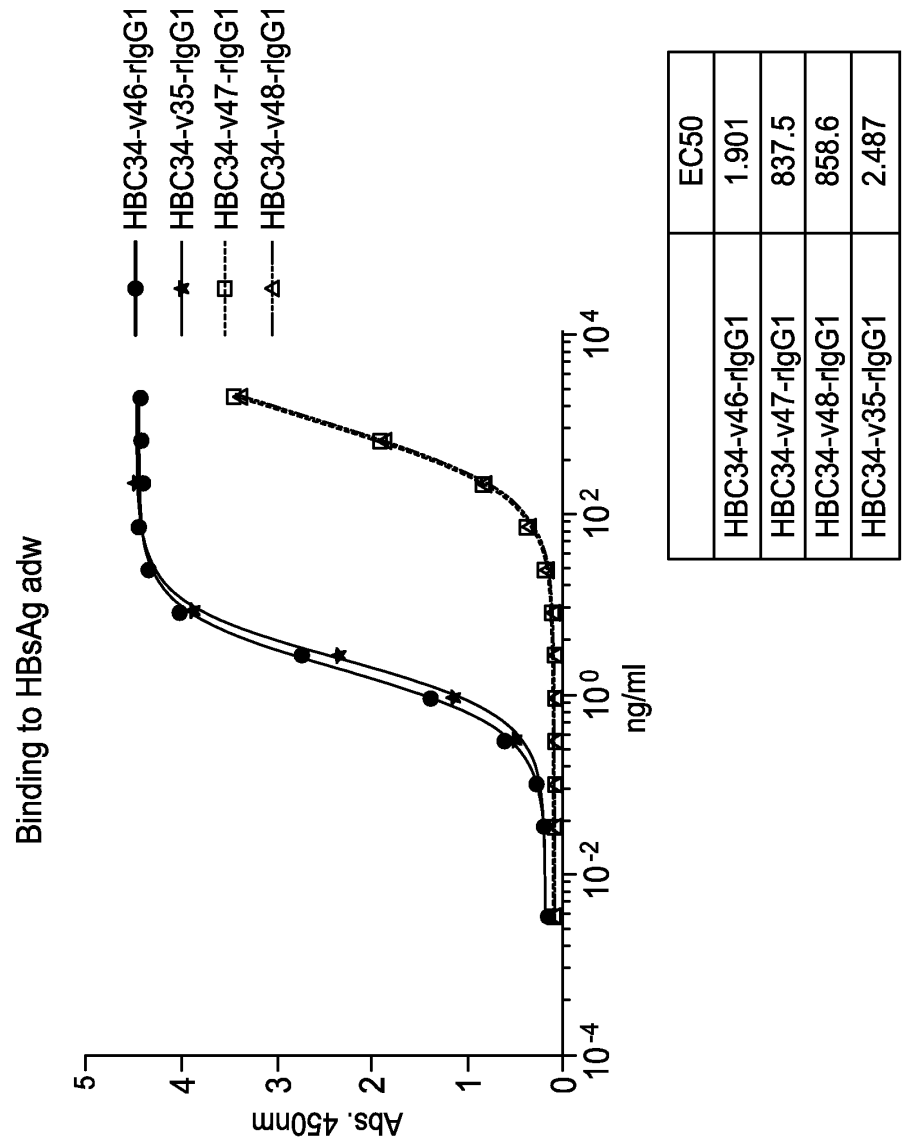


FIG. 14D

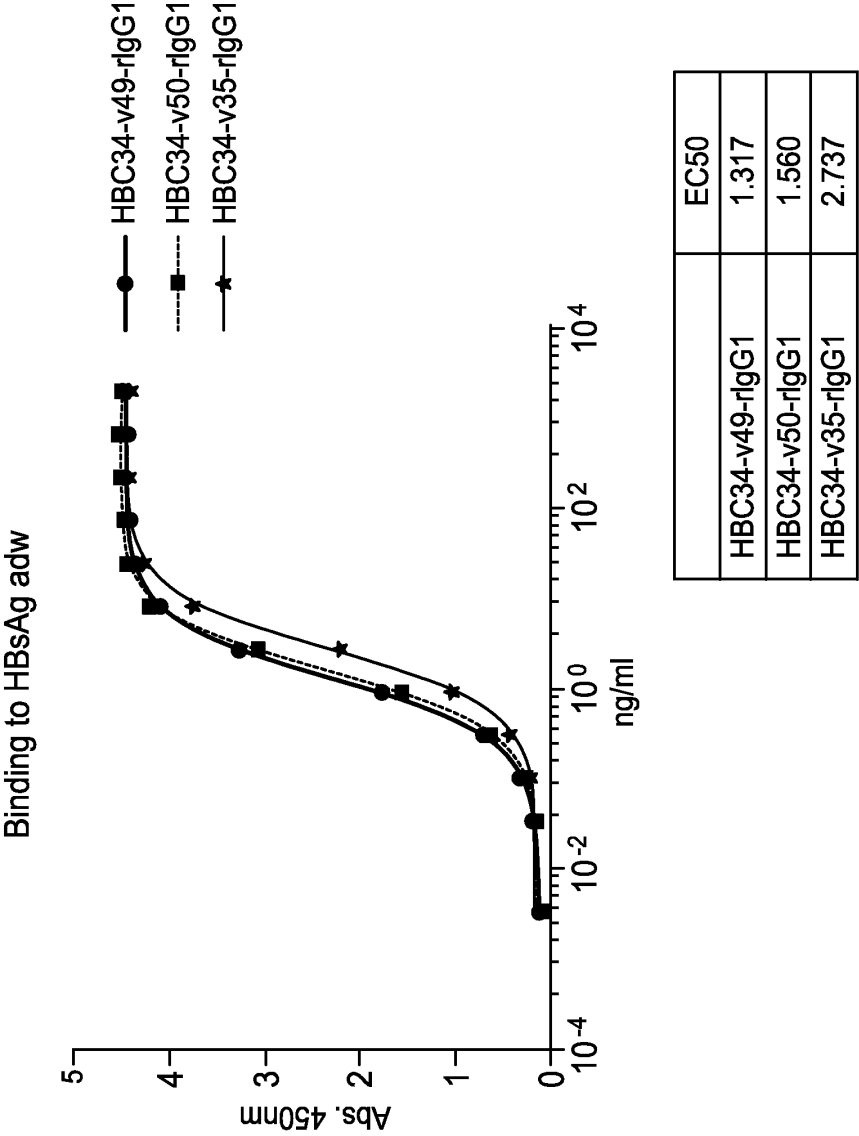


FIG. 14E

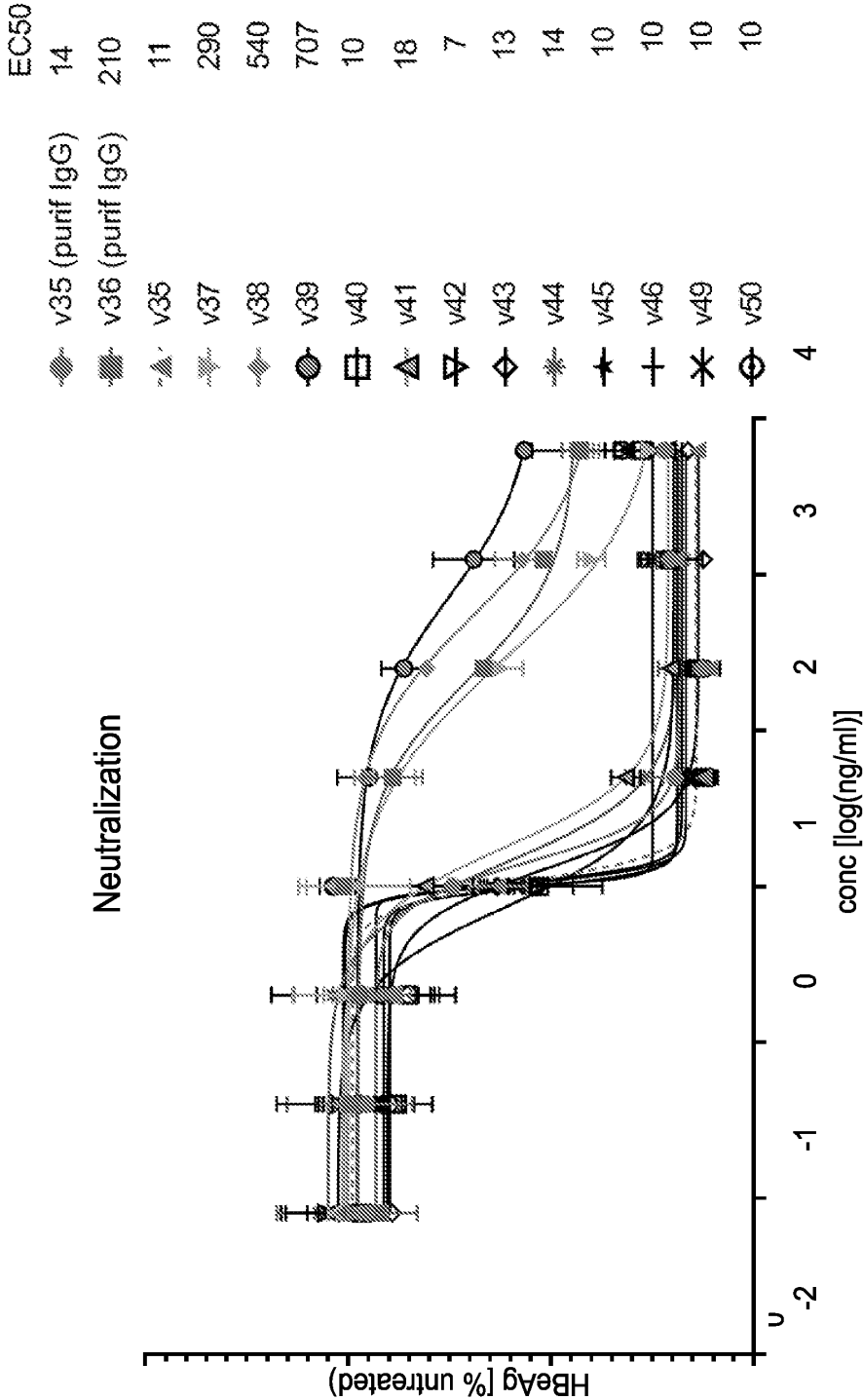


FIG. 15

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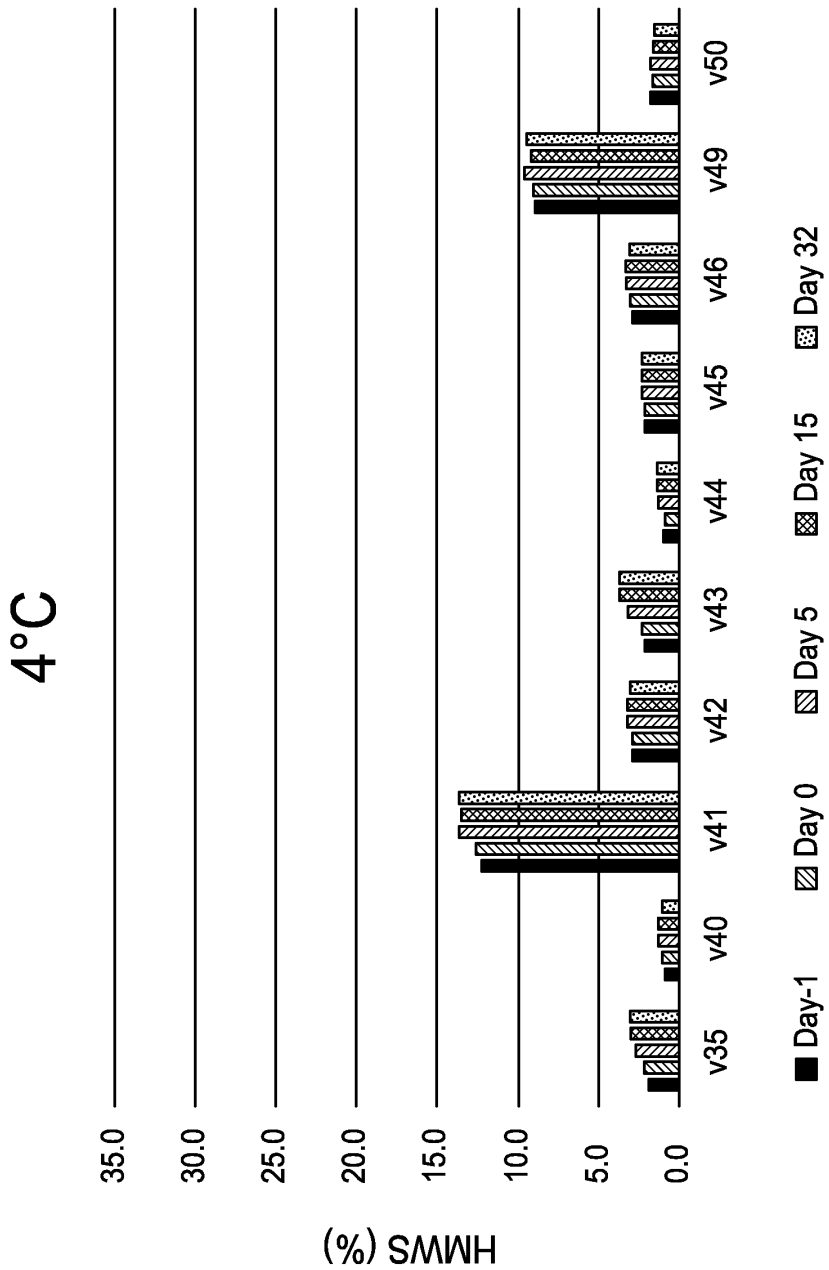


FIG. 16A

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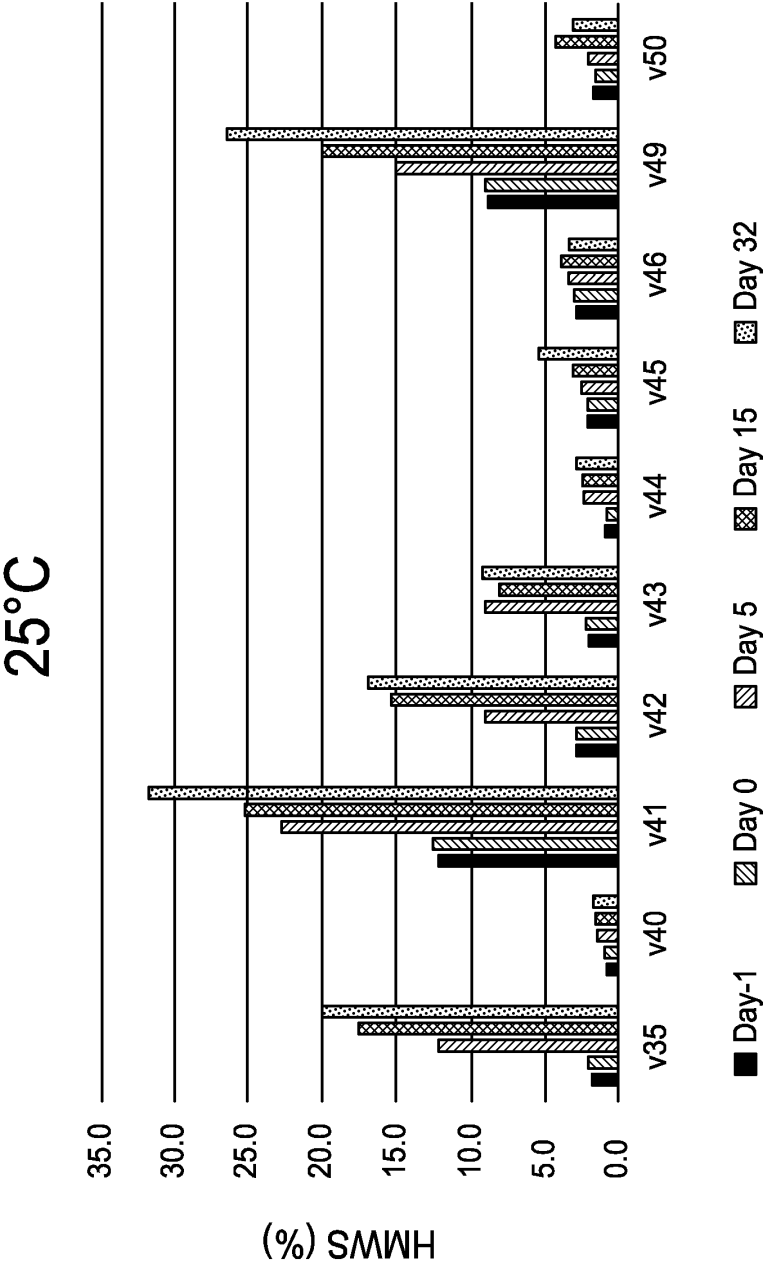


FIG. 16B

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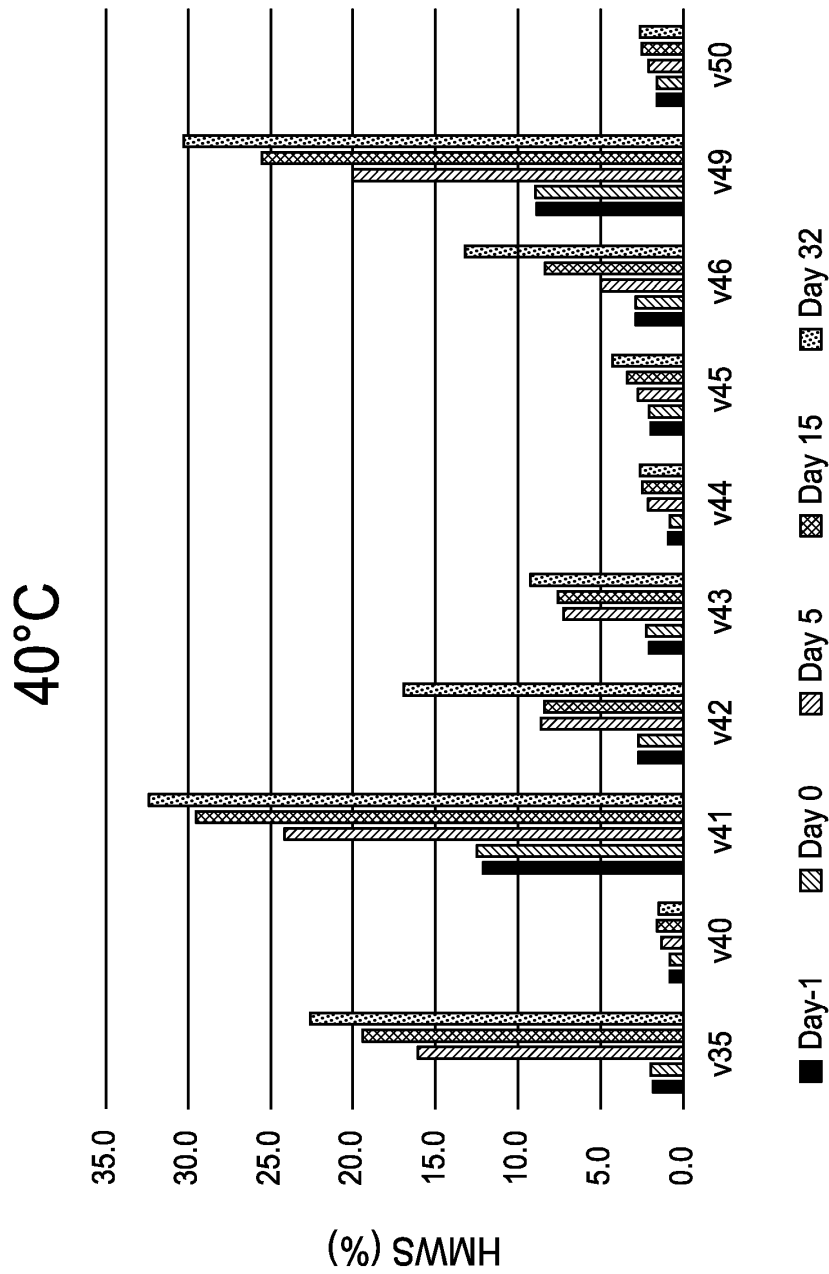


FIG. 16C

	V35 (WT)	V40	V41	V42	V43	V44	V45	V46	V49	V50
HMWS(%) 40C_day32	22.7	1.6	32.4	17.1	9.3	2.7	4.4	23.4	30.4	2.7

FIG. 16D

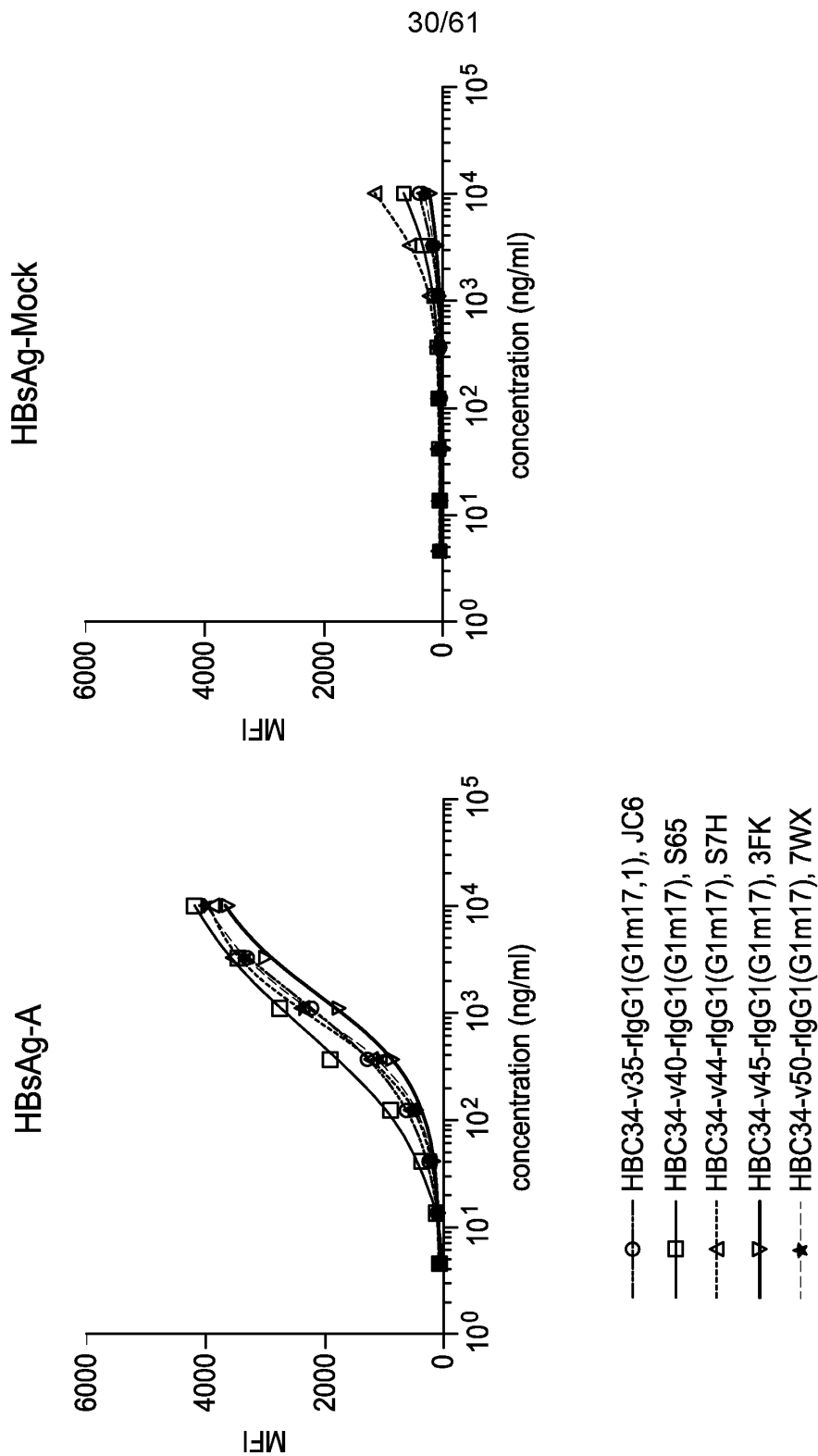
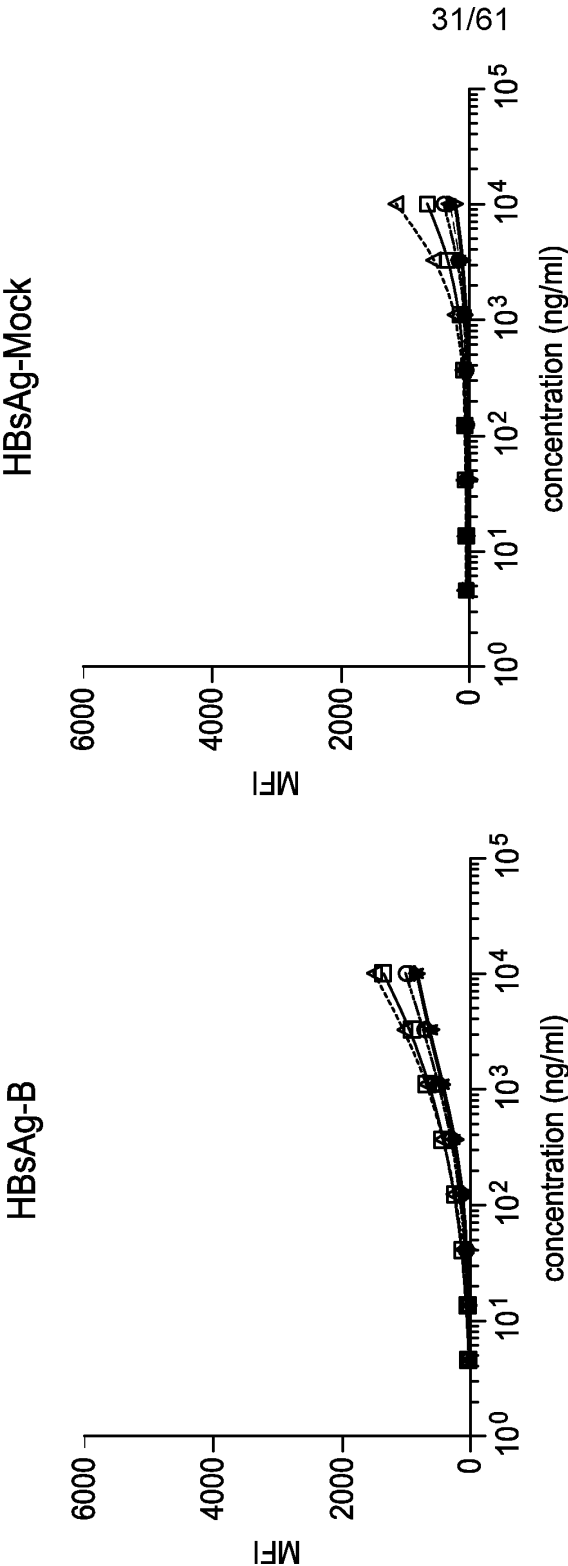
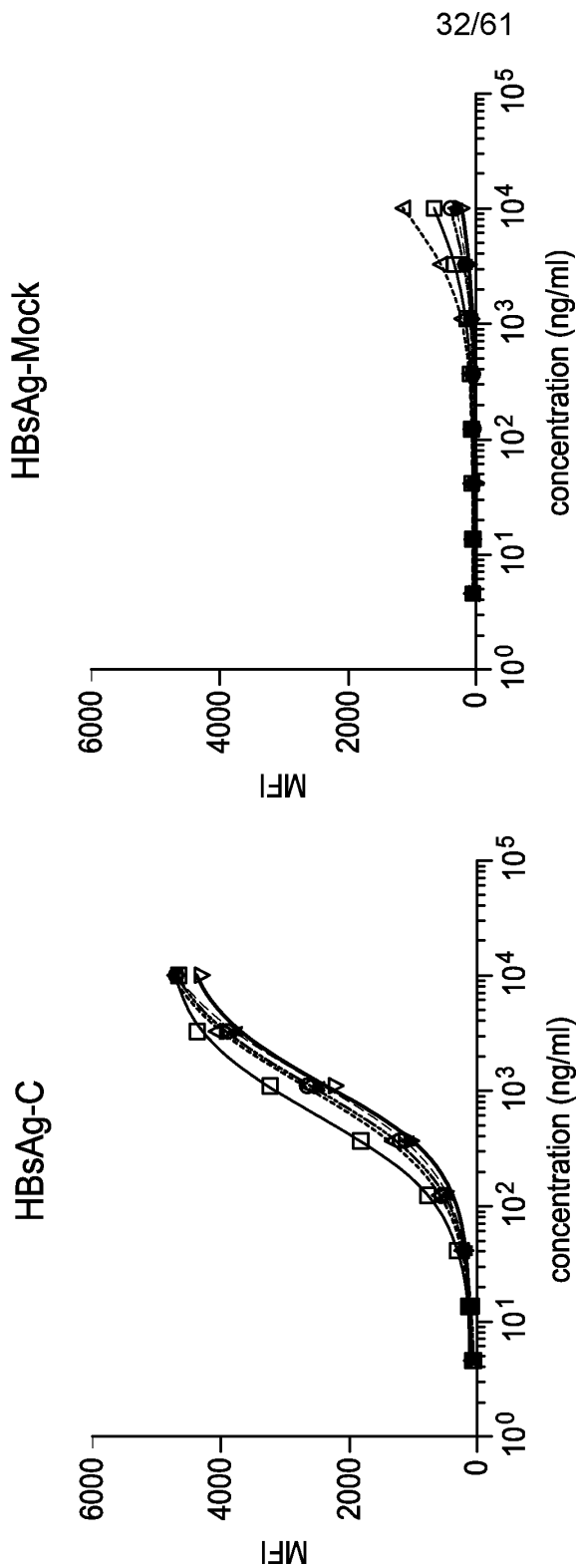


FIG. 17A



- HBC34-v35-rlgG1(G1m17,1), JC6
- HBC34-v40-rlgG1(G1m17), S65
- △ HBC34-v44-rlgG1(G1m17), S7H
- ▽ HBC34-v45-rlgG1(G1m17), 3FK
- ★ HBC34-v50-rlgG1(G1m17), 7WX

FIG. 17B



- HBC34-v35-rlgG1(G1m17,1), JC6
- HBC34-v40-rlgG1(G1m17), S65
- △ HBC34-v44-rlgG1(G1m17), S7H
- ▽ HBC34-v45-rlgG1(G1m17), 3FK
- ★ HBC34-v50-rlgG1(G1m17), 7WX

FIG. 17C

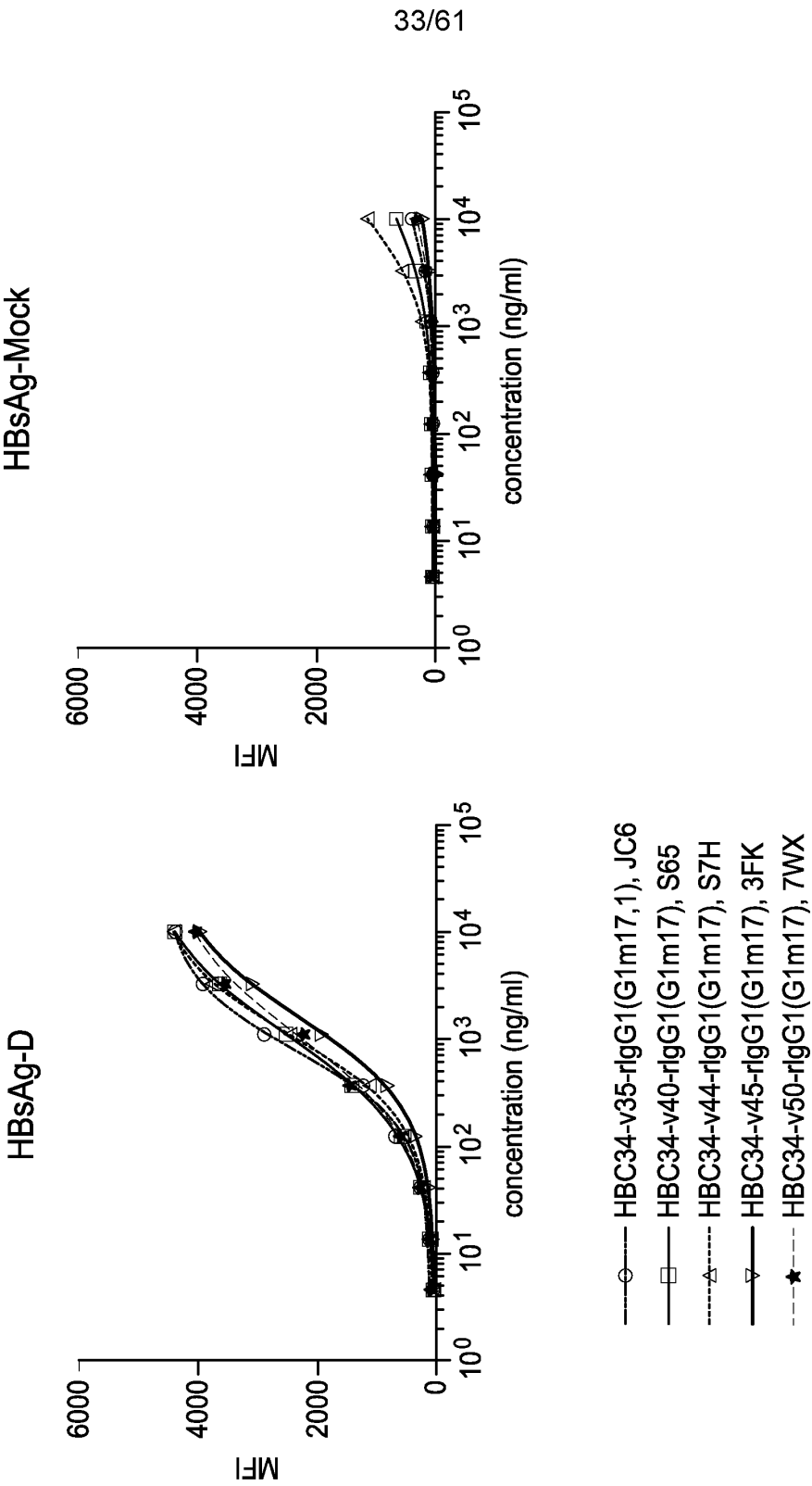


FIG. 17D

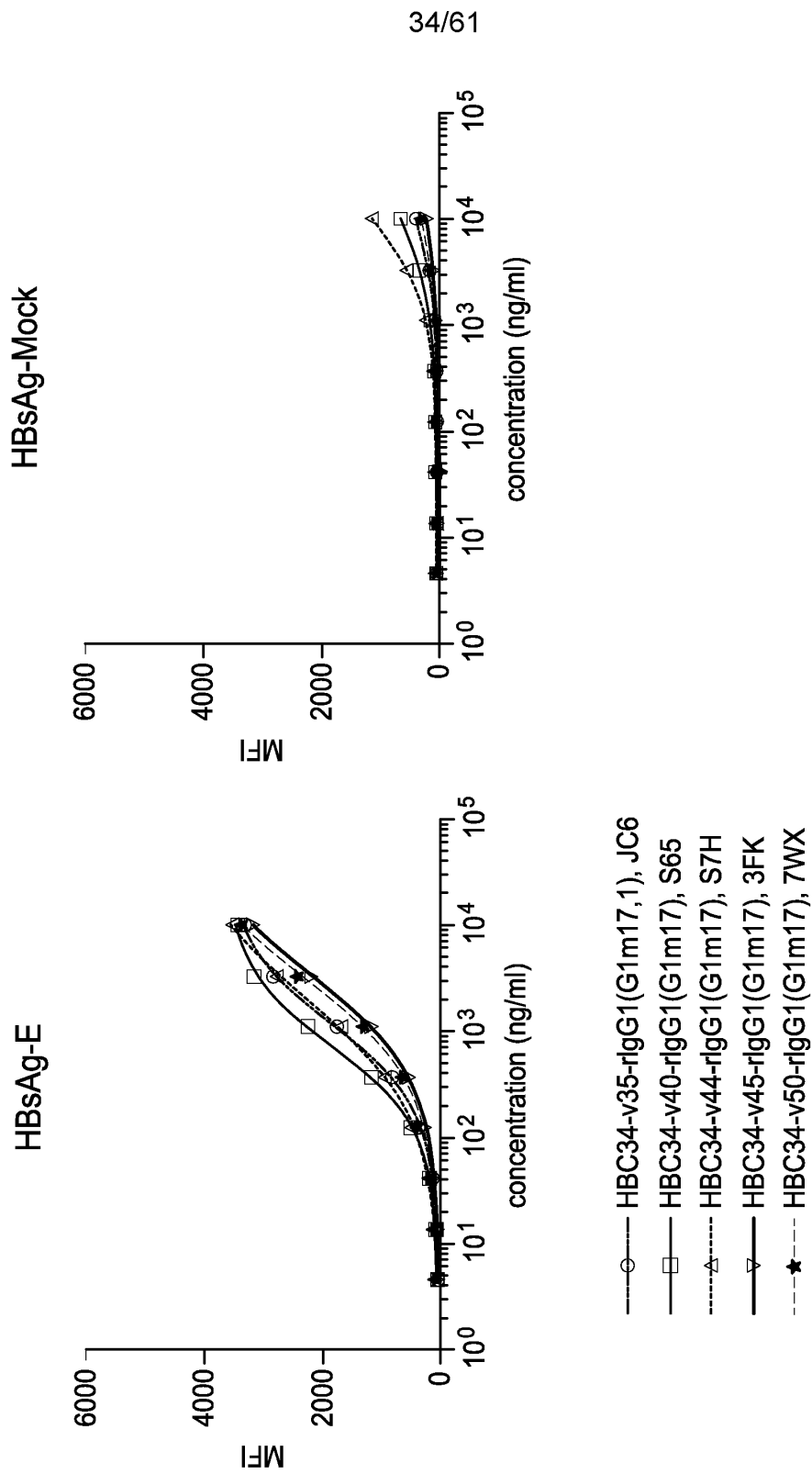


FIG. 17E

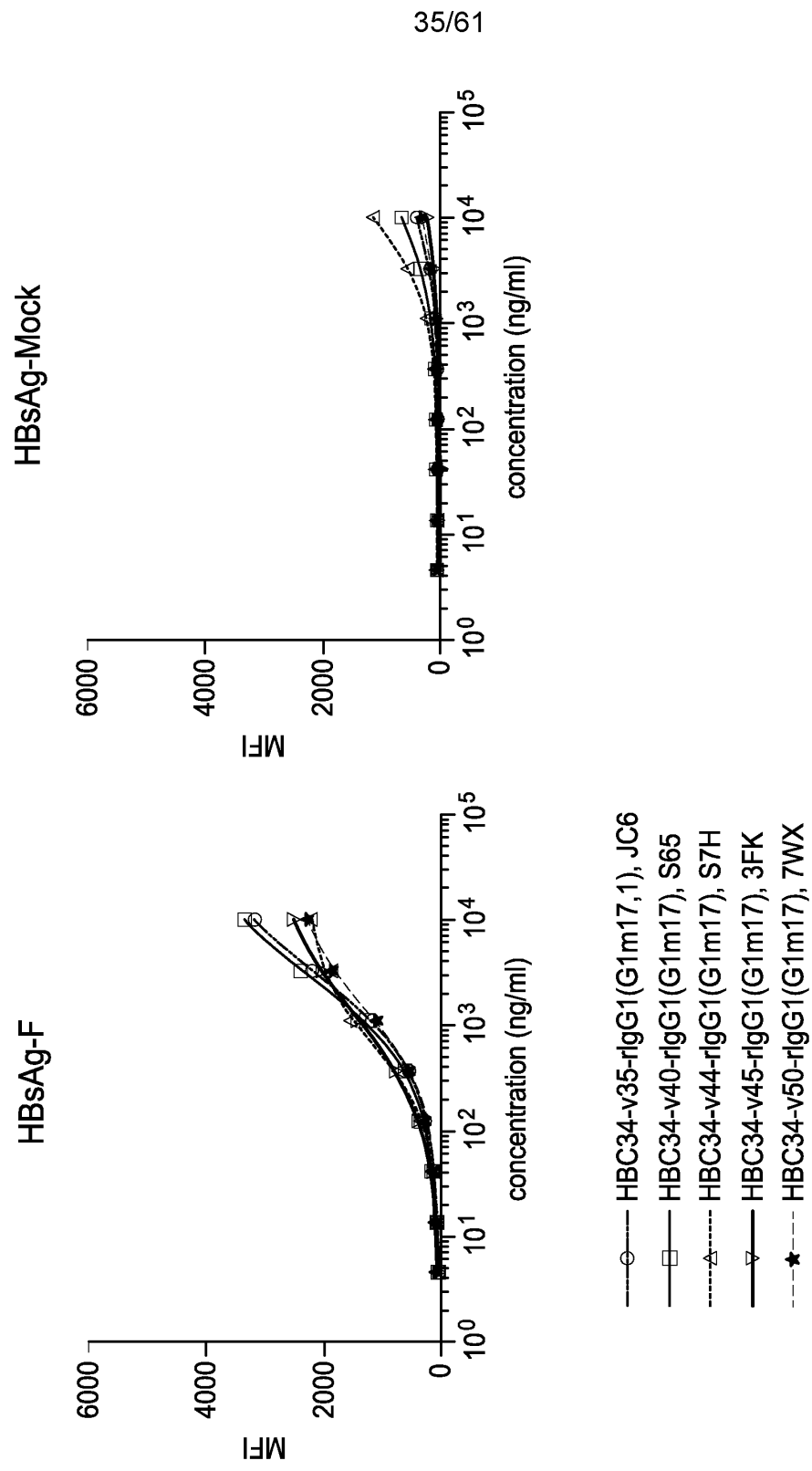


FIG. 17F

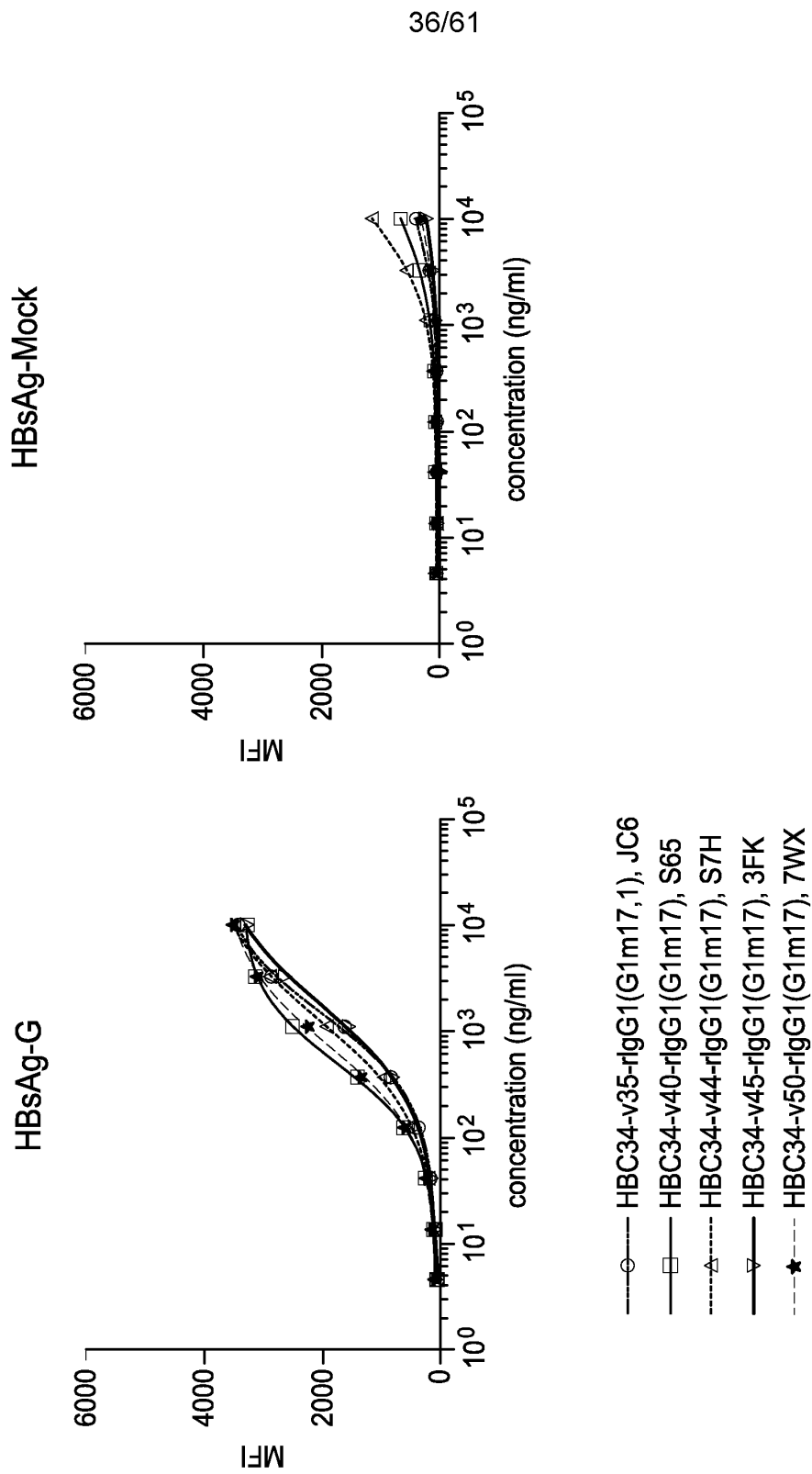


FIG. 17G

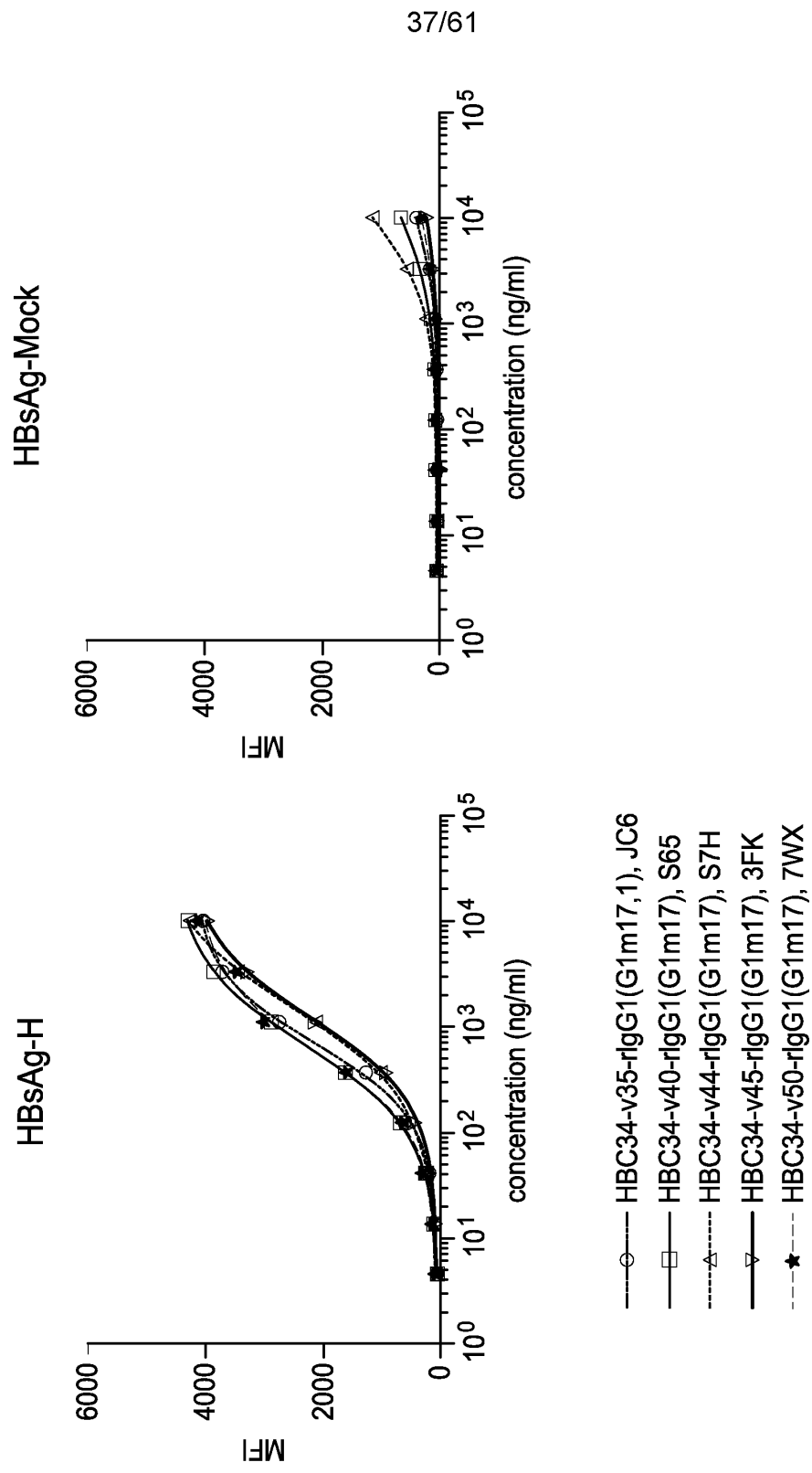


FIG. 17H

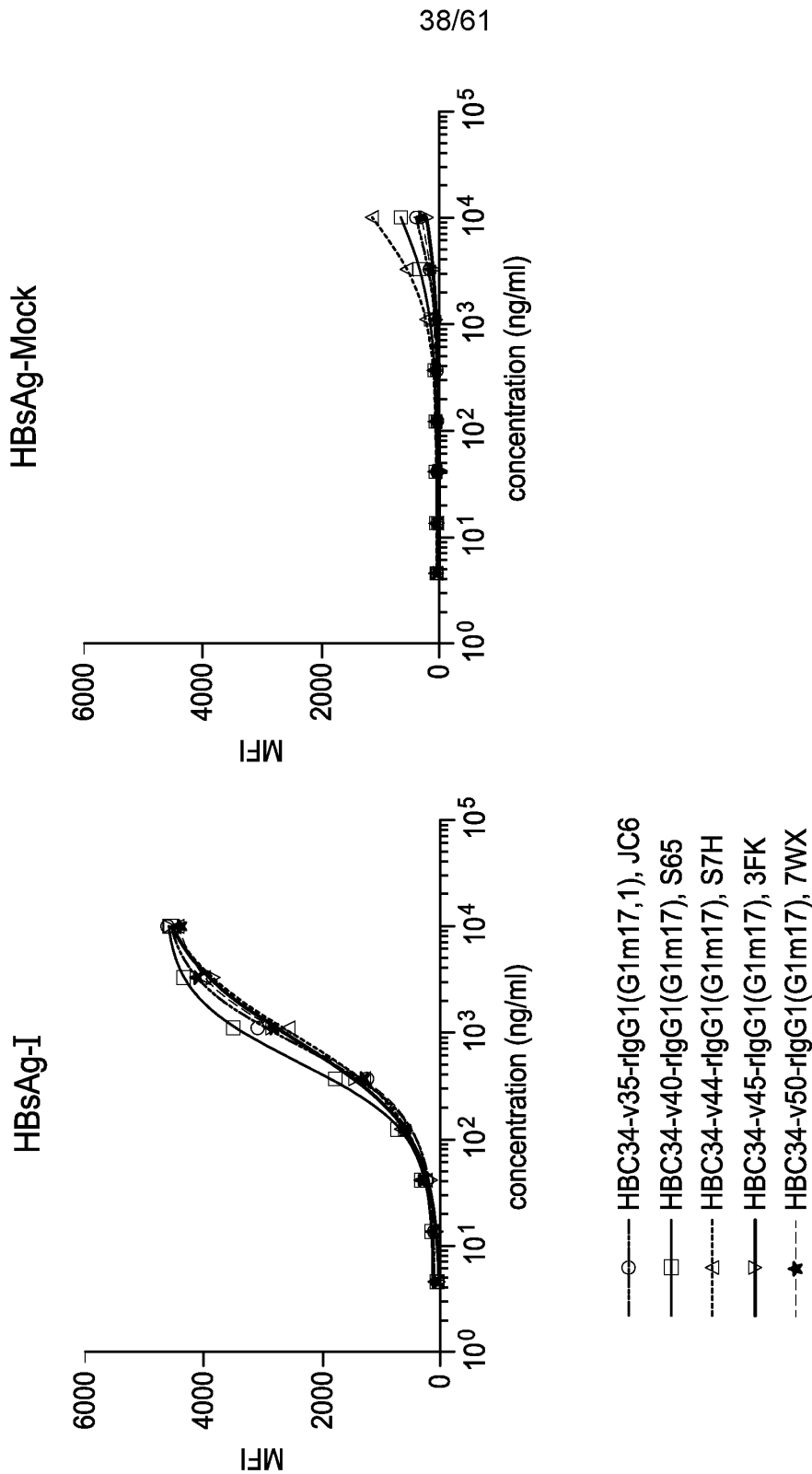


FIG. 17I

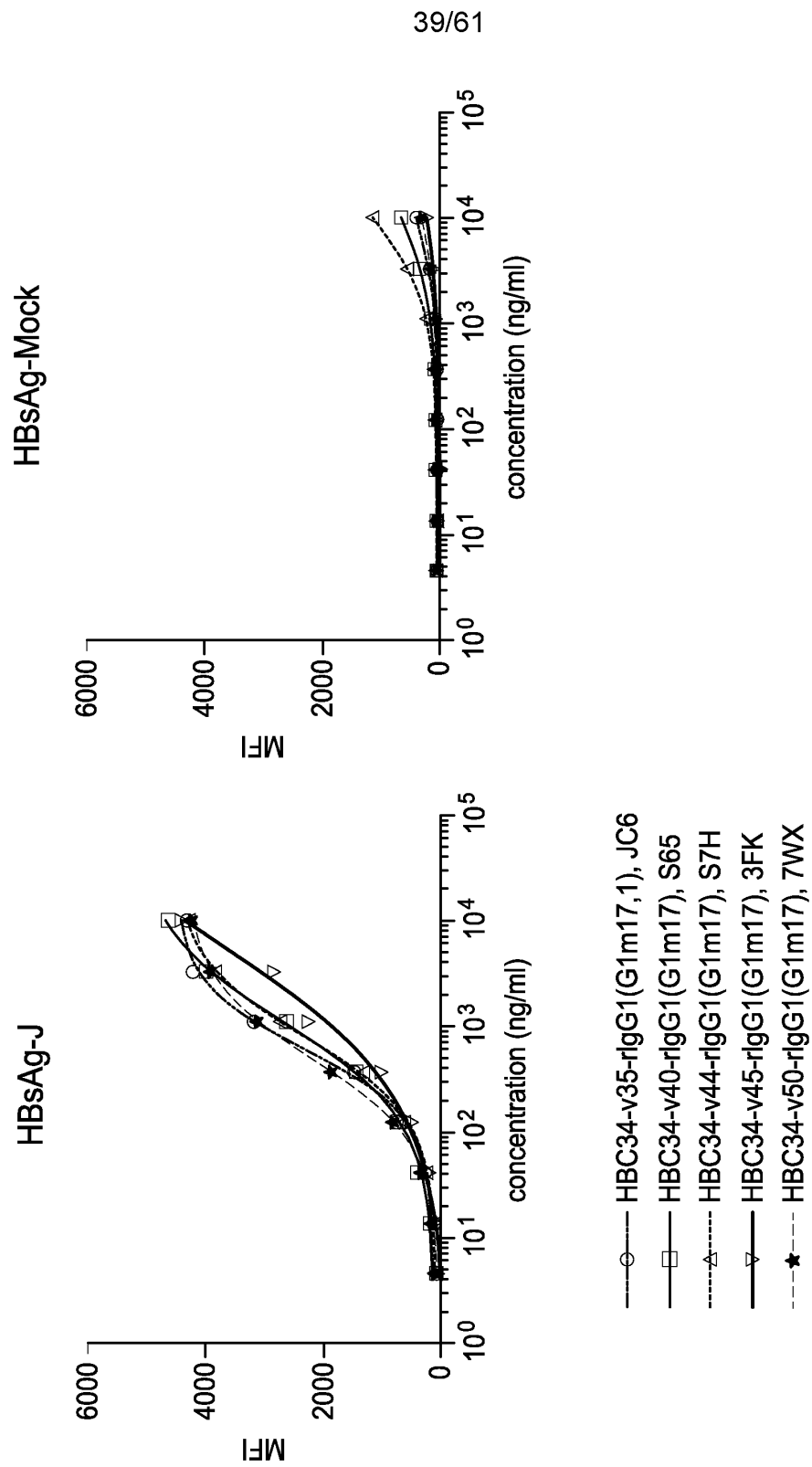


FIG. 17J

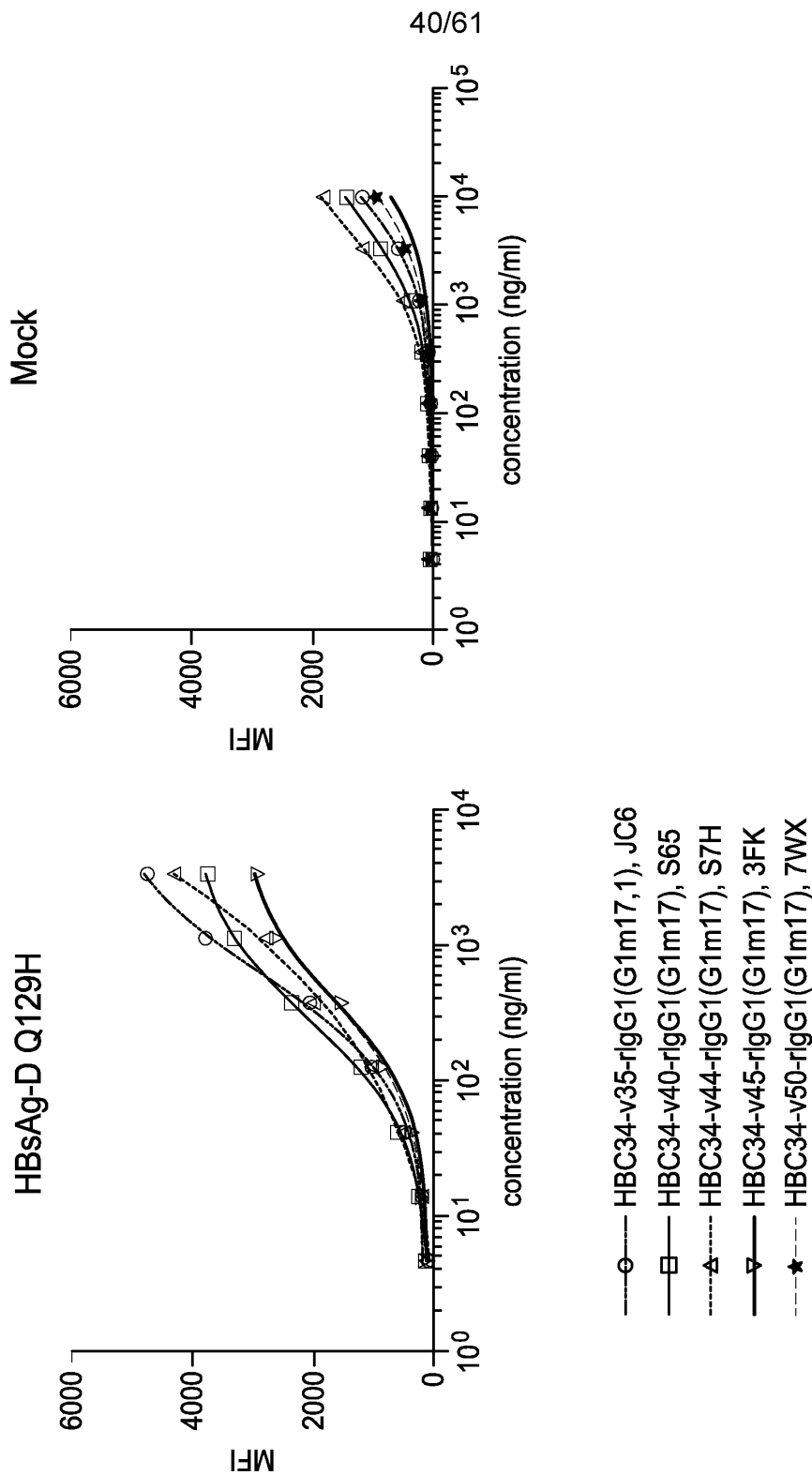
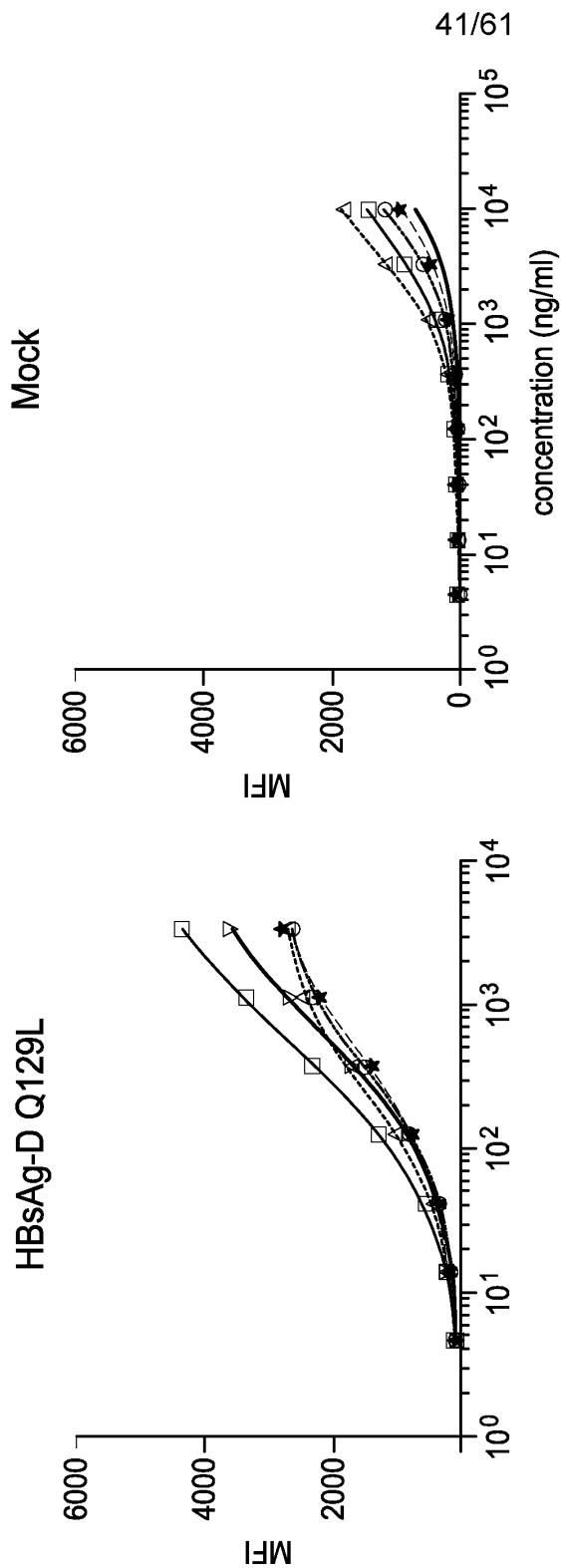


FIG. 18A



- HBC34-v35-rgG1(G1m17,1), JC6
- HBC34-v40-rgG1(G1m17), S65
- △ HBC34-v44-rgG1(G1m17), S7H
- ▽ HBC34-v45-rgG1(G1m17), 3FK
- ★ HBC34-v50-rgG1(G1m17), 7WX

FIG. 18B

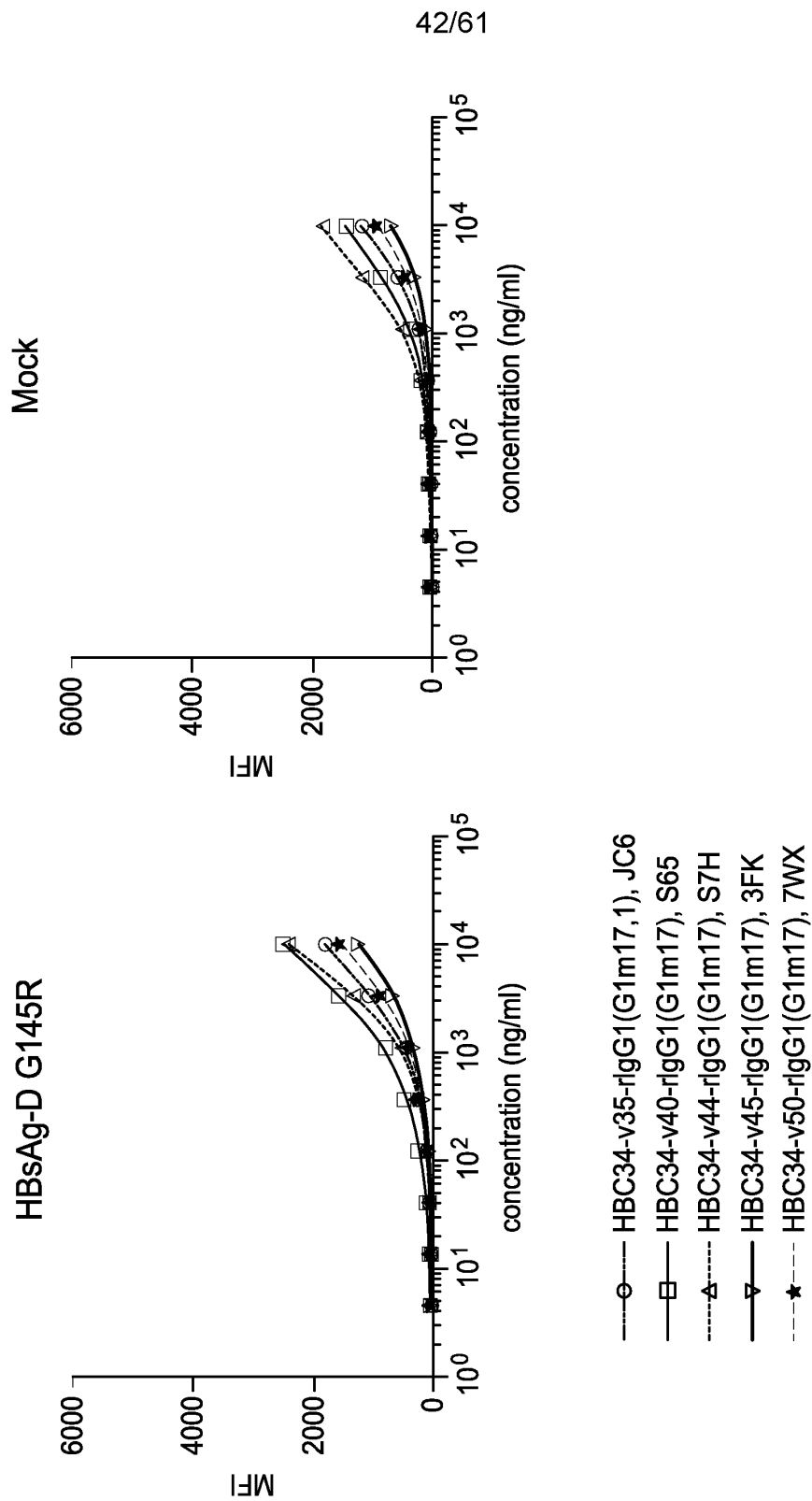


FIG. 18C

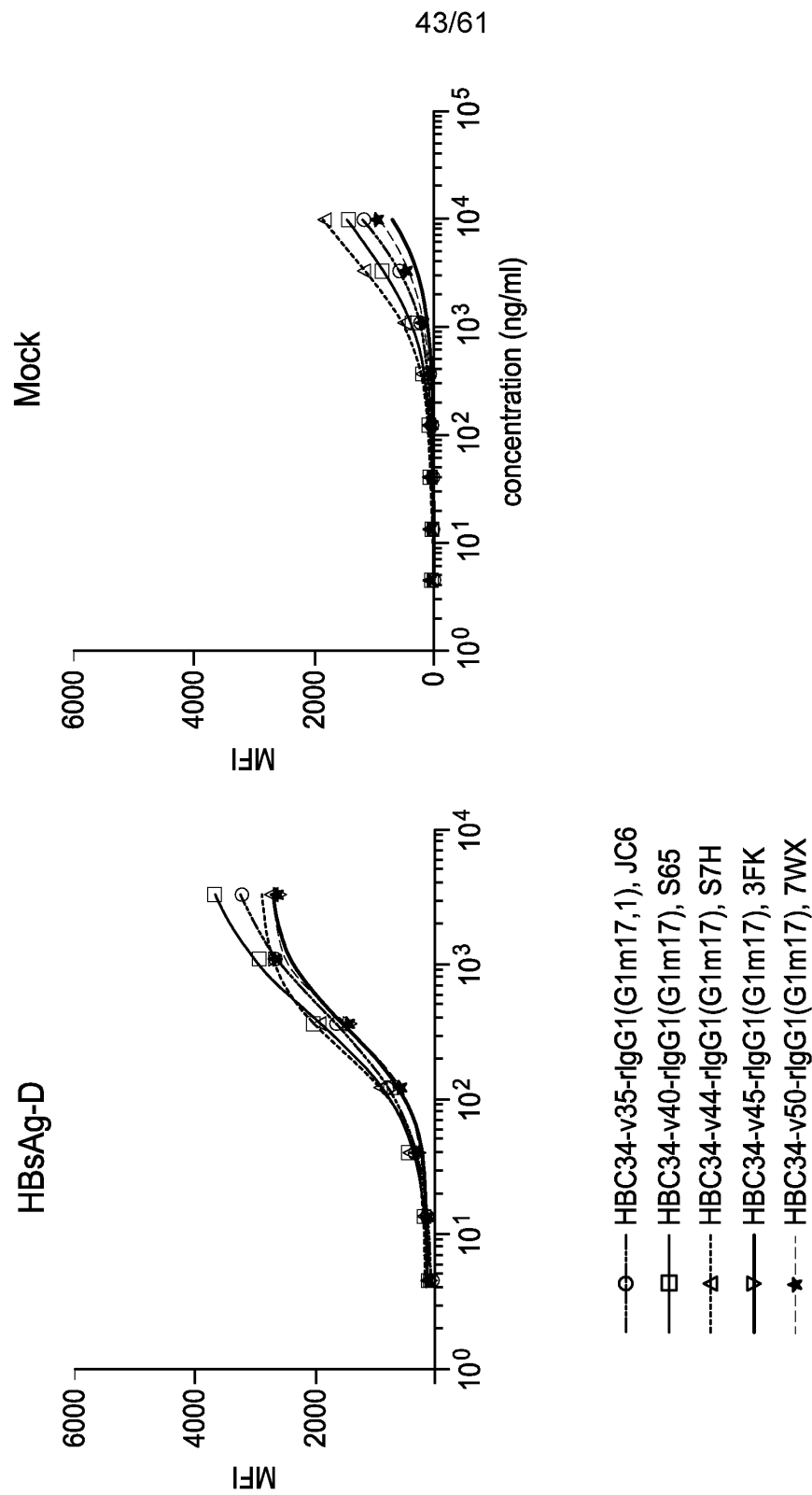


FIG. 18D

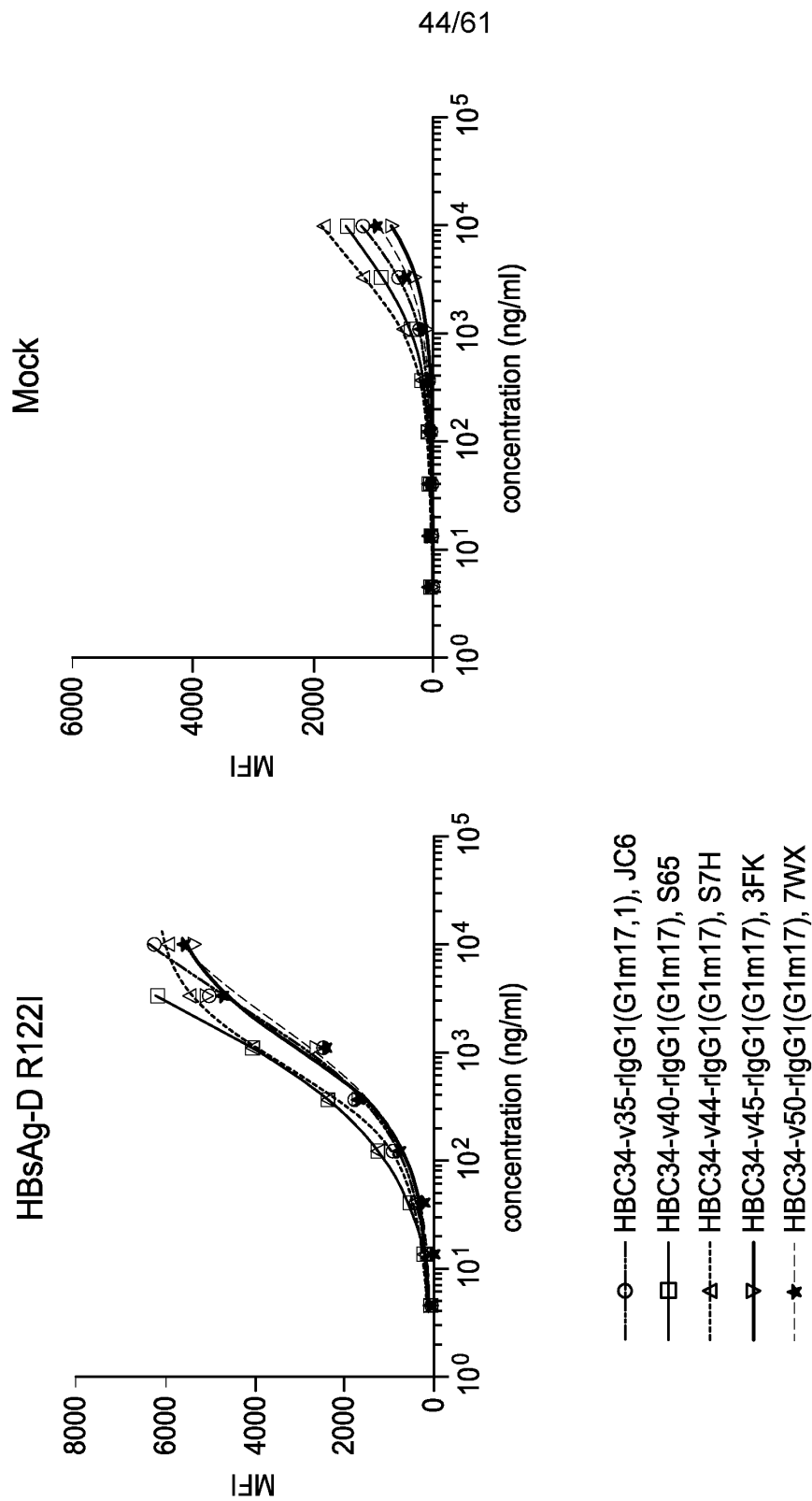


FIG. 18E

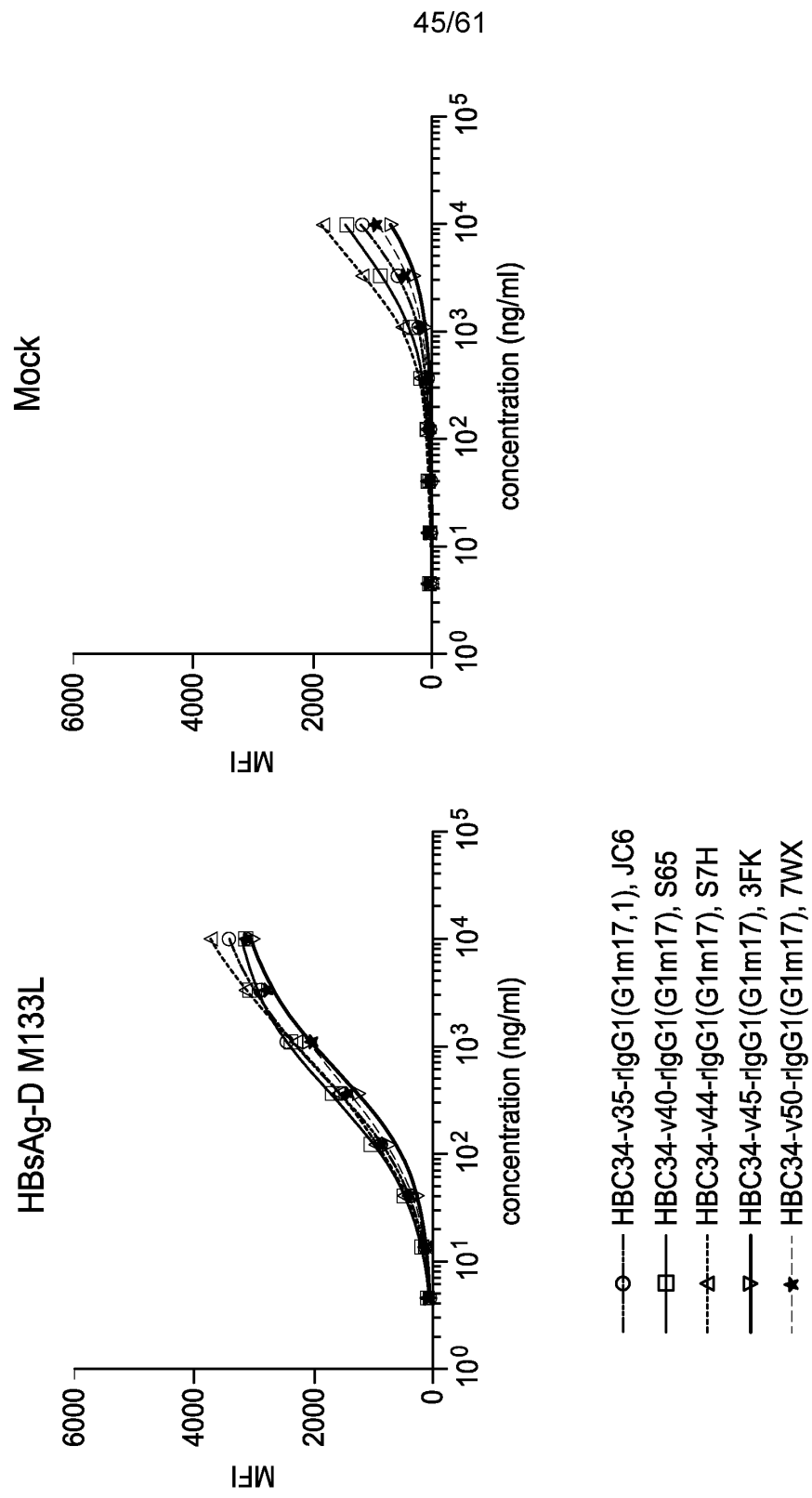
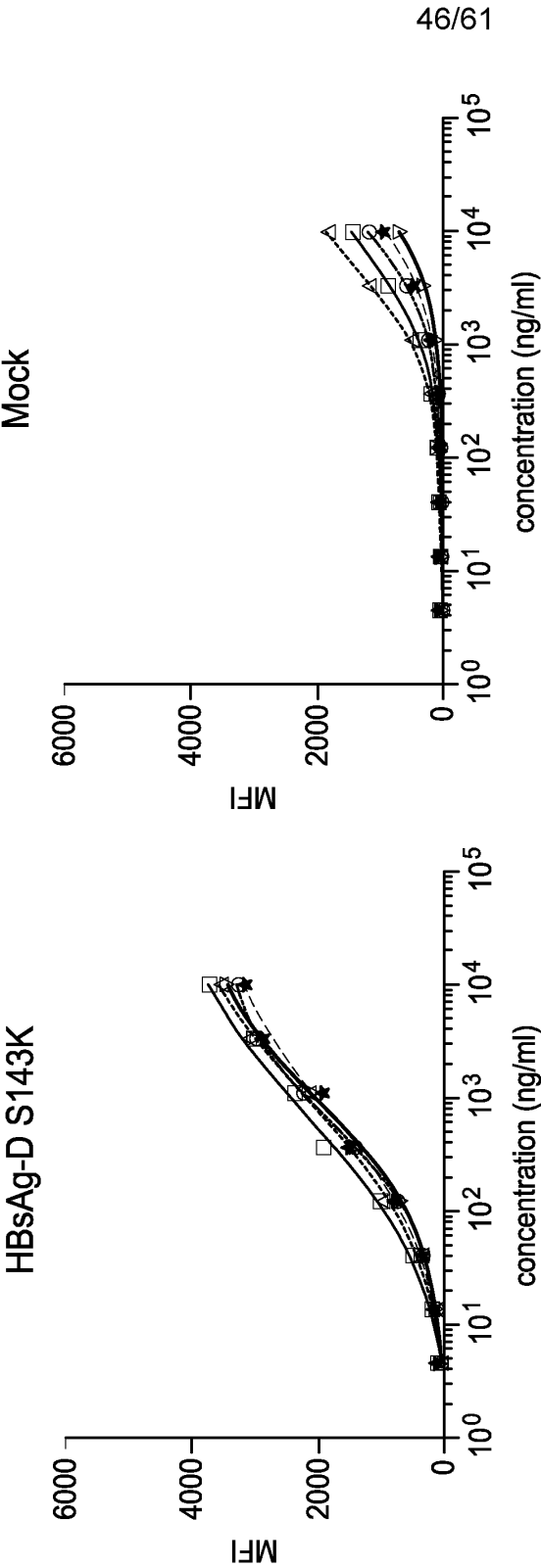


FIG. 18F



- HBC34-v35-rgG1(G1m17,1), JC6
- HBC34-v40-rgG1(G1m17), S65
- △ HBC34-v44-rgG1(G1m17), S7H
- ▽ HBC34-v45-rgG1(G1m17), 3FK
- ★ HBC34-v50-rgG1(G1m17), 7WX

FIG. 18G

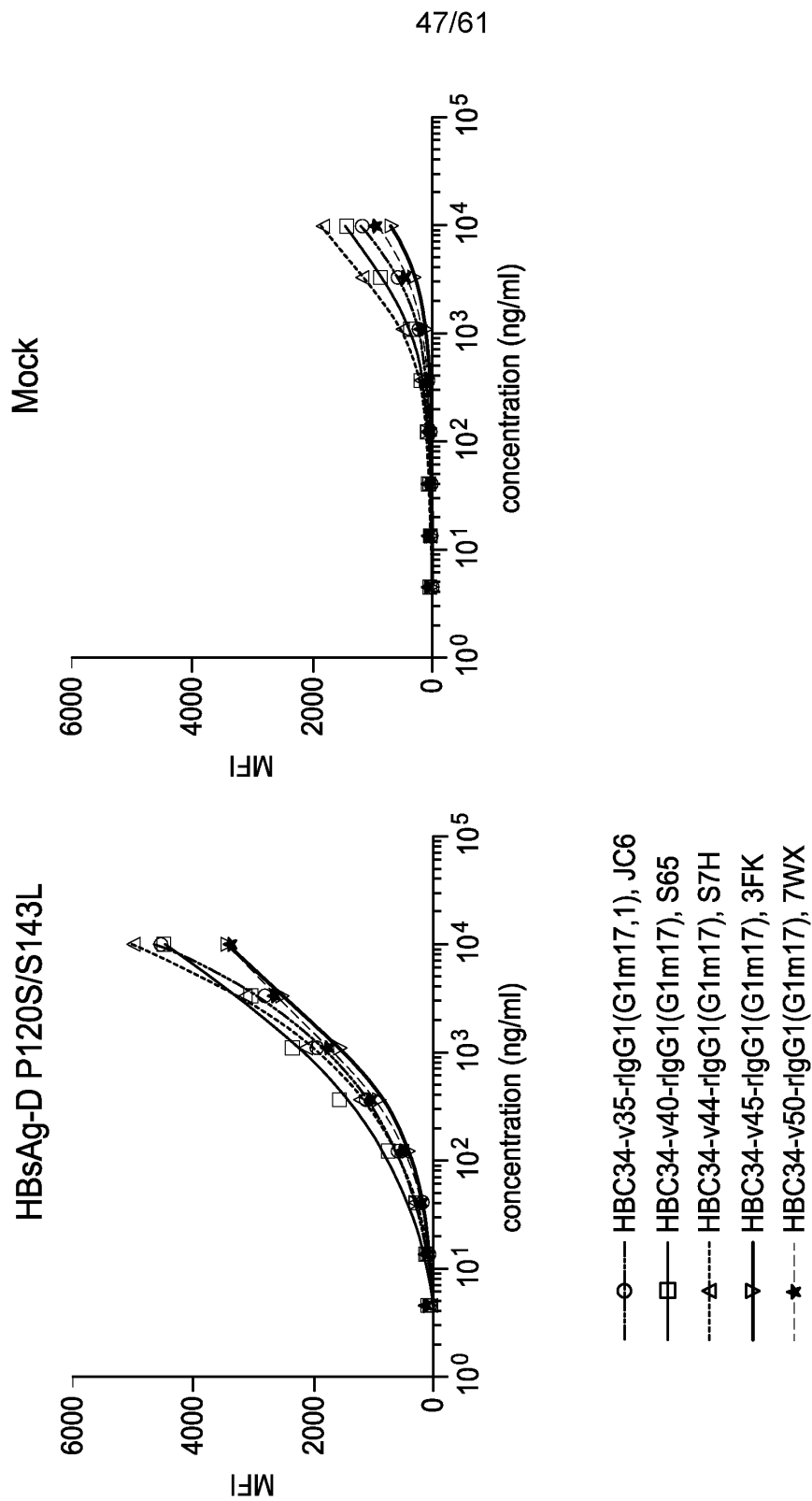


FIG. 18H

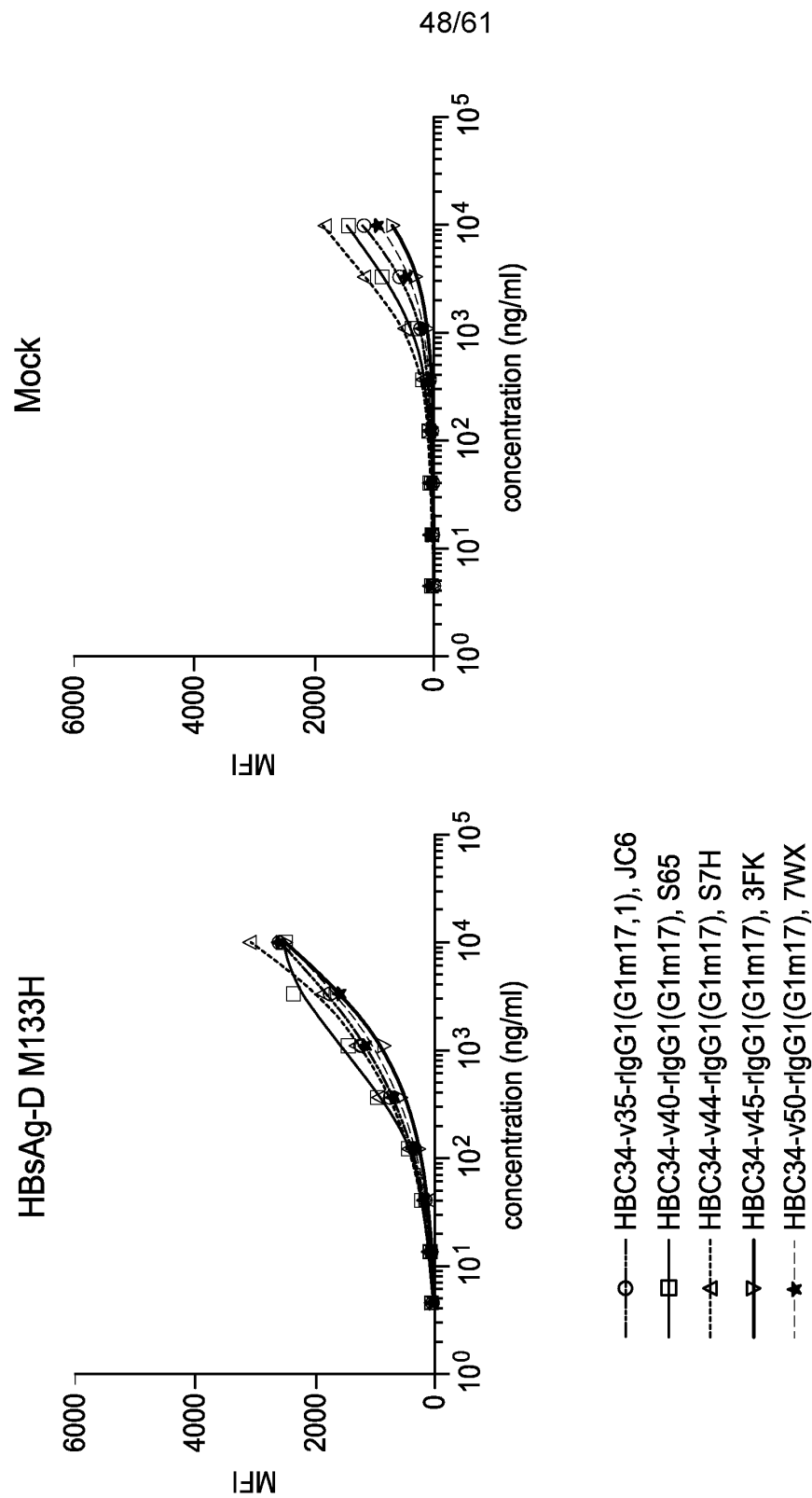


FIG. 18I

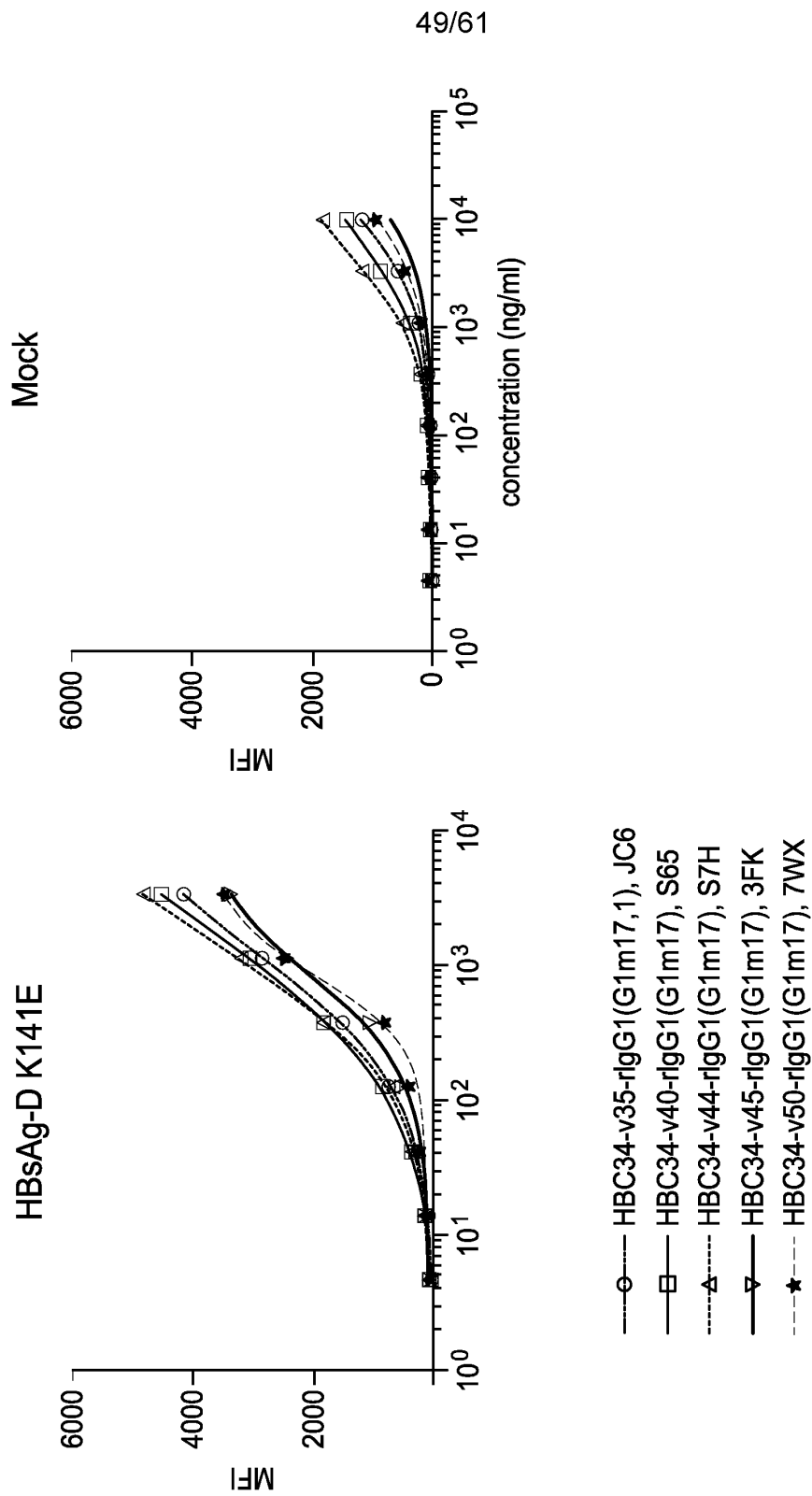


FIG. 18J

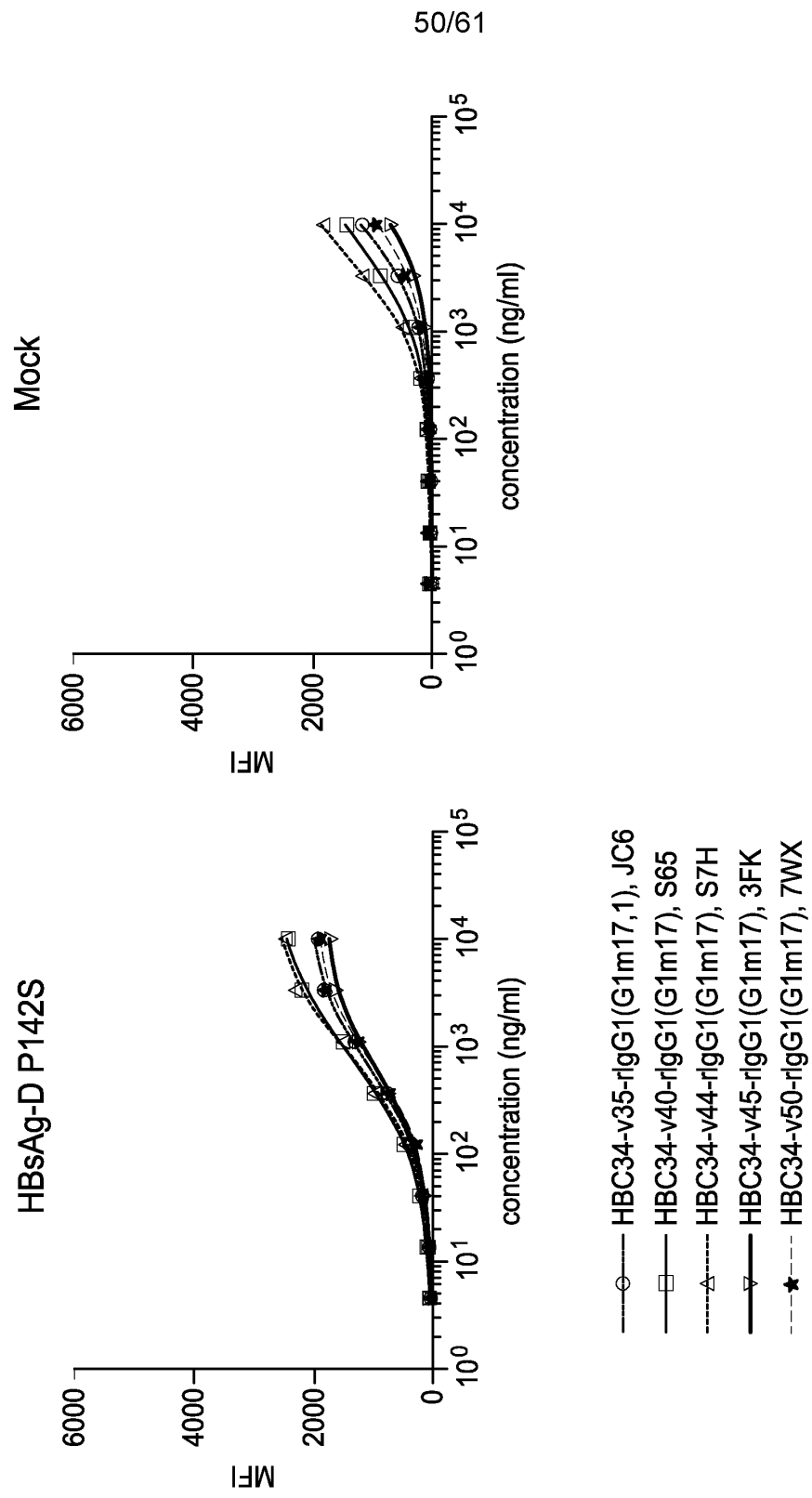


FIG. 18K

mAb name	titer 5 ml transfection (mg/L)	titer 100ml transfections (mg/L)	average titer in 100 ml scale (mg/L)
HBC34-v35-rlgG1 (G1m17,1)	89.4	149.0, 172.3, 212.0 (N=3)	177.8
HBC34-v40-rlgG1 (G1m17,1)	237.261	535.5, 583.0, 669.4 (N=3)	596.0
HBC34-v44-rlgG1 (G1m17,1)	157.8	588.2, 563.0 (N=2)	575.6
HBC34-v45-rlgG1 (G1m17,1)	140.9	269.2, 256.0 (N=2)	262.6
HBC34-v50rlgG1 (G1m17,1)	163.7	363.8, 371.0 (N=2)	367.4

FIG. 19

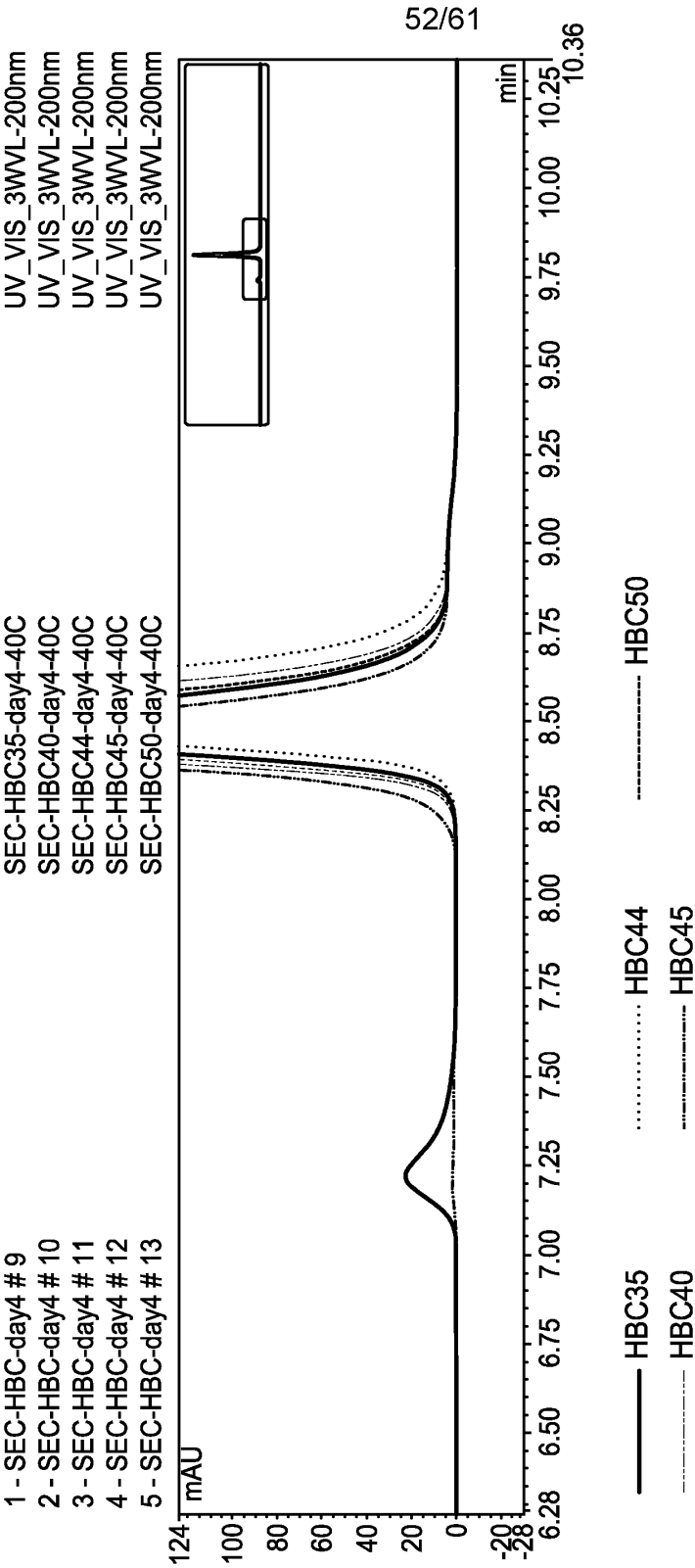


FIG. 20

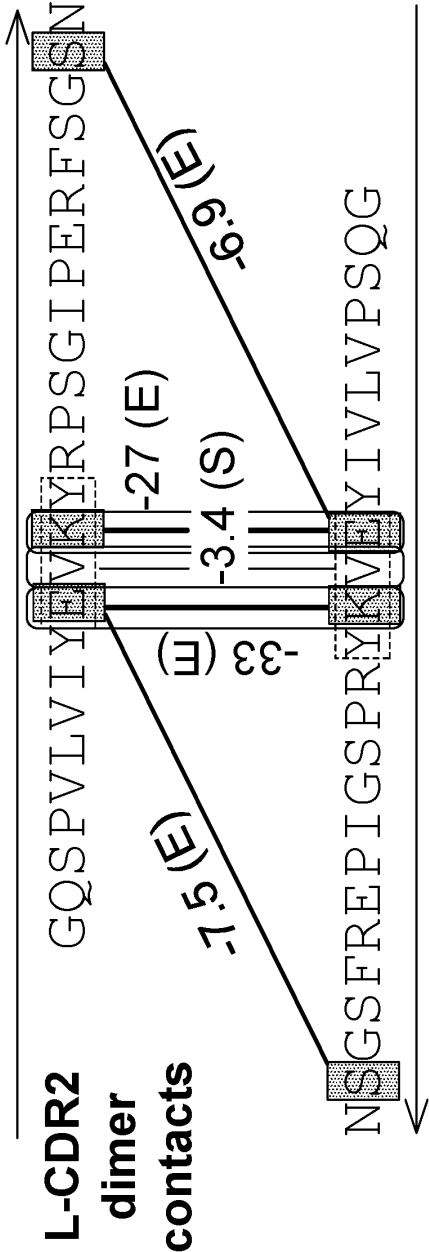


FIG. 21A

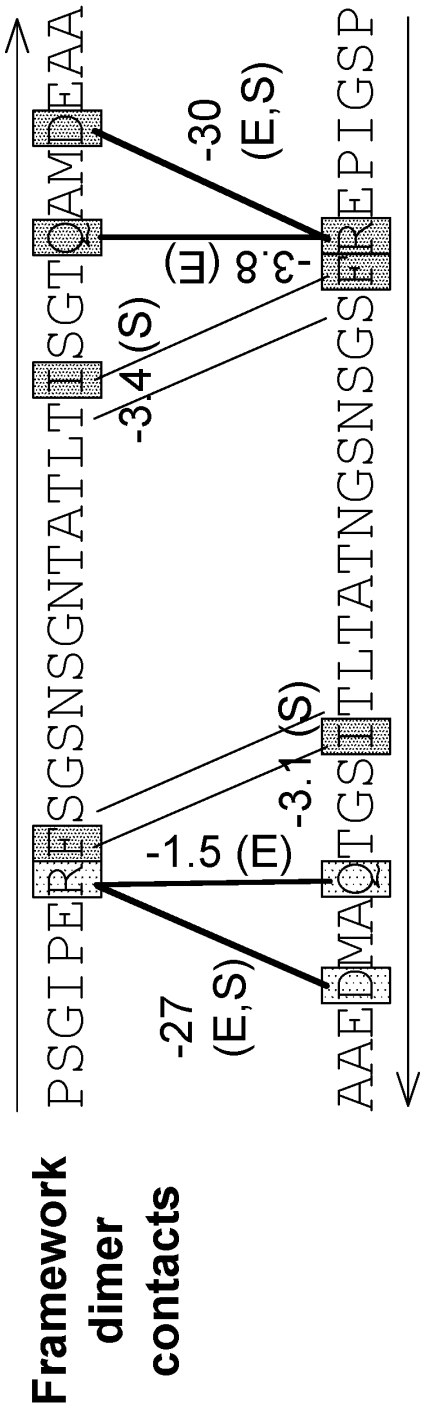


FIG. 21B

40	50	60	70	80	
v35	GQSPVLVIY E	VK Y RPSGIPE	RFSGSN S NGNT	ATLTISGT Q A	MDEAA Y FC – HBC34
v36	GQSPVLVIY Q	DSK R PSGIPE	RFSGSN S NGNT	ATLTISGT Q A	MDEAA Y FC – GL L2
v37	GQSPVLVIY E	DSK R PSGIPE	RFSGSN S NGNT	ATLTISGT Q A	MDEAA Y FC – v36 + Q49E
v38	GQSPVLVIY Q	VSK R PSGIPE	RFSGSN S NGNT	ATLTISGT Q A	MDEAA Y FC – v36 + D50V
v39	GQSPVLVIY Q	D K KRPSGIPE	RFSGSN S NGNT	ATLTISGT Q A	MDEAA Y FC – v36 + S51K
v40	GQSPVLVIY Q	DS Y RPSGIPE	RFSGSN S NGNT	ATLTISGT Q A	MDEAA Y FC – v36 + K52Y ← E49Q, V50D, K51S
v41	GQSPVLVIY Q	V S <u>Y</u> RPSGIPE	RFSGSN S NGNT	ATLTISGT Q A	MDEAA Y FC – v36 + D50V + K52Y
v42	GQSPVLVIY E	V S <u>Y</u> RPSGIPE	RFSGSN S NGNT	ATLTISGT Q A	MDEAA Y FC – HBC34 + K51S + S64A
v43	GQSPVLVIY Q	VK Y RPSGIPE	RFSGSN S NGNT	ATLTISGT Q A	MDEAA Y FC – HBC34 + E49Q
v44	GQSPVLVIY A	VK Y RPSGIPE	RFSGSN S NGNT	ATLTISGT Q A	MDEAA Y FC – HBC34 + E49A
v45	GQSPVLVIY E	VK Y RPSGIPE	RFSGSN S NGNT	ATLTISGT Q A	MDEAA Y FC – HBC34 + R60N
v46	GQSPVLVIY E	VK Y RPSGIPE	RFSGSN S NGNT	ATLTISGT Q A	MDEAA Y FC – HBC34 + R60A
v47	GQSPVLVIY E	V S <u>Y</u> RPSGIPE	RFSGSN S NGNT	ATLTASGT Q A	MDEAA Y FC – HBC34 + K51S + S64A + R60N + I74A
v48	GQSPVLVIY E	VK Y RPSGIPE	RFSGSN S NGNT	ATLTASGT Q A	MDEAA Y FC – HBC34 + R60N + S64A + + I74A
v49	GQSPVLVIY E	V S <u>Y</u> RPSGIPE	RFSGSN S NGNT	ATLTISGT Q A	MDEAA Y FC – HBC34 + K51S
v50	GQSPVLVIY E	VK Y RPSGIPE	KFSGSN S NGNT	ATLTISGT Q A	MDEAA Y FC – HBC34 + R60K

FIG. 21C

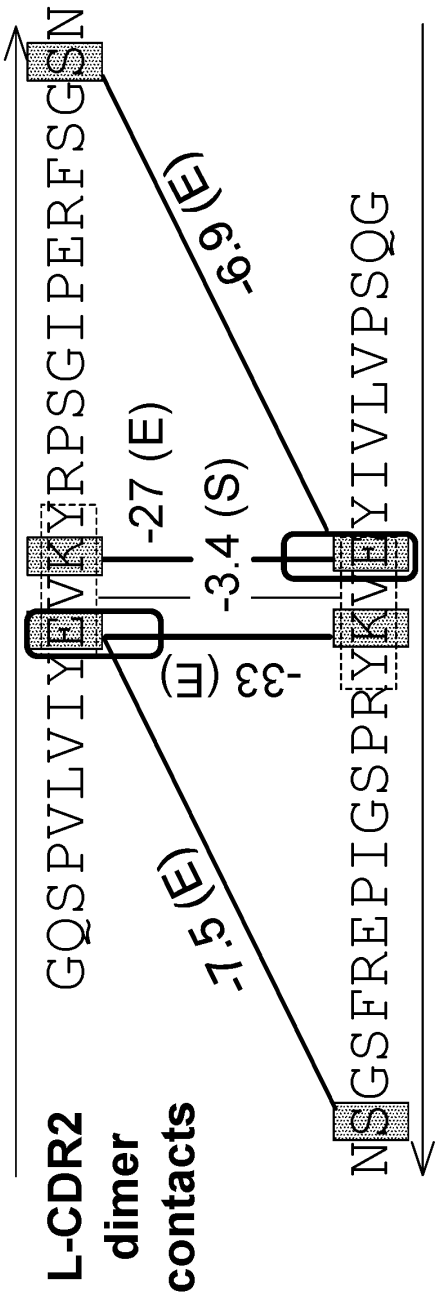


FIG. 22A

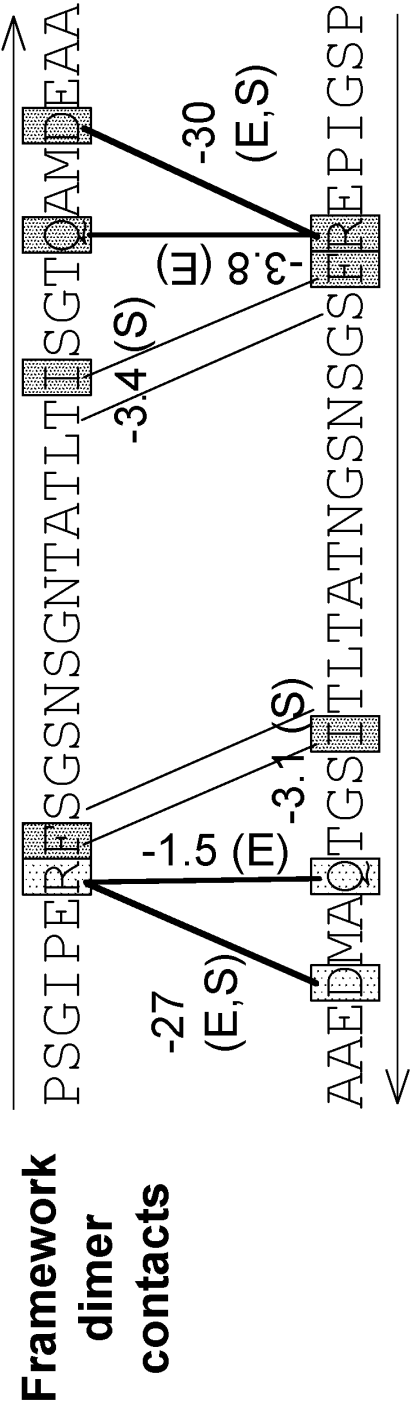


FIG. 22B

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E49A in L-CDR2

FIG. 22C

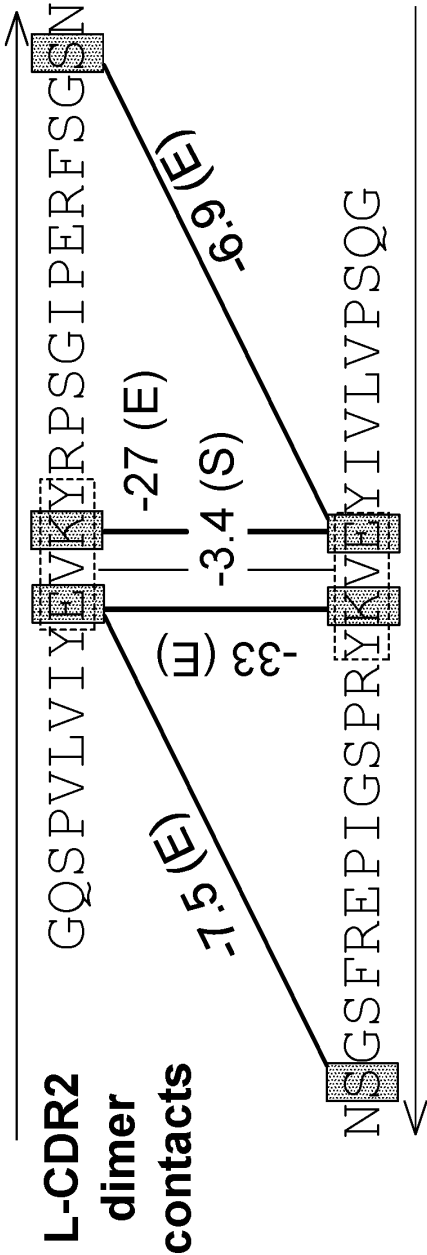


FIG. 23A

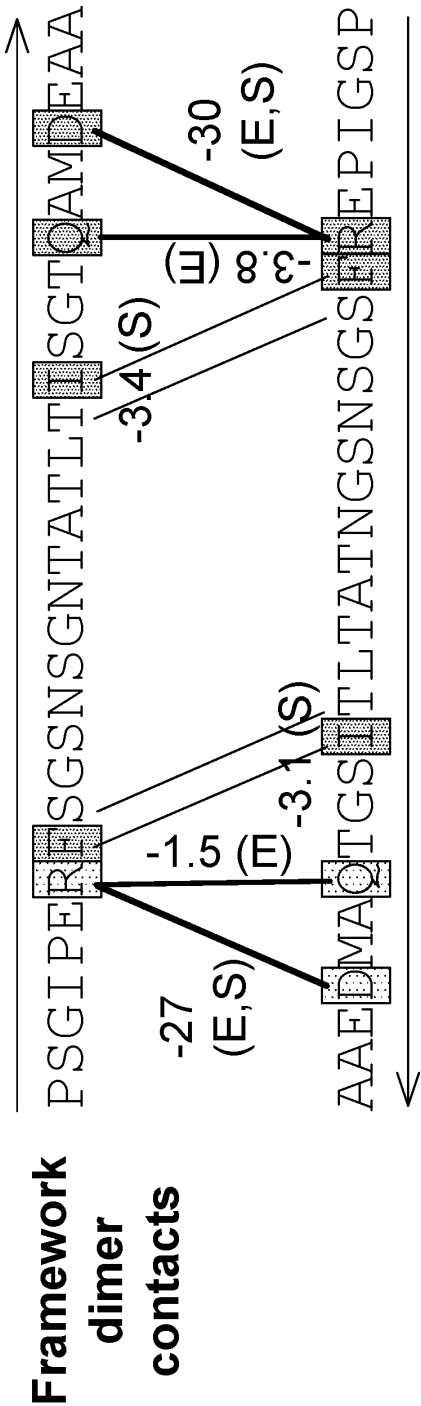


FIG. 23B

	40	50	60	70	80	
V35	GQSPVLVIYE	VKYRPSGIPE	RFSGSNSGNT	ATLTISGTQA	MDEAAAYFC	- HBC34
V36	GQSPVLVIYQ	DSKRPSGIPE	RFSGSNSGNT	ATLTISGTQA	MDEAAAYFC	- GL L2
V37	GQSPVLVIYE	DSKRPSGIPE	RFSGSNSGNT	ATLTISGTQA	MDEAAAYFC	- V36 + Q49E
V38	GQSPVLVIYQ	VSKRPSGIPE	RFSGSNSGNT	ATLTISGTQA	MDEAAAYFC	- V36 + D50V
V39	GQSPVLVIYQ	DKKRPSGIPE	RFSGSNSGNT	ATLTISGTQA	MDEAAAYFC	- V36 + S51K
V40	GQSPVLVIYQ	DSYRPSGIPE	RFSGSNSGNT	ATLTISGTQA	MDEAAAYFC	- V36 + K52Y
V41	GQSPVLVIYQ	VSYRPSGIPE	RFSGSNSGNT	ATLTISGTQA	MDEAAAYFC	- V36 + D50V + K52Y
V42	GQSPVLVIYE	VSYRPSGIPE	RFSGANSNT	ATLTISGTQA	MDEAAAYFC	- HBC34 + K51S + S64A
V43	GQSPVLVIYQ	VKYRPSGIPE	RFSGSNSGNT	ATLTISGTQA	MDEAAAYFC	- HBC34 + E49Q
V44	GQSPVLVIYA	VKYRPSGIPE	RFSGSNSGNT	ATLTISGTQA	MDEAAAYFC	- HBC34 + E49A
V45	GQSPVLVIYE	VKYRPSGIPE	NFSGSNSGNT	ATLTISGTQA	MDEAAAYFC	- HBC34 + R60N
V46	GQSPVLVIYE	VKYRPSGIPE	AFSGSNSGNT	ATLTISGTQA	MDEAAAYFC	- HBC34 + R60A
V47	GQSPVLVIYE	VSYRPSGIPE	NFSGANSNT	ATLTASGTQA	MDEAAAYFC	- HBC34 + K51S + S64A + R60N + I74A
V48	GQSPVLVIYE	VKYRPSGIPE	NFSGANSNT	ATLTASGTQA	MDEAAAYFC	- HBC34 + R60N + S64A + + I74A
V49	GQSPVLVIYE	VSYRPSGIPE	RFSGSNSGNT	ATLTISGTQA	MDEAAAYFC	- HBC34 + K51S
V50	GQSPVLVIYE	VKYRPSGIPE	KFSGSNSGNT	ATLTISGTQA	MDEAAAYFC	- HBC34 + R60K

R60 mutated
in framework

FIG. 23C