

STUDY REPORT

Original: 1/2

STUDY TITLE

**ACUTE DERMAL IRRITATION/CORROSION STUDY BIO-X KLEANZE EC IN
NEW ZEALAND WHITE RABBITS**

(As per OECD Guideline No. 404: Acute Dermal Irritation/Corrosion)

STUDY No.: BIO-ATX 2829

Study Completion Date: 12 January 2021

SPONSOR

OKADA ECOTECH PTE LTD
24 PIONEER CRESCENT #04-08
628557 SINGAPORE

TEST FACILITY

BIONEEDS INDIA PRIVATE LIMITED
DEVARAHOSAHALLY,
SOMPURA HOBLI, NELAMANGALA TALUK,
BANGALORE RURAL DISTRICT, PIN - 562 111,
KARNATAKA, INDIA
E-mail: bionees@bionees.in
Website: www.bionees.in
Tel No.: +91 816 - 2214400
Fax: +91 816 - 2214444

CONFIDENTIAL

TABLE OF CONTENTS

QUALITY ASSURANCE STATEMENT	4
STATEMENT OF GLP COMPLIANCE.....	5
DECLARATION.....	5
STATEMENT OF CONFIDENTIALITY	6
ABBREVIATIONS OF COMMONLY USED UNITS AND SYMBOLS	7
1. STUDY DETAILS	8
2. SUMMARY	10
3. STUDY COMPLIANCE.....	12
3.1 GLP Compliance	12
3.2 Regulatory Guideline.....	12
3.3 Animal Welfare	12
4. SAFETY PRECAUTIONS	12
5. OBJECTIVE.....	12
6. MATERIALS AND METHODS	12
6.1 Test Item Information.....	12
6.2 Test System	13
6.3 Husbandry.....	13
6.4 Acclimatization.....	14
6.5 Study Design	14
6.6 Preparation of Animals.....	15
6.7 Preparation of Test item	15
6.8 Dose Selection and Justification for Selection	15
6.9 Route of application and Justification for Selection.....	15
6.10 Method of Application of the Test Item	15
6.11 Test Procedure	15
6.11.1 Initial Test.....	15
6.11.2 Confirmatory Test	16
6.12 Observations	16
6.12.1 Clinical Signs of Toxicity and Mortality/Morbidity	16
6.12.2 Body Weight.....	17
6.12.3 Dermal Evaluations	17
6.12.4 Pathology.....	17

7.	INTERPRETATION OF RESULTS.....	17
8.	STUDY REPORT PREPARATION AND RESULTS.....	18
9.	AMENDMENTS AND DEVIATIONS	18
10.	STUDY REPORT DISTRIBUTION	18
11.	ARCHIVING.....	18
12.	REFERENCE	18
13.	RESULTS AND DISCUSSION.....	19
13.1	Clinical Signs of Toxicity and Mortality.....	19
13.2	Dermal Evaluations	19
13.3	Body Weight.....	19
14.	CONCLUSION	19
15.	TABLES.....	20
TABLE 1.	INDIVIDUAL ANIMAL CLINICAL SIGNS OF TOXICITY AND MORTALITY RECORD.....	21
TABLE 2.	INDIVIDUAL ANIMAL SKIN REACTIONS SCORING RECORD	22
TABLE 3.	INDIVIDUAL ANIMAL BODY WEIGHT (kg) AND PERCENT CHANGE IN BODY WEIGHT WITH RESPECT TO DAY 1	23
16.	ANNEXURES.....	24
ANNEXURE 1.	CERTIFICATE OF ANALYSIS OF BIO-X KLEANZE EC	25
ANNEXURE 2.	CONTAMINANT ANALYSIS TEST REPORT OF FEED.....	26
ANNEXURE 3.	CONTAMINANT ANALYSIS TEST REPORT OF WATER.....	28
ANNEXURE 4.	GLOBALLY HARMONIZED SYSTEM OF CLASSIFICATION AND LABELLING OF CHEMICALS (GHS)	31
ANNEXURE 5.	GLP CERTIFICATE	32


QUALITY ASSURANCE STATEMENT

The Study No.: BIO-ATX 2829, entitled “Acute Dermal Irritation/Corrosion Study of Bio-X Kleanze EC in New Zealand White Rabbits” has been inspected according to the OECD Principles of Good Laboratory Practice [C(97)186/Final].

The dates of inspections and dates of reporting to the Study Director and the Management have been listed below:

Inspection Dates	Inspection Phases	Reporting Dates	
		Study Director	Management
Initiation Phase			
14 December 2020	Study plan verification	14 December 2020	14 December 2020
07 January 2021	Study plan amendment No.1 verification	07 January 2021	07 January 2021
In-Life Phase			
22 December 2020	Test item application - Initial test	22 December 2020	22 December 2020
Reporting Phase			
07 January 2021	Draft report inspection	07 January 2021	07 January 2021
12 January 2021	Final report inspection	12 January 2021	12 January 2021

Inspections were performed according to the Standard Operating Procedures of the test facility’s Quality Assurance Unit. The study report was inspected against the approved study plan and pertinent raw data and accurately reflects the raw data.



(Signature)

Mr. PRAVEEN B.
Quality Assurance Unit

12 January 2021

(Date)

STATEMENT OF GLP COMPLIANCE

The Study No.: BIO-ATX 2829, entitled “Acute Dermal Irritation/Corrosion Study of Bio-X Kleanze EC in New Zealand White Rabbits” was performed in compliance with the OECD Principles of Good Laboratory Practice [C(97)186/Final].

DECLARATION

I hereby declare that the work was performed under my supervision and in accordance with the described procedures. It is assured that the reported results faithfully represent the raw data obtained during the experimental work. No circumstances have been left unreported which may have affected the quality or integrity of the data or which might have a potential bearing on the validity and reproducibility of this study.

I accept overall responsibility for the technical conduct of the study as well as the interpretation, analysis, documentation and reporting of the results.



(Signature)

Ms. D. JHANSI
Study Director



(Date)

STATEMENT OF CONFIDENTIALITY

This report contains **CONFIDENTIAL** and **PROPRIETARY** information of **OKADA ECOTECH PTE LTD., SINGAPORE** and will not be disclosed to anyone without the expressed or written approval of sponsor, except to the employees of the test facility wherever necessary and to persons authorized by law or judicial judgement.

D. Jhansi

(Signature)

Ms. D. JHANSI
Study Director

12 January 2021

(Date)



(Signature)

Dr. NITIN M. SHETTY
Deputy Test Facility Management

12 January 2021

(Date)

ABBREVIATIONS OF COMMONLY USED UNITS AND SYMBOLS

AAALAC	-	Association for Assessment and Accreditation of Laboratory Animal Care
B	-	Breadth
CPCSEA	-	Committee for the Purpose of Control and Supervision of Experiments on Animals
cm	-	Centimeter
ERY	-	Erythema
EDE	-	Oedema
GHS	-	Globally Harmonized System of Classification and Labelling of Chemicals
GLP	-	Good Laboratory Practice
IAR	-	Immediately after removal of the patch
g	-	Gram
h/hr(s)	-	Hour(s)
H	-	Height
IAEC	-	Institutional Animal Ethics Committee
kg	-	Kilogram
L	-	Length
M	-	Male
min	-	Minute
n	-	Number of animals
N	-	Normal
NAD	-	No Abnormality Detected
No.	-	Number
OECD	-	Organization for Economic Co-operation and Development
SD	-	Standard Deviation
TS	-	Terminal Sacrifice
°C	-	Degree Celsius

1. STUDY DETAILS

- 1.1 Study Title** : Acute Dermal Irritation/Corrosion Study of Bio-X Kleanze EC in New Zealand White Rabbits
- 1.2 Study Number** : BIO-ATX 2829
- 1.3 Study Code** : ADIN
- 1.4 Sponsor Details**
- Sponsor : Okada Ecotech Pte Ltd
24 Pioneer Crescent #04-08
628557 Singapore
- Sponsor's Representative : K. E. Tan
Okada Ecotech Pte Ltd
24 Pioneer Crescent #04-08
628557 Singapore
- Monitoring Scientist : A. Z. Tan
Okada Ecotech Pte Ltd
24 Pioneer Crescent #04-08
628557 Singapore
- 1.5 Test Facility** : Bionees India Private Limited
Devarahosahally,
Sompura Hobli, Nelamangala Taluk,
Bangalore Rural District, PIN - 562 111,
Karnataka, India
- 1.6 Study Responsibilities**
- Study Director : Ms. D. Jhansi., M.Sc
Bionees India Private Limited,
Devarahosahally,
Sompura Hobli, Nelamangala Taluk,
Bangalore Rural District, PIN - 562 111,
Karnataka, India
E-mail: bionees@bionees.in
- Study Co-ordinator : Ms. Amulya T. S., B. E. (Biotech)
- Study Personnel : Ms. Kowstubha G.D., M.Sc.
- Study Veterinarian : Dr. K. R Sneha., M.V.Sc.

1.7 Study Schedule

Study Initiation Date	:	16 December 2020
Experimental Starting Date	:	17 December 2020
Acclimatization Date	:	Start: 17 December 2020 End: 28 December 2020
Initial Test Date	:	22 December 2020
Confirmatory Test Date	:	29 December 2020
Experimental Completion Date	:	01 January 2021
Draft Report Submission Date	:	08 January 2021
Study Completion Date	:	12 January 2021

2. SUMMARY

The test item, Bio-X Kleanze EC was evaluated for Acute Dermal Irritation/Corrosion in New Zealand White rabbits.

The study was performed in two phases i.e. initial test and confirmatory test. Approximately 24 hours before the application of the test item, fur on the dorso-lateral area of the trunk of the animals was removed by clipping closely using an electric hair clipper (approximately 8 × 12 cm). Care was taken to avoid abrasion to the skin and the animals with healthy intact skin were used for experiment.

As there is no information on the test item, in initial test, three patches were applied for 3 minutes, 1 hour and 4 hour exposure period. The application site 1 (anterior left trunk region) of the animal was served as untreated control. On application site 2 (posterior left trunk region), site 3 (posterior right trunk region) and site 4 (anterior right trunk region) of the animal, 0.5 mL 80 dilutions of test item was applied for 3 minutes, 1 hour and 4 hours respectively. The first test patch was applied on site 2 and removed after three minutes. No skin reaction was observed after immediate observation, a second test patch was applied at site 3 and removed after one hour. After immediate observation, the observations at this stage indicated that exposure could be humanely allowed to extend to four hours, a third test patch was applied at site 4 and removed after four hours, and the response was graded. The application site 1 (anterior left trunk region) of the animal was covered with blank cotton gauze at the time of site 4 application and was removed along with application site 4. After removal of the test patches, the application sites were washed with distilled water and dried with absorbent cotton without altering the existing response or the integrity of the epidermis. The application sites 1, 2, 3 and 4 were scored immediately after patch removal whereas the application sites 1 and 4 were also scored approximately at 1, 24, 48 and 72 hours after the patch removal.

As there was no corrosive effect observed during initial test, the confirmatory test was performed using four additional rabbits (two animals with 80 dilutions and two animals with 160 dilutions of test item). In the confirmatory test, the patches were applied for 4 hours exposure period. Each animal had two application sites. The clipped area of skin at left trunk region and right trunk region were identified as application sites 1 and 2 respectively.

In the confirmatory test, the application site 1 (left trunk region) of each animal was served as untreated control covered with blank cotton gauze. On application site 2 (right trunk region) of each animal, 0.5 mL of test item was applied for 4 hours exposure period. After removal of the test patches the application sites were washed with distilled water and dried with absorbent cotton without altering the existing response or the integrity of the epidermis. The application sites 1 and 2 were scored approximately at 1, 24, 48 and 72 hours after patch removal.

The mean score across 3 scoring times (24, 48 and 72 hours after patch removal) for both initial test animal and confirmatory test animals was '0' for erythema and oedema grades.

No erythema and oedema was observed at the test item application site in initial and confirmatory test animals.

All the animals were observed once daily for clinical signs of toxicity and twice daily for mortality during the observation period. Body weight was recorded on the day of receipt, prior to administration of test item (day 1) and at termination. At termination,

all the animals were sacrificed by intravenous administration of sodium thiopentone and carcass was disposed.

No treatment related clinical signs of toxicity and mortality was observed in initial test animal and confirmatory test animals.

No treatment related changes were observed in body weight and percent change in body weight with respect to day 1 in initial test and confirmatory test animals. All animals revealed normal increase in the body weight during the observation period.

Conclusion

Based on the results of the experiment, it is concluded that single dermal application of Bio-X Kleanze EC was “non-irritant” to the skin of New Zealand White Rabbits and hence did not meet the classification criteria according to the Globally Harmonized System (GHS) of Classification and Labelling of Chemicals.

3. STUDY COMPLIANCE

3.1 GLP Compliance

The study was performed:

- a. In compliance with the OECD Principles of Good Laboratory Practice [C(97)186/Final].
- b. In accordance with the Standard Operating Procedures at Bionees India Private Limited and as per the mutually agreed study plan with the sponsor.

3.2 Regulatory Guideline

The study was performed in accordance with the OECD Guidelines for Testing of Chemicals No. 404 (Section 4: Health Effects), “Acute Dermal Irritation/Corrosion” adopted on 28 July 2015.

3.3 Animal Welfare

The study was performed in an AAALAC accredited facility:

- a. In accordance with the recommendation of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines for laboratory animal facility published in the Gazette of India, 2018.
- b. In accordance with the protocol approved by Institutional Animal Ethics Committee (IAEC) (Protocol No.: BIO-IAEC-4040 and Approval Date: 08/09/2020).

4. SAFETY PRECAUTIONS

Gloves, head cap, face mask and goggles were used in addition to protective body garments and slippers/shoes to ensure adequate personnel health and safety and to avoid ingestion, inhalation, eye and skin contact with the test item.

5. OBJECTIVE

The objective of this study was to assess the skin irritation and/or corrosive effects of the test item Bio-X Kleanze EC following single dermal application in New Zealand White Rabbits.

This also gives details on classification and labelling of chemical for safety and risk assessment.

6. MATERIALS AND METHODS

6.1 Test Item Information

The test item information provided by the sponsor as per Test Item Data Sheet and Certificate of Analysis is presented below:

Name of Test Item	:	Bio-X Kleanze EC
Physical appearance (with color)	:	Clear Brown liquid
Batch No.	:	2020061201
Date of Manufacture	:	12 June 2020
Date of Expiry	:	12 June 2023
Storage Conditions	:	Ambient (21 to 29°C)

Batch Produced by : Okada Ecotech Pte Ltd, Singapore
(Name and address)
Test Item Code by Test Facility : D1155-001

The responsibility for the correct identity and stability of the test item rests with the sponsor. The Certificate of Analysis provided by sponsor is presented as Annexure 1.

6.2 Test System

Animal Species : Rabbit (*Oryctolagus cuniculus*)
Strain : New Zealand White
Justification for Selection of Species : Rabbit is the preferable laboratory animal by national and international guidelines for dermal irritation/corrosion studies.
Source of Supply : Procured from approved breeder:
Adita Biosys Private Limited
Plot No.: SPL-26, 2nd Phase, KSSIDC
Industrial Estate, Madhugiri Road,
Antharasanahalli, Tumakuru-572106,
Karnataka, India
CPCSEA Registration No.
1868/PO/RcBt/S/16/CPCSEA
Group, No. of Animals / Test and Sex : G1A : 1 Male (80 dilutions of test item)
G1 : 2 Males (80 dilutions of test item)
G2 : 2 Males (160 dilutions of test item)
Initial Test : 1 Male
Confirmatory Test : 4 Males
(Total of 5 Males were received)
Age at Receipt : 4 months
Body Weight at Receipt : 2.07811 kg to 2.39064 kg
Animal Identification : Acclimatization period: Cage cards
Treatment period: Cage cards and last 4 digits of the animal number were written on the ear of each rabbit using black permanent marker pen.
Animal No.: Nb5968 to Nb5972

6.3 Husbandry

- a. Environmental Conditions** : Animals were housed under standard laboratory conditions, in an environmentally monitored air-conditioned room with adequate fresh air supply (12 to 15 air changes per hour), room temperature 19.3°C to 22.8°C and relative humidity 47% to 67% with 12 hours fluorescent lights and 12 hours dark cycle. The temperature and relative humidity were recorded once daily.
- b. Housing** : The animals were housed individually in stainless steel wire mesh cage (Size: L 24 x B 18 x H 18 inches) having facilities for holding pelleted feed and drinking water.

c. Feed : Altromin Maintenance Diet for rabbits (manufactured by Altromin Spezialfutter GmbH & Co. KG) was provided *ad libitum* to the rabbits throughout the experimental period. The contaminant analysis test report for the feed is presented as Annexure 2.

d. Water : Water was provided *ad libitum* throughout the experimental period. Deep bore-well water passed through reverse osmosis unit was provided in plastic water bottles with stainless steel sipper tubes.

The contaminant analysis test report for the water nearest to the experimental period is presented as Annexure 3.

6.4 Acclimatization

Healthy young adult animals used for initial test and confirmatory test were acclimatized for a period of five and twelve days respectively to laboratory conditions prior to treatment and were observed for clinical signs once daily. Veterinary examination of all the animals was performed on the day of receipt.

6.5 Study Design

The study was performed in two phases i.e initial test and confirmatory test. Initial test was performed using one rabbit, there was no corrosive and irritant effects observed in initial test. Hence, the confirmatory test was performed by using four additional rabbits (G1 with 0.5 mL of 80 dilutions test item and G2 with 0.5 mL of 160 dilutions test item).

The following study design was adopted for the study

Group : G1/G1A (80 dilutions of test item)									
Treatment	Quantity of test item applied (mL)	Initial Test (G1A)				Confirmatory Test (G1)			
		Animal No.: Nb5968				Animal No.: Nb5969		Animal No.: Nb5970	
		Lt. Trunk Region		Rt. Trunk Region		Lt. Trunk Region	Rt. Trunk Region	Lt. Trunk Region	Rt. Trunk Region
		Site 1	Site 2	Site 3	Site 4	Site 1	Site 2	Site 1	Site 2
Untreated Control	NA	Yes	No	No	No	Yes	No	Yes	No
Bio-X Kleanze EC	0.5	No	Yes (3 min)	Yes (1 hr)	Yes (4 hrs)	No	Yes (4 hrs)	No	Yes (4 hrs)
Confirmatory Test (G2) (160 dilutions of test item)									
Animal No.: Nb5971					Animal No.: Nb5972				
Lt. Trunk Region		Rt. Trunk Region			Lt. Trunk Region		Rt. Trunk Region		
Site 1		Site 2			Site 1		Site 2		
Yes		No			Yes		No		
No		Yes (4 hrs)			No		Yes (4 hrs)		

Rt.: Right, Lt.: Left, hr/s - Hour/s; min: Minutes

6.6 Preparation of Animals

Approximately 24 hours before the application of the test item, fur on the dorso-lateral area of the trunk of the animals was removed by clipping closely using an electric hair clipper (approximately 8 cm x 12 cm). Care was taken to avoid abrasion to the skin and the animals with healthy intact skin were used.

6.7 Preparation of Test item

For initial test:

80 dilutions: 0.13 mL of test item was taken and 10 mL of distilled water was added to get 80 dilutions of test item.

For Confirmatory test:

80 dilutions: 0.25 mL of test item was taken and 20 mL of distilled water was added to get 80 dilutions of test item.

160 dilutions: 0.13 mL of test item was taken and 20 mL of distilled water was added to get 160 dilutions of test item.

6.8 Dose Selection and Justification for Selection

As suggested in regulatory guidelines, 0.5 mL of diluted test item was used for the testing.

6.9 Route of application and Justification for Selection

The diluted test item was applied topically (dermal exposure). The dermal route was selected as it is one of the probable route of exposure to human.

6.10 Method of Application of the Test Item

Required amount of diluted test item was received, and 0.5 mL of diluted test item was applied to a small area (approximately 6 cm²) of skin on the application site covered with cotton gauze and wrapped with non-irritating adhesive tape. The patch was loosely held in contact with the skin by means of a suitable semi-occlusive dressing using crepe bandage for the duration of the exposure period. It was ensured that the test item was adhered to the skin in such a manner that there was good contact and uniform distribution of the test item on the skin.

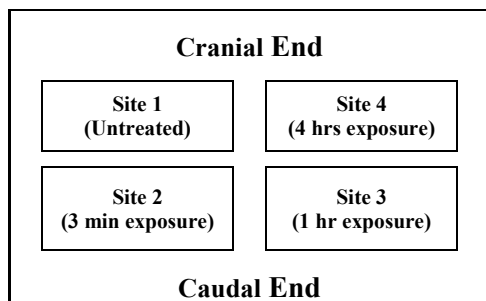
6.11 Test Procedure

6.11.1 Initial Test

In the initial test with 80 dilution (highest concentration) of Bio-X Kleanze EC three sequential test patches were applied step-by-step at different time points as per sponsor communication as there is no information on the test item. The clipped area of skin at left trunk region and right trunk region was divided into four application sites and it was identified as application sites 1, 2, 3 and 4 respectively.

The application site 1 (anterior left trunk region) of the animal was served as untreated control. On application site 2 (posterior left trunk region), site 3 (posterior right trunk region) and site 4 (anterior right trunk region) of the animal, 0.5 mL of test item was applied for 3 minutes, 1 hour and 4 hours respectively as per section 6.9. The first test patch was applied on site 2 and removed after three minutes. No skin reaction was observed after immediate observation, a second test patch was applied at site 3 and removed after one hour. After immediate observation, the observations at this stage indicated that exposure was humanely allowed to extend to four hours, a

third test patch was applied at site 4 and the response was graded. The application site 1 (anterior left trunk region) of the animal was covered with blank cotton gauze at the time of site 4 application and was removed along with application site 4. After removal of the test patches, the application sites were washed with distilled water and dried with absorbent cotton without altering the existing response or the integrity of the epidermis.

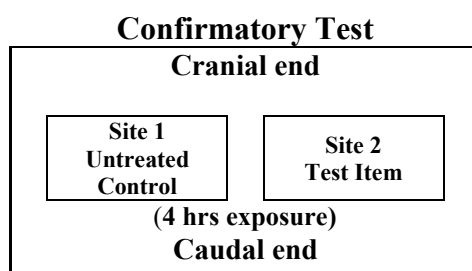


6.11.2 Confirmatory Test

There were no corrosive effects observed during initial test, hence the confirmatory test was performed by using four additional rabbits.

In confirmatory test with G1 (80 dilutions) and G2 (160 dilutions), the test patch was applied for 4 hours exposure period. Each animal had two application sites. The clipped area of skin at left trunk region and right trunk region was identified as application site 1 and 2 respectively.

The application site 1 (left trunk region) of each animal was served as untreated control covered with blank cotton gauze. On application site 2 (right trunk region) of each animal, 0.5 mL of undiluted test item was applied for 4 hours exposure period as per section 6.10. After removal of the test patches, the application sites were washed with distilled water and dried with absorbent cotton without altering the existing response or the integrity of the epidermis.



The details of distilled water used for study is as follows:

- Batch No. : 188B
- Manufactured Date : 10/12/2020
- Expiry Date : 09/12/2021
- Manufactured by : MRCL

6.12 Observations

The following observations were made during the experimental period.

6.12.1 Clinical Signs of Toxicity and Mortality/Morbidity

The animals were observed once daily for clinical signs of toxicity and twice daily for mortality/morbidity during the experimental period.

6.12.2 Body Weight

Body weights were recorded on the day of receipt, prior to application of test item (day 1) and at termination (day 4) of the experiment for both initial test animal and confirmatory test animals.

6.12.3 Dermal Evaluations

The animals were evaluated for signs of erythema and oedema and the responses were scored. In initial test, the application sites 2 and 3 were scored immediately after patch removal, sites 1 and 4 were scored immediately after patch removal and also scored approximately at 1, 24, 48 and 72 hours after patch removal. In confirmatory test, the application sites 1 and 2 were scored approximately at 1, 24, 48 and 72 hours after patch removal. The experiment was terminated after 72 hours observation after removal of test patch as there were no skin reactions.

Dermal reactions were graded and recorded according to the scores in the table below:

Table: Grading of Skin Reactions

1. Erythema and Eschar Formation	Score
No erythema.....	0
Very slight erythema (barely perceptible).....	1
Well defined erythema.....	2
Moderate to severe erythema.....	3
Severe erythema (beet redness) to eschar formation preventing grading of erythema... ..	4

Maximum possible score: 4

2. Oedema Formation	Score
No oedema	0
Very slight oedema (barely perceptible).....	1
Slight oedema (edges of area well defined by definite rising).....	2
Moderate oedema (raised approximately 1 millimetre)	3
Severe oedema (raised more than 1 millimetre and extending beyond area of exposure)	4

Maximum possible score: 4

6.12.4 Pathology

a. Necropsy

At the end of observation period, all the animals were humanely sacrificed by intravenous administration of sodium thiopentone (Batch No.: TP0002; Manufactured date: Mar 2020; Expiry date: Feb 2022; Manufactured by: Shree anand life sciences Ltd.) and the carcass was disposed.

7. INTERPRETATION OF RESULTS

The test item is classified according to the Globally Harmonized System (GHS) of Classification and Labelling of Chemicals (Refer Annexure 4).

The mean score was calculated across 3 scoring times (approximately at 24, 48 and 72 hours after patch removal) for each animal for erythema/eschar grades and for oedema grades separately.

8. STUDY REPORT PREPARATION AND RESULTS

Individual animal data is summarized and presented as tables. All findings presented in the study report are as per the standard reporting procedure of the test facility.

9. AMENDMENTS AND DEVIATIONS

One amendment was raised to correct the name of monitoring scientist as per revised test item data sheet and no deviations occurred during the conduct of the study.

10. STUDY REPORT DISTRIBUTION

Original: 1/2 - Sponsor

Original: 2/2 - Archives, Bionees India Private Limited

11. ARCHIVING

All materials and data generated in the study will be stored in the archives of the test facility. The study plan, raw data and study report will be maintained in the archives of Bionees India Private Limited for 9 years from the date of completion of the study. At the end of archiving period, the sponsor's instructions will be sought either to extend the archiving period or to return the archived material to the sponsor or for the disposal.

12. REFERENCE

The Globally Harmonized System of Classification and Labelling of Chemicals (GHS), 8th edition, 2019 (ST/SG/AC.10/30/REV.8).

13. RESULTS AND DISCUSSION

13.1 Clinical Signs of Toxicity and Mortality

No clinical signs of toxicity and mortality were observed in any of the animals of initial test and confirmatory test.

Refer Table 1.

13.2 Dermal Evaluations

No skin reactions like erythema and oedema were observed in any of the animals of initial test and confirmatory test.

The mean score across 3 scoring times (24, 48 and 72 hours after patch removal) for both initial test animal and confirmatory test animals was '0' for erythema and oedema grades

Refer Table 2.

13.3 Body Weight

No treatment related changes were observed in body weights and percent change in body weights with respect to day 1 in initial test and confirmatory test animals. All animals revealed normal increase in the body weight during the observation period.

Refer Table 3.

14. CONCLUSION

Based on the results of the experiment, it is concluded that single dermal application of Bio-X Kleanze EC was “non-irritant” to the skin of New Zealand White Rabbits and hence did not meet the classification criteria according to the Globally Harmonized System (GHS) of Classification and Labelling of Chemicals.

15. TABLES

TABLE 1. INDIVIDUAL ANIMAL CLINICAL SIGNS OF TOXICITY AND MORTALITY RECORD

Phase of the Experiment	Dose (mL/Patch)	Animal No.	Sex	Clinical Signs of Toxicity on Days			
				1	2	3	4
Initial Test	0.5mL of 80 dilutions	Nb5968	Male	N	N	N	N
		Nb5969	Male	N	N	N	N
Confirmatory Test	0.5mL of 80 dilutions	Nb5970	Male	N	N	N	N
		Nb5971	Male	N	N	N	N
	0.5mL of 160 dilutions	Nb5972	Male	N	N	N	N

N: Normal

TABLE 2. INDIVIDUAL ANIMAL SKIN REACTIONS SCORING RECORD

Phase of the Experiment	Animal No.	Sex	Exposure Duration	Application Site	Dose (mL/Patch)	Observations	Skin Reactions Score after Patch Removal					Mean Score
							IAR	1 hr	24 hrs	48 hrs	72 hrs	
Initial Test 0.5mL of 80 dilutions	Nb5968	Male	3 min	Site 2	0.5	ERY	0	-	-	-	-	-
						EDE	0	-	-	-	-	-
			1 hr	Site 3	0.5	ERY	0	-	-	-	-	-
						EDE	0	-	-	-	-	-
			4 hrs	Site 1	Untreated Control	ERY	0	0	0	0	0	0
						EDE	0	0	0	0	0	0
			4 hrs	Site 4	0.5	ERY	0	0	0	0	0	0
						EDE	0	0	0	0	0	0
Confirmatory Test 0.5mL of 80 dilutions	Nb5969	Male	4 hrs	Site 1	Untreated Control	ERY	-	0	0	0	0	0
						EDE	-	0	0	0	0	0
				Site 2	0.5	ERY	-	0	0	0	0	0
						EDE	-	0	0	0	0	0
	Nb5970	Male	4 hrs	Site 1	Untreated Control	ERY	-	0	0	0	0	0
						EDE	-	0	0	0	0	0
				Site 2	0.5	ERY	-	0	0	0	0	0
						EDE	-	0	0	0	0	0
Confirmatory Test 0.5mL of 160 dilutions	Nb5971	Male	4 hrs	Site 1	Untreated Control	ERY	-	0	0	0	0	0
						EDE	-	0	0	0	0	0
				Site 2	0.5	ERY	-	0	0	0	0	0
						EDE	-	0	0	0	0	0
	Nb5972	Male	4 hrs	Site 1	Untreated Control	ERY	-	0	0	0	0	0
						EDE	-	0	0	0	0	0
				Site 2	0.5	ERY	-	0	0	0	0	0
						EDE	-	0	0	0	0	0

ERY: Erythema; EDE: Oedema; 0: No Erythema/Oedema; min: Minutes; hr/hrs: Hour/Hours; IAR: Immediately after removal of the test patch; -: Not applicable

$$\text{Mean Score For Erythema/ Oedema} = \frac{24 \text{ hrs} + 48 \text{ hrs} + 72 \text{ hrs (Observations after patch removal)}}{3 \text{ (Observation time point)}}$$

TABLE 3. INDIVIDUAL ANIMAL BODY WEIGHT (kg) AND PERCENT CHANGE IN BODY WEIGHT WITH RESPECT TO DAY 1

Phase of the experiment	Dose (mL/animal)	Animal No.	Sex	Body weight (kg)		Percentage change in Body with respect to day
				1	4	1 to 4
Initial test (80 dilutions)	0.5	Nb5968	Male	2.21136	2.2497	1.73377
confirmatory test (80 dilutions)	0.5	Nb5969	Male	2.49162	2.52904	1.50183
		Nb5970		2.38111	2.42919	2.01923
			Mean	2.43637	2.47912	1.76053
			±SD	0.07814	0.07060	0.36585
		n	2	2	2	
confirmatory test (160 dilutions)	0.5	Nb5971	Male	2.30143	2.34086	1.71328
		Nb5972		2.18114	2.25064	3.18641
			Mean	2.24129	2.29575	2.44984
			±SD	0.08506	0.06380	1.04166
		n	2	2	2	


SD: Standard Deviation; n: Number of animals

16. ANNEXURES

ANNEXURE 1. CERTIFICATE OF ANALYSIS OF BIO-X KLEANZE EC**OKADA ECOTECH PTE LTD** (REG NO 199805584M)24 Pioneer Crescent, #04-08, West Park Bizcentral, Singapore 628557
Tel: (65) 6872 3515 Fax: (65) 6872 6558
Website: www.okada-ecotech.com**CERTIFICATE OF ANALYSIS**

Attention : **To whom it may concern**
Product Name : **Bio-X® Kleanze EC**
Batch Number : 2020061201
Date of Test : 1 December 2020

TEST	SPECIFICATIONS	RESULT
Appearance	Clear brown	OK
Odor	Pleasant	OK
Viscosity (cP) (BF DVII #1/100RPM/30Deg C)	20 ± 5 cps	20.0
Specific Gravity	0.95 ± 0.10	0.96
Dispersibility in Water	All proportion dispersible	OK


Tan Aik Zen
(Chemical Engineer)

ANNEXURE 2. CONTAMINANT ANALYSIS TEST REPORT OF FEED

Nr.: QA - 72
Aufbewahrungsdauer
15 Jahre nach Erstellen

Altromin Spezialfutter GmbH & Co. KG
Im Seelenkamp 20
D-32791 Lage
Tel.: +49 (0)5232 / 6088-0
Fax: +49 (0)5232 / 6088-20
E-Mail: analysen@altromin.de



Producer Certificate

Description	Maintenance diet for rabbits - Rich in crude fibre
Type	2123 4mm-pellets, 12.5 kg double plastic bags
Customer	ATNT Laboratories, India
Batch no. / Lot no.	202008241845
Order no.	Altromin Doc. No. 48867
Production date	24.08.2020
Expiry date	24.08.2021

Guaranteed nutritional values

% in air-dry substance	Value*	Tolerance**
Crude protein	13,7	12,0 – 15,4
Crude fat	3,0	2,0 – 5,0
Crude fibre	20,0	16,5 – 23,5
Crude ash	8,4	6,3 – 9,5
Moisture	11,4	< 12,5
NfE - Nitrogen free extracts	43,5	
Calcium	1,0	0,7 – 1,6
Phosphorus	0,5	0,2 – 0,8

* The producer guarantees that nutritional values of this batch are within the declared tolerance values.

** Tolerances according to Annex IV of Regulation (EU) Nr.767/2009.

Physical analysis

Pellet hardness kg/cm ² - Kahl	12
---	----

Sensory evaluation

Olfactory	ok
Visual	ok

This product is compliant with the specifications and quality requirements of Altromin and therefore has been approved for delivery.


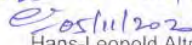
Accepted and released for use on 05/11/2020

Date: September 21st 2020

e-05/11/2020
Hans-Leopold Altrogge
QA-Manager

This is a computer printout and has therefore not been signed and dated by hand

ANNEXURE 2 (Contd...). CONTAMINANT ANALYSIS TEST REPORT OF FEED

Nr.: QA - 72-1 Aufbewahrungsdauer: 15 Jahre nach Erstellen	
Altromin Spezialfutter GmbH & Co. KG Im Seelenkamp 20 D-32781 Lage Tel.: +49 (0)5232 / 6088-0 Fax: +49 (0)5232 / 6088-20	
	
<h3>Producer Certificate</h3>	
Description	2123 Maintenance diet for rabbits
Customer	ATNT Laboratories, India
Batch no. / Lot no.	202008241845
Production date	24.08.2020
Expiry date	24.08.2021
Guaranteed diet status:	
Aflatoxins	
Aflatoxin B1	< 2.5 µg/kg
Aflatoxin B2	< 0.6 µg/kg
Aflatoxin G1	< 2.5 µg/kg
Aflatoxin G2	< 0.6 µg/kg
Sum B1, B2, G1, G2	below detection limit
Heavy metals	
Lead (Pb)	< 1.00 mg/kg
Cadmium (Cd)	< 0.20 mg/kg
Mercury (Hg)	< 0.05 mg/kg
Arsenic (As)	< 1.00 mg/kg
Polychlorinated Biphenyls	
PCB	below detection limit
Pesticides and residuals	
Chlorpyrifos-methyl	< 0.100 mg/kg
2-Phenylphenol	< 0.100 mg/kg
Diphenylamin	< 0.050 mg/kg
Ethoxyquin	< 5.000 mg/kg
Folpet	< 1.000 mg/kg
Piperonylbutoxid	< 0.500 mg/kg
Pirimiphos-methyl	< 0.500 mg/kg
all screened substances not mentioned are usually below detection limit (see attached list)	
Microbiological status	
Total aerobic count	< 10 ⁵ cfu/g
Yeasts	< 10 ² cfu/g
Moulds	< 10 ² cfu/g
E. coli	< 10 ¹ cfu/g
Salmonella in 25 g	not detectable
<i>Accepted and released for use on 05/11/2020</i>  Hans-Leopold Altrogge (Quality Manager)	
Date: September 21st 2020	
<small>This is a computer printout and has therefore not been signed and dated by hand.</small>	

ANNEXURE 3. CONTAMINANT ANALYSIS TEST REPORT OF WATER



INSTITUTE FOR ANALYSIS OF DAIRY, FOOD & CULTURES.
 #8, Siddhi Vinayaka Complex, Nagarabhavi 2nd Stage, 2nd Block
 Near BDA Complex, 80 Feet Ring Road, Bangalore-560 072
 Ph: +91-80-2318 6906 to 10, Cell : +91 8152881444/8152881222
 Mail: accounts@iadfac.com/bd@iadfac.com/qa@iadfac.com

CERTIFICATE OF ANALYSIS

BOOKING NO. : 0010
 CERTIFICATE NO. : 0010/2020-2021

NAME OF MANUFACTURER/PARTY :		BIONEEDS INDIA PRIVATE LIMITED Devarahosahalli, Sompura Hobali, Nelamangla Taluk, Bangalore Rural Dist, BANGALORE - 562111 KARNATAKA	
1. MFG. LIC. NO.	: NM	3. DATE	: 06/05/2020
2. REFERENCE NO.	: NM	5. NAME OF SAMPLE	: Drinking Water (R O Water)
4. DATE OF RECEIPT	: 06/05/2020		
6. DETAILS OF RAW MATERIAL / FINAL PRODUCTS (In Bulk/Finished Pack)			
(A) MANUFACTURER NAME	: NM	(B) BATCH NO.	: NM
(C) BATCH SIZE	: NM	(D) DATE OF MFG.	: NM
(E) SAMPLE QUANTITY	: 5Lx1 Can	(F) DATE OF EXPIRY	: NM
(G) PACKING	: Plastic Bottle	(H) STARTING DATE	: 08/05/2020
(I) SEALED	: Sealed	(J) ENDING DATE :	: 19/05/2020
(K) BRAND NAME	: NM	(L) SAMPLING PROTOCOL	: NA
(M) DATE OF SAMPLING/SAMPLE COLLECTION	: 06/05/2020	(N) REPORT GEN. DATE	: 19/05/2020

Specification as per IS 10500:2012

SR	TEST NAME	UNIT	RESULT	ACCEPTABLE LIMIT	PERMISSIBLE LIMIT	METHOD OF TEST
1	CHEMICAL TESTING Water, Residues in Water					
1	Colour	CU	<1	5 Max	15 Max	IS 3025 (Part-4) : 1983
2	Odour	-	Agreeable	Agreeable	Agreeable	IS 3025 (Part-5) : 2018
3	pH Value	-	6.6	6.5-8.5	No Relaxation	IS 3025 (Part-11) : 1983
4	Taste	-	Agreeable	Agreeable	Agreeable	IS 3025 (Part-7&Part-8) : 2017
5	Turbidity (as NTU)	-	<1	1 Max	5 Max	IS 3025 (Part-10) : 1984
6	Total Dissolved Solids	mg/l	23	500 Max	2000 Max	IS 3025 (Part-16) : 1984
7	Aluminium (as Al)	mg/l	<0.02	0.03 Max	0.2 Max	IS 3025 (Part-55) : 2003
8	Boron (as B)	mg/l	<0.1	0.5 Max	2.4 Max	IS 3025 (Part-57) : 2005
9	Calcium (as Ca)	mg/l	1	75 Max	200 Max	IS 3025 (Part-40) : 1991
10	Chloride (as Cl)	mg/l	2	250 Max	1000 Max	IS 3025 (Part-32) : 1988
11	Copper (as Cu)	mg/l	<0.05	0.05 Max	1.5 Max	IS 3025 (Part-42) : 1992
12	Fluoride (as F)	mg/l	<0.1	1.0 Max	1.5 Max	IS 3025 (Part-60) : 2013
13	Free residual Chlorine	mg/l	<0.1	0.2 Min	1.0 Max	IS 3025 (Part-26) : 1986
14	Iron (as Fe)	mg/l	<0.05	1.0 Max	No Relaxation	IS 3025 (Part-53) : 2003
15	Magnesium (as Mg)	mg/l	<1	30 Max	100 Max	IS 3025 (Part-46) : 1994
16	Manganese (as Mn)	mg/l	<0.1	0.1 Max	0.3 Max	IS 3025 (Part-59) : 2006

Remarks : <i>Accepted and released for use @ 21/05/2020</i>	For IADFAC Laboratories Pvt. Ltd. <i>Karan</i> Authorised Signatory Karunakara A.C. (ID No-132) Senior Manager-Chemical	CONTD. ON NEXT PAGE..... AUTHORISED SIGNATORY
--	---	---

Note :

- The results listed, refer only to the samples analysed & applicable parameters, Endorsement products is neither inferred nor implied.
- Total liability of our institute is limited to the invoiced amount.
- The report cannot be reproduced, completely or in part, in any form of media (including print) without an explicit written permission from IADFAC Lab.
- Sample drawn and submitted by the party for Analysis unless otherwise stated.
- Analysed Food samples are destroyed within one month. Analysed Packaged Drinking Water samples destroyed after 3 months.

ANNEXURE 3 (Contd...). CONTAMINANT ANALYSIS TEST REPORT OF WATER

INSTITUTE FOR ANALYSIS OF DAIRY, FOOD & CULTURES.
 #8, Siddhi Vinayaka Complex, Nagarabhavi 2nd Stage, 2nd Block
 Near BDA Complex, 80 Feet Ring Road, Bangalore-560 072
 Ph: +91-80-2318 6906 to 10, Cell : +91 8152881444/8152881222
 Mail: accounts@iadfac.com/bd@iadfac.com/qa@iadfac.com



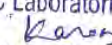
CERTIFICATE OF ANALYSIS

BOOKING NO. : 0010
 CERTIFICATE NO. : 0010/2020-2021

NAME OF MANUFACTURER/PARTY :		BIONEEDS INDIA PRIVATE LIMITED Devarahosahalli, Sompura Hoball, Nelamangla Taluk, Bangalore Rural Dist, BANGALORE - 562111 KARNATAKA	
1. MFG. LIC. NO.	: NM	3. DATE	: 06/05/2020
2. REFERENCE NO.	: NM	5. NAME OF SAMPLE	: Drinking Water (R O Water)
4. DATE OF RECEIPT	: 06/05/2020		
6. DETAILS OF RAW MATERIAL / FINAL PRODUCTS (In Bulk/Finished Pack)			
(A) MANUFACTURER NAME	: NM	(B) BATCH NO.	: NM
(C) BATCH SIZE	: NM	(D) DATE OF MFG.	: NM
(E) SAMPLE QUANTITY	: 5Lx1 Can	(F) DATE OF EXPIRY	: NM
(G) PACKING	: Plastic Bottle	(H) STARTING DATE	: 08/05/2020
(I) SEALED	: Sealed	(J) ENDING DATE :	: 19/05/2020
(K) BRAND NAME	: NM	(L) SAMPLING PROTOCOL	: NA
(M) DATE OF SAMPLING /SAMPLE COLLECTION	: 06/05/2020	(N) REPORT GEN. DATE	: 19/05/2020

Specification as per IS 10500:2012

SR	TEST NAME	UNIT	RESULT	ACCEPTABLE LIMIT	PERMISSIBLE LIMIT	METHOD OF TEST
17	Nitrate (as NO ₃)	mg/l	1.16	45 Max	No Relaxation	IS 3025 (Part-34) : 1988
18	Selenium (as Se)	mg/l	<0.01	0.01 Max	No Relaxation	IS 3025 (Part-56) : 2003
19	Sulphate (as SO ₄)	mg/l	<1	200 Max	400 Max	IS 3025 (Part-24) : 1986
20	Total Alkalinity as calcium carbonate	mg/l	8.0	200 Max	600 Max	IS 3025 (Part-23) : 1986
21	Total Hardness (as CaCO ₃)	mg/l	4	200 Max	600 Max	IS 3025 (Part-21) : 2009
22	Cadmium (as Cd)	mg/l	<0.003	0.003 Max	No Relaxation	IS 3025 (Part-41) : 1992
23	Lead (as Pb)	mg/l	<0.01	0.01 Max	No Relaxation	IS 3025 (Part-47) : 1994
24	Mercury (as Hg)	mg/l	<0.001	0.001 Max	No Relaxation	IS 3025 (Part-48) : 1994
25	Total Arsenic (as As)	mg/l	<0.01	0.01 Max	No Relaxation	IS 3025 (Part-37) : 1988
26	Total Chromium (as Cr)	mg/l	<0.05	0.05 Max	No Relaxation	Annexure- J of IS 13428 : 2005
Pesticide residues						
1	Endosulfan					
a	Alpha Endosulfan	µg/l	<0.01	0.4 Max	No Relaxation	FSSAI Manual of water 2016
b	Beta Endosulfan	µg/l	<0.01	0.4 Max	No Relaxation	FSSAI Manual of water 2016
c	Endosulfan sulphate	µg/l	<0.01	0.4 Max	No Relaxation	FSSAI Manual of water 2016
2	Ethion	µg/l	<0.01	3 Max	No Relaxation	FSSAI Manual of water 2016

Remarks : *Accepted and released for use @ 21/05/2020* For IADFAC Laboratories Pvt. Ltd.

 Authorised Signatory
 Karunakara A.C. (ID No-132)
 Senior Manager-Chemical

CONTD. ON NEXT PAGE.....
AUTHORISED SIGNATORY

Note :

- The results listed, refer only to the samples analysed & applicable parameters, Endorsement products is neither inferred nor implied.
- Total liability of our institute is limited to the invoiced amount.
- The report cannot be reproduced, completely or in part, in any form of media (including print) without an explicit written permission from IADFAC Lab.
- Sample drawn and submitted by the party for Analysis unless otherwise stated.
- Analysed Food samples are destroyed within one month. Analysed Packaged Drinking Water samples destroyed after 3 months.

ANNEXURE 3 (Contd...). CONTAMINANT ANALYSIS TEST REPORT OF WATER



INSTITUTE FOR ANALYSIS OF DAIRY, FOOD & CULTURES.
 #8, Siddhi Vinayaka Complex, Nagarabhavi 2nd Stage, 2nd Block
 Near BDA Complex, 80 Feet Ring Road, Bangalore-560 072
 Ph: +91-80-2318 6906 to 10, Cell : +91 8152881444/8152881222
 Mail: accounts@iadfac.com/bd@iadfac.com/qa@iadfac.com

CERTIFICATE OF ANALYSIS

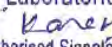
BOOKING NO. : 0010
 CERTIFICATE NO. : 0010/2020-2021

NAME OF MANUFACTURER/PARTY :		BIONEEDS INDIA PRIVATE LIMITED Devarahosahalli, Sompura Hobali, Nelamangla Taluk, Bangalore Rural Dist, BANGALORE - 562111 KARNATAKA	
1. MFG. LIC. NO.	: NM	3. DATE	: 06/05/2020
2. REFERENCE NO.	: NM	5. NAME OF SAMPLE	: Drinking Water (R O Water)
4. DATE OF RECEIPT	: 06/05/2020		
6. DETAILS OF RAW MATERIAL / FINAL PRODUCTS (In Bulk/Finished Pack)			
(A) MANUFACTURER NAME	: NM	(B) BATCH NO.	: NM
(C) BATCH SIZE	: NM	(D) DATE OF MFG.	: NM
(E) SAMPLE QUANTITY	: 5Lx1 Can	(F) DATE OF EXPIRY	: NM
(G) PACKING	: Plastic Bottle	(H) STARTING DATE	: 08/05/2020
(I) SEALED	: Sealed	(J) ENDING DATE :	: 19/05/2020
(K) BRAND NAME	: NM	(L) SAMPLING PROTOCOL	: NA
(M) DATE OF SAMPLING /SAMPLE COLLECTION	: 06/05/2020	(N) REPORT GEN. DATE	: 19/05/2020

Specification as per IS 10500:2012

SR	TEST NAME	UNIT	RESULT	ACCEPTABLE LIMIT	PERMISSIBLE LIMIT	METHOD OF TEST
3	Monocrotophos	µg/l	<0.01	1 Max	No Relaxation	FSSAI Manual of water 2016
--	--	--	-- End of Report --	--	--	--

Remarks :
 Accepted & released for use @ 21/05/2020 For IADFAC Laboratories Pvt. Ltd.


 Authorised Signatory
 Karunakara A.C. (ID No-132)
 Senior-Manager-Chemical
AUTHORISED SIGNATORY

Note :

1. The results listed, refer only to the samples analysed & applicable parameters, Endorsement products is neither inferred nor implied.
2. Total liability of our Institute is limited to the invoiced amount.
3. The report cannot be reproduced, completely or in part, in any form of media (including print) without an explicit written permission from IADFAC Lab.
4. Sample drawn and submitted by the party for Analysis unless otherwise stated.
5. Analysed Food samples are destroyed within one month. Analysed Packaged Drinking Water samples destroyed after 3 months.

ANNEXURE 4. GLOBALLY HARMONIZED SYSTEM OF CLASSIFICATION AND LABELLING OF CHEMICALS (GHS)

Categories	Criteria
*Category 1	Destruction of skin tissue, namely, visible necrosis through the epidermis and into the dermis, in at least one tested animal after exposure ≤ 4 h
Sub-category 1A	Corrosive responses in at least one animal following exposure ≤ 3 min during an observation period ≤ 1 h
Sub-category 1B	Corrosive responses in at least one animal following exposure > 3 min and ≤ 1 h and observations ≤ 14 days
Sub-category 1C	Corrosive responses in at least one animal after exposures > 1 h and ≤ 4 h and observations ≤ 14 days
Irritant (Category 2)	<ol style="list-style-type: none"> (1) Mean score of ≥ 2.3 and ≤ 4.0 for erythema/eschar or for oedema in at least 2 of 3 tested animals from grading at 24, 48 and 72 hours after patch removal or, if reactions are delayed, from grades on 3 consecutive days after the onset of skin reactions; or (2) Inflammation that persist to the end of the observation period normally 14 day in at least 2 animals, particularly taking into account alopecia (limited area), hyperkeratosis, hyperplasia, and scaling; or (3) In some cases where there is pronounced variability of response among animals, with very definite positive effects related to chemicals exposure in a single animal but less than the criteria above.
Mild Irritant (Category 3)	Mean score of ≥ 1.5 and < 2.3 for erythema/eschar or for oedema from gradings in at least 2 of 3 tested animals from grades at 24, 48 and 72 hours or, if reactions are delayed, from grades on 3 consecutive days after the onset of skin reactions (when not included in the irritant category above).

*: This category may be further divided into three sub-categories (1A, 1B and 1C) which can be used by those authorities requiring more than one designation for corrosivity. Corrosive test item should be classified in category 1 where sub-categorization is not required by a competent authority or where data are not sufficient for sub-categorization. When data are sufficient and where required by a competent authority test item may be classified in one of the three sub-categories (1A, 1B and 1C) in accordance with the criteria as per the above mentioned table.

ANNEXURE 5. GLP CERTIFICATE

National Good Laboratory Practice (GLP) Compliance Monitoring Authority (NGCMA)
Department of Science and Technology
GOVERNMENT OF INDIA

Certificate of GLP Compliance

This is to certify that

Bionees India Private Limited
Devarahosahally, Sompura Hobli, Nelamangala Taluk
Bengaluru Rural District - 562111, Karnataka (India)

is a GLP certified test facility in compliance with the NGCMA's Document No. GLP-101 "Terms & Conditions of NGCMA for obtaining and maintaining GLP certification by a test facility" and OECD Principles of GLP.

The test facility conducts the below-mentioned tests/ studies:

- **Physical-chemical Testing (Including Five Batch Analysis)**
- **Toxicity Studies**
- **Mutagenicity Studies**
- **Environmental Toxicity Studies on Aquatic and Terrestrial Organisms**
- **Studies on Behaviour in Water, Soil and Air; Bioaccumulation**
- **Residue Studies**
- **Analytical and Clinical Chemistry Testing**
- **Others**

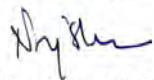
The specific areas of expertise, test items and test systems are listed in the annexure overleaf.

Validity: September 23, 2020 – September 22, 2023

Certificate No. : GLP/C-153/2020

Issue Date : 13-10-2020




(Dr. Neeraj Sharma)
Head, NGCMA

ANNEXURE 5 (Contd...). GLP CERTIFICATE

National GLP Compliance Monitoring Authority (NGCMA)

Annexure to Certificate of GLP Compliance No. GLP/C-153/2020

Areas of Expertise:

- **Physical-chemical Testing (Including Five Batch Analysis)**

- **Toxicity Studies**

- o Acute Toxicity
- o Developmental and Reproductive Toxicity
- o Eye Irritation/ Corrosion (*in vitro* and *in vivo*)
- o Guinea Pig Maximization
- o Immunogenicity
- o Inhalation Toxicity
- o Local Lymph Node Assay (LLNA)
- o Local Tolerance
- o Neurotoxicity
- o Phototoxicity
- o Pyrogen Test
- o Repeated Dose Toxicity
- o Skin Irritation/ Corrosion (*in vitro* and *in vivo*)
- o Skin Sensitization (*in vitro* and *in vivo*)

- **Mutagenicity Studies**

- o 3T3 NRU Assay (*in vitro*)
- o Bacterial Reverse Mutation (AMES) Test
- o Cell Gene Mutation Test (*in vitro* and *in vivo*)
- o Chromosomal Aberration Test (*in vitro* and *in vivo*)
- o Comet Assay
- o Cytotoxicity (*in vitro*)
- o Micronucleus Test (*in vitro* and *in vivo*)
- o Mouse Lymphoma Assay (MLA)
- o MTT Assay

- **Environmental Toxicity Studies on Aquatic and Terrestrial Organisms**

- **Studies on Behaviour in Water, Soil and Air; bioaccumulation**

- **Residue Studies**

- **Analytical and Clinical Chemistry Testing**

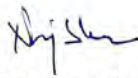
- **Others**

- o ADME Studies
- o Bioanalysis
- o Biocompatibility Studies
- o Drug Metabolism & Pharmacokinetic (DMPK)
- o Hemocompatibility Studies
- o Implantation Studies
- o In chemico Skin Sensitization: Direct Peptide Reactivity Assay
- o Maximum Tolerated Dose (MTD) Studies
- o Method Development
- o Method Validation
- o Skin Absorption (*in vitro*)

Test Item(s): Agrochemicals, Cosmetics Products, Feed Additives, Food Additives, Industrial chemicals, Medical Devices (*Applicable only for Bio-compatibility, not applicable for Batch Release parameters required as per MDR, 2017*) and Pharmaceuticals (Human and Veterinary)

Test System(s): Algae, Bovine, Cell lines, Chicken, Collembolan, Crop plant seeds, Cyanobacteria, Daphnia, Diatoms, Earthworm, *E-Coli*, Fish, Guinea Pigs, Hamsters, Honeybees, Human Cavader Skin, Human Lymphocytes, Japanese quail, Lemna, Mallard duck, Mice, Pigeon, Predatory Mites, Rabbit, Rat, *Salmonella typhimurium*, Silkworm and Tissue Culture.




(Dr. Neeraj Sharma)
 Head, NGCMA