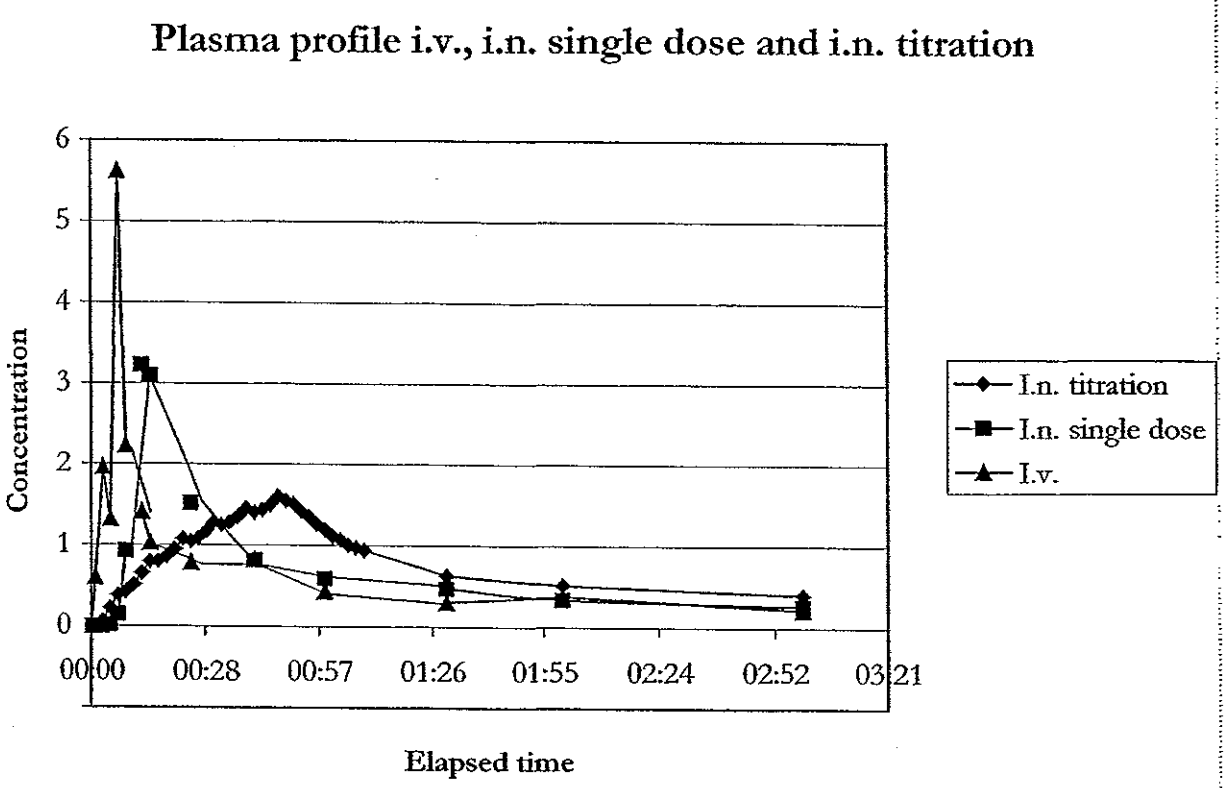
3 0 DEC 2004

Figure 1



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Figure 1A

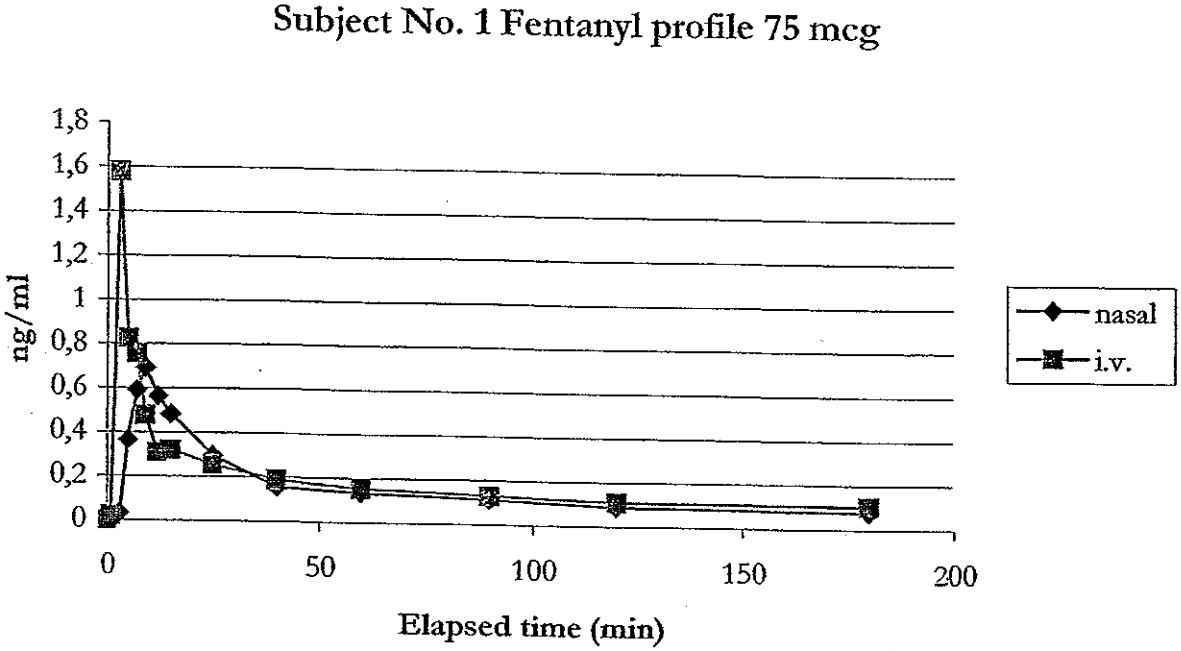


Figure 1B

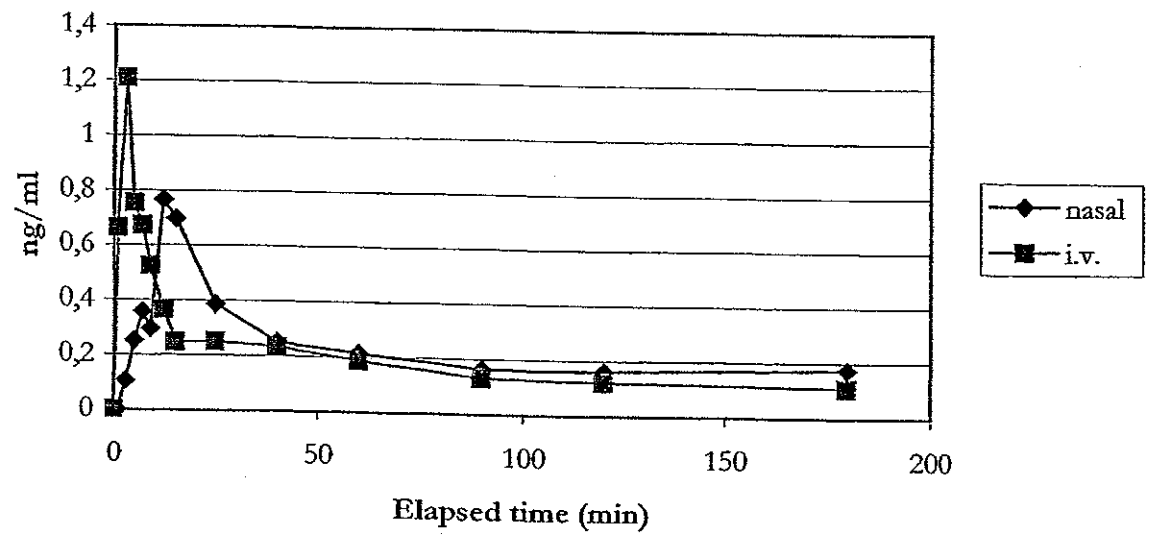
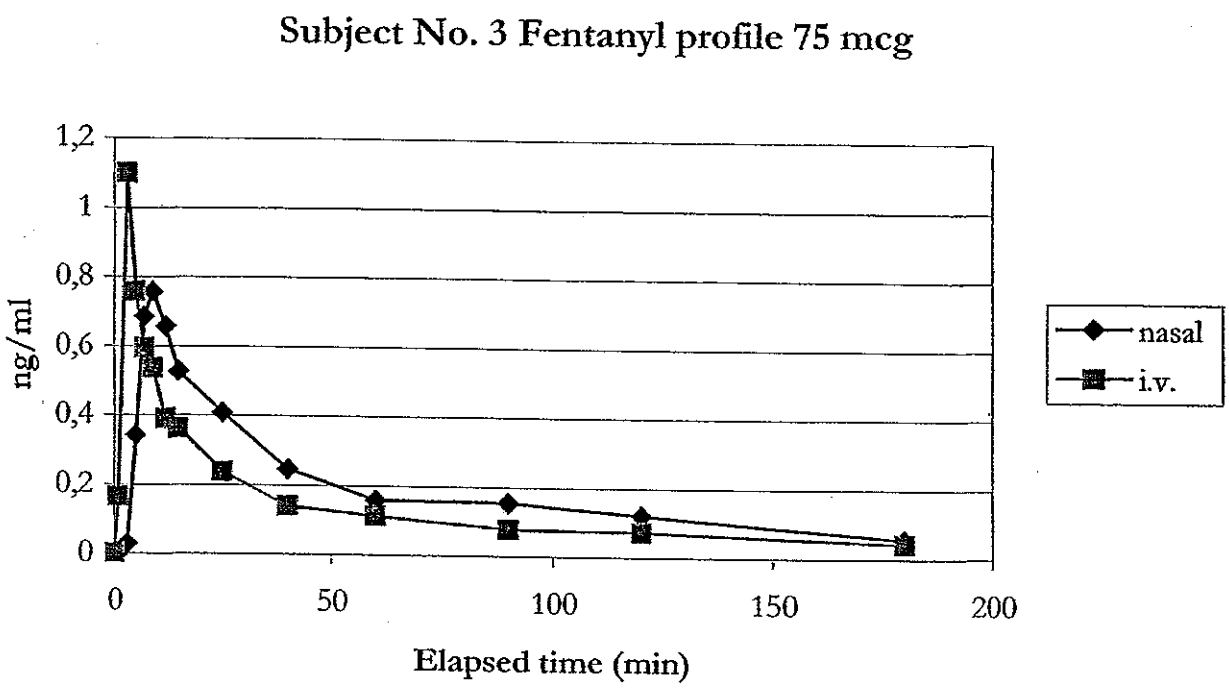


Figure 1C


Subject No. 3 Fentanyl profile 75 mcg
1,2
1
0,8
0,6
0,4
0,2
0
ng/ml
0
50
100
150
200
Elapsed time (min)
nasal
i.v.

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Figure 2A

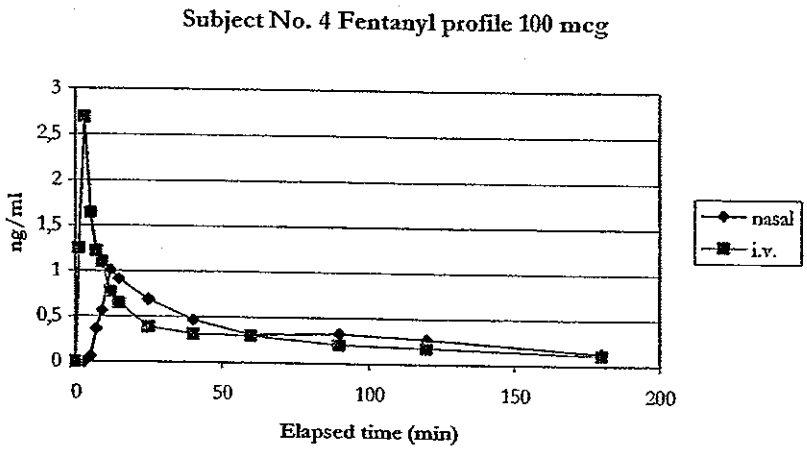
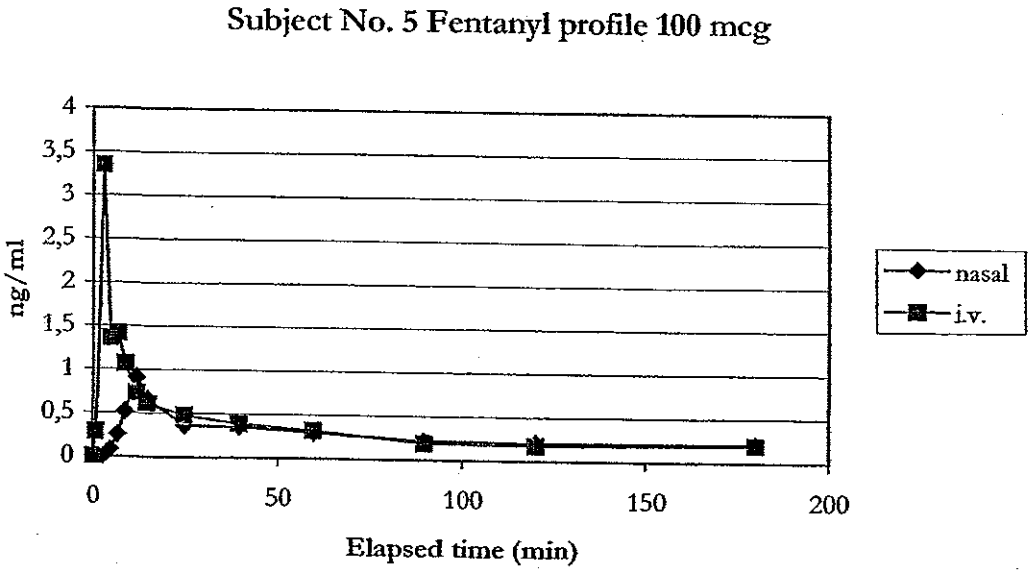


Figure 2B



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Figure 2C

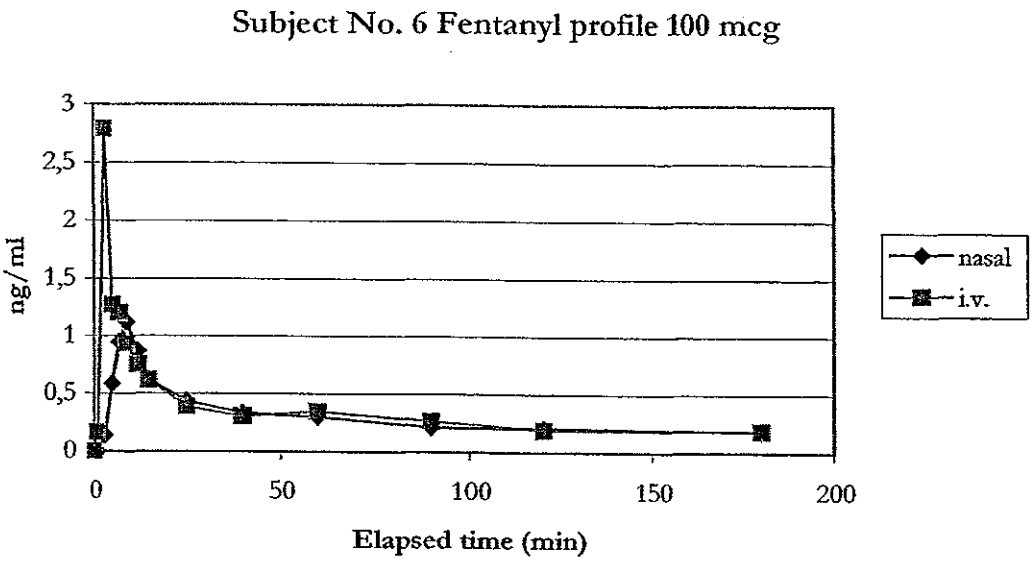


Figure 2D

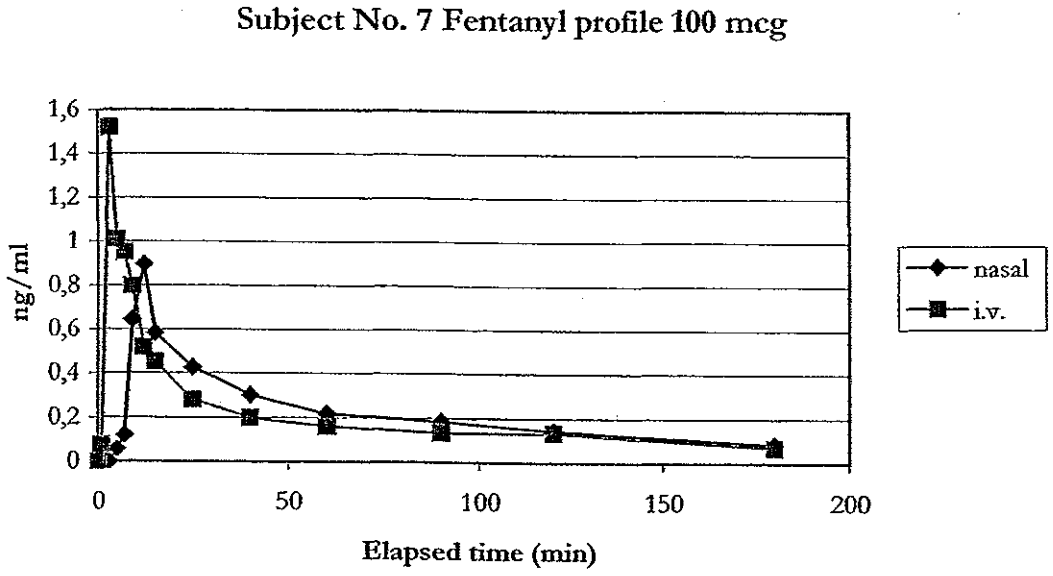


Figure 3A

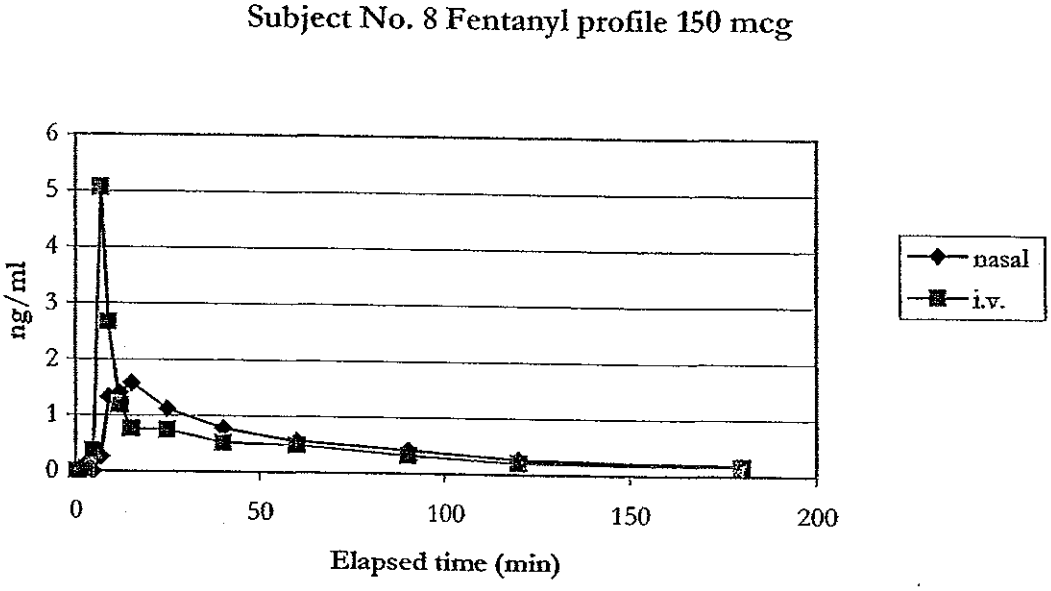
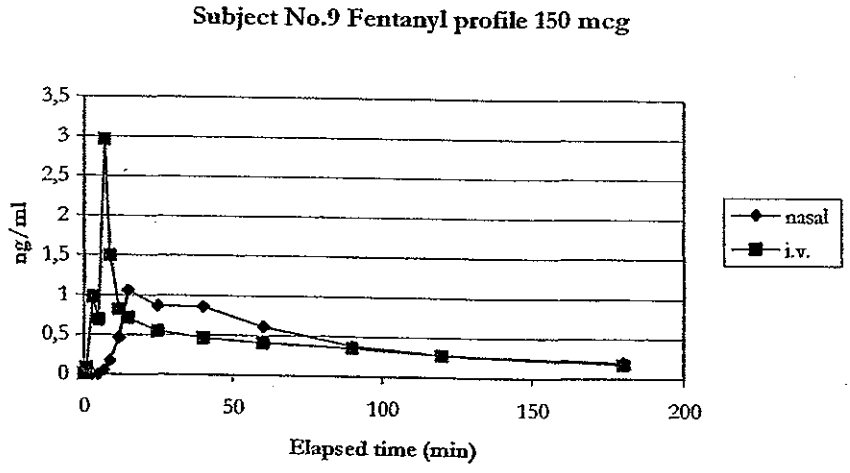


Figure 3B



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Figure 3C

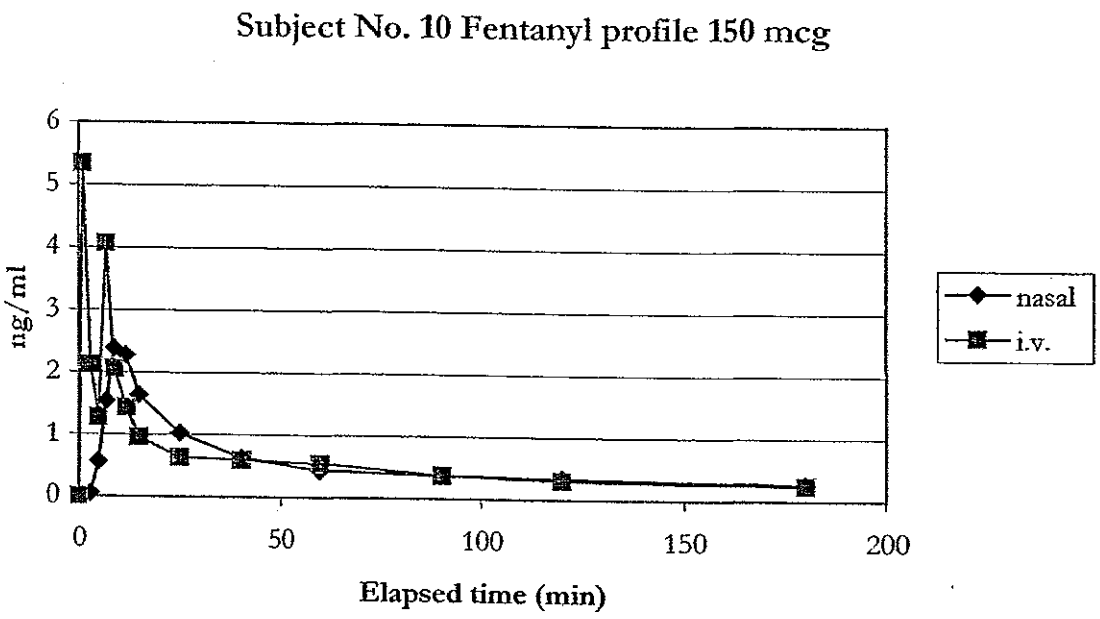


Figure 4A

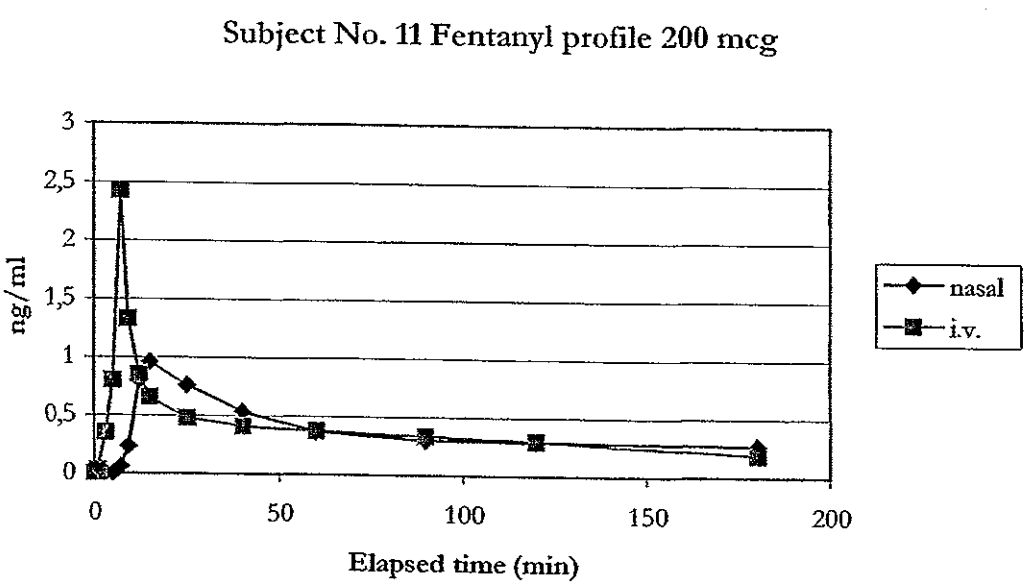
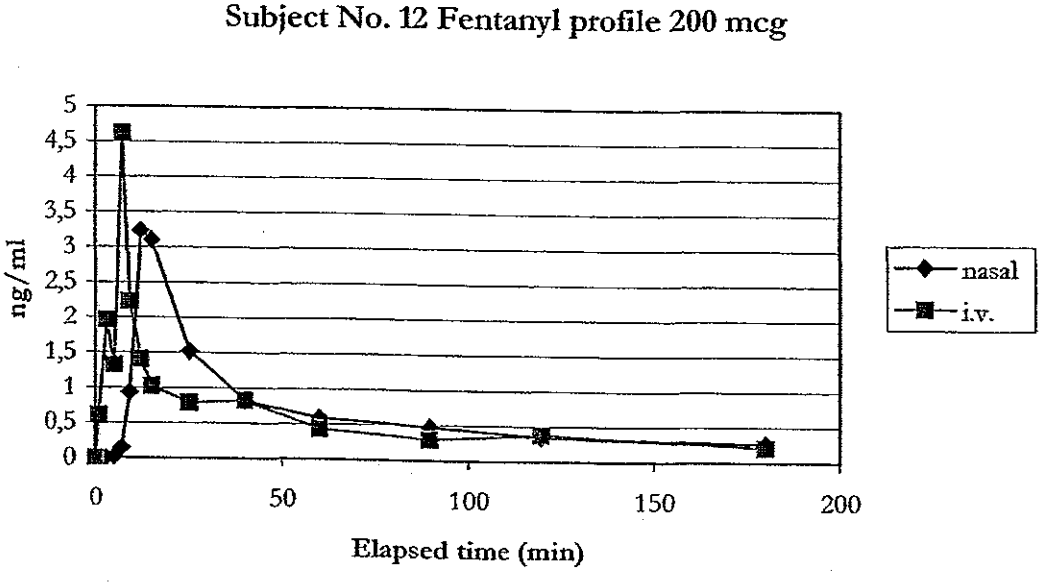


Figure 4B



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4c Figure

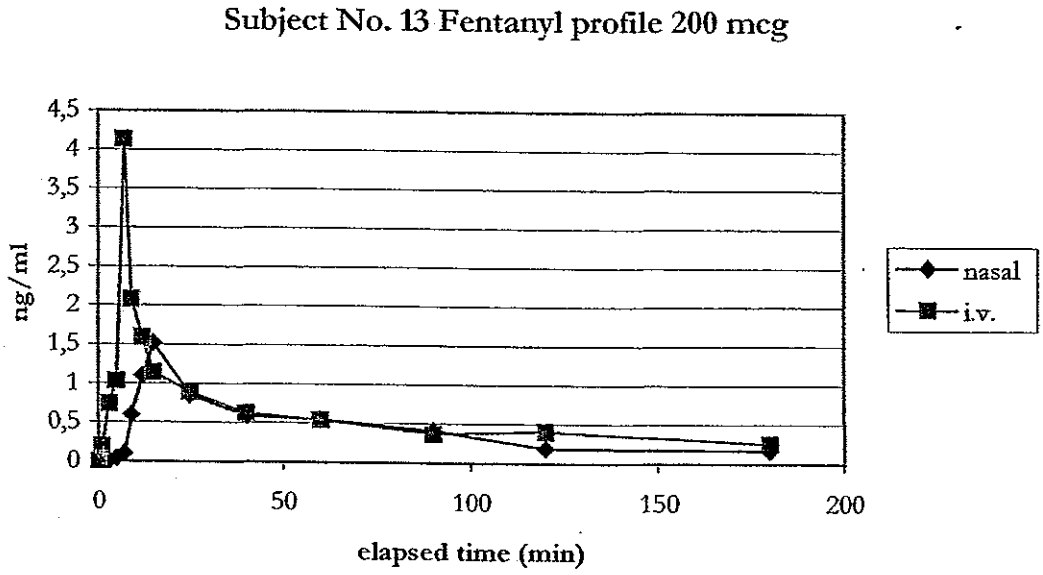


Figure 5

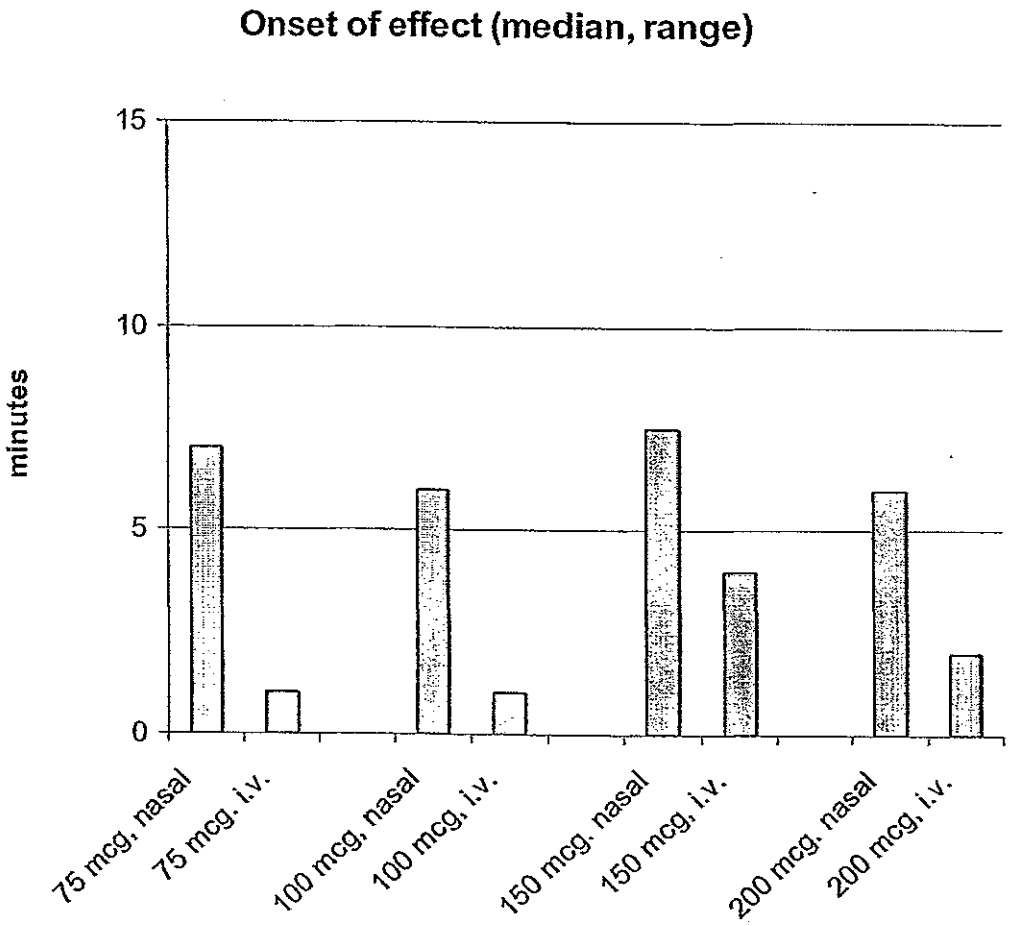

Onset of effect (median, range)
minutes
15
10
5
0
75 mcg, nasal
75 mcg, i.v.
100 mcg, nasal
100 mcg, i.v.
150 mcg, nasal
150 mcg, i.v.
200 mcg, nasal
200 mcg, i.v.

Figure 6a

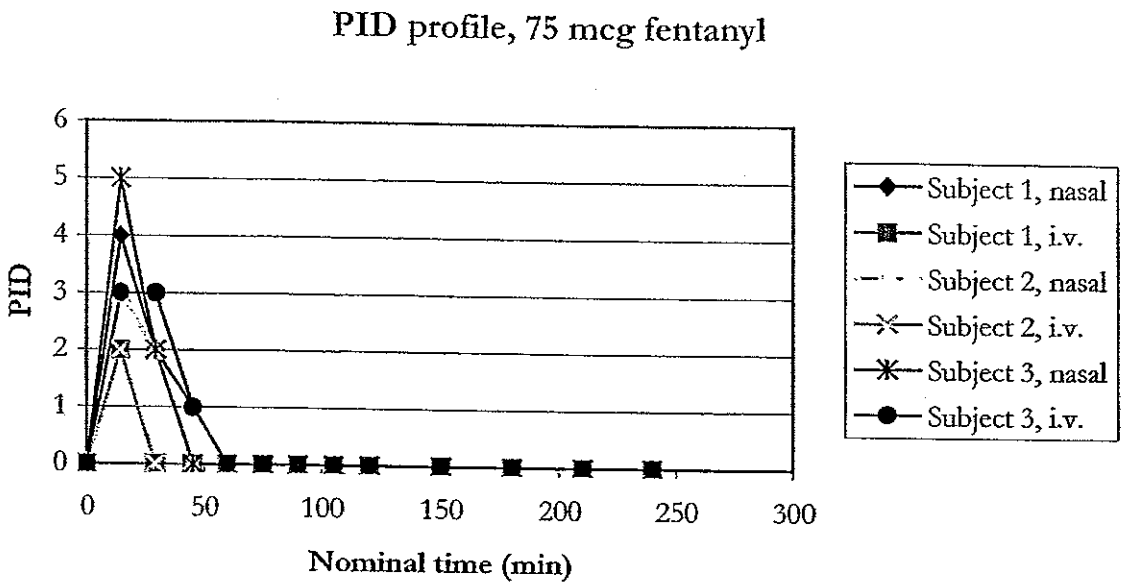


Figure 6b

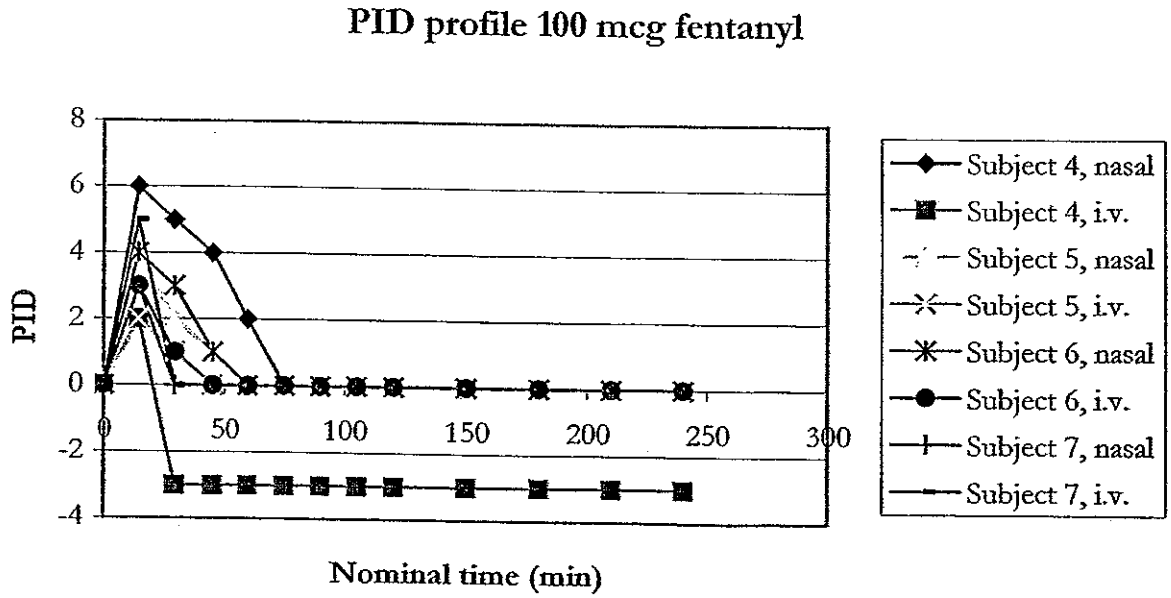


Figure 6c

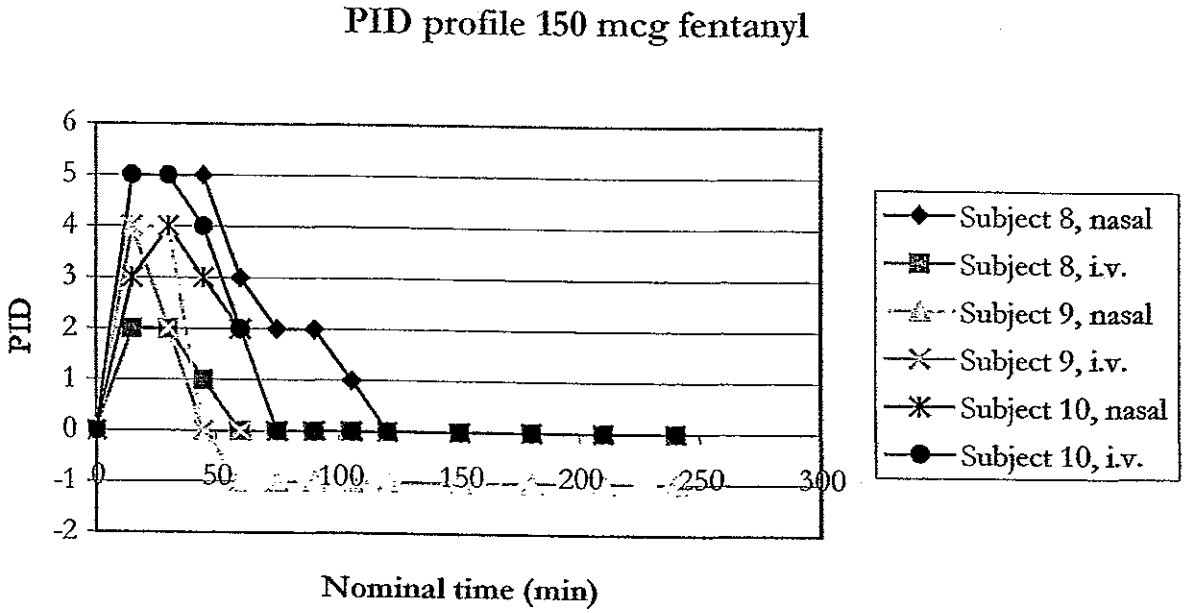


Figure 6d

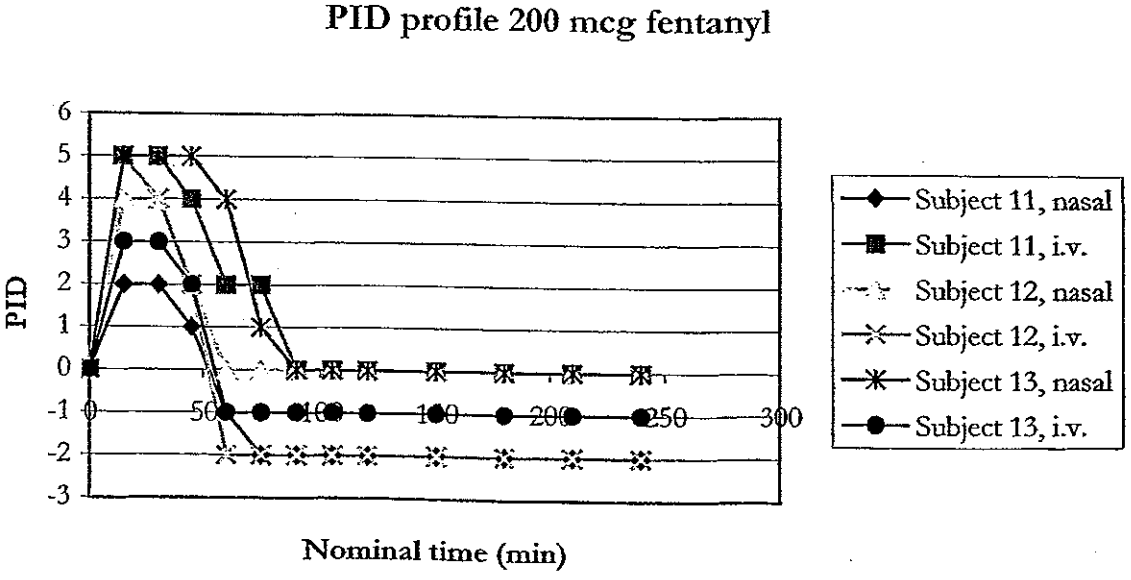


Figure 7

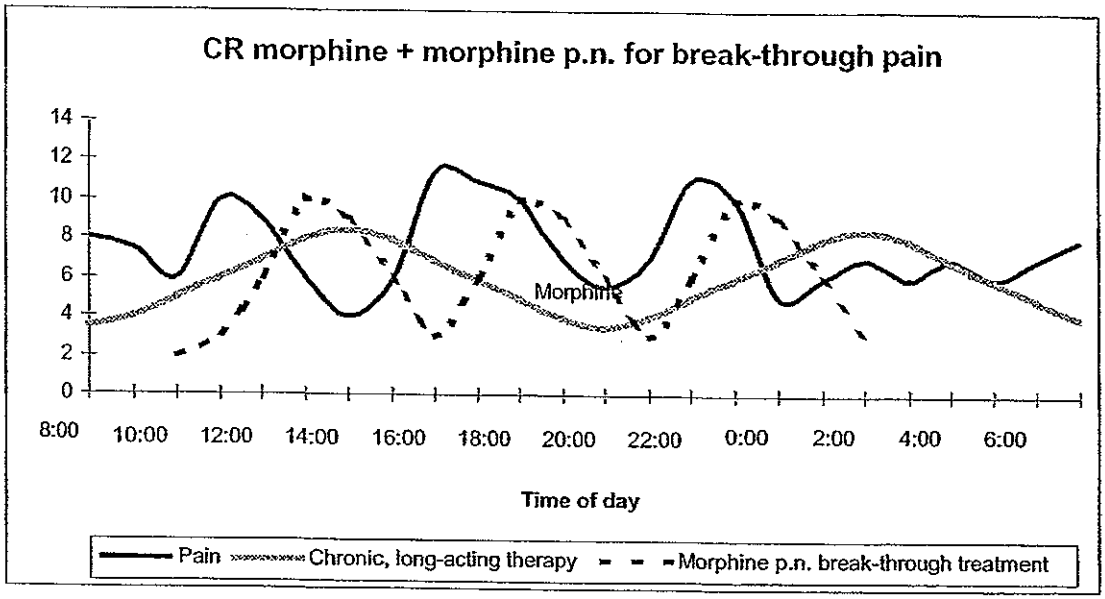


Figure 8

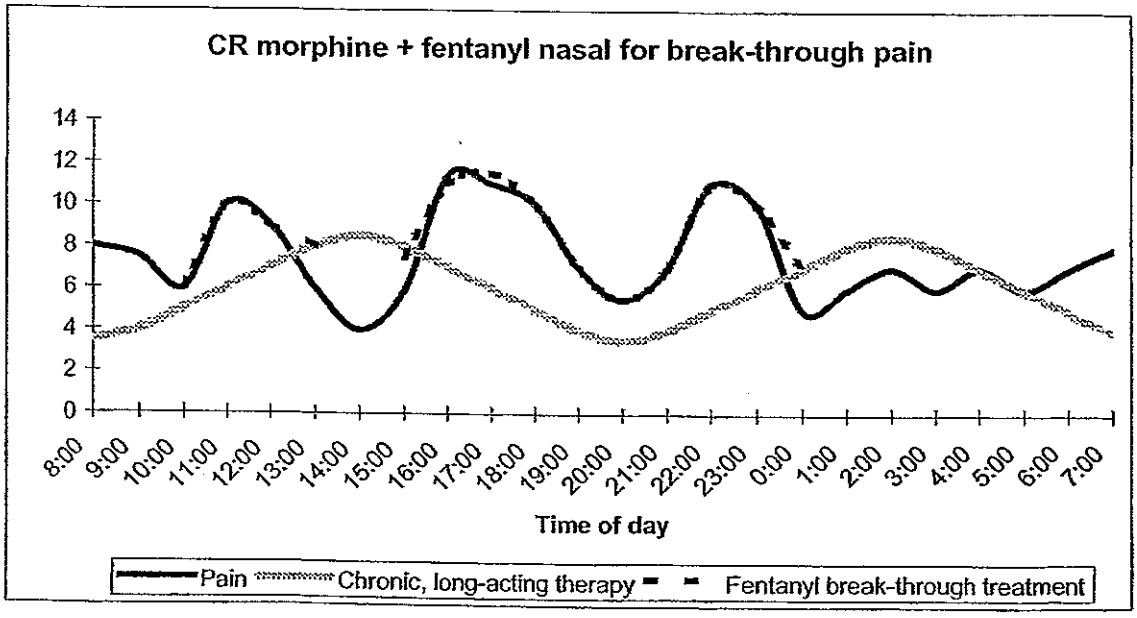


Table 1

	75 µg Fentanyl					
subject no.	**1**		**2**		**3**	
	Concentration (ng/ml)		Concentration (ng/ml)		Concentration (ng/ml)	
Nominal Time (min)	Nasal	i.v.	Nasal	i.v.	Nasal	i.v.
0	< 0,02	< 0,02	< 0,02	< 0,02	< 0,02	< 0,02
1	< 0,02	0,0223	< 0,02	0,665	< 0,02	0,165
3	0,0322	1,58	0,107	1,21	0,0290	1,10
5	0,366	0,826	0,253	0,756	0,343	0,758
7	0,592	0,756	0,359	0,673	0,686	0,596
9	0,692	0,479	0,297	0,527	0,758	0,537
12	0,564	0,311	0,767	0,368	0,658	0,392
15	0,483	0,321	0,699	0,248	0,528	0,364
25	0,298	0,255	0,388	0,251	0,408	0,238
40	0,157	0,189	0,251	0,234	0,247	0,140
60	0,136	0,154	0,215	0,187	0,158	0,113
90	0,113	0,131	0,165	0,132	0,154	0,0781
120	0,0882	0,111	0,162	0,122	0,120	0,0728
180	0,0796	0,106	0,174	0,109	0,0564	0,0436

Table 2

100 µg Fentanyl							
4		5		6		7	
Concentration (ng/ml)		Concentration (ng/ml)		Concentration (ng/ml)		Concentration (ng/ml)	
Nasal	i.v.	Nasal	i.v.	Nasal	i.v.	Nasal	i.v.
< 0,02	< 0,02	< 0,02	< 0,02	< 0,02	< 0,02	< 0,02	< 0,02
< 0,02	1,25	< 0,02	0,284	< 0,02	0,162	< 0,02	0,0753
< 0,02	2,69	< 0,02	3,35	0,138	2,79	< 0,02	1,52
0,0566	1,64	0,0838	1,36	0,588	1,27	0,0566	1,01
0,361	1,22	0,255	1,42	0,948	1,20	0,120	0,952
0,565	1,10	0,520	1,07	1,12	0,938	0,643	0,798
1,01	0,776	0,912	0,735	0,872	0,755	0,897	0,519
0,914	0,649	0,661	0,609	0,622	0,618	0,584	0,453
0,689	0,385	0,365	0,479	0,437	0,390	0,428	0,281
0,462	0,312	0,358	0,389	0,336	0,308	0,303	0,200
0,308	0,297	0,297	0,321	0,300	0,346	0,218	0,161
0,326	0,205	0,217	0,189	0,214	0,268	0,183	0,133
0,273	0,176	0,208	0,173	0,206	0,191	0,142	0,133
0,132	0,112	0,208	0,197	0,185	0,186	0,0836	0,0698

Table 3

Subject No.		150 µg Fentanyl					
		8		9		10	
		Concentration (ng/ml)		Concentration (ng/ml)		Concentration (ng/ml)	
Nominal Time (min)	Nasal	i.v.	Nasal	i.v.	Nasal	i.v.	i.v.
0	< 0,02	< 0,02	< 0,02	< 0,02	< 0,02	< 0,02	< 0,02
1	< 0,02	< 0,02	< 0,02	0,0822	< 0,02	5,35	0,186
3	0,119	0,0422	< 0,02	0,976	0,0522	2,12	0,738
5	NS	0,370	< 0,02	0,688	0,566	1,28	1,03
7	0,261	5,07	0,0587	2,96	1,54	4,07	4,13
9	1,33	2,67	0,175	1,50	2,39	2,06	2,08
12	1,41	1,19	0,464	0,823	2,28	1,44	1,59
15	1,58	0,771	1,06	0,714	1,64	0,964	1,14
25	1,12	0,751	0,866	0,547	1,03	0,640	0,893
40	0,78	0,530	0,857	0,464	0,627	0,597	0,626
60	0,559	0,489	0,610	0,407	0,44	0,548	0,538
90	0,418	0,325	0,383	0,359	0,373	0,380	0,371
120	0,267	0,211	0,278	0,278	0,333	0,303	0,407
180	0,182	0,170	0,202	0,177	0,264	0,242	0,257

Table 4

200 µg Fentanyl				
11	**12**		**13**	
Concentration (ng/ml)	Concentration (ng/ml)		Concrentation (ng/ml)	
Nasal	i.v.	Nasal	i.v.	Nasal
< 0,02	< 0,02	< 0,02	< 0,02	< 0,02
< 0,02	0,0291	< 0,02	0,602	< 0,02
< 0,02	0,352	< 0,02	1,96	< 0,02
< 0,02	0,802	0,0220	1,32	0,0399
0,0622	2,43	0,148	4,62	0,101
0,233	1,33	0,930	2,23	0,595
0,802	0,853	3,23	1,41	1,10
0,961	0,657	3,10	1,03	1,52
0,761	0,479	1,52	0,788	0,854
0,535	0,409	0,819	0,828	0,588
0,367	0,374	0,590	0,432	0,542
0,302	0,334	0,478	0,302	0,409
0,292	0,297	0,343	0,381	0,193
0,269	0,188	0,263	0,215	0,167

Table 5

	75 µg Fentanyl											
Subject No.	**1**				**2**				**3**			
Nominal Time (min)	Nasal		i.v.		Nasal		i.v.		Nasal		i.v.	
	PI	PID	PI	PID	PI	PID	PI	PID	PI	PID	PI	PID
0	5	0	3	0	8	0	4	0	6	0	3	0
15	1	4	0	2	5	3	2	2	1	5	0	3
30	3	2	0	0	6	2	4	0	4	2	0	3
45	4	1	2	0	8	0	4	0	6	0	2	1
60	5	0	3	0	8	0	4	0	6	0	3	0
75	5	0	3	0	8	0	4	0	6	0	3	0
90	5	0	3	0	8	0	4	0	6	0	3	0
105	5	0	3	0	8	0	4	0	6	0	3	0
120	5	0	3	0	8	0	4	0	6	0	3	0
150	5	0	3	0	8	0	4	0	6	0	3	0
180	5	0	3	0	8	0	4	0	6	0	3	0
210	5	0	3	0	8	0	4	0	6	0	3	0
240	5	0	3	0	8	0	4	0	6	0	3	0

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Table 6

100 µg Fentanyl															
4				5				6				7			
Nasal		i.v.		Nasal		i.v.		Nasal		i.v.		Nasal		i.v.	
PI	PID	PI	PID	PI	PID	PI	PID	PI	PID	PI	PID	PI	PID	PI	PID
7	0	3	0	5	0	3	0	5	0	4	0	3	0	6	0
1	6	1	2	1	4	1	2	1	4	1	3	0	3	1	5
2	5	6	-3	3	2	2	1	2	3	3	1	3	0	6	0
3	4	6	-3	4	1	3	0	4	1	4	0	3	0	6	0
5	2	6	-3	5	0	3	0	5	0	4	0	3	0	6	0
7	0	6	-3	5	0	3	0	5	0	4	0	3	0	6	0
7	0	6	-3	5	0	3	0	5	0	4	0	3	0	6	0
7	0	6	-3	5	0	3	0	5	0	4	0	3	0	6	0
7	0	6	-3	5	0	3	0	5	0	4	0	3	0	6	0
7	0	6	-3	5	0	3	0	5	0	4	0	3	0	6	0
7	0	6	-3	5	0	3	0	5	0	4	0	3	0	6	0
7	0	6	-3	5	0	3	0	5	0	4	0	3	0	6	0
7	0	6	-3	5	0	3	0	5	0	4	0	3	0	6	0
7	0	6	-3	5	0	3	0	5	0	4	0	3	0	6	0

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Table 7

	150 µg Fentanyl											
Subject No.	**8**				**9**				**10**			
Nominal Time (min)	Nasal		i.v.		Nasal		i.v.		Nasal		i.v.	
	PI	PID	PI	PID	PI	PID	PI	PID	PI	PID	PI	PID
0	5	0	2	0	5	0	4	0	4	0	5	0
15	0	5	0	2	1	4	0	4	1	3	0	5
30	0	5	0	2	1	4	2	2	0	4	0	5
45	0	5	1	1	5	0	4	0	1	3	1	4
60	2	3	2	0	6	-1	4	0	2	2	3	2
75	3	2	2	0	6	-1	4	0	4	0	5	0
90	3	2	2	0	6	-1	4	0	4	0	5	0
105	4	1	2	0	6	-1	4	0	4	0	5	0
120	5	0	2	0	6	-1	4	0	4	0	5	0
150	5	0	2	0	6	-1	4	0	4	0	5	0
180	5	0	2	0	6	-1	4	0	4	0	5	0
210	5	0	2	0	6	-1	4	0	4	0	5	0
240	5	0	2	0	6	-1	4	0	4	0	5	0

Table 8

200 µg Fentanyl											
11				12				13			
Nasal		i.v.		Nasal		i.v.		Nasal		i.v.	
PI	PID	PI	PID	PI	PID	PI	PID	PI	PID	PI	PID
2	0	6	0	5	0	6	0	5	0	3	0
0	2	1	5	1	4	1	5	0	5	0	3
0	2	1	5	1	4	2	4	0	5	0	3
1	1	2	4	3	2	4	2	0	5	1	2
3	-1	4	2	5	0	8	-2	1	4	4	-1
4	-2	4	2	5	0	8	-2	4	1	4	-1
4	-2	6	0	5	0	8	-2	5	0	4	-1
4	-2	6	0	5	0	8	-2	5	0	4	-1
4	-2	6	0	5	0	8	-2	5	0	4	-1
4	-2	6	0	5	0	8	-2	5	0	4	-1
4	-2	6	0	5	0	8	-2	5	0	4	-1
4	-2	6	0	5	0	8	-2	5	0	4	-1
4	-2	6	0	5	0	8	-2	5	0	4	-1