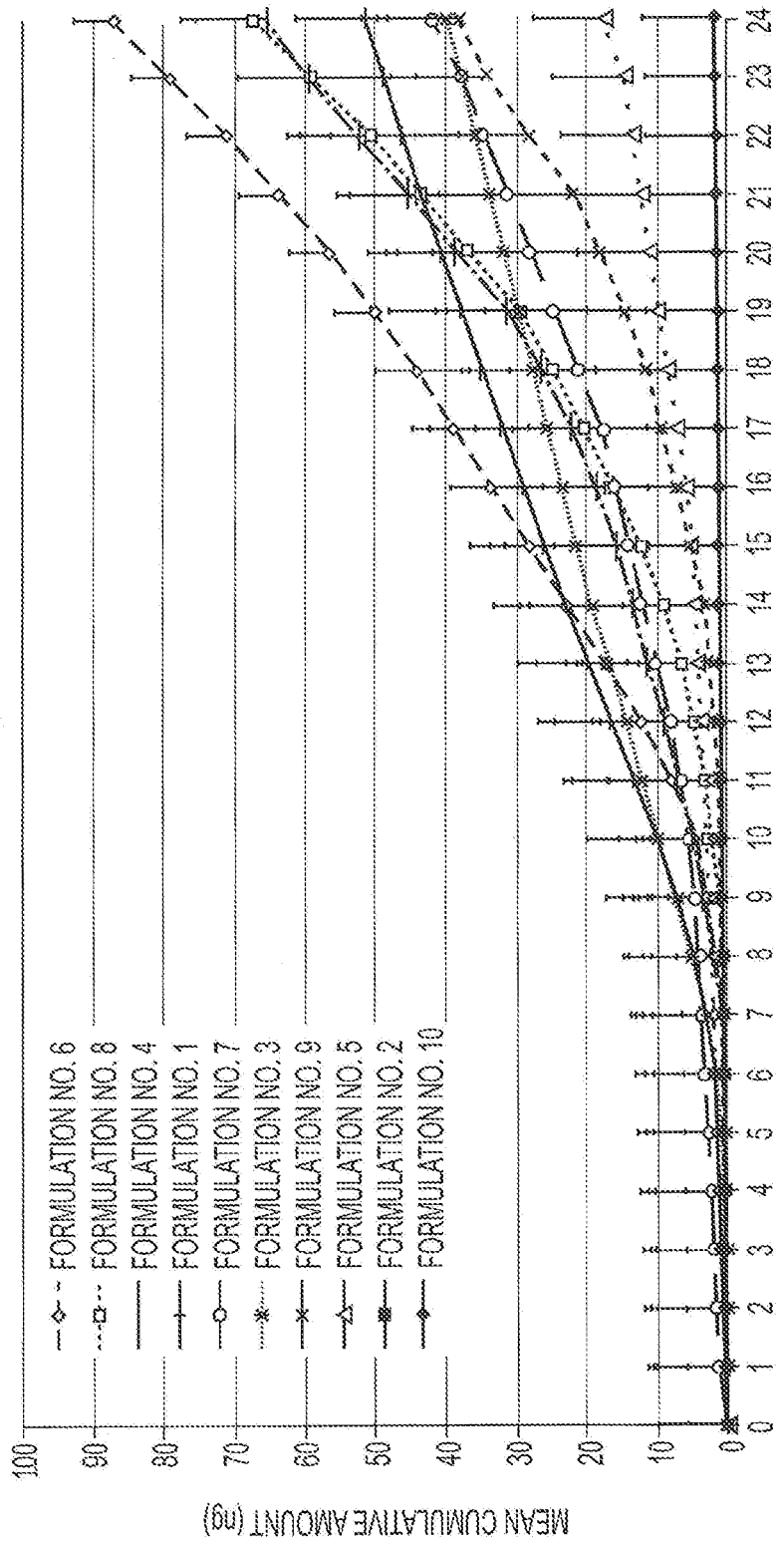

IN VITRO SKIN PENETRATION ASSAY RESULTS
N31506-1, R1, R2, R3 AND R4, MEAN CUMULATIVE AMOUNT OF API (ng) AFTER 24 HRS, 4 SKIN DONORS, N = 12 TO 17
FORMULATION NO. 6
FORMULATION NO. 8
FORMULATION NO. 4
FORMULATION NO. 1
FORMULATION NO. 7
FORMULATION NO. 3
FORMULATION NO. 9
FORMULATION NO. 5
FORMULATION NO. 2
FORMULATION NO. 10
MEAN CUMULATIVE AMOUNT (ng)
TIME (HRS)

FIG. 1

Figure 2 Simulated distributions of palm and axilla size in adult males.

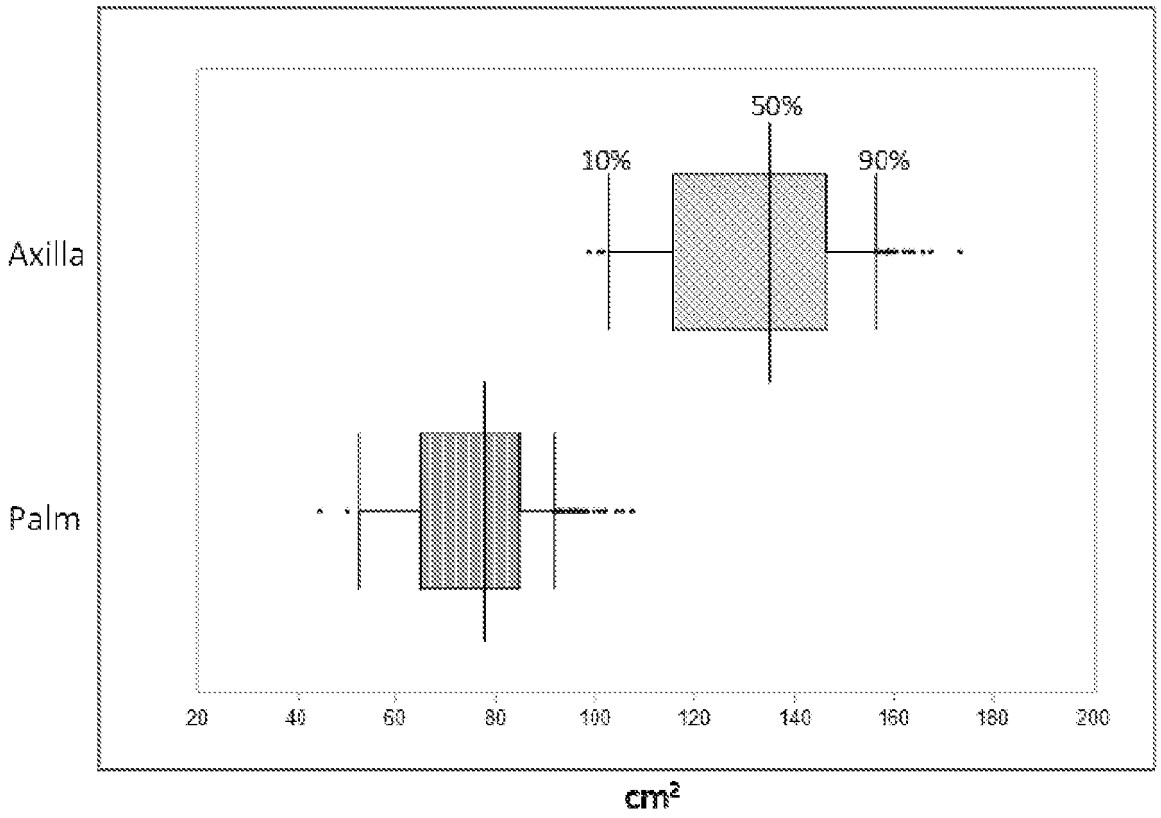
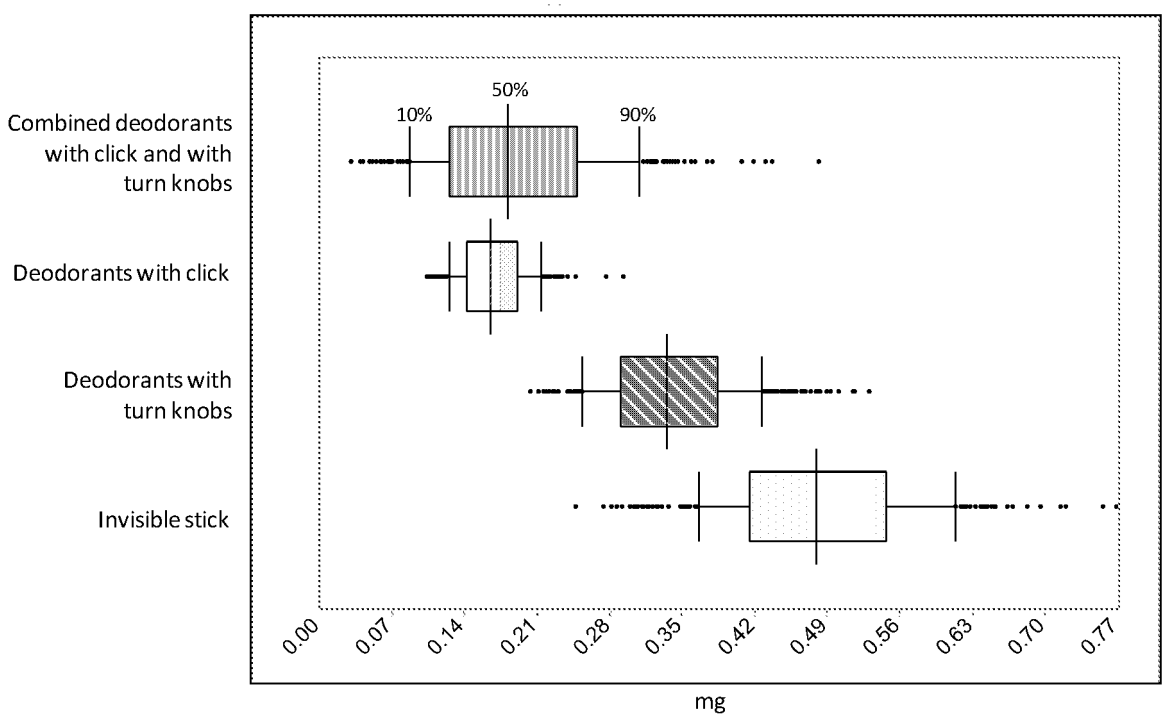


Figure 3 Distributions of the amount of product applied by different types of metered deodorants.



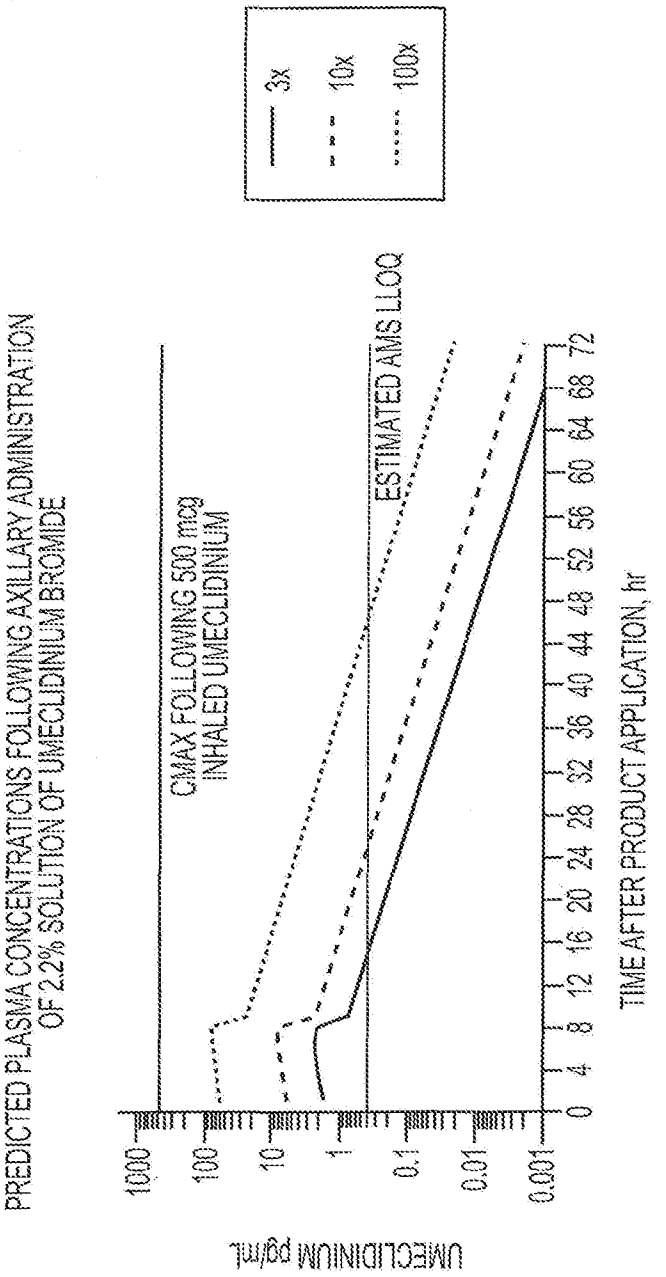
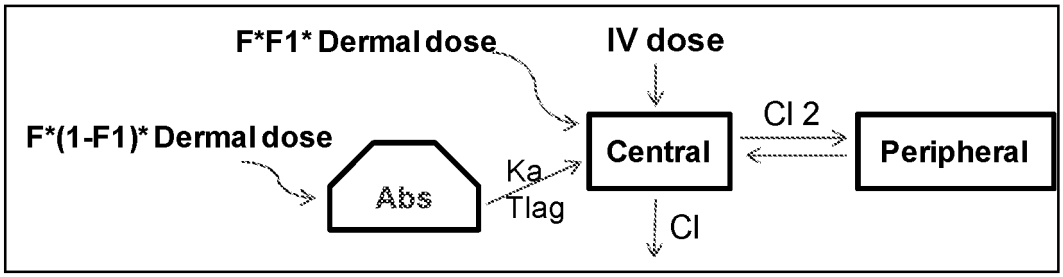

PREDICTED PLASMA CONCENTRATIONS FOLLOWING AXILLARY ADMINISTRATION OF 2.2% SOLUTION OF UMECLIDINIUM BROMIDE
CMAX FOLLOWING 500 mcg INHALED UMECLIDINIUM
ESTIMATED AMS LLOQ
3x
10x
100x
UMECLIDINIUM pg/mL
1000
100
10
1
0.1
0.01
0.001
0 4 8 12 16 20 24 28 32 36 40 44 48 52 56 60 64 68 72
TIME AFTER PRODUCT APPLICATION, hr

FIG. 4

Figure 5 Structure of the population pharmacokinetic model describing a combine dataset of plasma concentrations following IV and dermal administration to occluded axilla.



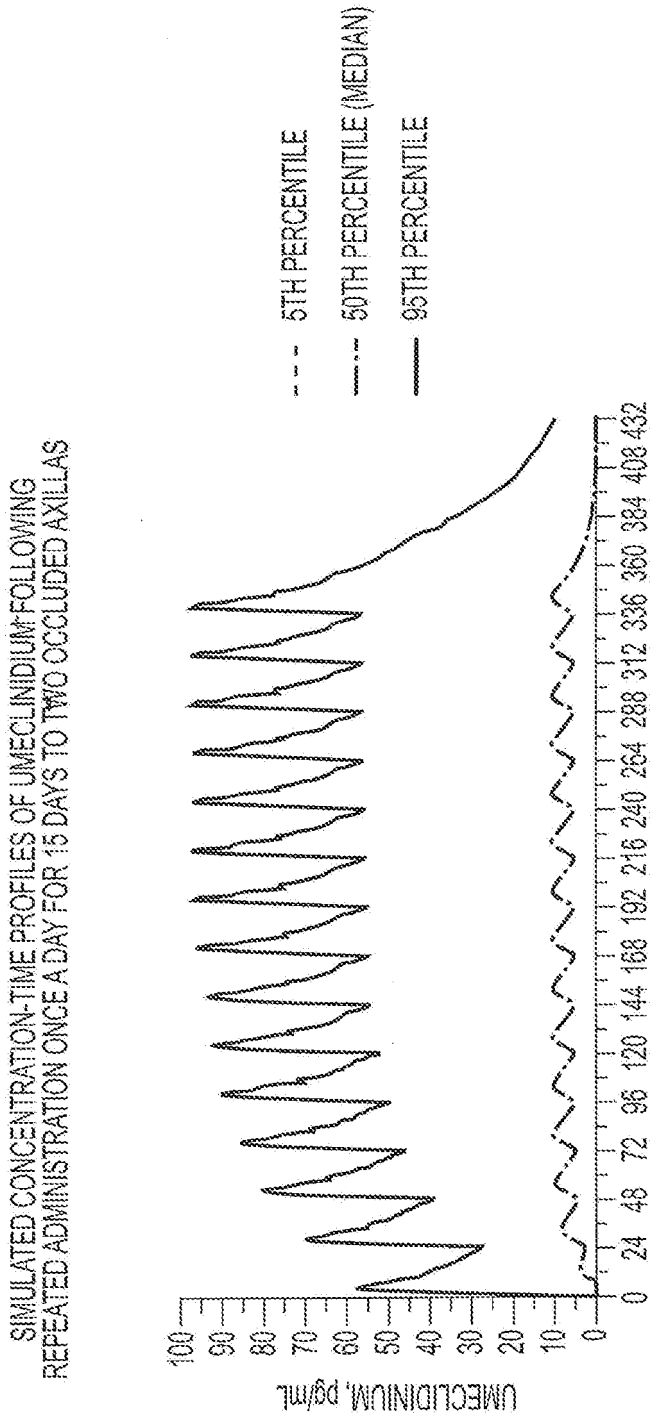
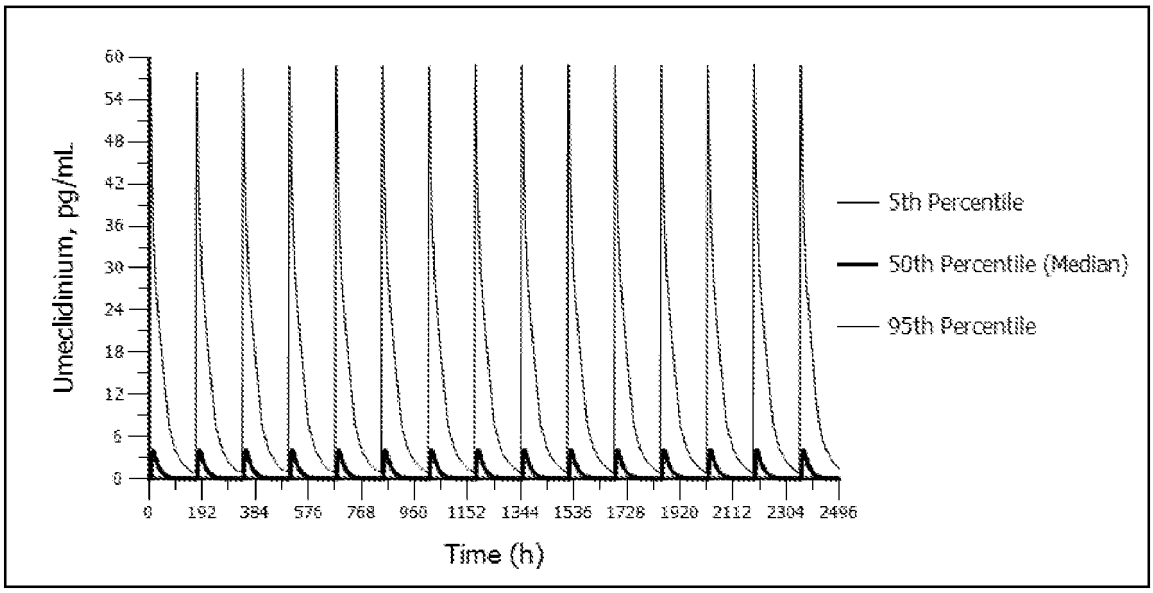

SIMULATED CONCENTRATION-TIME PROFILES OF UMECLINIDIUM FOLLOWING REPEATED ADMINISTRATION ONCE A DAY FOR 15 DAYS TO TWO OCCLUDED AXILLAS
5TH PERCENTILE
50TH PERCENTILE (MEDIAN)
95TH PERCENTILE
UMECLIDINIUM, pg/mL
100
90
80
70
60
50
40
30
20
10
0
0 24 48 72 96 120 144 168 192 216 240 264 288 312 336 360 384 408 432
TIME (h)

FIG. 6

Figure 7 Simulated concentration-time profiles of Umeclidinium following repeated administration once a week for 15 days to two occluded axillas.



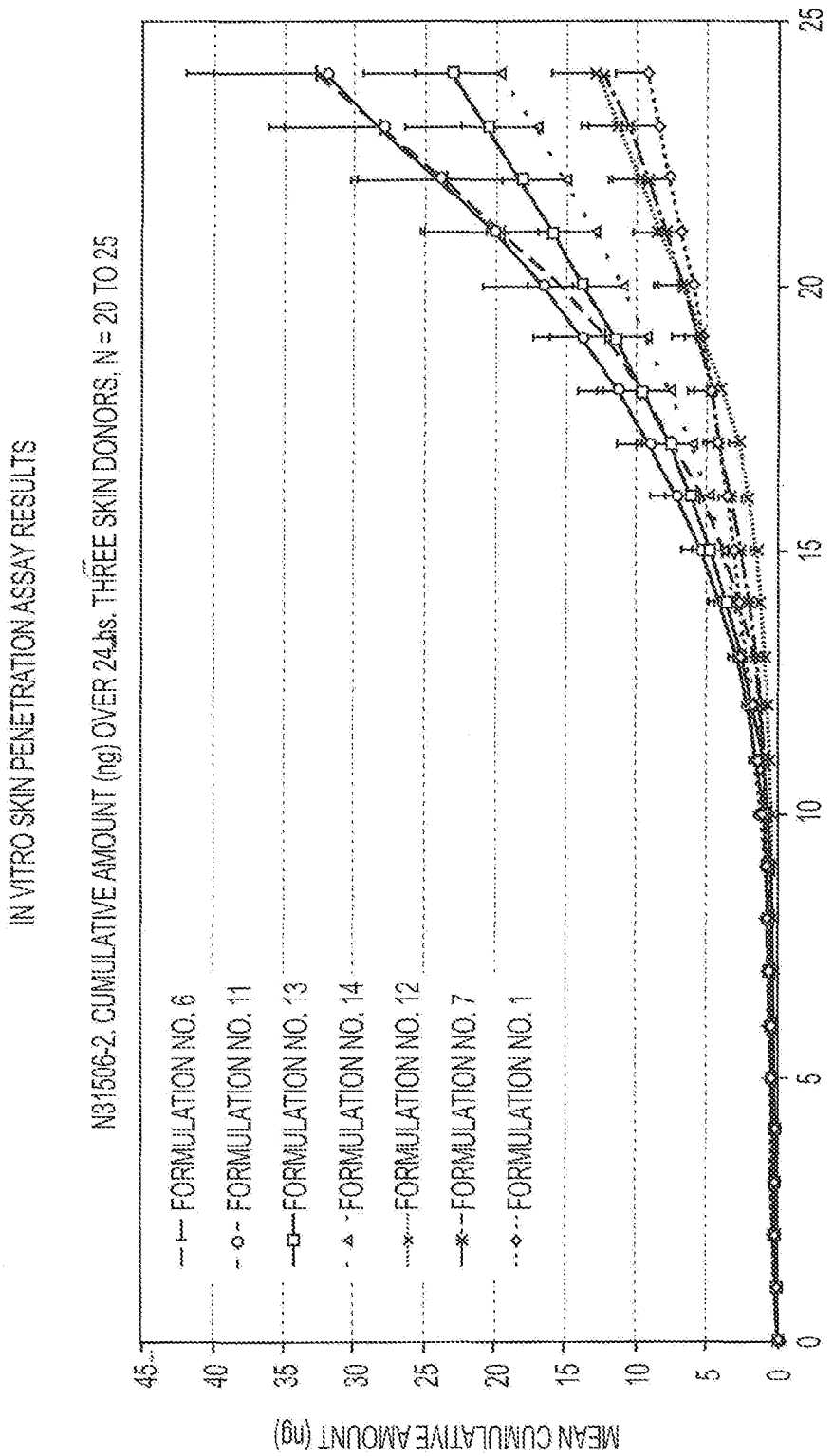

IN VITRO SKIN PENETRATION ASSAY RESULTS
N31506-2. CUMULATIVE AMOUNT (ng) OVER 24 hs. THREE SKIN DONORS, N = 20 TO 25
FORMULATION NO. 6
FORMULATION NO. 11
FORMULATION NO. 13
FORMULATION NO. 14
FORMULATION NO. 12
FORMULATION NO. 7
FORMULATION NO. 1
MEAN CUMULATIVE AMOUNT (ng)
TIME (hs)
0
5
10
15
20
25
30
35
40
45

FIG. 8