

**NONCLINICAL DRUG SAFETY
ASSESSMENT REQUIREMENTS TO OPEN
AN IND/FIH TRIAL
GENERAL & SPECIAL CASES
PHARMATEK U. PRESENTATION**

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POINTS TO CONSIDER



- THERE ARE MORE THAN 7,000 PHARMACEUTICAL COMPANIES (AT LEAST 3,800 IN THE U.S ALONE)
- OVER 16,000 ACTIVE DRUGS IN R&D IN 2007
- ORPHAN DRUGS SAME AS OTHERS FOR REGULATORY REQUIREMENTS
- NDAs come in all flavors:
 - 505(b)(1)//505(b)(2)//ANDA

NON-CLINICAL SAFETY ASSESSMENT



NON-CLINICAL SAFETY ASSESSMENT SERVES FOUR SEPARATE STAGES IN DRUG/DEVICE DEVELOPMENT

0) SCREENING TO ID LEADS

1) TO SUPPORT FIRST IN MAN TRIALS (IND/IDE)

2) TO SUPPORT CONTINUED CLINICAL DEVELOPMENT

3) TO SUPPORT MARKETING APPROVAL

SCREENING STUDIES TO IDENTIFY LEADS



- 1) GENERALLY NON-GLP. THIS DOES NOT INCLUDE “EXPANDED ACUTES” FOR EXPLORATORY INDs
- 2) SCREENING AMES, hERG (10 μ M), SINGLE DOSE ACUTES MOST COMMON

FOR REQUIRED TESTS



- Must be GLP
- Should have audited draft report for FDA filing

TOXICOLOGY STUDIES



TOXICOLOGY STUDIES CAN BE CONSIDERED
AS EITHER:

A) HAZARD SCREENS

OR

B) SYSTEMIC TOXICOLOGY

(B) ARE DRIVEN ONLY BY CLINICAL
EXPOSURE LEVELS

SPECIES SELECTION



<u>RODENT</u>	<u>NONRODENT</u>	<u>SPECIAL USE</u>
Mouse	Dog	Rabbit*
Rat	Primate	Hamster
	Pig	Ferret

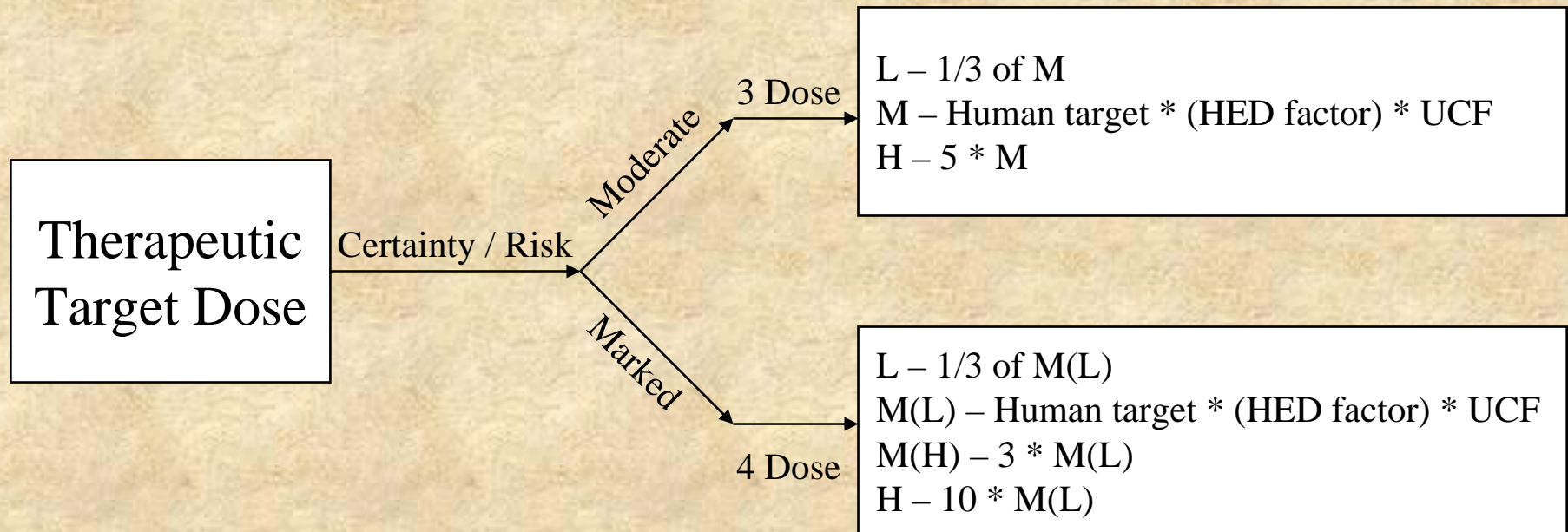
*May also be used as nonrodents

REPEAT DOSE STUDY: Dose Selection



- The low dose should show no (toxicological) effect and preferably exceed the expected human AUC
- The high dose should show clear toxicity
- Intermediate dose(s) should show minor (beginning) effects
- The dose range should reflect the expected human dose, route and regimen.

Two Dose Selection Schemes



General Guidelines for Maximum Dose Volume

General Guidelines for Maximum Dose Volumes by Route

Route	Volume should not exceed (ml/kg)	Notes
Oral	20	Fasted animals
Dermal	2	Limit is accuracy of dosing per available body surface
Intravenous	1	Over 5 minute
Intramuscular	0.5	At one site
Perocular	0.01 ml	
Rectal	0.5	
Vaginal	0.2 ml in rat 1 ml in rabbit	
Inhalation	2 mg/liter	
Nasal	0.1 ml per nostril in monkey or dog	

(Baker et al., 1979; Garramone, 1986)

THE GENERAL CASE NEVER FULLY APPLIES

- BIOLOGICS
- OPHTHALMICS
- TOPICALS
- PARENTERALS
- GENERAL SAFETY TESTS-21 CFR SECT.610.9 >
DAYS ADMIN IN MICE AND GUINEA PIGS
- THE ANIMAL RULE
- NOT ALL DRUGS REQUIRE IND FOR FIM
(RADIO PHARMACEUTICALS AND IMAGING
AGENTS)

General Case: Oral Route

TEST REQUIRMENT	SPECIES
INITIAL CLINICAL TRIAL/IND REQUIREMENTS	
1) Acute toxicity in rodents (Oral and IV*)	R/M
2) Acute toxicity in nonrodents (Oral)	D/S/P
3) 7-day DRF toxicity in rodents (Oral)	R/M
4)7-day DRF toxicity in nonrodents(Oral)	D/S/P
5) Genotoxicity: Bacterial mutagenicity (Ames)	<i>In vitro</i>
6) Genotoxicity: <i>In vitro</i> clastogenicity (CHO chromosome aberration)	<i>In vitro</i>
7) Genotoxicity: <i>In vivo</i> (mouse or rat micronucleus)	R/M
8) * Safety pharmacology: CV-hERG	<i>In vitro</i>
9) Safety pharmacology: CV <i>in vivo</i>	D/P/S
10) Safety pharmacology: FOB/Irwin	R/M
11) Safety pharmacology: Respiratory- Rodent	R
12) Pivotal/repeat dose in rodents (14-28 day oral)	R/M
13) Pivotal/repeat dose in nonrodents (14-28 day oral)	D/P/S
14)* CYP induction/inhibition	<i>In vitro</i>
15)* Five species micrososome metabolic panel	<i>In vitro</i>
16) Develop Bioanalytical for 3 species (man/rodent/nonrodent)	NA

General Case: Oral Route (Cont.)

TEST REQUIRMENT	SPECIES
TO SUPPORT CONTINUED CLINICAL DEVELOPMENT	
17) Developmental Tox (Seg II) – rat and rabbit pilots and rat and rabbit studies	R/B
18) Immunotoxicity	TBD
19) Pivotal/repeat dose in rodents (3/6 month oral)	R/M
20) Pivotal/repeat dose in nonrodents (3/9-12 month oral)	D/P/S
TO SUPPORT MARKETING APPROVAL	
21) Reproductive Toxicity – Seg I	R
22) Reproductive Toxicity – Seg III	R
23) Tumorigenicity/Carcinogenicity - Rat	R
24) Tumorigenicity/Carcinogenicity - Mouse	M
<p>* Recommended ** May be required SPECIES: R= Rat M= Mouse D= Dog S= Pig P= Primate B=Rabbit TBD= To be determined All studies described above must be performed GLP.</p>	

General Case: Oral Exploratory / Phase 0 IND

TEST REQUIRMENT	SPECIES
INITIAL CLINICAL TRIAL/IND REQUIREMENTS	
1) Enhanced Acute toxicity in rodents (Oral)	R/M
2) Enhanced Acute toxicity in nonrodents (Oral)	D/S/P
TO SUPPORT CONTINUED CLINICAL DEVELOPMENT	
17) Developmental Tox (Seg II) - rat and rabbit pilots and rat and rabbit studies	R/B
18) Immunotoxicity	TBD
19) Pivotal/repeat dose in rodents (3/6 month oral)	R/M
20) Pivotal/repeat dose in nonrodents (3/9-12 month oral)	D/P/S
TO SUPPORT MARKETING APPROVAL	
21) Reproductive Toxicity - Seg I	R
22) Reproductive Toxicity - Seg III	R
23) Tumorigenicity/Carcinogenicity - Rat	R
24) Tumorigenicity/Carcinogenicity - Mouse	M
No route to approval or more than initial study	

Special Case: Non-Oral/Non-Topical Route

TEST REQUIRMENT	SPECIES
INITIAL CLINICAL TRIAL/IND REQUIREMENTS	
1) Acute toxicity in rodents	R/M
2) Acute toxicity in nonrodents	D/S/P
3) 7-day DRF toxicity in rodents	R/M
4)7-day DRF toxicity in nonrodents	D/S/P
5) Genotoxicity: Bacterial mutagenicity (Ames)	<i>In vitro</i>
6) Genotoxicity: <i>In vitro</i> clastogenicity (CHO chromosome aberration)	<i>In vitro</i>
7) Genotoxicity: <i>In vivo</i> (mouse or rat micronucleus)	R/M
8) * Safety pharmacology: CV-hERG	<i>In vitro</i>
9) Safety pharmacology: CV <i>in vivo</i>	D/P/S
10) Safety pharmacology: FOB/Irwin	R/M
11) Safety pharmacology: Respiratory- Rodent	R
12) Pivotal/repeat dose in rodents (14-28 day)	R/M
13) Pivotal/repeat dose in nonrodents (14-28 day)	D/P/S
14)* CYP induction/inhibition	<i>In vitro</i>
15)* Five species microsome metabolic panel	<i>In vitro</i>
16) Develop Bioanalytical for 3 species (man/rodent/nonrodent)	NA
17) Local Irritation (Venous/Muscle- Clinical formulation) Redo as formulation change	B

Special Case: Non-Oral/Non-Topical Route (Cont.)

TEST REQUIRMENT	SPECIES
TO SUPPORT CONTINUED CLINICAL DEVELOPMENT	
18) Developmental Tox (Seg II) – rat and rabbit pilots and rat and rabbit studies	R/B
19) Hemolysis (Clinical formulation)	<i>In vitro</i>
20) Immunotoxicity	TBD
21) Pivotal/repeat dose in rodents (3/6 month oral)	R/M
22) Pivotal/repeat dose in nonrodents (3/9-12 month oral)	D/P/S
TO SUPPORT MARKETING APPROVAL	
23) Reproductive Toxicity – Seg I	R
24) Reproductive Toxicity – Seg III	R
25) Tumorigenicity/Carcinogenicity – Rat	R
26) Tumorigenicity/Carcinogenicity - Mouse	M

* Recommended

** May be required

SPECIES: R= Rat M= Mouse D= Dog S= Pig P= Primate B=Rabbit TBD= To be determined

All studies described above must be performed GLP.

Special Case: Topical Agents

TEST REQUIRMENT	SPECIES
INITIAL CLINICAL TRIAL/IND REQUIREMENTS	
1) Acute toxicity in rodents (IV*)	R/M
2) Acute toxicity in nonrodents	D/S/P
3) 7-day DRF toxicity in rodents	R/M
4)7-day DRF toxicity in nonrodents	D/S/P
5) Genotoxicity: Bacterial mutagenicity (Ames)	<i>In vitro</i>
6) Genotoxicity: <i>In vitro</i> clastogenicity (CHO chromosome aberration)	<i>In vitro</i>
7) Genotoxicity: <i>In vivo</i> (mouse or rat micronucleus)	R/M
8) * Safety pharmacology: CV-hERG	<i>In vitro</i>
9) Safety pharmacology: CV <i>in vivo</i>	D/P/S
10) Safety pharmacology: FOB/Irwin	R/M
11) Safety pharmacology: Respiratory- Rodent	R
12) Pivotal/repeat dose in rodents (14-28 day Intended route***)	R/M
13) Pivotal/repeat dose in nonrodents (14-28 day Intended route***)	D/P/S
14)* CYP induction/inhibition	<i>In vitro</i>
15)* Five species micrososome metabolic panel	<i>In vitro</i>
16) Develop Bioanalytical for 3 species (man/rodent/nonrodent)	NA
17) Local Irritation *** (Clinical formulation)	R
18) Of dermal - sensitization	G

Special Case: Topical Agents (Cont.)

TEST REQUIRMENT	SPECIES
TO SUPPORT CONTINUED CLINICAL DEVELOPMENT	
19) Developmental Tox (Seg II) – rat and rabbit pilots and rat and rabbit studies	R/B
20) Immunotoxicity***(If immune modulatory claim or there are findings in 14/28 dog studies	TBD
21) Pivotal/repeat dose in rodents (3/6 month oral)	R/M
22) Pivotal/repeat dose in nonrodents (3/9-12 month oral)	D/P/S
TO SUPPORT MARKETING APPROVAL	
23) Reproductive Toxicity – Seg I	R
24) Reproductive Toxicity – Seg III	R
25) Tumorigenicity/Carcinogenicity - Rat	R
26) Tumorigenicity/Carcinogenicity - Mouse	M
<p>* Recommended ** May be required SPECIES: R= Rat M= Mouse D= Dog S= Pig P= Primate B= Rabbit G= Guinea Pig TBD= To be determined ***Dermal/Ophthalmic/Vaginal/Rectal All studies described above must be performed GLP.</p>	

Special Case: Imaging Agents

TEST REQUIRMENT	SPECIES
INITIAL CLINICAL TRIAL/IND REQUIREMENTS***	
1) Acute toxicity in rodents (IV) - Expanded	R/M
2) Acute toxicity in nonrodents (IV) - Expanded	D/S/P
3) Genotoxicity: Bacterial mutagenicity (Ames)	<i>In vitro</i>
4) Genotoxicity: <i>In vitro</i> clastogenicity (CHO chromosome aberration)	<i>In vitro</i>
5) Genotoxicity: <i>In vivo</i> (mouse or rat micronucleus)	R/M
6) Safety pharmacology: CV <i>in vivo</i>	D/P/S
7) Safety pharmacology: Respiratory- Rodent	R
8) Pivotal/repeat dose in nonrodents (14-28 day oral)	D/P/S
9) Develop Bioanalytical for 2 species (man/nonrodent)	NA
10) Hemolysis	<i>In vitro</i>
TO SUPPORT MARKETING APPROVAL	
11) Reproductive Toxicity – Seg I	R
<p>* Recommended ** May be required ***Initial single dose clinical study at a single academic center may not require an IND. SPECIES: R= Rat M= Mouse D= Dog S= Pig P= Primate B=Rabbit TBD= To be determined All studies described above must be performed GLP.</p>	

Special Case: Oncology Agents (Cytotoxic)

TEST REQUIRMENT	SPECIES
INITIAL CLINICAL TRIAL/IND REQUIREMENTS	
1) Acute toxicity in rodents (IV)	R/M
2) Acute toxicity in nonrodents (IV)	D/S/P
3) 7-day DRF toxicity in rodents (IV)	R/M
4)7-day DRF toxicity in nonrodents (IV)	D/S/P
5) * Safety pharmacology: CV-hERG	<i>In vitro</i>
6) Pivotal/repeat dose in rodents (14-28 day IV)	R/M
7) Pivotal/repeat dose in nonrodents (14-28 day IV)	D/P/S
8)* CYP induction/inhibition	<i>In vitro</i>
9)* Five species microsome metabolic panel	<i>In vitro</i>
10) Develop Bioanalytical for 3 species (man/rodent/nonrodent)	NA
TO SUPPORT CONTINUED CLINICAL DEVELOPMENT	
10) Pivotal/repeat dose in rodents (3/6 month oral)	R/M
11) Pivotal/repeat dose in nonrodents (3/9-12 month oral)	D/P/S
MARKETING APPROVAL	
<p>* Recommended ** May be required SPECIES: R= Rat M= Mouse D= Dog S= Pig P= Primate B=Rabbit TBD= To be determined All studies described above must be performed GLP.</p>	

Special Case: Oncology Agents (Protein-Targeted Molecules)

TEST REQUIREMENT	SPECIES
INITIAL CLINICAL TRIAL/IND REQUIREMENTS	
1) Acute toxicity in rodents (IV)	R/M
2) Acute toxicity in nonrodents (IV)	D/S/P
3) 7-day DRF toxicity in rodents (IV)	R/M
4) 7-day DRF toxicity in nonrodents (IV)	D/S/P
5) Safety pharmacology: CV <i>in vivo</i>	D/P/S
6) Safety pharmacology: FOB/Irwin	R/M
7) Safety pharmacology: Respiratory- Rodent	R
8) Pivotal/repeat dose in rodents (14-28 day IV)	R/M
9) Pivotal/repeat dose in nonrodents (14-28 day IV)	D/P/S
10)* CYP induction/inhibition	<i>In vitro</i>
11)* Five species microsome metabolic panel	<i>In vitro</i>
12) Develop Bioanalytical for 3 species (man/rodent/nonrodent)	NA

Special Case: Oncology Agents (Protein-Targeted Molecules) (Cont.)

TEST REQUIRMENT	SPECIES
TO SUPPORT CONTINUED CLINICAL DEVELOPMENT	
13) Developmental Tox (Seg II) – rat and rabbit pilots and rat and rabbit studies	R/B
14) Immunotoxicity	TBD
15) Pivotal/repeat dose in nonrodents (3/6 month oral)	D/P/S
TO SUPPORT MARKETING APPROVAL	
16) Reproductive Toxicity – Seg I	R
17) Reproductive Toxicity – Seg III	R
<p>* Recommended ** May be required SPECIES: R= Rat M= Mouse D= Dog S= Pig P= Primate B=Rabbit TBD= To be determined All studies described above must be performed GLP.</p>	

Special Case: HIV/ALS

TEST REQUIRMENT	SPECIES
INITIAL CLINICAL TRIAL/IND REQUIREMENTS	
1) Acute toxicity in rodents (Intended clinical route)	R/M
2) Acute toxicity in nonrodents (Intended clinical route)	D/S/P
3) 7-day DRF toxicity in rodents (Intended clinical route)	R/M
4)7-day DRF toxicity in nonrodents (Intended clinical route)	D/S/P
5) Genotoxicity: Bacterial mutagenicity (Ames)	<i>In vitro</i>
6) Genotoxicity: <i>In vitro</i> clastogenicity (CHO chromosome aberration)	<i>In vitro</i>
8) * Safety pharmacology: CV-hERG	<i>In vitro</i>
9) Safety pharmacology: CV <i>in vivo</i>	D/P/S
10) Safety pharmacology: FOB/Irwin	R/M
11) Safety pharmacology: Respiratory- Rodent	R
12) Pivotal/repeat dose in rodents (14-28 day Intended clinical route)	R/M
13) Pivotal/repeat dose in nonrodents (14-28 day Intended clinical route)	D/P/S
14)* CYP induction/inhibition	<i>In vitro</i>
15)* Five species micrososome metabolic panel	<i>In vitro</i>
16) Develop Bioanalytical for 3 species (man/rodent/nonrodent)	NA
17) If route other than oral – local tissue irritation	

Special Case: HIV/ALS (Cont.)

TEST REQUIRMENT	SPECIES
TO SUPPORT CONTINUED CLINICAL DEVELOPMENT	
18) Developmental Tox (Seg II) – rat and rabbit pilots and rat and rabbit studies	R/B
19) Immunotoxicity (Required)	TBD
20) Pivotal/repeat dose in rodents (3/6 month Intended clinical route)	R/M
21) Pivotal/repeat dose in nonrodents (3/9-12 month Intended clinical route)	D/P/S
TO SUPPORT MARKETING APPROVAL	
22) Reproductive Toxicity – Seg I	R
23) Reproductive Toxicity – Seg III	R
24) Tumorigenicity/Carcinogenicity - Rat	R
25) Tumorigenicity/Carcinogenicity - Mouse	M
<p>* Recommended ** May be required SPECIES: R= Rat M= Mouse D= Dog S= Pig P= Primate B=Rabbit TBD= To be determined All studies described above must be performed GLP.</p>	

Special Case: Life Threatening Short Use*** Indications

TEST REQUIRMENT	SPECIES
INITIAL CLINICAL TRIAL/IND REQUIREMENTS	
1) Acute toxicity in rodents (Intended route)	R/M
2) Acute toxicity in nonrodents (Intended route)	D/S/P
3) 7-day DRF toxicity in rodents (Intended route)	R/M
4)7-day DRF toxicity in nonrodents (Intended route)	D/S/P
5) Genotoxicity: Bacterial mutagenicity (Ames)	<i>In vitro</i>
6) * Safety pharmacology: CV-hERG	<i>In vitro</i>
7) Safety pharmacology: CV <i>in vivo</i>	D/P/S
8) Pivotal/repeat dose in rodents (14-28 day oral)	R/M
9) Pivotal/repeat dose in nonrodents (14-28 day oral)	D/P/S
10)* CYP induction/inhibition	<i>In vitro</i>
11)* Five species microsome metabolic panel	<i>In vitro</i>
12) Develop Bioanalytical for 3 species (man/rodent/nonrodent)	NA
TO SUPPORT CONTINUED CLINICAL DEVELOPMENT	
13) Pivotal/repeat dose in rodents (3/6 month oral)	R/M
14) Pivotal/repeat dose in nonrodents (3/9-12 month oral)	D/P/S
<p>* Recommended ** May be required ***Less than 14 days clinical use SPECIES: R= Rat M= Mouse D= Dog S= Pig P= Primate B=Rabbit TBD= To be determined</p>	
All studies described above must be performed GLP.	

Special Case: 505b(2) Registrations

TEST REQUIRMENT	SPECIES
INITIAL CLINICAL TRIAL/IND REQUIREMENTS	
1) Acute toxicity in rodents (Intended route)	R/M
2) Acute toxicity in nonrodents (Intended route)	D/S/P
3) 7-day DRF toxicity in rodents (Intended route)	R/M
4)7-day DRF toxicity in nonrodents (Intended route)	D/S/P
5) * Safety pharmacology: CV-hERG	<i>In vitro</i>
6) Safety pharmacology: CV <i>in vivo</i>	D/P/S
7) Pivotal/repeat dose in nonrodents (14-28 day oral)	D/P/S
8)* CYP induction/inhibition	<i>In vitro</i>
9)* Five species microsome metabolic panel	<i>In vitro</i>
10) Develop Bioanalytical for 3 species (man/rodent/nonrodent)	NA
TO SUPPORT CONTINUED CLINICAL DEVELOPMENT	
11) Developmental Tox (Seg II) – rat and rabbit pilots and rat and rabbit studies	R/B
12) Pivotal/repeat dose in nonrodents (3/9-12 month oral)	D/P/S
TO SUPPORT MARKETING APPROVAL	
13) Bioequivalence study in appropriate species	

* **Recommended**

** **May be required** SPECIES: R= Rat M= Mouse D= Dog S= Pig P= Primate B=Rabbit TBD= To be determined

All studies described above must be performed GLP.

Special Case: ANDA

TEST REQUIRMENT	SPECIES
INITIAL CLINICAL TRIAL/IND REQUIREMENTS	
2) Acute toxicity in nonrodents (Oral)	D/S/P
13) Pivotal/repeat dose in nonrodents (28 day oral bioequivalency)	D/P/S
16) Develop Bioanalytical for 3 species (man/rodent/nonrodent)	NA
TO SUPPORT MARKETING APPROVAL	
21) In Silico and Human bioequivalence	
<p>* Recommended ** May be required SPECIES: R= Rat M= Mouse D= Dog S= Pig P= Primate B=Rabbit TBD= To be determined All studies described above must be performed GLP.</p>	

Special Case: Biotechnology Derived Drugs

TEST REQUIRMENT	SPECIES
INITIAL CLINICAL TRIAL/IND REQUIREMENTS	
1) Acute toxicity in rodents (Oral and IV*)	R/M
2) Acute toxicity in nonrodents (Oral)	D/S/P
3) 7-day DRF toxicity in rodents (Oral)	R/M
4)7-day DRF toxicity in nonrodents(Oral)	D/S/P
5) Genotoxicity only if appropriate (species cases)	
6) Safety pharmacology: CV <i>in vivo</i>	D/P/S
7) Safety pharmacology: Respiratory- Rodent	R
8) Pivotal/repeat dose in rodents (14-28 day oral)	R/M
9) Pivotal/repeat dose in nonrodents (14-28 day oral)	D/P/S
10)* Five species microsome metabolic panel	<i>In vitro</i>
11) Develop Bioanalytical for 3 species (man/rodent/nonrodent)	NA
12) Antibody based assay to select appropriate species	

Special Case: Biotechnology Derived Drugs (Cont.)

TO SUPPORT CONTINUED CLINICAL DEVELOPMENT	
13) Immunotoxicity	TBD
14) Pivotal/repeat dose in rodents (3/6 month oral)	R/M
15) Pivotal/repeat dose in nonrodents (3/9-12 month oral)	D/P/S
TO SUPPORT MARKETING APPROVAL	
16) Reproductive Toxicity – Seg I	R
17) Reproductive Toxicity – Seg III	R
* Recommended	
** May be required	
SPECIES: R= Rat M= Mouse D= Dog S= Pig P= Primate B=Rabbit	
TBD= To be determined	
All studies described above must be performed GLP.	

Special Case: Vaccines

TEST REQUIRMENT	SPECI ES
INITIAL CLINICAL TRIAL/IND REQUIREMENTS	
1) Acute toxicity in rodents (Oral and IV*)	R/M
2) Acute toxicity in nonrodents (Oral)	D/S/P
8) Pivotal/repeat dose in rodents (14-28 day oral)	R/M
9) Pivotal/repeat dose in nonrodents (14-28 day oral)	D/P/S
TO SUPPORT CONTINUED CLINICAL DEVELOPMENT & TO SUPPORT MARKETING APPROVAL	
13) Immunotoxicity	TBD
<p>* Recommended ** May be required SPECIES: R= Rat M= Mouse D= Dog S= Pig P= Primate B=Rabbit TBD= To be determined All studies described above must be performed GLP.</p>	

Special Case: Biologics

TEST REQUIREMENT	SPECIES
INITIAL CLINICAL TRIAL/IND REQUIREMENTS	
1) Acute toxicity in rodents (Oral and IV*)	R/M
2) Acute toxicity in nonrodents (Oral)	D/S/P
3) 7-day DRF toxicity in rodents (Oral)	R/M
4) 7-day DRF toxicity in nonrodents (Oral)	D/S/P
5) Genotoxicity: Bacterial mutagenicity (Ames)	<i>In vitro</i>
6) Pivotal/repeat dose in rodents (28 day oral)	R/M
7) Pivotal/repeat dose in nonrodents (28 day oral)	D/P/S
8) Develop Bioanalytical for 3 species (man/rodent/nonrodent)	NA
TO SUPPORT CONTINUED CLINICAL DEVELOPMENT	
9) Developmental Tox (Seg II) – rat and rabbit pilots and rat and rabbit studies	R/B
10) Neoantigenicity	B
TO SUPPORT MARKETING APPROVAL	

* Recommended

** May be required

SPECIES: R= Rat M= Mouse D= Dog S= Pig P= Primate B=Rabbit TBD= To be determined

All studies described above must be performed GLP.

Special Case: Excipients

TEST REQUIRMENT	SPECIES
INITIAL CLINICAL TRIAL/IND REQUIREMENTS	
1) Acute toxicity in rodents (Oral and IV*)	R/M
2) Acute toxicity in nonrodents (Oral)	D/S/P
3) 7-day DRF toxicity in rodents (Oral)	R/M
4)7-day DRF toxicity in nonrodents(Oral)	D/S/P
5) Genotoxicity: Bacterial mutagenicity (Ames)	<i>In vitro</i>
6) Genotoxicity: <i>In vitro</i> clastogenicity (CHO chromosome aberration)	<i>In vitro</i>
7) Genotoxicity: <i>In vivo</i> (mouse or rat micronucleus)	R/M
8) * Safety pharmacology: CV-hERG	<i>In vitro</i>
9) Safety pharmacology: CV <i>in vivo</i>	D/P/S
10) Safety pharmacology: FOB/Irwin	R/M
11) Safety pharmacology: Respiratory- Rodent	R
12) Pivotal/repeat dose in rodents (14-28 day oral)	R/M
13) Pivotal/repeat dose in nonrodents (14-28 day oral)	D/P/S
14)* CYP induction/inhibition	<i>In vitro</i>
15)* Five species micrososome metabolic panel	<i>In vitro</i>
16) Develop Bioanalytical for 3 species (man/rodent/nonrodent)	NA

Special Case: Excipients (Cont.)

TEST REQUIREMENT	SPECIES
TO SUPPORT CONTINUED CLINICAL DEVELOPMENT	
17) Developmental Tox (Seg II) – rat and rabbit pilots and rat and rabbit studies	R/B
18) Immunotoxicity	TBD
19) Pivotal/repeat dose in rodents (3/6 month oral)	R/M
20) Pivotal/repeat dose in nonrodents (3/9-12 month oral)	D/P/S
TO SUPPORT MARKETING APPROVAL	
21) Reproductive Toxicity – Seg I	R
23) Tumorigenicity/Carcinogenicity - Rat	R
<p>* Recommended ** May be required SPECIES: R= Rat M= Mouse D= Dog S= Pig P= Primate B=Rabbit TBD= To be determined All studies described above must be performed GLP.</p>	

CONTRACT LABORATORIES



THE BIG

Covance*	Charles River*	MPI	Battelle	WIL
SNBL*	MDS Pharma		Huntingdon*	CIT

THE MID-SIZE

BASi	Toxikon	Stillmeadow	Ricerca	LABs
ITR	Calvert	IITRI	SRI	RTI
Aptuit	USG	Bridge*	Southern Research	Harlan*

THE SPECIALIZED

NAMSA	INVITROGEN	In Vitro Tech	SITEK	BRT
CHAN Test	Liberty Labs	Skeletech	Midwest Bioresearch	Parsolt

THE EXTINCT

Bushy Run	Oread	FDRL	Tegaris	UTBL
Midatlantic	Litton Bionetics	U. Miami	IBT	Cannon Labs

*Multiple site Tox. CRO's

TOXICOLOGY LAB LISTINGS

Lab	Location	Phone #	Website	Additional Services	Rat	Rabbits	Dog	Carcinogen icity	DART	Inhalation	Primate	Pig	IV Infusion	Genotoxic	Devices	Metabolism	Analytical	Special Studies	
ABC Labs.	Missouri, IA N. Ireland, UK	(573) 474-8579 44 (0) 2870 320 639	www.abclabs.com	Bioanalysis, methods development	X											X	X		
ADMETRx	Kalamazoo	(269)-372-3272	www.admetrx.com	Yes															
Applied Preclinical Services	Oxford, NJ	(908) 637-4427	NO		X		X			X		X					X		
Apptec	St. Paul, Minn. Camden, N.J	800-622-8820	www.apptecls.com	microbiology										X	X				
Aptuit	Ledbury, UK & US	44 (0) 131 451 2560 878-988-2100	www.quintiles.com	Yes, clinical development, +	X	X	X	X	X			X	X	X	X	X	X	X	SP
Austrian Research Center	Seibersdorf, Austria	43(0) 50550-0	www.arcs.ac.at/		X	X			X										SP
BAS	West Lafayette, IN	(800) 845-4246	www.bioanalytical.com	Yes	X	X	X	X	X		X	X	X	X	X	X	X	X	
Battelle	Columbus, OH Richland, WA	(800) 201-2011	www.battelle.org	Yes	X	X	X	X	X	X	X	X	X				X	X	
BEC Labs	Toledo, OH	(419) 693-5307 (888) BEC-LABS	www.beclabs.com	Yes												X			
Bioagri	Piracicaba, Campinas and Sao Paulo- BRAZIL	+55-19-3429-7720	www.bioagri.com.br	None	X	X	X	X						X		X	X		
Biocon	Rockville, MD	800-826-8426	www.bioconinc.com	ferrets, disease models	X	X													
Bio-Life	Neillsville, WI	(715) 743-3171	NO	Yes											X			WL	
Bio-Quant	San Diego, CA	858-450-0048	www.bio-quant.com	Tumor models, Disease models	X		X					X					X		
BioReliance / Invitrogen	Rockville, MD	(800) 738-1000	www.bioreliance.com	*Full range Genotoxicity, Transgenic mouse CA models, MPI p53	X	X							X	X			X		
Biotechnics	Hillsborough, NC	(919) 245-3114	www.biotechnics-inc.com	Yes	X	X	X							X					
BRI	Vancouver, BC	(604) 432-9237	www.bripharm.com	Yes, Pharmaceutical, Development, +	X									X		X	X		

TOXICOLOGY LAB LISTINGS (Cont.)

Lab	Location	Phone #	Website	Additional Services	Rat	Rabbits	Dog	Carcinogenicity	DART	Inhalation	Primate	Pig	IV Infusion	Genotoxic	Devices	Metabolism	Analytical	Special Studies		
BRIDGE	Beijing, China Gaithersburg, MD	+650-859-3853	www.bridgepharmaceuticals.com	regulatory consulting	X		X				X		X	X		X	X			
BRT	Raleigh, NC	(919) 851-4499	www.futureciy.com/westwood/saks/135/brt/location.html	*Specialty immunotox	X	X									X					
BTC	Irvine, CA	(949) 660-3185	www.biologicaltestcenter.com	Yes, Pediatrics, +	X	X	X					X	X	X	X	X	X			
Calvert	Olyphant, PA	(570) 586-2411	www.calvertlabs.com	Yes	X	X	X	X	X		X	X	X		X	X	X	SP		
CEDRA	Austin, TX	(512) 834-7766	www.cedracorp.com	Yes														X		
Celsis	St. Louis, MO	(314) 487-6776	www.celsislabs.com	Yes, stability, methods	X			X	X	X				X	X	X	X	X		
Central Toxicology Labs. (Sygenta)	Alderley Park Macclesfield SK10 4TJ UK	+44 16255 15852 (p) +44 16255 17314 (f)	www.syngenta.com	Yes	X	X	X	X	X	X	X		X	X		X	X	SP		
Cerep	Redmond, WA	(425) 895-8666	www.cerep.com	Chemistry, in vitro PK, hERG										X				SP		
CeeTox Inc.	Kalamazoo, MI	269.353.5555	www.ceetox.com	Chemistry, in vivo, cell culture													X	X		
Chantest	Cleveland, OH	(216) 332-1665 (p) (216) 332-1706 (f)	www.chantest.com	hERG, ion channels																
Charles River	Worcester, MA	(508) 890 -0100	www.criver.com	Tumor models, implant studies	X	X	X				X	X	X		X	X	X	SP		
	Redfield, AR	(501) 397-2540		Ocular Tox IOP's	X	X	X	X				X	X							
	Sparks, NV*	(775) 331-2201		*Primate DART, immunotox					X		X		X				X	X	SP	
	Horsham, PA**	(215) 443-8710		** Photocarc Ferret emesis	X	X			X										SP	
	Spencerville, OH	(419) 647-4196		Acute Testing	X	X	X	X	X	X	X		X	X						
	Tranent, Scotland (Inveresk)	440 187 561 4555		Clinical, Ferret emesis	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	SP WL
	Montreal, QU (CTBR)	(514) 630-8200		Clinical, ferret emesis, Immunotox	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	SP
Cirion	Canada	(450) 688-6445	www.cirion.ca	Yes, clinical	X	X	X				X	X		X	X	X				

TOXICOLOGY LAB LISTINGS (Cont.)

Lab	Location	Phone #	Website	Additional Services	Rat	Rabbits	Dog	Carcinogen idiv	DART	Inhalation	Primate	Pig	IV Infusion	Genotoxic	Devices	Metabolism	Analytical	Special Studies
CIT – Centre Internat. De Toxicologie	Cedex France	+33 2 32 292626 (p) +33 2 32 678705 (f)	www.citox.com		X	X	X	X	X		X	X	X	X		X	X	SP
Clintox Bioservices	Hyderabad, India	91(40)55153222	www.clintoxbio.com	Phototox Hamsters	X	X										X		SP
Commonwealt h Biotechnologi es Inc.	Richmond, VA	(804) 648-3820	www.cbi-biotech.com	Genomics		X												
Comparative Biosciences	Sunnyvale, CA	(408)-504-8871 (408) 738-9278	www.compbio.com	*Special discovery, models	X	X							X		X	X	X	
CorDynamics	Chicago, IL	312-421-8876	www.cordynamics.com	CV safety only														
Covance	Vienna, VA Madison, WI Harrogete, U.K. Muenster, FRG	(888) COVANCE (888) 541-LABS	www.covance.com	Clinical, consulting	X	X	X	X	X		X	X	X	X	X	X	X	SP SP
CPTC	Fairfield, NJ	(973) 808-7111	www.cptclabs.com	Yes, clinical +	X	X									X		X	
Dermtech	San Diego, CA	(800) 808-2774	www.dermtechintl.com	Yes, consulting						X	X							
Enviro-Bio- Tech-Ltd.	Bernville, PA	(610) 488-7664	NO	(chicken, cattle) (food animals)														X WL
Experimur	Chicago, IL	312-842-9700	http://www.experimur.com	PK	X	X	X	X	X		X	X	X					
Exygen	State College, PA	(800) 281-3219 (p) (800) 272-1019 (f)	www.exygen.com	Methods, development												X	X	
Fraunhofer ITA	Nikolai-Fuchs Str. D-30625 Hannover Germany	+49 511 5353 0 (p) +49 511 5353 155(f)	www.ita.fhg.de		X	X	X	X	X	X				X		X	X	
Frontier Biosciences	China – US office	301-251-0231	www.frontierbsi.com	Animal disease models	X	X	X	X	X				X	X		X		SP
Genelogic	Gaithersburg, MD	(301) 330-3733 800-436-3564	www.genelogic.com	Yes	X	X	X	X	X		X	X	X			X	X	SP
Gibraltar Laboratories, Inc.	Fairfield, NJ	(973)-227-6882(p) (973)-227-0812(f)	www.gibraltarlabsinc.com	Microbiology	X	X								X	X			
Gwathmey	Cambridge, MA	(617) 491-0022 (p) (617) 492-5545 (f)	www.gwathmey.com	Consulting, biology	X	X									X	X		
Harlan	Rehovot ISRAEL	972 (0) 8-9409451	[none]	Bioproducts, Breeder	X		X									X	X	SP

TOXICOLOGY LAB LISTINGS (Cont.)

Lab	Location	Phone #	Website	Additional Services	Rat	Rabbits	Dog	Carcinogen idity	DART	Inhalation	Primate	Pig	IV Infusion	Genotoxic	Devices	Metabolism	Analytical	Special Studies
Haskell Laboratory	Wilmington, DE	(306)- 366-5200		Yes	X	X	X	X	X					X		X	X	
Huntingdon	East Millstone, NJ Cambridgeshire, UK	(732) 873-2550 44 (0) 1480 892000	www.huntingdon.com	Discovery support	X X	X X	X	X X ^a	X X	X X	X	X	X	X		X	X X	SP
Industrial Toxicology Research Center (ITRC)	Lucknow Nadu, India	+91-522-2211547; Fax : +91-522 2228227	www.itrcindia.org/index.html	Irritation, behavioural				X	X					X				
Intox	Pune, India	+91 22923633	www.intoxlab.com/html/profile.htm	Irritation, Farm animals	X	X		X	X					X				
Inveresk	Tranent, Scotland Montreal, QU	44 (0) 1875 614555 (514) 630-8200	www.inveresk.com	Clinical, ferret emesis	X X	X X	X X	X X	X X	X X	X	X	X	X		X	X X	SP SP
Irvine Analytical Labs, Inc.	Irvine, CA	(877) 445-6554	www.ialab.com	Yes						X							X	
Intl. Inst. of Biotech and Toxicology	Tamil Nadu, India	+91-4111-274246 +91-4111-274455		Biotechnology, Entomology, Agronomy													X	
Intl. Hungary Ltd.	Veszprem, Hungary	+36-1-4314840 fax +36-88-545-301	www.trc.hu	Yes toxicology	X	X	X	X		X			X			X		
IPS Therapeutique	Sherbrooke Quebec	819-564-5391 (p) 819-820-6831 (f)	www.ipstherapeutique.com/	hERG testing CV, safety pharm														
ITL Labs Ltd.	Delhi, India	91-11-27915654	www.indiamart.com/itl/														X	
ITR	Montreal, OU	(514) 457-7400	www.itrlab.com	Affiliated labs	X	X	X	X	X	X	X		X	X		X	X	SP
ITRI	Albuquerque, NM	(408) 428-9988	www.itri.com	Yes	X			X		X							X	
Jai Research Foundation International	Gujarat, India	+ 44 1684 891519	www.jrfonline.com		X	X	X	X	X					X		X	X	
JSW Research	Austria		www.jswresearch.com	Yes	X			X	X		X			X		X	X	
KIT (Korean Institute of Technology)	Korea	+82-42-610-8105	www.kitox.re.kr/eng_about.html	Yes	X	X	X	X			X	X	X	X				
LABS	Laval, Canada Veszprem, HU	(450) 973-2240 (416) 815-0700	www.preclin.com www.trc.hu	Yes	X X	X X	X X	X X		X			X X			X X		
Liberty Research	Waverly, NY	(607) 565-8131 (p) (607) 565-7420 (f)	NO	Cats, Ferrets			X											

TOXICOLOGY LAB LISTINGS (Cont.)

Lab	Location	Phone #	Website	Additional Services	Rat	Rabbits	Dog	Carcinogen idity	DART	Inhalation	Primate	Pig	IV Infusion	Genotoxic	Devices	Metabolism	Analytical	Special Studies	
Lovelace	Albuquerque, NM	(505) 348-9456	www.lrri.org	Clinical						X									
LPT	Hamburg, GE	40-70-20-20 40-70-20-22-99	www.LPT-pharm-tox.de		X	X	X	X	X	X	X	X	X	X	X	X	X	X	SP
LyChron	Mountain View, CA	650-938-3675	www.lychron.com	Pig Device Implant Studies								X							
Maccine	Singapore	+65-6778-7305	www.maccine.com	Yes	X	?	?			?			X			X	X		
MB Research	Spinnerstown, PA	(215) 536-4110	www.mbresearch.com	In vitro and alternative models	X	X	X								X				
MDS Pharma Services	Lincoln, NE L'Arbresle, France Geneva, Switzerland	(514) 333-0033	www.mdsp.com	Clinical, receptor screening	X	X	X	X	X		X			X	X	X	X	X	SP SP
MicaGenix	Greenfield, IN	888-779-5500	www.micagenix.com	Histology Image analysis Non-GLP mice & rats										X					
Micro Test	Agawam, MA	(800) 631-1680	www.microtestlabs.com	Yes											X				
Midwest Bio Research	Evanston, IL	847-682-6141(p) 847-556-6560(f)	www.midwestbioresearch.com	consultation										X		X			
MPI	Mattawan, MI	(269) 668-3336	www.mpiresearch.com	Yes	X	X	X	X	X		X	X	X		X	X	X	X	SP
MSI	Minato-ku, Tokyo, Japan	81 3 3454 7571	www.ankaken.co.jp	Yes				X		X	X					X			
MWRI	Kansas City, MO	(816) 753-7600	www.mriresearch.org	Yes	X			X											
NAMSA	Toledo, OH Irvine, CA Kennesaw, GA	(419) 666-9455 (949) 951-3110 (770) 427-3101	www.namsa.com	Yes										X X	X X				
Nelson Labs	Salt Lake City, UT	(800) 826-2088	www.nelsonlabs.com	Yes											X		X		
Next Century, INC	Newark, Delaware	(302) 453-0571	www.nextcenturyinc.com	Yes	X	X	X	X		X	X	X	X		X				
Northern Biomedical Research	Muskegon, MI	(231) 759-2333		Yes, Surgery, Large animals	X	X	X				X	X	X			X			
Northview	Northbrook, IL Spartan, SC	(847) 564-8181 (864) 574-7728	www.northviewlabs.com	Yes											X				
NOTOX	s'Hertogenbosch the Netherlands	31 73 640 67 00 (p) 31 73 640 67 99 (f)	www.notox.nl	Yes, Birds, +	X	X	X	X	X			X	X	X	X	X			WL

TOXICOLOGY LAB LISTINGS (Cont.)

Lab	Location	Phone #	Website	Additional Services	Rat	Rabbits	Dog	Carcinogenicity	DART	Inhalation	Primate	Pig	IV Infusion	Genotoxic	Devices	Metabolism	Analytical	Special Studies	
Nucro-Technics	Ontario, Canada	(416) 438-6727 (p) (416) 438-3463 (f)	www.nucro-technics.com	Microbiology	X	X	X	X						X	X		X		
Pacific Biolabs (PBL)	Hercules, CA	(510) 694-9000	www.northviewlabs.com	Yes	X	X	X	X	X					X	X	X	X		
Perry Scientific	San Diego, CA	(858) 560-9000 (p) (858) 467-9608 (f)	www.perryscientific.com	Yes; Large animals	X	X	X	X	X			X	X		X	X	X	SP	
Porsolt & Partners	Boulogne-Billancourt, FRANCE	+33146109990	http://www.porsolt.com/	Yes	X	X	X				X		X			X	X		
Product Safety Labs	Dayton, NJ	(732) 438-5100 (732) 254-9200	www.productsafetylabs.com	Environmental, Ferret Emesis Studies	X	X		X	X	X			X	X	X		X	WL	
Provident Preclinical, Inc	Doylestown, PA	215-348-3868(p) 215-348-5081(f)	www.ppicro.com	Yes	X	X	X	X		X	X	X			X				
Quest	Newark, Delaware	(302) 369-5601	www.questpharm.com	Yes	X	X	X		X		X			X		X	X		
Rallis Research Center	Bangalore, India	+91-80-28394959 +91-80-28394015	www.rallis.co.in	Yes	X	X		X						X		X	X		
RCC Ltd.	Zelgliweg 1 CH-4452 Itegen Switzerland	(410) 385-1666 – US sales office +41 61 975 1111 (p)	www.rcc.ch	Consulting, regulatory	X	X	X	X	X	X		X	X	X	X	X	X	X	SP
Ricerca	Concord, OH	(888) 763-4797	www.ricerca.com	*Synthesis, product development	X	X	X	X	X	X						X	X		
RTC S.p.A.	Via Tito Speri 12 I-40 Pomezia (Rom) Italy	+39 06 910 951 (p) +39 06 910 5737 (f)	www.rtc.it	Yes, Consulting, Regulatory	X	X	X	X	X			X		X				SP WL	
RTI	RTP, NC	(919) 541-6000	www.rti.org	Yes	X			X	X								X	X	
SafePharm	Derby, UK	00 44 (0) 1332 792896	www.safepharm.com	Yes, (fish+)	X			X	X	X				X	X	X	X	SP	
SCANTOX	Hestehavevej 36a DK-4623 Lille Skensved, Denmark	+45 56 82 11 00 (p) +45 56 82 12 02 (f)	www.scantox.com		X	X	X	X	X	X		X	X	X	X				
Sequani Limited	Bromyard Road Herefordshire HR8 1LH Ledbury, U.K.	+44 1531 634121 (p) +44 1531 634753 (f)	www.sequani.com		X	X	X	X	X			X	X	X	X				

TOXICOLOGY LAB LISTINGS (Cont.)

Lab	Location	Phone #	Website	Additional Services	Rat	Rabbits	Dog	Carcinogen idity	DART	Inhalation	Primate	Pig	IV Infusion	Genotoxic	Devices	Metabolism	Analytical	Special Studies
SGS Life Sciences Division	Fairfield, NJ	(800) 747-8782	www.ustesting.sgsna.com	Implant, combustion, fish, industrial, consumer products	X	X		X						X	X		X	SP, WL
Sinclair	PO Box 658	573-387-4400	www.sinclairresearch.com	Radiolabeled; cats; other				X				X	X		X	X		
Sitek	Rockville, MD	(301) 926-4900	www.siteklabs.com	Yes	X									X	X	X		
Skeletech	Bothell, WA	(425) 424-2663	www.skeletech.com	*Bone, CNS	X	X	X				X	X	X		X			
SNBL	Kagoshima, Japan	81 (0) 99-294-2600 81 (0) 99-294-3196 (f)	www.snbl.com	Yes, Clinical, +, Irritation`	X	X	X	X	X		X	X	X	X	X			SP
SNBL USA Ltd.	6605 Merrill Creek Parkway Everett, WA 98203	(425) 407 0121 (p) (425) 407 8601 (f)	http://www.snblusa.com/	Formulation, ferrets	X	X		X	X	X	X		X				X	SP
Southern RI	Birmingham, AL	(888) 322-1166	www.southernreaserch.org	Yes, formulation, development, tumor models	X	X	X	X	X		X	X	X	X	X	X	X	SP
SP1-bio	France	33 (0) 169 53 14 00	www.spibio.com	Clinical	X											X	X	
Spring Valley Lab.	Woodbine, MD	(800) 864-1839	www.springvalleylabs.com	Ferrets	X	X		X	X						X			
SRI	Palo Alto, CA	(650) 859-2000 866-451-5998	www.sri.com	Formulation, CTM	X	X	X	X				X		X	X	X	X	
Stillmeadow Inc.	Sugarland, TX	(281) 240-8828	www.stillmeadow.com	Companion animal studies	X	X	X			X		X					X	
STS duo Tek	Rush, NY He nrietta, NY	(716) 321-1130 (800) 836-4850	www.stsduotek.com	Yes, ocular	X	X							X	X	X			
Tandem Labs	Ewing, NJ	(609) 434-0044	www.tandemlabs.com	Yes													X	
TNO Pharma	Utrechtseweg 48 NL-3700AJ Zeist 3704 HE The Netherlands	+31 30 694 4806 (p) +31 30 694 4845 (f)	www.voeding.tno.nl	Yes, packaging, food & nutrition, clinical	X	X	X	X	X	X	X	X	X	X	X	X	X	SP, WL
Torrent Pharmaceutica Is Ltd.	Gujarat, India		www.torrentpharma.com					X	X					X				
TOXIKON Corp.	15 Wiggins Ave. Bedford, MA 01730	(781) 275 3330 (p) (781) 271-1136 (f)	www.toxikon.com	Yes	X	X	X	X	X			X	X	X	X	X		WL

TOXICOLOGY LAB LISTINGS (Cont.)

Lab	Location	Phone #	Website	Additional Services														
					Rat	Rabbits	Dog	Carcinogen idiv ^a	DART	Inhalation	Primate	Pig	IV Infusion	Genotoxic	Devices	Metabolism	Analytical	Special Studies
UIC Tox Research Lab	Chicago, IL	(312) 996-2123	www.uic.edu/labs/tox	Yes	X	X	X		X	X	X		X			X	X	
Vivo Bio Tech, Ltd.	Hyderabad, India	92-40-55784714 (p) 91-40-55776112 (f)	www.vivobio.com	immuno-deficient mice	X	X			X					X		X		
VIZON SciTec	Vancouver, BC CANADA	604-224-4331	www.vizonscitec.com	Ecotox														
VIMTA	Hyderabad, India	+91-40-2726 4141	www.vimta.com	Clinical					X					X			X	
WIL Research Labs, Inc.	1407 George Rd. Ashland, OH 44805	(419) 289 8700 (p) (419) 289 3650 (f)	www.wilresearch.com	Yes	X	X	X	X	X	X	X	X	X			X	X	SP, WL
XenoBiotics	Plainsboro, NJ	(609) 799-2295 (609) 799-7497	www.xbl.com	Clinical	X	X	X									X		
Xenotech	Lenexa, Kansas	(913) 438-7450	www.xenotech.com	Yes												X		

- A “Yes” or “+” listed in the additional services column indicates that there are more services available than just those listed.
- SP in the special studies column indicates safety pharmacology, WL in this column indicates wildlife/ environmental testing is available, EN in this column indicates that environmental testing in available.
- * Limited

^a Hamster carcinogenicity is available