

:

	H		G	P	T	1	-	1
--	---	--	---	---	---	---	---	---

.....	1
.....	1
.....	2
.....	4
.....	5
.....	6
.....	7
.....	16

Acute toxicity test Single dose toxicity test

24

[1]

[1 2]

"

"

[1 ~ 4]

1

2

3

4

5

20%

[1 ~ 4]

[1 ~ 4]

()

/

[1, 2, 4, 5]

[1, 2, 4, 5]

1

2

[6]

3

4

5

LD₅₀

6

-

No observed adverse effect

level, NOAEL

Maximal tolerance dose, MTD

Minimal lethal dose, MLD

Median lethal dose, LD₅₀

50%

1 CDER, FDA. Guidance for industry: single dose acute toxicity testing for pharmaceuticals (Final). 1996

2

2002 11-14

3 European Union. Single dose toxicity. European Union Medicinal Products for Human Use Guidelines (3BS1a), 1987

4 Cordier A. Single dose toxicity: Industry perspectives. In: P.F. D'Arcy and D.W.G. Harron edited, Proceedings of the First International Conference on Harmonization. Brussels 1991, 189-191

5 Outcome - Single dose toxicity. In: P.F. D'Arcy and D.W.G. Harron edited, Proceedings of the First International Conference on Harmonization. Brussels 1991, 184

6 Louis C D, Hayes A W. Acute toxicity and eye irritancy. In: Hays A W edited, Principles and methods of toxicology. Fourth edition, 2001: 853-916

7 OECD. Acute oral toxicity-fixed dose procedure. OECD guideline for testing of chemicals. 2001

8 British Toxicology Society Working Party on Toxicity (1984). Special report a new approach to the classification of substances and preparations on the basis of their acute toxicology. Human Toxicol, 1984 (3): 85-92

9 OECD. Guideline 425: Acute Oral Toxicity-Up and Down Procedure. OECD Guidelines for testing of chemicals. 2001

10 EPA. EPA OPPTS Harmonized Test guideline 870.1100 Acute Oral Toxicity.1998

[6]

I.	A.	1.	
		2	
	B.		
	C.		
	D.		
	E.		
	II.	A.	

	B.		
	C.		CNS
	D.		CNS
	E.		CNS
	F.		CNS
	G.	:	CNS
	H.		CNS
	I.		CNS
	J.		CNS
III. ()	A.		CNS
	B.		CNS
	C.	-	CNS
	D.		CNS
	E.	:	CNS
IV.	A.		
	B.	:	
	C.		CNS
	D.		
	E.	()	
	F.	()	
V.	A.		
	B.		
	C.		
	D.		

	E.		
	F.		
	G.		
	H.		
VI.	A.		
	B.		
	C.		CNS
	D.		CNS
	E.		CNS
VII.	A.		
VIII.	A.		
IX.	A.	()	CNS
X.	A.		
	B.		
XI.			
()	A.		
	B.		
	A.		CNS, ()
	A.		
	B.		
XII.	A.		
	B.		

1

6 Beagle 4-6
2-3
50%

2

24 ()
5g/kg) 10-20

14

3 Fixed-dose procedure [7]

1984 [8]

5 50 500 2000mg/kg

5000mg/kg

6-12

3-4

500mg/kg

2000 mg/kg

5

24

7

7

7

10

50mg/kg

2

1

(mg/kg)			
	< 100%	100%	100%
5	(Very toxic) (LD ₅₀ 25mg/kg)	Toxic LD ₅₀ 25-200mg/kg	50mg/kg
50	5mg/kg	Harmful LD ₅₀ 200-2000mg/kg	500mg/kg
500	50mg/kg	LD ₅₀ > 2000mg/kg	2000mg/kg
2000	500mg/kg		

4

Up and down method [9,10]

Dixon Mood

1985 Bruce

OECD EPA

LD₅₀

5

2000 mg/kg

5000 mg/kg

2000 mg/kg

:

1

4

5 1

: 3 3 LD₅₀ 2000mg/kg 3 3
LD₅₀ 2000 mg/kg 3

5000mg/kg : 5000mg/kg

1

2

2

LD₅₀

5000mg/kg

14

2

1

2

2

1

1

3

3

LD₅₀

5000 mg/kg

3

3

LD₅₀

5000mg/kg

:

1

48

LD₅₀

1/ -
 2 32
 32
 1.75 5.5 17.5 55 175
 550 2000mg/kg 1.75 5.5 17.5 55 175 550 1750
 5000mg/kg 175mg/kg
 20
 05
 32

48

LD₅₀

LD₅₀ (

EPA

AOT 425StatPgm)

a 3

b 6 5 /

c 4 LD₅₀

25

4

LD₅₀

/

4-6

C

-

15

[11]

LD₅₀

<http://www.epa.gov/oppfead1/harmonization/>

5

Pyramiding dosage design

8

4

2

1 3 10 30 100 300 1000 3000mg/kg

10 20 40 80 160 320 640 1280 mg/kg

MLD

LD₅₀

MLD LD₅₀

MLD

LD₅₀

5-7

6

LD₅₀

