Advinus REACH Capabilities

Advinus Corporate Overview

Key Facts

- Regulatory Testing facility in Bangalore, India, since 1982
- Promoted by the TATA group – India's premier and one of the largest business houses
- Management team of US and global experience with over 150 years

People

- More than 275 professionals
- >74% with Masters and PhD degrees

Vision: To be the leading and most admired life science R&D company from India creating value for its customers and stakeholders

Advinus Laboratory Services, Bangalore

Infrastructure

- Laboratory operations on one 8 acre campus
- Facility spread over 220,000 sq. ft of modern laboratory space

Data Management Systems

- Watson
- Nova LIMS
- SDMS
- Provantis (for regulatory toxicology)

Our Experience

- 25 years of operation
- 17 years of conducting GLP studies
- Over 3300 GLP studies
- Over 100 sponsors
- Studies as per
  - OECD
  - EPA
  - JMAFF

Our Commitment

- Stringent systems for
  - Quality
  - Confidentiality
  - Data security
- Strict adherence to SOPs and schedules
- Reliability of data

Project Management

- Client and Study team interface
- Dedicated project manager for each client
- Internal project tracking
- Ensuring timely communication and real time project status update
- Resource allocation
- Coordination between disciplines
- Timely project completion with quality deliverables
- Provide assistance with inward and outward sample shipment

Safety Assessment - People Strength

- 124 Professional staff members
- US Board Certified Toxicologist (DABT)
- 65% of the staff have either a Ph.D., M.S. (biology) or D.V.M.
- Thirty five Study Directors
- Twenty two veterinarians
- Each Study Director is with the company for an average of 10 years

Regulatory Inspections

- Total of 9 Government Inspections
- Inspection by BfR –German Health Ministry for GLP qualification
  - 1992,1996, 2000, 2005
- Inspection by W& V The Netherlands for GLP qualification
  - 1999, 2003, 2007
- Indian GLP Monitoring Authority
  - 2005, 2008
- No regulatory inspections “For Cause”

Accreditations

voedsel en waren autoriteit

ENDORSEMENT OF COMPLIANCE

WITH THE OECD PRINCIPLES OF
GOOD LABORATORY PRACTICE

Pursuant to the Netherlands GLP Compliance Monitoring Programme and according to Directive 2004/9/EC the conformity with the OECD Principles of GLP was assessed on 29 January – 2 February 2007 at

Advinus Therapeutics Private Limited
21 & 22 Phase II, Peenya Industrial Area
Bangalore - 560 058 INDIA

It is herewith confirmed that the afore-mentioned test facility is currently operating in compliance with the OECD Principles of Good Laboratory Practice in the following areas of expertise: physical-chemical testing, toxicity studies, mutagenicity studies, environmental studies on aquatic and terrestrial animals, and analytical and clinical chemistry.

Den Haag, 2 April 2007

Dr Th. Helder
Manager GLP Compliance Monitoring Program

Food and Consumer Product Safety Authority (VWA)
Prinses Beatrixlaan 2, 2595 AL Den Haag
Postbus 19506, 2500 CM Den Haag, The Netherlands

NATIONAL GLP COMPLIANCE MONITORING AUTHORITY

GOOD LABORATORY PRACTICE

GLP CERTIFICATE

GLP Inspection was carried out at Advinus Therapeutics Private Limited, Plot Nos. 21 & 22, Phase-II , Post Box No. 5813, Peenya Industrial Area, Bangalore-560 058, India in the following areas of expertise:

- physical-chemical testing
- toxicity studies
- mutagenicity studies
- environmental toxicity studies on aquatic & terrestrial organisms
- residue studies
- analytical and clinical chemistry testing

Based on the Inspection Report and the follow-up actions taken by the test facility, it is confirmed that the test facility is capable of conducting the above-mentioned tests/studies in compliance with OECD Principles of Good Laboratory Practice (GLP) and Norms, as adopted by the National GLP Compliance Monitoring Authority.

This GLP Certificate is valid for a period of three years from the date of issue, subject to the condition that the test facility complies with the Terms & Conditions of the National GLP Compliance Monitoring Authority's Document Number GLP-101.

Certificate No.: GLP/C-006

Issue Date : 07-11-2005

(R.S.HOA)
Head
National GLP Compliance Monitoring Authority
Department of Science & Technology
Technology Bhavan New Delhi-110016

BfR –German Health Ministry since 1992

W& V The Netherlands since 1999

AAALAC International since 2001
(1st AAALAC facility in India)

Indian GLP Authorities since 2005

Drug Control Dept of Karnataka since June 2003

BfR

GUTE LABORPRAXIS /
GOOD LABORATORY PRACTICE

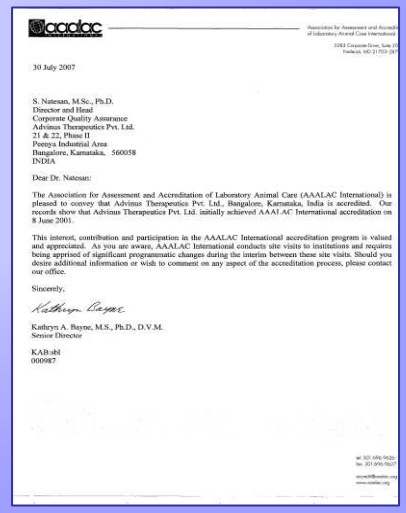
Advinus Therapeutics Private Limited

Prüfbereiche / Area of Expertise

- Prüfungen zur Bestimmung der physikalisch-chemischen Eigenschaften und Gehaltsbestimmungen / Physico-chemical testing
- Prüfungen zur Bestimmung der toxikologischen Eigenschaften / Toxicity studies
- Prüfungen zur Bestimmung der erbgutverändernden Eigenschaften (in vitro, in vivo) / Mutagenicity studies
- Ökotoxikologische Prüfungen zur Bestimmung der Auswirkungen auf aquatische und terrestrische Organismen / Environmental toxicity studies on aquatic and terrestrial organisms
- Prüfungen zum Verhalten im Boden im Wasser und in der Luft, Metabolismus / Studies on behaviour in soil, water and air, biotransformation
- Prüfungen zur Bestimmung von Rückständen / Residue studies
- Spezielle Wirksamkeits-, sowie Sicherheitsprüfungen von Arzneimitteln / Implantate / Medizinische Prothesen, as well as safety studies with drugs / vaccines

Datum der Inspektion / Date of inspection

February 19-22 , 2008



aaalac

Association for Assessment and Accreditation of Laboratory Animal Care International

30 July 2007

S. Natesan, M.Sc., Ph.D.
Director and Head
Corporate Quality Assurance
Advinus Therapeutics Pvt. Ltd.
21 & 22, Phase II
Peenya Industrial Area
Bangalore, Karnataka, 560058
INDIA

Dear Dr. Natesan:

The Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC International) is pleased to convey that Advinus Therapeutics Pvt. Ltd., Bangalore, Karnataka, India is accredited. Our records show that Advinus Therapeutics Pvt. Ltd. initially achieved AAALAC International accreditation on 8 June 2001.

This interest, contribution and participation in the AAALAC International accreditation program is valued and appreciated. As you are aware, AAALAC International conducts site visits to institutions and requires being apprised of significant programmatic changes during the interim between these site visits. Should you desire additional information or wish to comment on any aspect of the accreditation process, please contact our office.

Sincerely,

Kathryn A. Bayne, M.S., Ph.D., D.V.M.
Senior Director

KAB:sbl
000987

Test Systems Available

Rats	Wistar, Brown Norway, Sprague Dawley
Mice	Swiss Albino, Balb/C, Of1
Rabbits	New Zealand White
Guinea pigs	Duncan Hartley
K-9	Beagle
Chicken	White Leghorn
Pigeons	Columba livia
Quail	Coturnix coturnix japonica
Fresh water fish	Carp, Zebra, Guppies
Algae & Daphnia	*Selenestrum capricornutum & Daphnia magna*
Earthworms	Eisenia foetida foetida, Eudrilus eugeniae

Acute and Sub-acute studies

- Routes:
  - Oral (Gavage or dietary)/ Dermal/ Subcutaneous/ Intramuscular/ Intraperitoneal/ Intravenous/ Inhalation routes – single or multiple doses in different species
- Skin sensitization tests
  - Local Lymph Node Assay
- Skin / Eye irritation tests
- Short / long term by all routes
  - rats/mice
  - non-rodents

Sub-chronic and Chronic Studies

- Studies with administration through Dietary/ Gavage/ Subcutaneous/ Intramuscular/ Intraperitoneal/ Intravenous routes
- Sub-chronic 28/90 day studies
- Chronic 6/12 months studies
- Oncogenicity/ Carcinogenicity/ Life span studies
- Combined chronic and carcinogenicity studies
- 1/2/3 generation reproduction studies
- Teratology
  - Rats
  - Rabbits
- Fertility and early embryonic development in rats
- Peri-natal and Post-natal development toxicity studies in rats

Genotoxicity Studies

- *In vitro* mutagenicity
  - Ames test
  - Chromosomal aberration test – CHO cells
  - Gene Mutation test – CHO cells
    – mouse lymphoma cells
- *In vivo* mutagenicity
  - Micronucleus test – rats & mice
  - Chromosomal aberration test – mice
  - Dominant lethal test - rats & mice

List of acute studies

Guideline/s	Study Type
TOXICOLOGICAL STUDIES – ACUTE / SHORT-TERM	
OECD 420/423	Acute Oral Toxicity (Rats)
OECD 402	Acute Dermal Toxicity (Rats) (Full test)
OECD 403	Acute Inhalation Toxicity (Rats) - Limit test - Full test
OECD 404	Acute Dermal Irritation/ Corrosion (Rabbits)
OECD 405	Acute Eye Irritation/ Corrosion (Rabbits)
OECD 406	Skin Sensitization study (Guinea pigs) - Beuhler test - M & K Test

Sub chronic and chronic studies

Guideline/s	Study Type
OECD 407	Dose range finding study (14 days) in rats (without HP)
OECD 407	Repeated dose (28 day) study in rats (with recovery)
OECD	Repeated dose (28 day) study in dogs (with recovery)
OECD 408	Repeated dose (90 day) study in rats (with recovery)
OECD 409	Repeated dose (90 day) study in dogs (with recovery)
OECD 451	Carcinogenicity study in rats
OECD 451	Carcinogenicity study in mice
OECD 452	Chronic toxicity study in rats (1 year)
OECD 453	Combined chronic and carcinogenicity study
OECD 414	Teratogenicity –rats (including pre-study)
OECD 414	Teratogenicity – rabbits (including pre-study)
OECD 416	Two generation reproduction study in rats

Genotox capabilities

Guideline/s	Study Type
MUTAGENICITY STUDIES	
OECD 471	Bacterial reverse mutation assay (Ames test)
OECD 473	In vitro chromosome aberration test in CHO Cells
OECD 474	In vivo mammalian erythrocyte micronucleus test.
OECD 476	In vitro mammalian cell gene mutation test (HPRT) – CHO Cells
OECD 476	In vitro mammalian cell gene mutation test (TK) – mouse lymphoma Cells

Ecotoxicology studies

Studies on

- Fish
- Algae
- Daphnia
- Earthworms

Eco-Tox Capabilities

Guideline/s	Study Type
ECOTOX STUDIES	
OECD 201	Algal growth inhibition test
OECD 202	Daphnia acute immobilization test
OECD 211	Daphnia reproduction test
OECD 301B OECD 301D	Ready Biodegradation – Carbon dioxide Evolution Ready Biodegradation – Closed Bottle
OECD 203	Fish acute toxicity test – Static
OECD 204	Fish prolonged toxicity test – 21 day
OECD 207	Earthworm Acute toxicity
OECD 401	Acute oral in Japanese quails
OECD 401	Acute oral in Chicken
OECD 205	Avian Dietary study in Japanese quails
OECD 206	Avian reproduction in Japanese quails

Analytical Chemistry – Residue / Analytical

Analytical Chemistry & Product Properties Studies

- Physical and Chemical properties
- Five batch analysis according to
  - ➢ USEPA (OPPTS) / OECD / SETAC Guidelines
  - ➢ EEC/CIPAC methods

Phys-Chem Capabilities

Guideline/s	Study Type
PHYSICO-CHEMICAL STUDIES	
OECD 102, EEC A.1, OPPTS 830.7200, CIPAC /MT2	Melting point/melting range
OECD 103, OPPTS 830.7220, EEC A.2	Boiling point/ Boiling range
OECD 109, EEC A.3, OPPTS 830.7300, CIPAC MT 3	Specific gravity and density
OECD 104, OPPTS 830.7950	Vapour pressure
OECD 115, EEC A5	Surface tension of liquids
OECD 105, OPPTS830.7840, EEC A.6, MT 157	Solubility in water
OECD 107/117, OPPTS 830.7550, EEC A.8	Octonal-water partition coefficient
OPPTS 830.6315, EEC A.9, CIPAC MT 12	Flash point
OPPTS 830.6315, EEC A.10	Flammability (solids)
OPPTS 830.6314, EEC A.17	Oxidizing property
OECD 112, OPPTS 830.7370	Dissociation constant
OECD 114, OPPTS 830.7100, CIPAC MT 22	Viscosity of liquids
OECD 121, EEC C.19	Adsorption/desorption screening
OECD 111, OPPTS 835.2130, EEC C.7	Hydrolysis as a function of pH

Analytical Chemistry - Residue / Analytical

Residue & E-fate Studies

- Persistence, Residue and Environmental fate studies of pesticides
- Analysis of Pesticide residues and their metabolites in diverse substrates viz.,
  - soil
  - water
  - air
  - plants
  - animal feed
  - tissues

REACH registration – Phys chem. studies

TONNAGE	TESTS TO BE DONE
> 1 TO > 99 TONNES	Physical state at 20 degree C and 101.3 kPa, Melting Point/ Freezing Pt, Boiling Point, Relative density, Vapour Pressure, Surface Tension, Water Solubility, Octanol-Water Partition Coefficient, Flash Point / Flammability, Explosive Properties, Self-Ignition Temp, Oxidizing properties, Granulometry
> 100 TO > 1000 TONNES	All the above studies + stability in organic solvents, Dissociation Constant, Viscosity

Currently under development

REACH registration - Tox studies

TONNAGE	TESTS TO BE DONE
> 1 TONNE	In vitro Skin/Eye (irritation /Corrosion), Skin sensitisation / LLNA, Ames, Acute oral toxicity
> 10 TONNES	All the above studies +In vivo Skin/Eye Irritation, In vitro Cytogenicity, In vitro gene mutation, Acute dermal, Acute inhalation, 28 Day repeated dose, Repro tox (421), Developmental tox (421 or 422), Toxicokinetics assessment.
> 100 TONNES	All the above studies + Repeated dose toxicity (90 days), 2-gen repro tox (416), Teratogenicity
> 1000 TONNES	All the above studies + Immunotox, Neurotox, Long term (12 months) repeated toxicities studies, carcinogenicity study.

Currently under development

REACH registration – E-Fate studies

TONNAGE	TESTS TO BE DONE
> 1 TONNE	Acute daphnia toxicity, Acute algae lc50, Biodegradation
> 10 TONNES	All the above studies + Acute fish LC50, Bacterial (sludge) inhibition, H Hydrolysis as a function of pH, Adsorption/Desorption screening
> 100 TONNES	All the above studies + long term daphnia toxicity, Long term fish toxicity, Identification of degradation products, Earthworms, Simulation Testing (soil, water, sediment), Soil micro-organisms, Plants, Fish ELS/Fish embryo and sac-fry stages/Fish juvenile growth, Further adsorption/Desorption studies, Bioconcentration in fish.
> 1000 TONNES	All the above studies + Further E-Fate/ behaviours and biotic degradation, long term testing on earthworms, soil invertebrates, plants sediment organism, Toxicity to birds.

Currently under development

Contact Information

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