SM-403 STANDARD OPERATING PROCEDURE FOR SUBJECT MANAGEMENT WHILE ON STUDY

I. INTRODUCTION AND PURPOSE

The safety and well-being of subjects is of paramount concern to the research team. This standard operating procedure (SOP) describes the steps for fulfilling the regulatory and clinical requirements to ensure adherence to study procedures for the evaluation of a subject's response to the investigational article. Through close monitoring and careful assessment of subjects, adverse events can be detected early and treated appropriately. By following these procedures, close attention is paid to subject well-being and to integrity of the data.

2. SCOPE

This SOP applies to the activities involved in managing subjects on clinical studies conducted at this investigative site subject to investigational new drug (IND) regulations for drugs and biologics during all phases of development.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 50.20	General requirements for informed consent
21 CFR 56.109	IRB review of research
21 CFR 312.60	General responsibilities of investigators
21 CFR 312.62	Investigator recordkeeping and record retention

4. REFERENCES TO OTHER APPLICABLE SOP'S

GA-102	Responsibilities of the Research Team
SM-401	Informed Consent Development and Implementation
SM-402	Subject Recruitment and Screening
SM-404	Adverse Event Reporting
SM-405	Specimen Collection and Handling
DM-501	Data Management

5. ATTACHMENTS

A. Medical History

B. Physical Examination
C. Concomitant Medication Log
D. Adverse Event/Intercurrent Illness Log
E. Patient Summary

6. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in ensuring the appropriate clinical management of all clinical trial activity. This includes the following:

- Principal investigator
- Sub-investigator
- Research coordinator

7. DEFINITIONS

The following definitions from the International Conference on Harmonisation, Good Clinical Practice: Consolidated Guideline apply to this SOP.

Adverse Event (AE): An AE is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

Randomization: The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.

Subject/Trial Subject: An individual who participates in a clinical trial, either as a recipient of the investigational product(s) or as a control.

Well-being (of the trial subjects): The physical and mental integrity of the subjects participating in a clinical trial.

8. PROCESS OVERVIEW

A. Enrollment assessments and management
B. Follow-up, completion and early termination from the study
C. Communication with primary or referring medical providers
D. Management of ineligible subjects

9. PROCEDURES

A. ENROLLMENT ASSESSMENTS AND MANAGEMENT

RESPONSIBILITY	DESCRIPTION OF PROCEDURE

PI Research coordinator	Elicit and document the subject's medical history (Attachment A, Medical History). Perform a complete or directed physical examination (Attachment B, Physical Examination). Establish the subject's baseline signs and symptoms. Review with the subject the use of any current medication (Attachment C, Concomitant Medication Log). Inform the subject about the required study procedures and visits. Collect specimens as directed by the protocol Order tests/procedures as directed by the protocol. Provide contact information to the subject. Schedule the follow-up visit.
PI Research coordinator	Randomize and dispense the test article. Review with the subject the use of any study aids, such as a diary.

B. FOLLOW-UP, COMPLETION AND EARLY TERMINATION FROM THE STUDY

RESPONSIBILITY	DESCRIPTION OF PROCEDURE
PI Research coordinator	Perform a complete or directed physical examination. Assess the subject for signs and symptoms of any intercurrent illness and document adverse events appropriately (Attachment D, Adverse Event/Intercurrent Illness Log or Sponsor's source). Collect specimens as directed by the protocol. Order diagnostic tests and procedures as necessary. Institute appropriate therapy if required by the subject's condition. Review any use of concomitant medication. Schedule follow-up visits per protocol.
PI Research coordinator	Assess the subject's compliance with the test article. Collect unused test article, if appropriate. Dispense additional test article, as required.

PI Sub-investigator	Diagnose and document any intercurrent illness and endpoints. Review the subject's laboratory and other test results.

C. COMMUNICATION WITH PRIMARY OR REFERRING MEDICAL PROVIDERS

RESPONSIBILITY	DESCRIPTION OF PROCEDURE
Research coordinator	Depending on sponsor requirements and individual request, inform the subject's primary care provider about the subject's progress while on study, if the subject agrees. Ensure that the primary care provider receives copies of the subject's laboratory test results and reports of procedures, etc. if the subject requests. Confer with the primary care provider, as appropriate.

D. MANAGEMENT OF INELIGIBLE SUBJECTS

RESPONSIBILITY	DESCRIPTION OF PROCEDURE
PI Research coordinator	Document the reason for ineligibility. Retain any supporting data available. Complete any clinical and laboratory assessments required by the protocol. Collect any unused test article and any used test article containers, and record data in the investigational drug log. Discuss treatment alternatives with the subject. Follow the subject as required by the protocol. Notify the sponsor as required.

Attachment A

MEDICAL HISTORY

Patient Name: _____ Date: ____/____/____

Please check the appropriate box and, if abnormal, describe.

Normal	Abnormal		Describe the abnormality
❑	❑	Ears, nose and throat	_____
❑	❑	Ophthalmic	_____
❑	❑	Respiratory:	_____
		Smoker Yes ____ No ____	# packs/week _____
❑	❑	Cardiovascular	_____
❑	❑	Gastrointestinal	_____
❑	❑	Hepatic	_____
❑	❑	Renal	_____
❑	❑	Urogenital	_____
❑	❑	Neurological	_____
❑	❑	Endocrine	_____
❑	❑	Musculoskeletal	_____

❑ ❑ Skin _____

_____

❑ ❑ Psychiatric _____

_____

❑ ❑ Drug allergies _____

_____

Signature_____ Date:

____/____/____

Attachment B

PHYSICAL EXAMINATION

Patient Name: _____ Date: ____/____/____

Please check the appropriate box and, if abnormal, describe.

	Normal	Abnormal	Describe the abnormality
HEENT	❑	❑	_____
Respiratory	❑	❑	_____
Abdomen	❑	❑	_____
Musculoskeletal	❑	❑	_____
Cardiovascular	❑	❑	_____
Lymph Nodes	❑	❑	_____
Skin	❑	❑	_____
Neurological	❑	❑	_____

Height _____ ❑ ins ❑ cms Weight _____ ❑ kg ❑ lb

Vital Signs: Temp_____ ❑ F ❑ C B/P _____ P_____

Comments:

_____

_____

_____

_____

_____

Signature_____ Date: ____/____/____

Attachment C

CONCOMITANT MEDICATIONS LOG

Patient #: _____

Patient initials: _____

Medication/Dose	Indication	Start Date	Stop Date

Attachment D

ADVERSE EVENT and INTERCURRENT ILLNESS LOG

Patient #: _____

Patient initials:_____

Adverse Event **Adverse Event/Intercurrent Illness**	**Seriousness**	**Start Date**	**Stop Date**	**Relation to IP** **Study drug**	**PI initials /date**

PI Signature_____ Date: ____/____/____

Attachment E

PATIENT SUMMARY

Protocol #: _____ **Protocol Title:** _____

Pt. initials _____ **Wt. at baseline** _____ **(kg)**

Date enrolled ___/___/___ **Date completed** ___/___/___ **Total time on study** _____

Date of first dose ___/___/___ **Baseline dose** _____ **Date of last dose** ___/___/___

Dose changes

Date	Rationale
_____/_____/_____	_____
_____/_____/_____	_____
_____/_____/_____	_____

Adverse events

Date	SAE?		Description	IRB report?	
____/____/____	Y ❑	N ❑	_____	Y ❑	N ❑
____/____/____	Y ❑	N ❑	_____	Y ❑	N ❑
____/____/____	Y ❑	N ❑	_____	Y ❑	N ❑
____/____/____	Y ❑	N ❑	_____	Y ❑	N ❑
____/____/____	Y ❑	N ❑	_____	Y ❑	N ❑

Protocol deviations

Date	Description
____/____/____	_____
____/____/____	_____

ICF amendments signed ❑ ___/___/___ ❑ ___/___/___ ❑ ___/___/___

Comments: _____