Figure 1

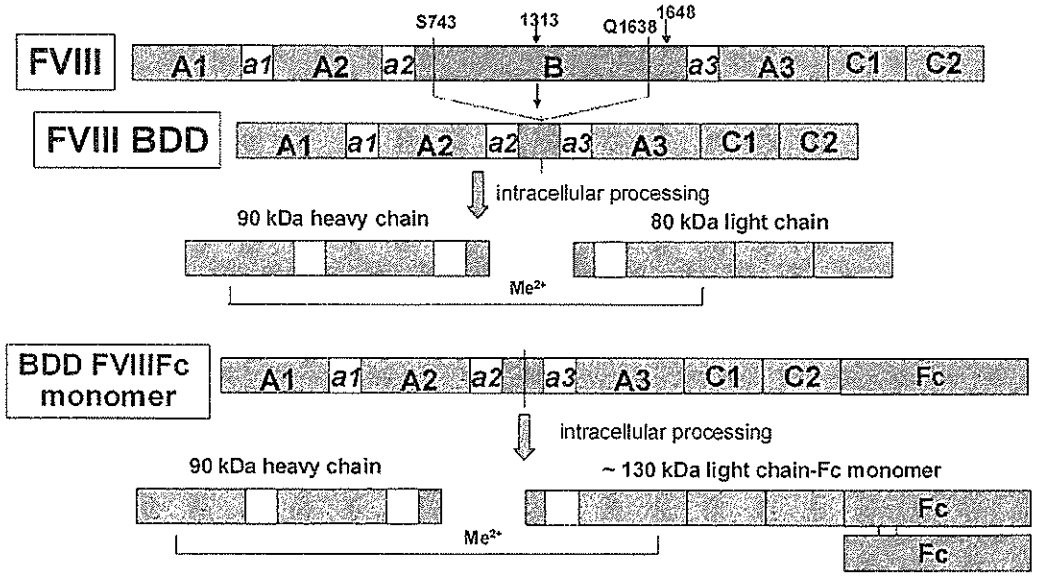

FVIII
S743
1313
Q1638
1648
A1
a1
A2
a2
B
a3
A3
C1
C2
FVIII BDD
intracellular processing
90 kDa heavy chain
80 kDa light chain
Me2+
BDD FVIIIFc monomer
Fc
~ 130 kDa light chain-Fc monomer

Figure 2

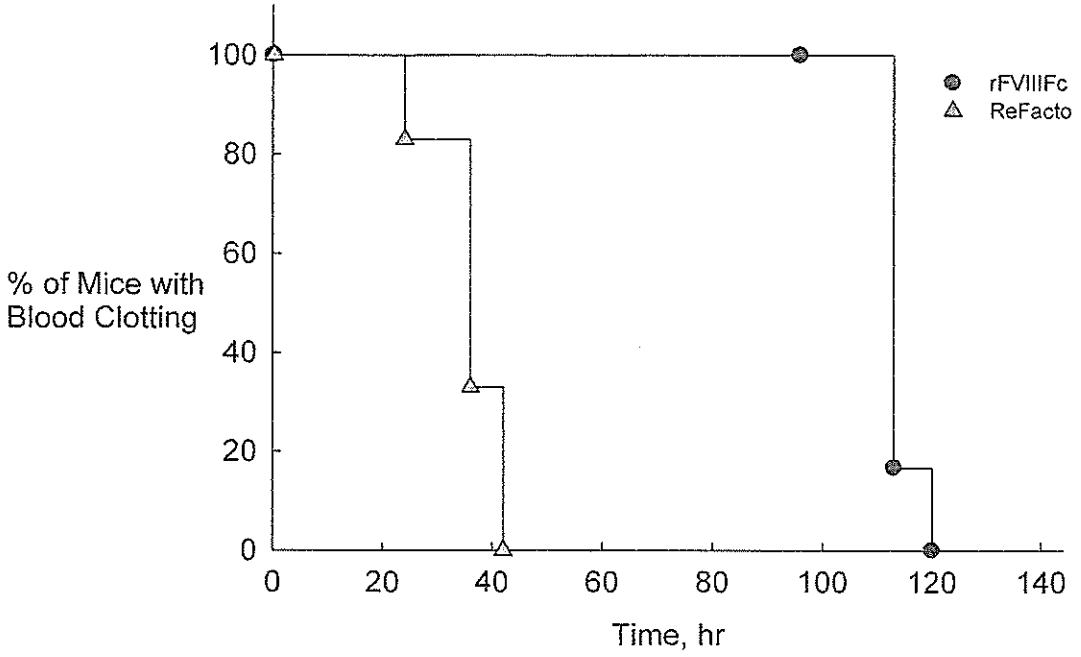

100
80
60
40
20
0
% of Mice with Blood Clotting
0
20
40
60
80
100
120
140
Time, hr
rFVIIIFc
ReFacto

Figure 3

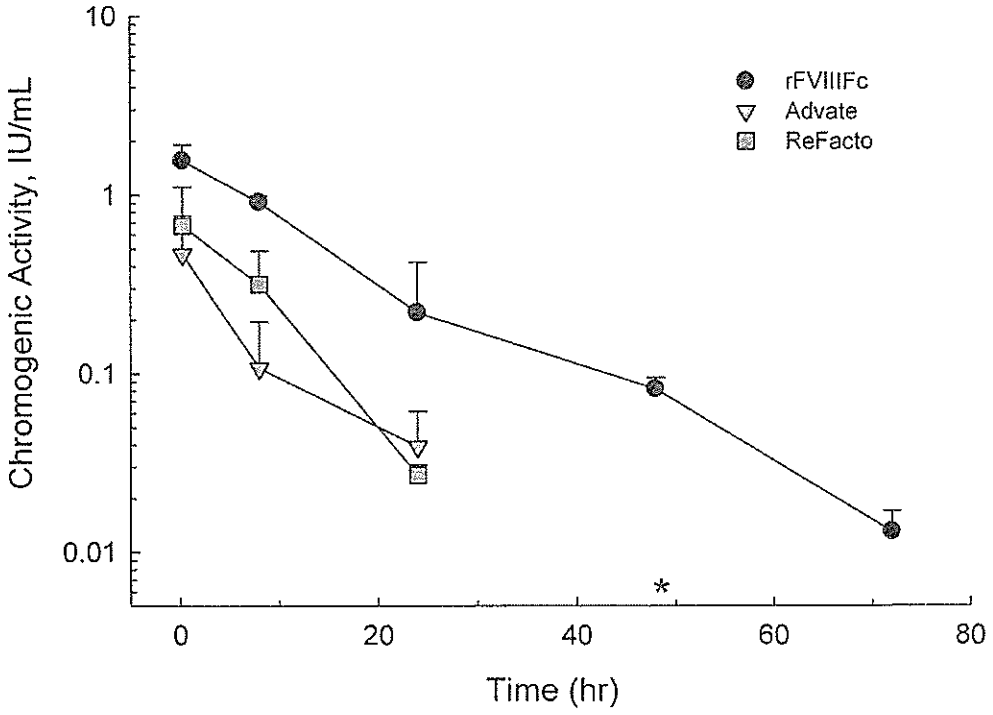

10
1
0.1
0.01
Chromogenic Activity, IU/mL
0
20
40
60
80
Time (hr)
rFVIIIFc
Advate
ReFacto
*

Figure 4A

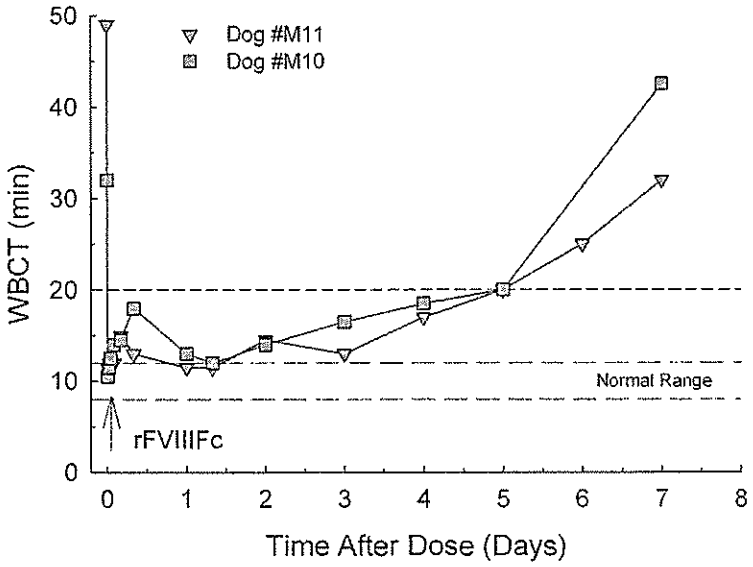

Dog #M11
Dog #M10
WBCT (min)
Normal Range
rFVIIIFc
Time After Dose (Days)
0
10
20
30
40
50
0
1
2
3
4
5
6
7
8

Figure 4B

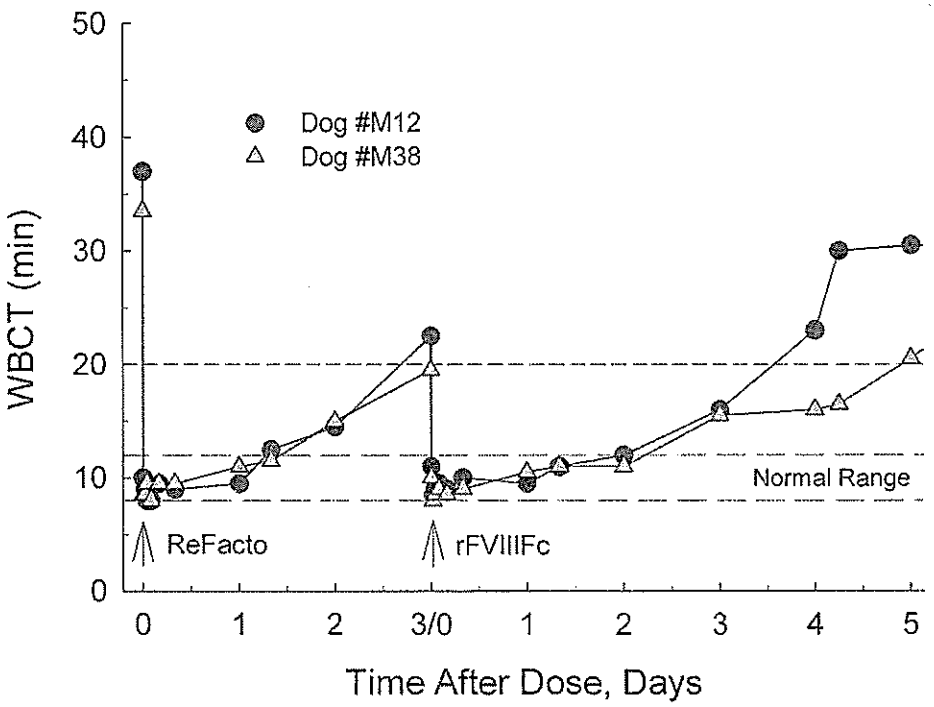

50
40
30
20
10
0
WBCT (min)
Dog #M12
Dog #M38
Normal Range
ReFacto
rFVIIIFc
0
1
2
3/0
1
2
3
4
5
Time After Dose, Days

Figure 5

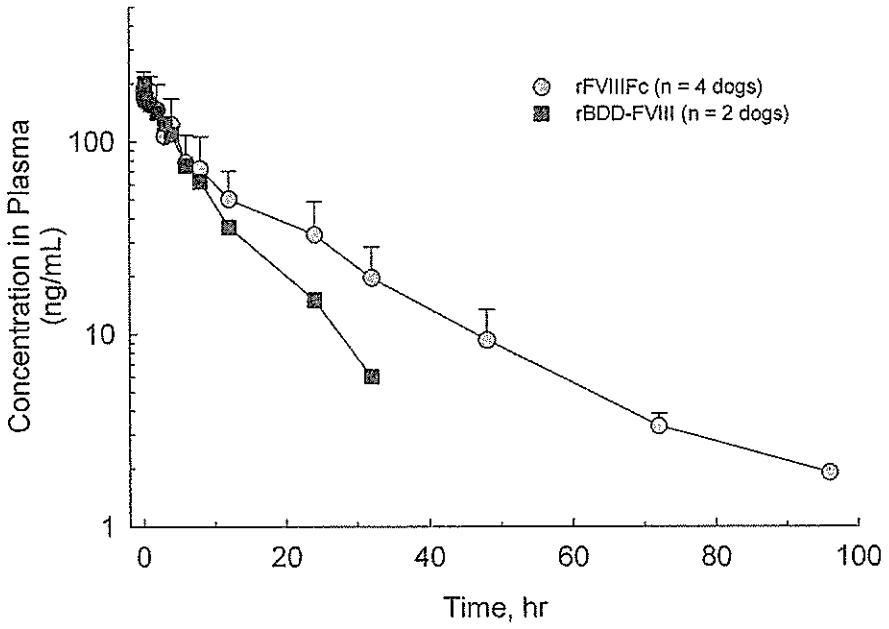

rFVIIIFc (n = 4 dogs)
rBDD-FVIII (n = 2 dogs)
Concentration in Plasma (ng/mL)
100
10
1
0
20
40
60
80
100
Time, hr

Figure 6

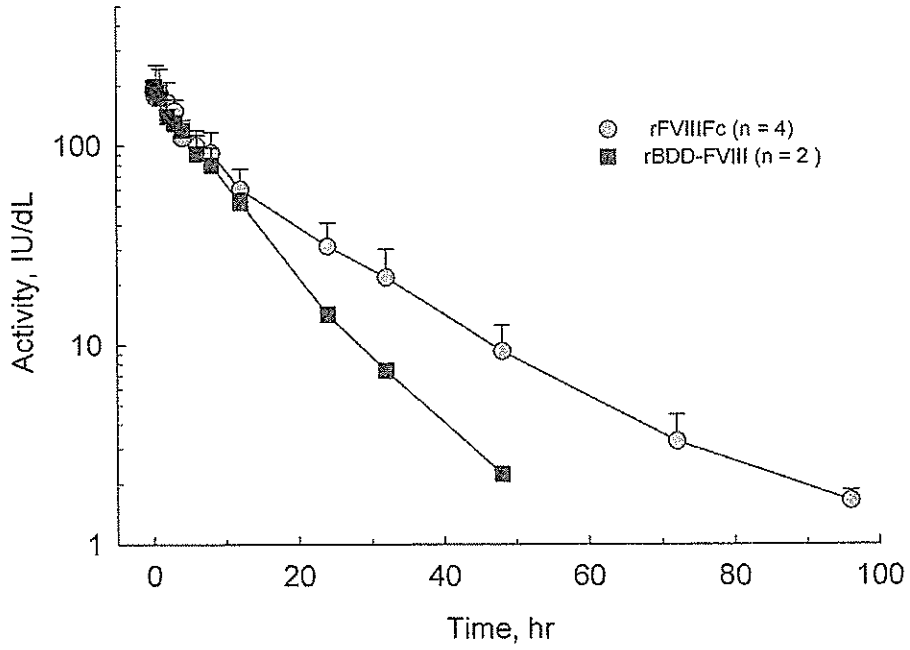

rFVIIIFc (n = 4)
rBDD-FVIII (n = 2)
Activity, IU/dL
100
10
1
0
20
40
60
80
100
Time, hr

Figure 7

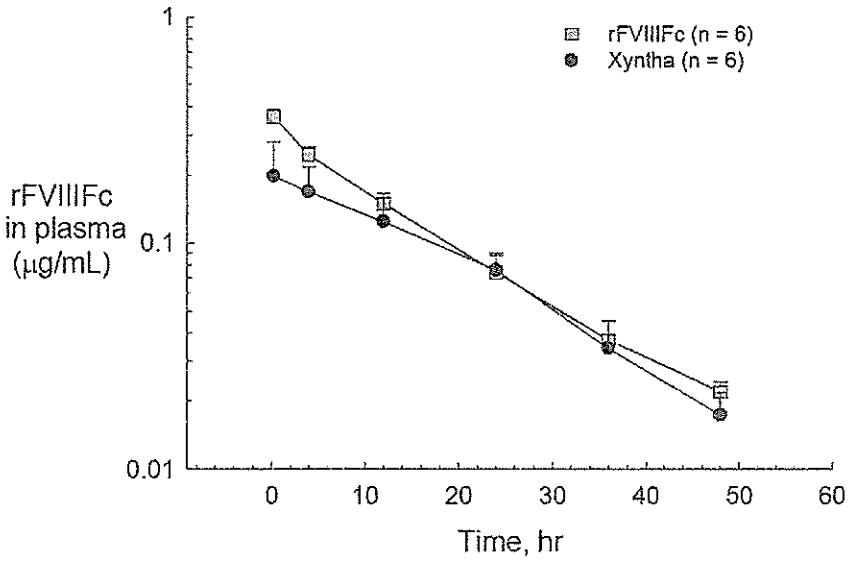
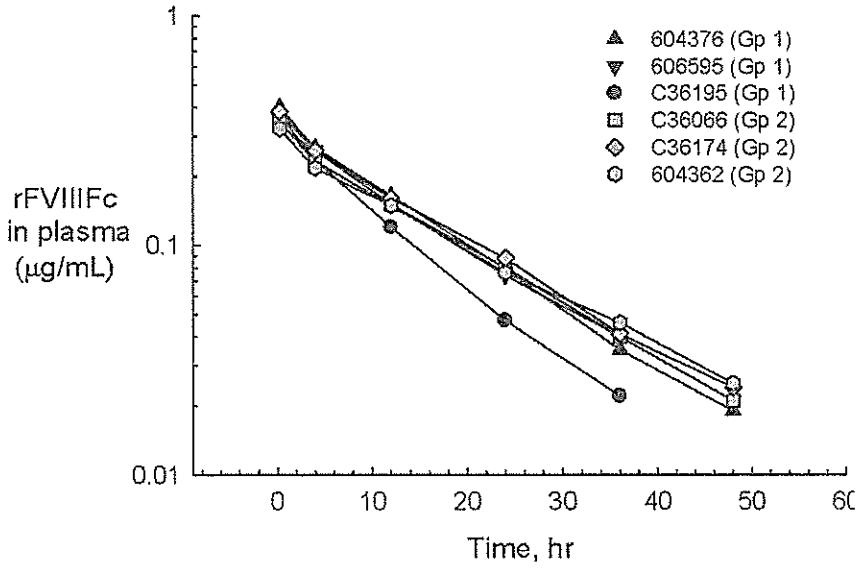

rFVIIIFc (n = 6)
Xyntha (n = 6)
rFVIIIFc in plasma (μg/mL)
1
0.1
0.01
0
10
20
30
40
50
60
Time, hr

Figure 8

A.


1
0.1
0.01
rFVIIIFc
in plasma
(μg/mL)
0
10
20
30
40
50
60
Time, hr
604376 (Gp 1)
606595 (Gp 1)
C36195 (Gp 1)
C36066 (Gp 2)
C36174 (Gp 2)
604362 (Gp 2)

B.

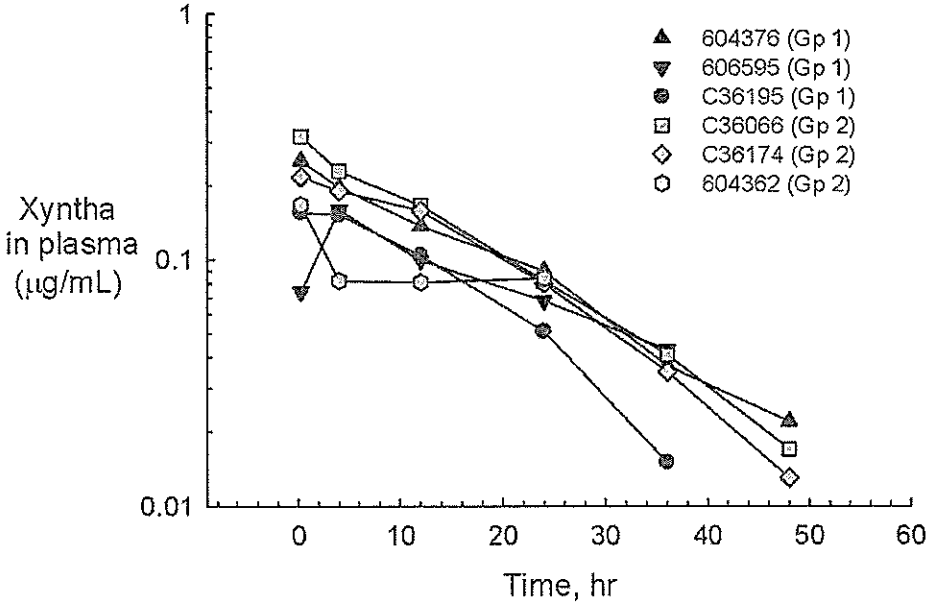

1
0.1
0.01
Xyntha
in plasma
(μg/mL)
0
10
20
30
40
50
60
Time, hr
604376 (Gp 1)
606595 (Gp 1)
C36195 (Gp 1)
C36066 (Gp 2)
C36174 (Gp 2)
604362 (Gp 2)

Figure 9

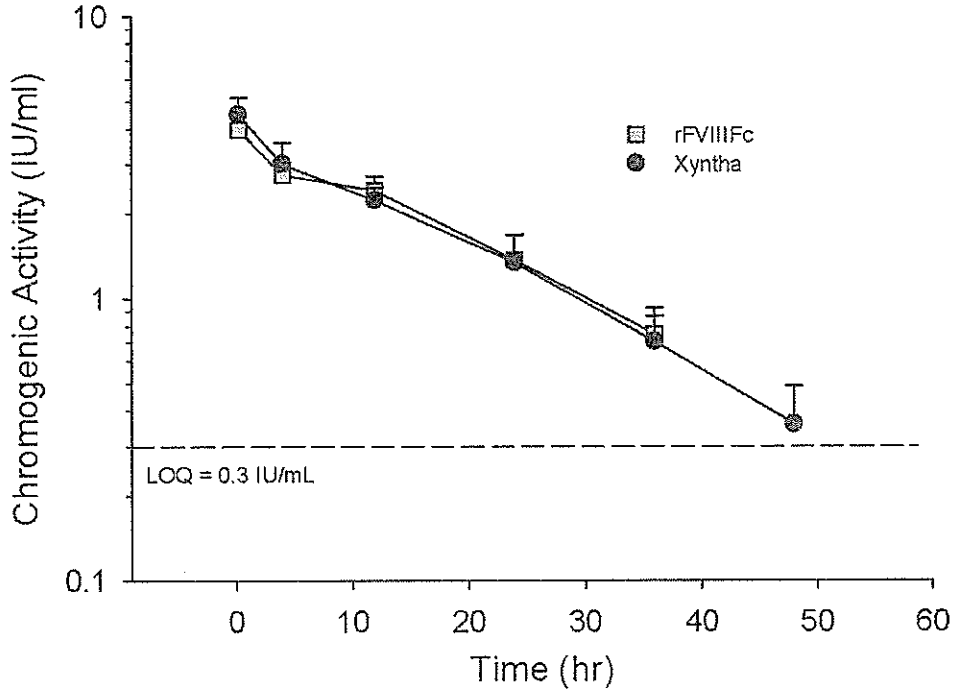
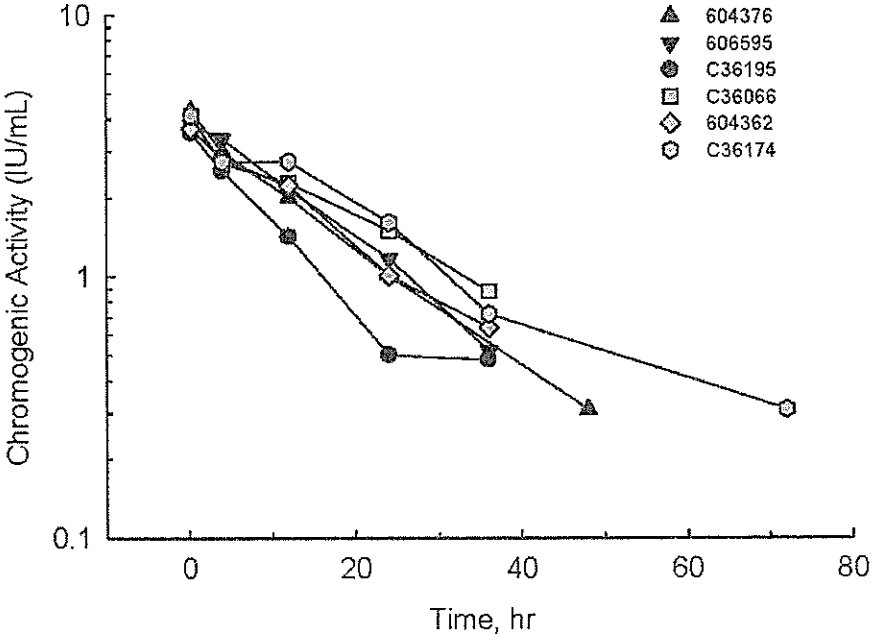

10
1
0.1
Chromogenic Activity (IU/ml)
rFVIIIFc
Xyntha
LOQ = 0.3 IU/mL
0
10
20
30
40
50
60
Time (hr)

Figure 10

A.


10
1
0.1
Chromogenic Activity (IU/mL)
0
20
40
60
80
Time, hr
604376
606595
C36195
C36066
604362
C36174

B.

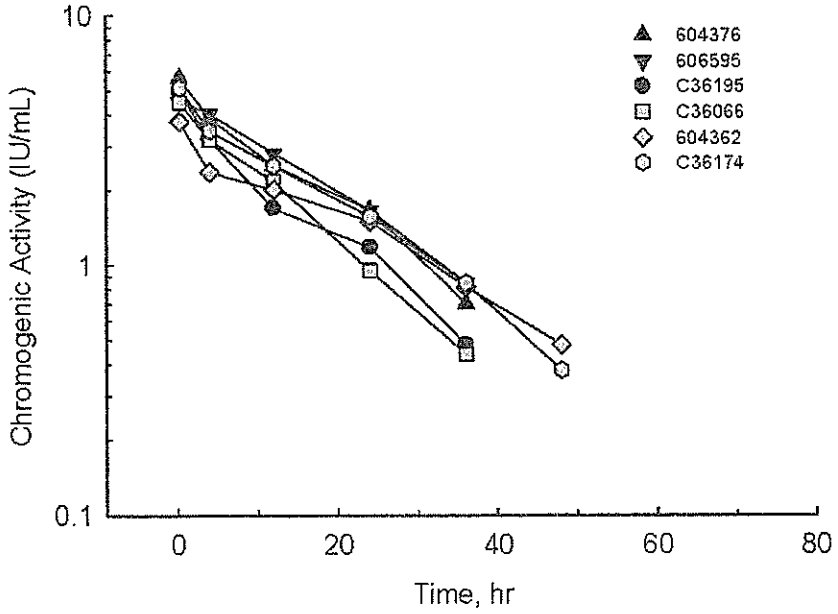

10
1
0.1
Chromogenic Activity (IU/mL)
0
20
40
60
80
Time, hr
604376
606595
C36195
C36066
604362
C36174

Figure 11

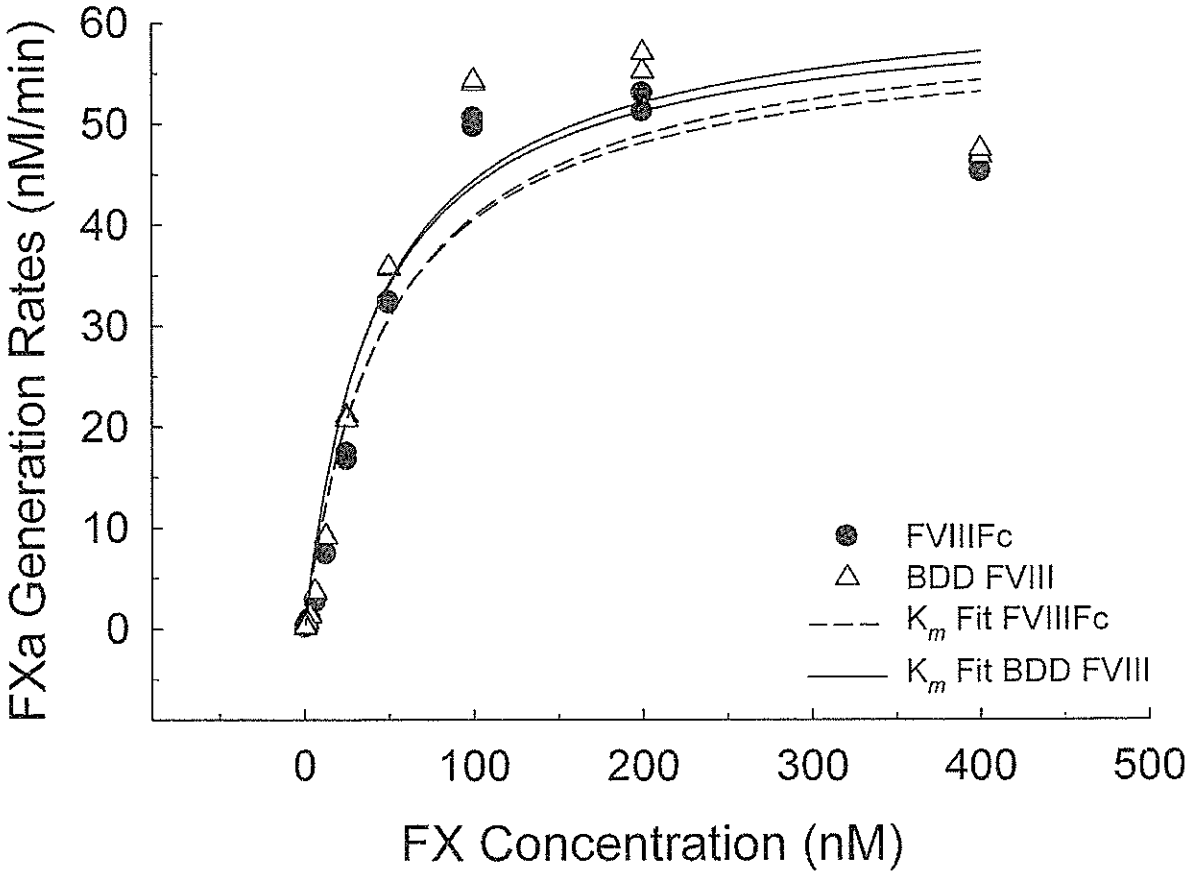

FXa Generation Rates (nM/min)
60
50
40
30
20
10
0
0
100
200
300
400
500
FX Concentration (nM)
FVIIIFc
BDD FVIII
K_m Fit FVIIIFc
K_m Fit BDD FVIII

Figure 12

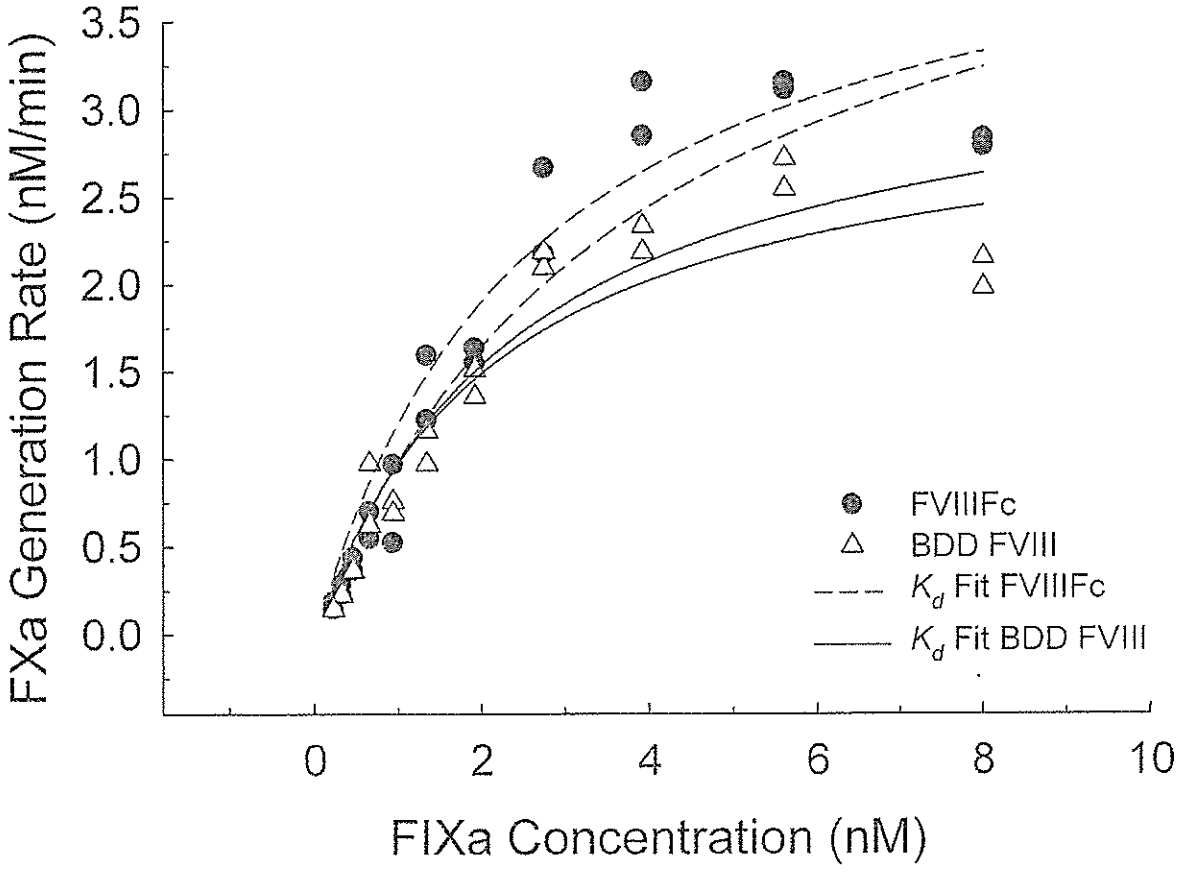

FXa Generation Rate (nM/min)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
2
4
6
8
10
FIXa Concentration (nM)
FVIIIFc
BDD FVIII
K_d Fit FVIIIFc
K_d Fit BDD FVIII

Figure 13A

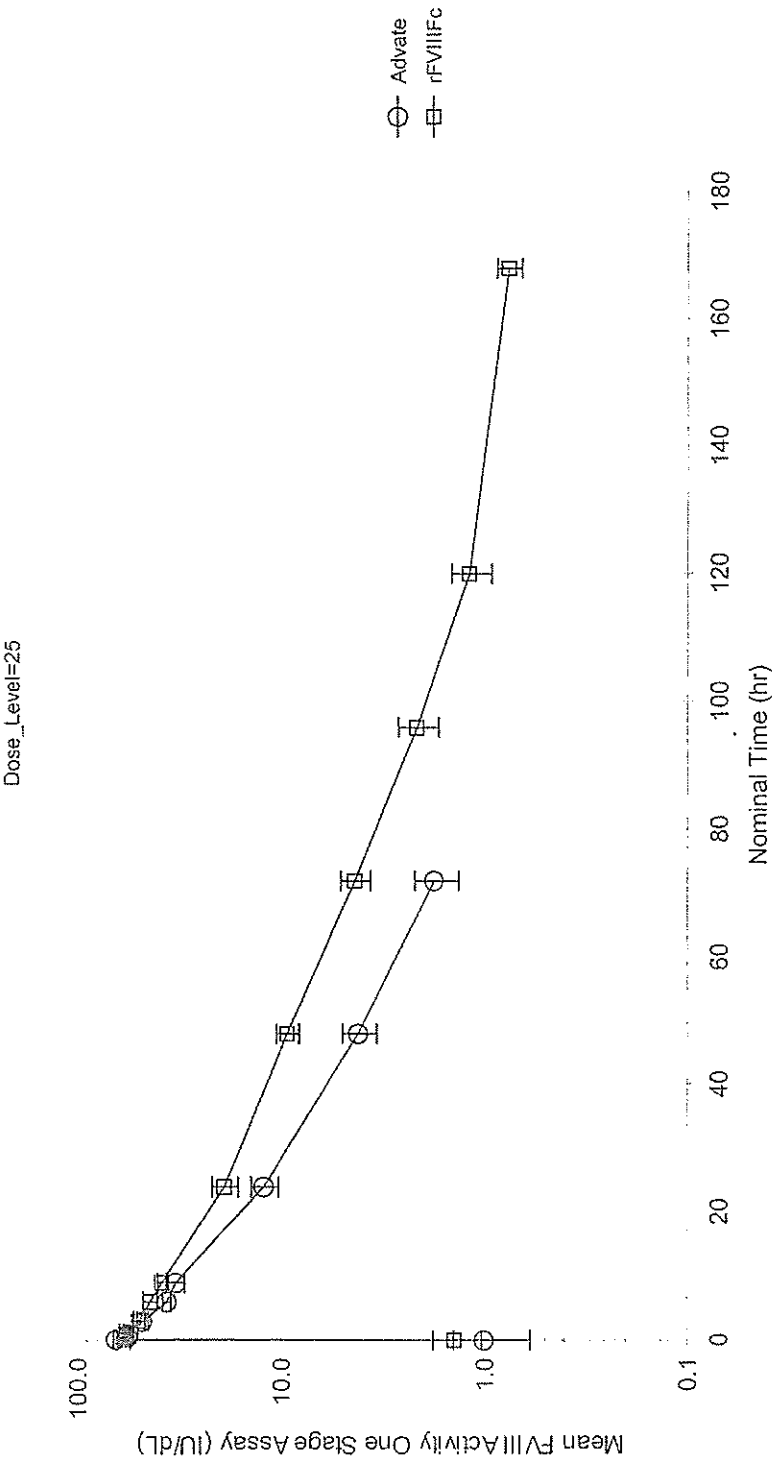

Dose_Level=25
Advate
rFVIIIFc
Mean FVIII Activity One Stage Assay (IU/dL)
100.0
10.0
1.0
0.1
0
20
40
60
80
100
120
140
160
180
Nominal Time (hr)

Figure 13B

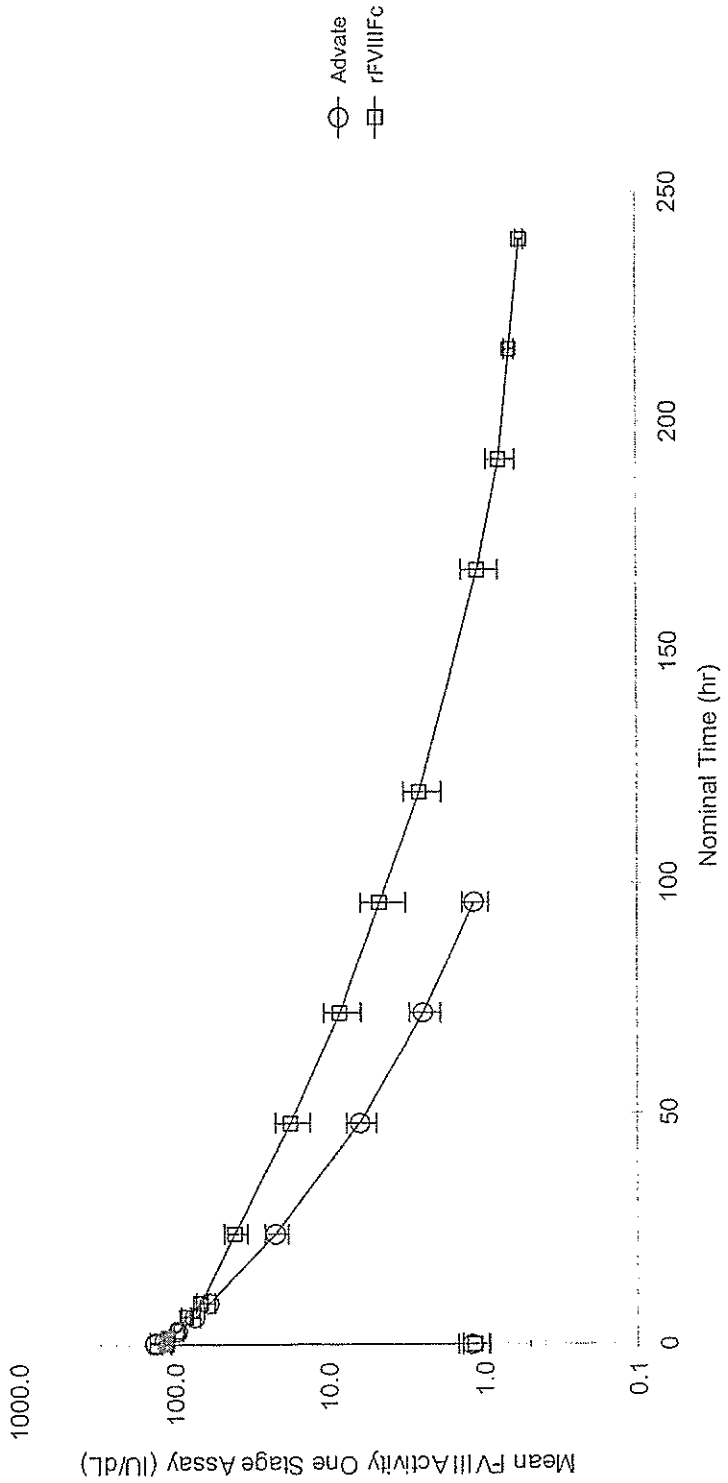

Advate
rFVIIIFc
Dose_Level=65
Mean FVIII Activity One Stage Assay (IU/dL)
1000.0
100.0
10.0
1.0
0.1
0
50
100
150
200
250
Nominal Time (hr)

Figure 13C

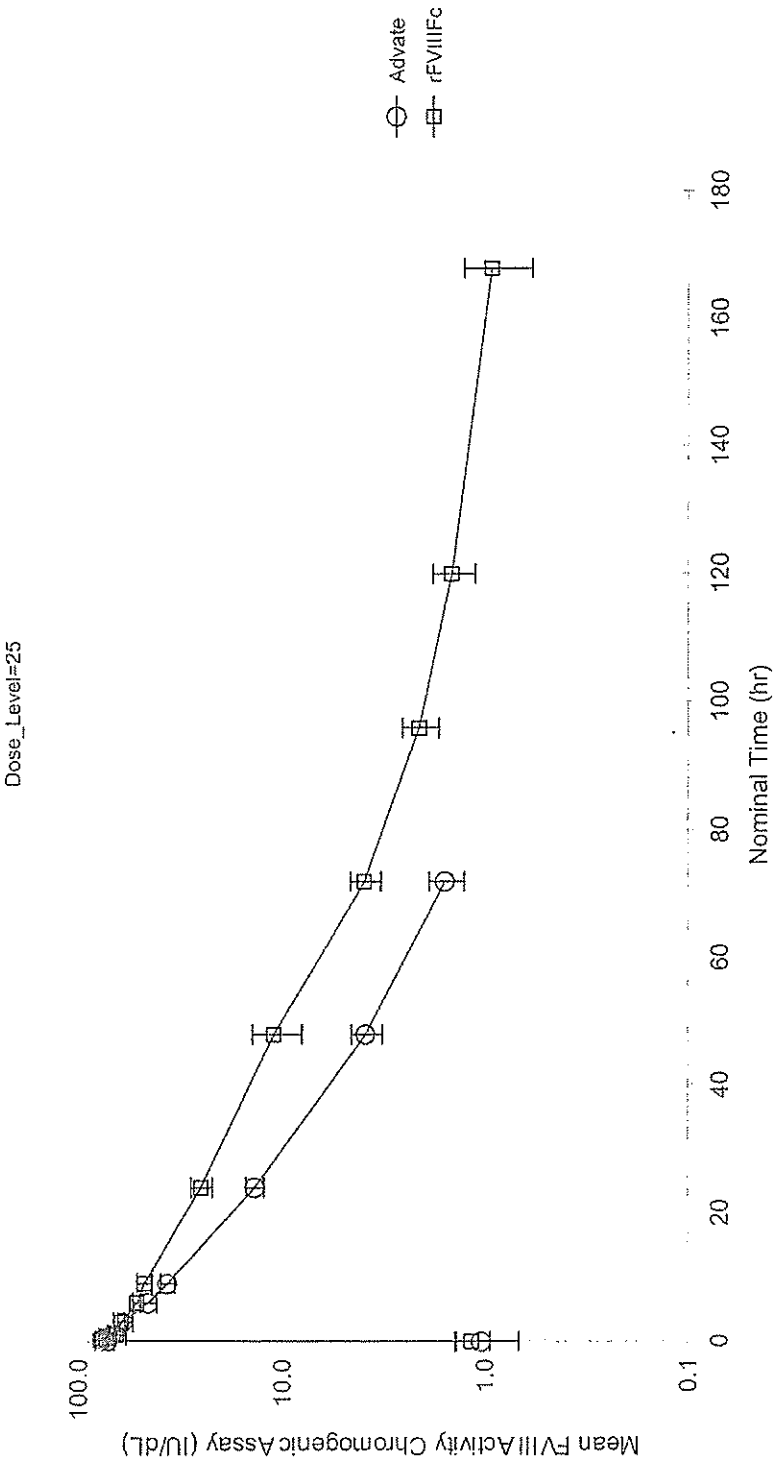

Dose_Level=25
Advate
rFVIIIFc
Mean FVIII Activity Chromogenic Assay (IU/dL)
100.0
10.0
1.0
0.1
0
20
40
60
80
100
120
140
160
180
Nominal Time (hr)

Figure 13D

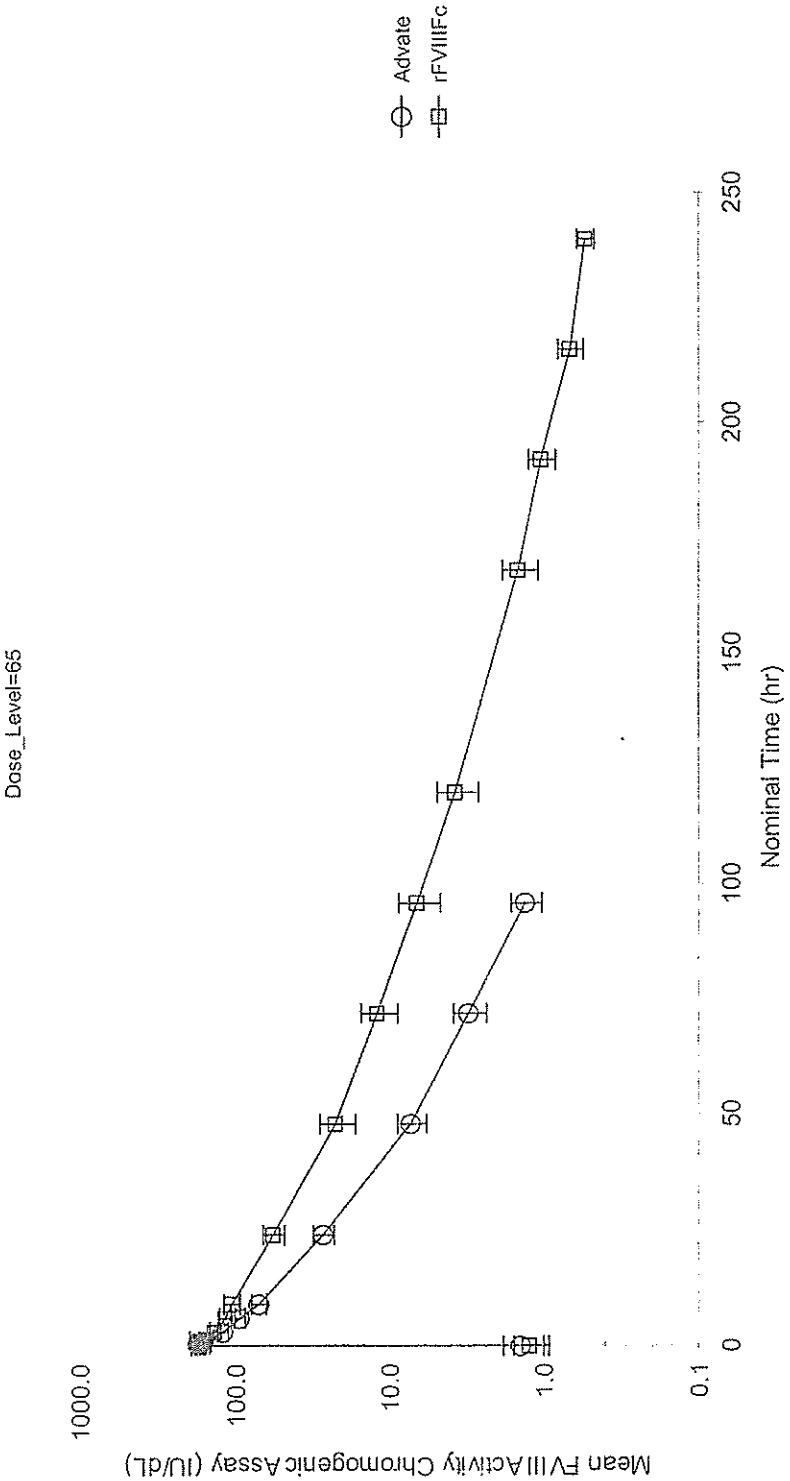

Advate
rFVIIIFc
Dose_Level=65
Mean FVIII Activity Chromogenic Assay (IU/dL)
1000.0
100.0
10.0
1.0
0.1
0
50
100
150
200
250
Nominal Time (hr)

Figure 14A

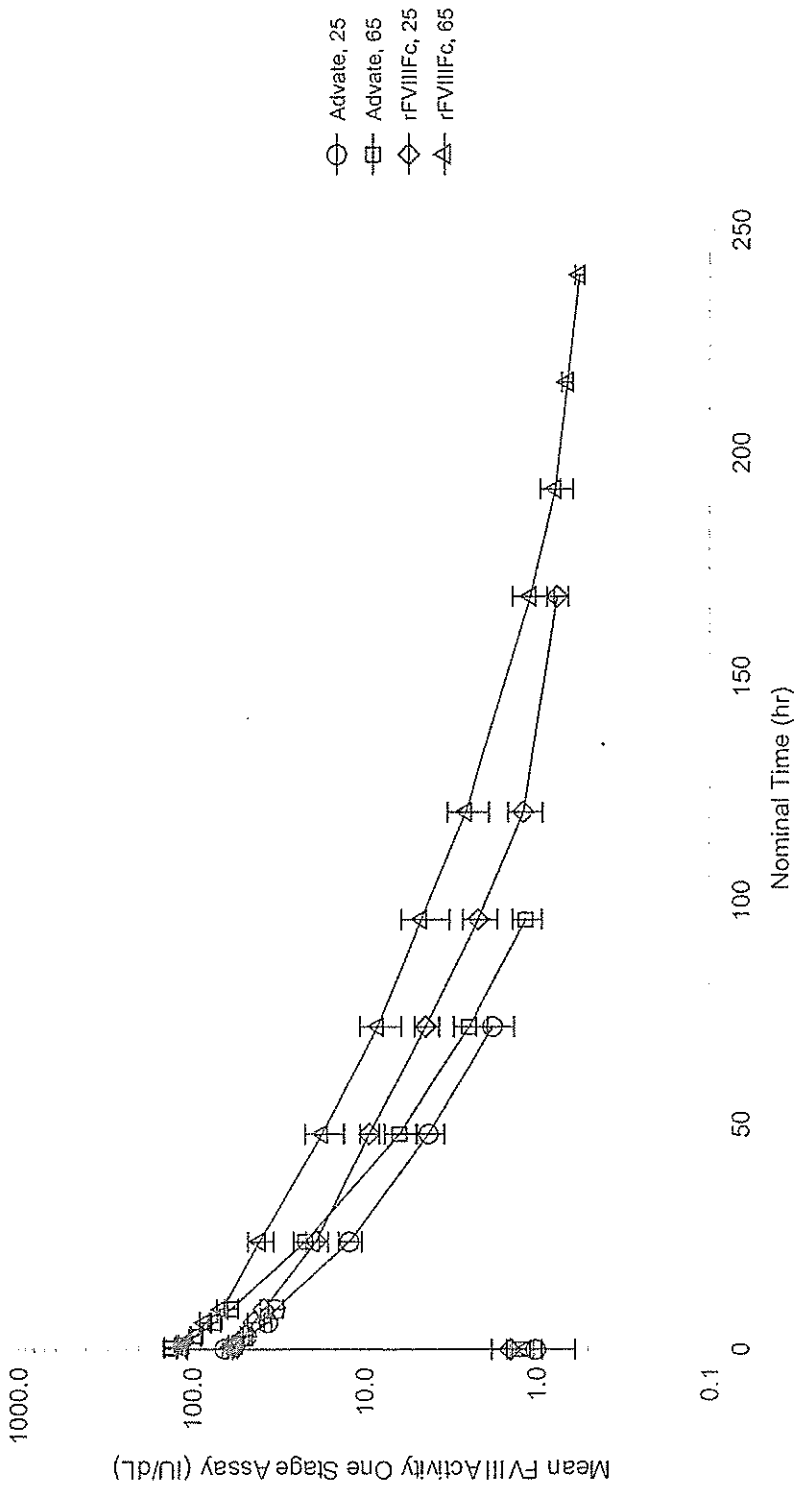
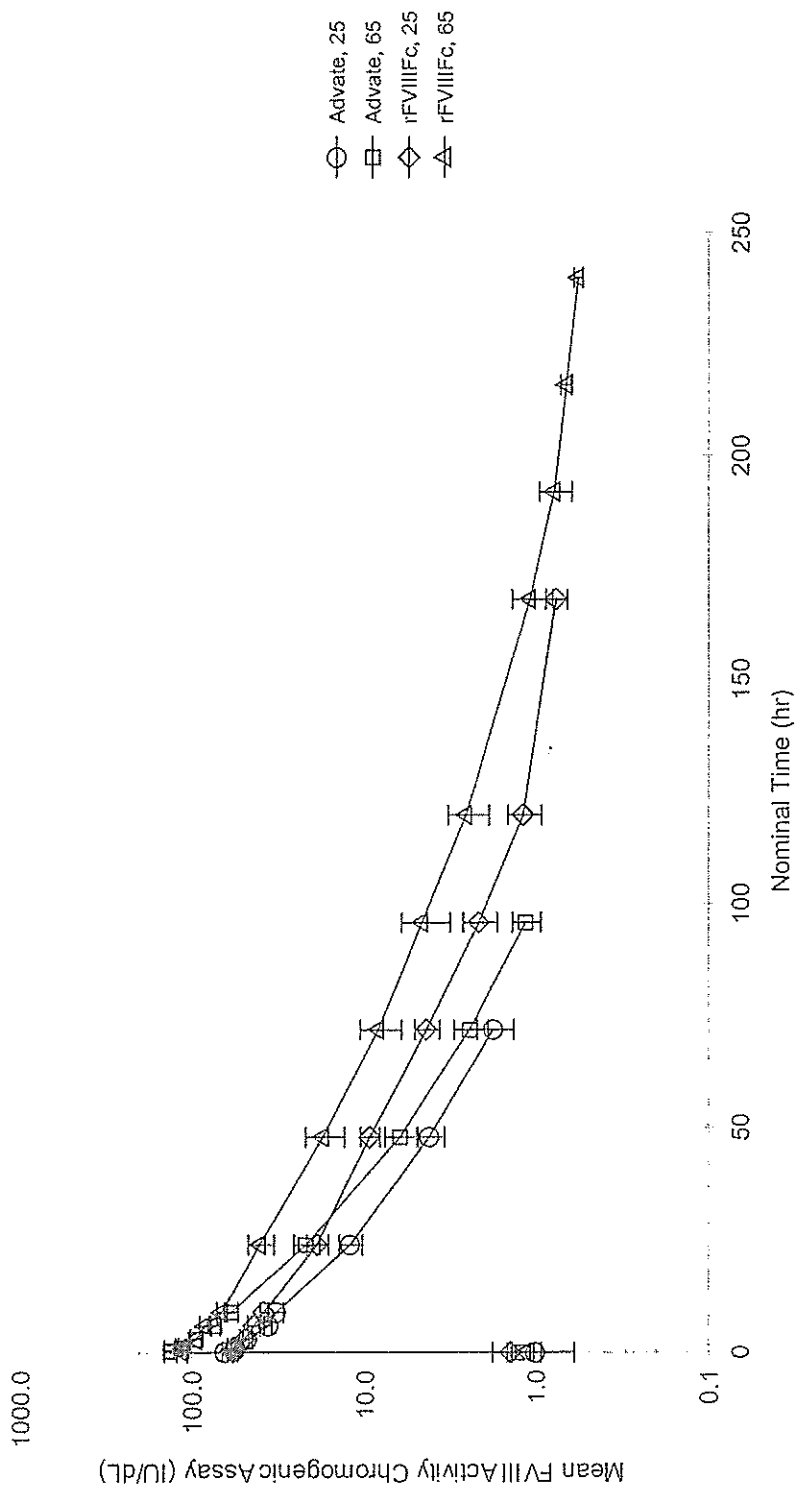

Advate, 25
Advate, 65
rFVIIIFc, 25
rFVIIIFc, 65
Mean FVIII Activity One Stage Assay (IU/dL)
1000.0
100.0
10.0
1.0
0.1
0
50
100
150
200
250
Nominal Time (hr)

Figure 14B


Advate, 25
Advate, 65
rFVIIIFc, 25
rFVIIIFc, 65
Mean FVIII Activity Chromogenic Assay (IU/dL)
1000.0
100.0
10.0
1.0
0.1
0
50
100
150
200
250
Nominal Time (hr)