Study of Acute Systemic Toxicity
for the Test Item

SMART PRINT BIO VITALITY

Final Report

REFERENCE METHOD: ISO 10993-11:2017

STUDY DIRECTOR: Fabiana de Oliveira Branchini

STUDY COMPLETION DATE: September 20th, 2024

PERFORMING LABORATORY:
MEDLAB PRODUTOS DIAGNÓSTICOS LTDA.
Rua Octávio Teixeira Mendes Sobrinho, 35
Vila Santa Catarina – CEP: 04376-070
São Paulo, SP – Brazil

IDENTIFICATION:
Study code: **BTAS2**
Study number: **12918-1/2024.0**

SPONSOR:
MMTECH PROJETOS TECNOLÓGICOS IMPORTAÇÃO E EXPORTAÇÃO LTDA
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GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

Study title: Study of Acute Systemic Toxicity for the Test Item SMART PRINT BIO VITALITY

Study number: 12918-1/2024.0

This study was conducted under my responsibility in accordance with NIT-DICLA-035 (INMETRO, Oct/19, Rev. 04) and its complementary documents, which meets the principles of Good Laboratory Practice as published by the OECD (N° 1 [ENV/MC/CHEM (98) 17]).
This study was conducted in accordance with the study plan, approved by the Sponsor and Test Facility Manager and to the standard operating procedures. This report represents a true and accurate record of the obtained results. There were no major known circumstances that may have affected the quality or integrity of the study.
All original raw data, including electronic records, documentation, signed study plan, possible additions to the study plan, final report and test item rate will be retained in the GLP files of Medlab Produtos Diagnósticos Ltda.

Fabiana de Oliveira Branchini
Analista de Toxicologia
CRBio: 68308/01-D

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Study Director
Medlab Produtos Diagnósticos Ltda

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STATEMENT OF QUALITY ASSURANCE

Study title: Study of Acute Systemic Toxicity for the Test Item SMART PRINT BIO VITALITY

Study number: 12918-1/2024.0

Based on the Quality Assurance review, this final report was considered an accurate and true record of the data generated during the study.

This final report has been inspected for the respective study plan, standard operating procedure, and raw data. Study procedures were monitored through process inspection.

The inspections were conducted in accordance with the standard operating procedures of the Quality Assurance of Medlab Produtos Diagnósticos Ltda.

Inspection dates and respective reporting dates to the Study Director and Test Facility Manager are presented below. These inspection reports are kept in the GLP files of Medlab Produtos Diagnósticos Ltda.

Inspection	Date of Inspection	Reporting dates	
		Study Director	Test Facility Manager
Study plan	08/30/2024	08/30/2024	08/30/2024
Experimental phase*	05/28 and 05/29/2024	07/02/2024	07/02/2024
Raw data	09/19/2024	09/19/2024	09/19/2024
Final Report	09/20/2024	09/20/2024	09/20/2024

* Process inspection performed at least annually

Emine Oshiro Sakaue
Emine Sakaue
Garantia da Qualidade

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Quality Assurance
Medlab Produtos Diagnósticos Ltda

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GENERAL INFORMATION

Contributors

Fabiana de Oliveira Branchini	Study Director
Roberta dos Santos Machado	Test Facility Manager
Emine Oshiro Sakaue	Quality Assurance
Suellen Karoline Bezerra	Technical Support
Paloma Oliveira	Technical Support

Study dates

Study start date:	September 6th, 2024
Experimental phase start:	September 6th, 2024
Experimental phase end:	September 13th, 2024
Study completion date:	September 20th, 2024
English version	September 20th, 2024

Performing laboratory

This study was conducted at Medlab Produtos Diagnósticos Ltda, located at Rua Octávio Teixeira Mendes Sobrinho, 35 – CEP:04376-070, São Paulo – SP, Brazil.

Adherence to the study plan

No deviations were registered to the study plan.

Archives

All raw data and original study records are the property of the Sponsor. The data will be correctly registered, signed and kept at Medlab Produtos Diagnósticos Ltda for five years. Test items will be held until the expiration date, after which it will be discarded.

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1. ABSTRACT

Systemic toxicity results from absorption and distribution of a substance in the organism, causing signs of toxicity and/or mortality. The aim of the study was to evaluate the acute systemic response to the test item **SMART PRINT BIO VITALITY** provided MMTECH PROJETOS TECNOLÓGICOS IMPORTAÇÃO E EXPORTAÇÃO LTDA. The method used was ISO 10993-11:2017.

Two groups of five female Swiss mice (*Mus musculus*) were treated by intravenous (polar extract) and intraperitoneal (nonpolar extract) administration of the test item. Two other groups of five animals were treated with the extraction vehicles. Body weights were recorded before administration (day 0) and daily for a period of 72 hours. The animals were observed individually after application and daily for a period of 72 hours for the presence of clinical signs of toxicity. At the end of the study, the animals were euthanized in a carbon dioxide (CO_2) chamber. No clinical signs of toxicity or death were observed among the animals.

Under test conditions, the test item **SMART PRINT BIO VITALITY** was considered in accordance with the adopted methodology.

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2. INTRODUCTION

2.1. Study objective

The aim of the present study was to evaluate the systemic response to the test item **SMART PRINT BIO VITALITY** through the intravenous and intraperitoneal injection of the test item extract in mice (*Mus musculus*).

2.2. Reference guideline

The study was performed according to ISO 10993-11: *Tests for systemic toxicity*, 2017.

2.3. Weight of evidence analysis

For reasons related to animal welfare, prior to conducting the study, an analysis of the evidence was performed, with available and relevant data from the test item. The testing strategy includes an assessment of human and/or animal data related to toxic effects. Test substance known to cause pain and discomfort due to corrosive or severely irritating properties need not be tested.

2.4. Animal welfare

Animals are maintained in the testing facility in accordance with local and international requirements outlined in the Standard Operating Procedures. Animals with ongoing signs of severe discomfort and/or pain at any stage of the study are humanely euthanized and the test item properly evaluated. Animal care procedures and decision criteria for euthanasia of moribund and severely distressed animals are described in detail in the Standard Operating Procedures.

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3. MATERIAL AND METHOD

3.1. Test item[1]

Identification:	**SMART PRINT BIO VITALITY**
Received date at Medlab:	August 6th, 2024
Category:	Health Products
Batch:	PVA3 004/24
Manufacturing date:	April/2024
Expiration date:	April/2026
Active ingredient(s):	Not applicable
CAS number of the active ingredient(s):	Not applicable
Declared composition:	Amorphous Silica < 5%; Silanized Silica > 50%; Dispersant <4%; Photoinitiator <4%; Methacrylic Monomers >40%; Pigments <0.07%
Physical state:	Solid
Other information:	Dimensions: 50x50x1.2mm | Weight: 5g
Provided by:	MMTECH PROJETOS TECNOLÓGICOS IMPORTAÇÃO E EXPORTAÇÃO LTDA

[1] Information supplied by the Sponsor

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3.2. Test system

Species:	*Mus musculus* (mice)
Strain:	Swiss
Source:	Anilab, Paulínia – SP
Justification for the test system:	Mice are a species widely used in systemic toxicity studies, and recommended in the test method
Number and sex:	20 nulliparous and non-pregnant females, being 10 animals per group of extraction (5 for test group and 5 for control group)
Body weight:	The body weight variation among the animals on day 0 did not exceed 20% of the average for each group
Date of birth:	08/08/2024
Receiving date:	09/05/2024
Acclimatization:	The animals were acclimated to laboratory conditions for 5 days before starting the test; animals with any signs of abnormality were not used in the study
Accommodation:	The animals were kept in conventional cages for the species during the acclimation and test period, in 5 animals per cage
Identification:	The test system was individually identified by marking with a hydrographic pen on the tail; the cages were identified by labels containing the study number, lot of animals and dates of the experimental phase.
Feeding:	Commercial feed for the species (Qualy Nutrição Animal Rodents, batch 123-1, manufacture date:

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	05/02/2024, expiry date: 10/29/2024, was supplied *ad libitum* during the acclimatization period; the feed is analyzed at each batch to verify the presence of microbiological contaminants. The feed provided did not show contamination that could affect the purpose or integrity of the study
Water:	Filtered water was provided *ad libitum* in the acclimatization periods; the water is periodically analyzed for the presence of chemical and microbiological contaminants. The filtered water provided did not show contamination that could affect the purpose or integrity of the study.

3.3. Environmental conditions

The environmental conditions of the test room were monitored and recorded during the experimental period. The average temperature was 22.9ºC and the average relative humidity was 45.8%. The animals were kept under automatic control of the 12/12 hours photoperiod.

3.4. Method administration and reason for choice

The test item extracts were injected intravenously (polar extract) in the tail vein of the test system, and intraperitoneally (non-polar extract), as described in the methodology.

3.5. Reference item (control)

It was used 0.9% sodium chloride solution (polar vehicle) and sunflower oil (non-polar vehicle) as test item extraction vehicles.

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3.6. Material, reagents and equipment

Materials: Flask with lid, gauze, syringe, sterile needle, hydrographic pen, rodent restrainer.
Reagents: 0.9% sodium chloride solution and sunflower oil.
Equipament: Semi-analytical scale, water bath and incubator.

3.7. Test item preparation

Extraction of the test item was performed in accordance with ISO 10993-12 (2021). The test item was extracted at 50°C for 72 hours in an incubator in two vehicles (polar and non-polar) in a ratio of 3 cm² of test item to 1 mL of vehicle. The extracts were used within 24 hours of preparation.

Total prepared for polar solution: 50 cm² of the test item to 16.7 mL of 0.9% sodium chloride solution. The liquid resulting from this process (extract) presented a homogeneous and colorless appearance, as per the original color of the vehicle, without the presence of particulates, and was not submitted to any other additional process.

Total prepared for non-polar solution: 50 cm² of test item to 16.7 mL of vegetable oil. The liquid resulting from this process (extract) presented a homogeneous and yellow appearance, according to the original color of the vehicle, without the presence of particulates, and was not submitted to any other additional process.

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3.8. Experimental design

The animals were randomly selected, identified and separated into four groups, test and control for each extraction vehicle. The polar extract was injected intravenously, and the nonpolar extract was injected intraperitoneally, at a dose of 50 mL/kg of body weight, and 0.9% sodium chloride solution and vegetable oil were used as a control, applied in the same conditions as the test item.

The animals were weighed before the application of extracts and daily for 3 days after application.

The animals were regularly observed for the presence of toxic signs, such as changes in the skin, eyes, respiratory, cardiovascular and gastrointestinal systems, changes in motor activity, salivation, seizures, piloerection, body weight loss and death.

3.9. Results evaluation / acceptance criterion

The test item is evaluated according to pharmacopoeial criteria. If all animals survive and do not show significant clinical signs of toxicity, the test item is considered in accordance with the adopted requirements. If two or more animals die, or if two or more animals show severe clinical signs of toxicity, the test item is deemed not to comply with the requirements of the method. If even one animal presents mild to severe clinical signs or mortality, a retest should be performed with 10 more animals for each extract and 5 control animals for each vehicle. In the retest, if no significant clinical signs of toxicity are observed, the test item is considered to comply with the adopted requirements.

4. RESULTS

4.1. Body weight

Tables 1 and 2 show the initial and final body weight of the test systems, as well as the body weight variation. During the experimental period, no clinical signs of toxicity or deaths were observed, and at the end of the study the animals showed weight gain.

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4.2. Mortality and clinical signs of toxicity

Tables 3 and 4 show the mortality and clinical signs of toxicity during the experimental period. No clinical signs of toxicity or mortality were observed among the animals treated, either with the polar or non-polar extract.

5. CONCLUSION

Under test conditions, the test item **SMART PRINT BIO VITALITY** was considered in accordance with the adopted method.

6. REFERENCES

INMETRO: NIT-DICLA-035 – Principles of Good Laboratory Practices – GLP, Rev. 04, October/2019 e and its complementary documents.

ISO 10993-11: Tests for systemic toxicity, 2017.

ISO 10993:12 – Biological evaluation of medical devices. Part 12: Sample Preparation and Reference Materials, 2021.

OECD Environmental Health and Safety Publications, Series on Principles of Good Laboratory Practice and Compliance Monitoring. No. 1.,41p., Paris, 1998 (17).

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TABLE 1: Individual body weight (g) of the test system – polar extract (intravenous route)

Body weight (g)					
Control Group	**Pre-injection**	**24 hours**	**48 hours**	**72 hours**	**Variation**
1	19.78	19.97	20.57	21.11	1.33
2	18.36	18.13	18.77	18.77	0.41
3	19.28	19.24	19.91	19.53	0.25
4	18.64	17.71	18.04	18.78	0.14
5	18.89	20.06	20.81	22.23	3.34
Test Group	**Pre-injection**	**24 hours**	**48 hours**	**72 hours**	**Variation**
1	17.11	17.61	17.87	17.36	0.25
2	19.36	20.02	20.82	20.75	1.39
3	17.29	18.66	18.89	19.39	2.10
4	15.69	18.67	19.34	21.40	5.71
5	18.98	19.53	19.98	20.87	1.89

TABLE 2: Individual body weight (g) of the test system – nonpolar extract (intraperitoneal route)

Body weight (g)					
Control Group	**Pre-injection**	**24 hours**	**48 hours**	**72 hours**	**Variation**
1	21.87	22.07	23.69	24.30	2.43
2	22.27	22.75	23.40	24.42	2.15
3	21.82	21.15	22.29	22.85	1.03
4	22.16	21.50	22.76	23.40	1.24
5	21.50	20.82	21.88	22.80	1.30
Test Group	**Pre-injection**	**24 hours**	**48 hours**	**72 hours**	**Variation**
1	15.71	20.50	17.32	18.67	2.96
2	19.10	19.36	20.19	20.98	1.88
3	19.51	20.43	20.97	23.16	3.65
4	20.03	20.74	21.53	22.36	2.33
5	20.13	21.19	21.26	22.46	2.33

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TABLE 3: Clinical evaluation of the test system – polar extract (intravenous route)

Group	Test system	Evaluation Day 0	Evaluation 24 hours	Evaluation 48 hours	Evaluation 72 hours	Mortality
Control	**1**	NO	NO	NO	NO	**0 / 5**
	2	NO	NO	NO	NO	
	3	NO	NO	NO	NO	
	4	NO	NO	NO	NO	
	5	NO	NO	NO	NO	
Test	**1**	NO	NO	NO	NO	**0 / 5**
	2	NO	NO	NO	NO	
	3	NO	NO	NO	NO	
	4	NO	NO	NO	NO	
	5	NO	NO	NO	NO	

NO: No observations.

TABLE 4: Clinical evaluation of the test system – nonpolar extract (intraperitoneal route)

Group	Test system	Evaluation Day 0	Evaluation 24 hours	Evaluation 48 hours	Evaluation 72 hours	Mortality
Control	**1**	NO	NO	NO	NO	**0 / 5**
	2	NO	NO	NO	NO	
	3	NO	NO	NO	NO	
	4	NO	NO	NO	NO	
	5	NO	NO	NO	NO	
Test	**1**	NO	NO	NO	NO	**0 / 5**
	2	NO	NO	NO	NO	
	3	NO	NO	NO	NO	
	4	NO	NO	NO	NO	
	5	NO	NO	NO	NO	

NO: No observations.

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ANNEX 1 – CERTIFICATE OF RECOGNITION OF COMPLIANCE WITH THE PRINCIPLES OF GOOD LABORATORY PRACTICES

National Institute of Metrology, Quality and Technology – Inmetro
General Coordination for Accreditation

Statement of GLP Compliance

GLP Recognition No. GLP BPL 0041 — Initial Recognition: March 06th, 2014

Medlab Produtos Diagnósticos Ltda.
Rua Octavio Teixeira Mendes Sobrinho, 35 - Vila Santa Catarina - São Paulo – SP - Brasil

General Coordination for Accreditation of Inmetro grants to the above mentioned test facility the recognition of compliance with the OECD Principles of Good Laboratory Practice as part of the Brazilian GLP Monitoring Program to carry out non-clinical health and environmental safety studies, as described in the scope below:

Areas of expertise	Categories of Test Items
Toxicity Studies, Efficacy Studies; Citotoxicity Studies	Pesticides, Their Components and Suchlike; Pharmaceutical Products; Veterinary Drugs; Sanitizers; Industrial Chemicals; Health Products; Medical Devices; Cosmetics; Food Additives

Note: Categories of test items "pesticides", "pharmaceutical products", "cosmetics", "wood preservative", "feed additives", "veterinary drugs", "sanitizers", "industrial chemicals", "remedial for treatments of effluents and natural ecosystems" and "medical devices" are covered by Brazil´s full adherence to the OECD Council Acts related to the Mutual Acceptance of Data (MAD) on Good Laboratory Practice.

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MARCOS VALERIO BARRADAS
General Coordinator for Accreditation Substitute

The current status of recognition must be checked on the email address http://www.inmetro.gov.br/monitoramento_BPL/certificados

MOD-CGCRE-027 – Rev. 09 – Apr. OUT/23 – Pg. 2/03

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