SAFETY MANAGEMENT PLAN

Product: Lercanidipine

Study code: ISS-000157

Final version
Date: 22May2026

RECORDATI Industria Chimica e Farmaceutica S.p.A, via Civitali, 1 - 20148 Milan, Italy, (hereinafter referred to as "Recordati HQ").

SPONSOR - INVESTIGATOR: Prof.ssa Carollo C. - Centro U.O.S.D. di Nefrologia e Dialisi, Azienda Ospedaliera Universitaria Policlinico Paolo Giaccone, via Del Vespro 129, Palermo.

Approved by Recordati (signature and date):

22-May-2026 | 10:06:12 BST

Signed by:

Cecilia Maffei

Signer Name: Cecilia Maffei
Signing Reason: I approve this document
Signing Time: 22-May-2026 | 10:06:10 BST

2D361C6F054B4C7FB390744BBD2A6497

Cecilia Maffei - QPPV for SPC Business Unit

Approved by Sponsor (signature and date):

26-mag-2026 | 17:14:51 BST

Firmato da:

Caterina Carollo

Nome firmatario: Caterina Carollo
Motivo per la firma: Approvo il documento
Ora firma: 26-mag-2026 | 17:14:42 BST

7982FD7E88874DC78653EC4419C179AC

Prof.ssa Caterina Carollo - Sponsor/Investigator

Firmato digitalmente da: Caterina Carollo
Luogo: palermo
Data: 09/06/2026 17:26:34

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ABBREVIATIONS

ADR	Adverse Drug Reaction
AE	Adverse Event
AESI	Adverse Event of Special Interest
ASR	Annual Safety Report
CEC	Central Ethics Committee
CRO	Contract Research Organisation
CRF	Case Report Form
EC	Ethics Committee
EU	European Union
EV	EudraVigilance
HQ	Recordati Headquarter in Milan
ICSR(s)	Individual Case Safety Report(s)
IME	Important Medical Event
IP	Investigational Product
LEC	Local Ethics Committee
MedDRA	Medical Dictionary for Regulatory Activities
NCA	National Competent Authority
NIP	Nominated Individual for Pharmacovigilance at National level
PV	Pharmacovigilance
PVU	Pharmacovigilance Unit
QPPV	Qualified Person responsible for Pharmacovigilance
SADR	Serious Adverse Drug Reaction
SAE	Serious Adverse Event
SSE	Serious Side effect (for food supplement)
SUE	Serious Undesirable Effect (for cosmetic)
SOP	Standard Operating Procedure

Version History

Document Version	Date	Reason for update
01	22May2026	First release

1 STUDY INFORMATION

This document describes the management of safety information arising from the investigator sponsored study *"Influence of Lercanidipine on renal, metabolic and cardiovascular (CV) parameters of subjects attending an ambulatory of Nephrocardiology*" with study ID ISS-000157 supported by Recordati HQ, in compliance to ICH guidelines and all applicable laws and regulations.

The following assumptions are valid:

Study code	*ISS-000157*
Study design	*Observational retrospective study*
Product under study	*Lercanidipine*
Countries	*Italy*

2 CONTACT INFORMATION

		Address **Phone/Fax**	**e-mail**
SPONSOR - INVESTIGATOR	PRINCIPAL INVESTIGATOR	Prof.ssa Caterina Carollo Centro U.O.S.D. di Nefrologia e Dialisi, Azienda Ospedaliera Universitaria Policlinico Paolo Giaccone, via Del Vespro 129, Palermo. Dott.ssa Ilaria Morreale Pharmacovigilance Responsible Person Azienda Ospedaliera Universitaria Policlinico - Palermo	caterina.carollo@unipa.it Ilaria.morreale@policlinico.pa.it

		Phone: +39 0916553258	
RECORDATI HQ PV UNIT	SPC QPPV	Cecilia Maffei SPC QPPV Via Matteo Civitali, 1 20148 Milan - Italy Phone: +39 02 48787097 Fax: +39 0248787668 Mobile: +39 3440630500	Maffei.C@recordati.it; QPPVOffice@recordati.it
	Mailbox for the exchange of safety information	ICSR Processing Group Via Matteo Civitali, 1 20148 Milan - Italy	ICSR-RecordatiHQ@recordati.it

3 SCOPE

This document describes the responsibilities of all persons involved in safety information exchange with respect to management ADR, incident, pregnancy and other safety data handling and the management of aggregates safety reports for the study with protocol number ISS-000157 supported by Recordati, to assure compliance with all applicable worldwide laws and regulations.

4 STUDY RESPONSIBILITIES

In addition to points 4.1 and 4.2, please refer to Addendum 1 for details on task responsibilities.

4.1 Investigator's responsibility

Investigator, unless otherwise defined, is responsible for the following tasks:

-Ensure the proper collection and reporting to Recordati HQ PVU of any adverse event (e.g., serious adverse events; non-serious adverse events and/or laboratory abnormalities);

-Fill in and send to Recordati HQ PVU the specific form;

-Assign a local ID to each AE in order to speed up reconciliation process;

-Report to Recordati HQ PVU any other safety issues requiring notifications;

-Electronic submissions of the expedite reports to the NCAs, when appropriate;

-Send the acknowledge of submission to Recordati HQ PVU;

-Submit the reports to ECs, as appropriate;

-Maintain and update a local database/tracker;

-Monthly reconciliation with Recordati HQ PVU;

-Perform follow-up attempts as requested by Recordati, if applicable;

-Periodic safety updates, if applicable.

4.2 Recordati HQ PVU's responsibility

Recordati HQ PVU, unless otherwise defined, is responsible for the following tasks:

-Ensure the Sponsor receives an ad hoc PV training;

-Entering and managing all safety information arose in the study, including SAEs, SSEs, SUEs into the Recordati Safety database according to Recordati case processing procedures;

-Electronic distributions to partners/affiliates, as appropriate;

-Perform monthly reconciliation with the investigator;

-Send to the investigator follow-up requests, as appropriate.

5 SAFETY REPORTING REQUIREMENTS

5.1 Safety Reporting Form

Investigator must carefully fill in the ad hoc safety reporting form for the AEs, including special situations and device deficiencies within the agreed timeline settled in the protocol:

• if serious, the reports should be sent to the Recordati HQ PVU *within 1 working day.*
• if non-serious, the reports should be sent to the Recordati HQ PVU *within 1 working day*.

With the same timeframe and format, **all further follow-up safety information** must be reported by Sponsor to the PVU.

Any Adverse Events (serious and non-serious), Pregnancies and special situations, associated or not with an AE, occurring in non-interventional studies with primary data collection (including special situations of use) have to be carefully documented by the healthcare professional on the trial database via Case Report Form (eCRF if applicable) / tracker, as specified in the protocol.

Any Adverse Drug Reaction (AE related to the study drug)/Incident/Pregnancy/Special situation report form has to be sent from study centre - within 1 working day of awareness - via e-mail to Recordati HQ PVU. E-mail address: ICSR-RecordatiHQ@recordati.it.
Pregnancy and special situation cases will be expedited for reporting only if the event results in a reportable ICSR/incident.

The forms to be used for immediate transmission to Recordati are:

FRM 01-C_SOP-PV50 - Solicited Adverse Event Report Form
FRM 02-C_SOP-PV50 - Pregnancy/Drug Exposure In Utero Solicited Report Form
FRM 03-C_SOP-PV50 - Solicited Report Form for Incident, Adverse Event, Suspected Complaint
FRM 01-C_SOP-PV60 - Safety Report - Reconciliation form

5.2 Narrative section

To fill in FRM-01 in the **narrative** section, the following narrative template could be used.

Subject ID is a *XX* years old *(race/gender)* subject enrolled in study *(code/title)* on *(dd/mmm/yyyy)* due to *(specify indication).* Subject medical history included *(specify concomitant diseases).* Concomitant medication at the start of the event included *(specify concomitant medications).*

At the onset of the event, subject was performing the *wash-out/run-in/double-blind (specify according to the study design)* phase of the study.

The subject had received his/her first dose of study drug/medical device on (*dd/mmm/yyyy) (specify, as appropriate dose, frequency, route)*. The most recent dose before event onset was received on (*dd/mmm/yyyy) (specify as appropriate dose, frequency, route).*

On *(dd/mmm/yyyy)*, the subject experienced *"investigator's verbatim".*

Describe event:

- admission/initial condition (vital signs, lab tests/procedures performed);
- seriousness criteria;
- relationship with study drug/medical device (investigator's assessment);
- action taken with the drug/medical device;
- other action taken (specify);
- course of event;
- data on dechallenge, rechallenge (if any);
- outcome (ongoing/resolved).

In case of relevant laboratory data, insert lab test information, if provided.
The action taken with THE SUSPECT DRUG (API)/MEDICAL DEVICE*: insert action taken with the suspect drugs.*
The dechallenge and rechallenge were*: insert dechallenge/rechallenge information.*
At the time of report, the outcome of event was: *insert outcome of the event.*
The event was considered*: insert information about the seriousness of the event/s.*
The reporter's assess the event: *insert information about the report's causality of the event/s.*

5.3 Notification to Recordati (example)

The investigator will be responsible to notify the safety information on the product to Recordati HQ PVU.

See Attachment 1 for example of email for sending of Safety forms from the Investigator to Recordati HQ PVU.

6 REPORTING REQUIREMENTS: Reporting ADR to Competent Authorities/Investigators

The safety reporting starts:

- After the patient(s) provided informed consent

Ends:

- until XX (30) calendar days after the patient(s) discontinued the Study drug (Lercanidipine) during the study conduct or until 30 calendar days after the last patient visit if the patient is still receiving the Study drug (Lercanidipine).

Once the safety report is received by Recordati HQ PVU, it is managed into ARGUS safety database, according to the Recordati safety procedures.

The reports must be transmitted to NCA, as appropriate, within the defined regulatory timelines by the Investigator:

Valid Serious ADR related to suspect drug in the concerned trial (domestic/foreign) within **15 calendar days**;

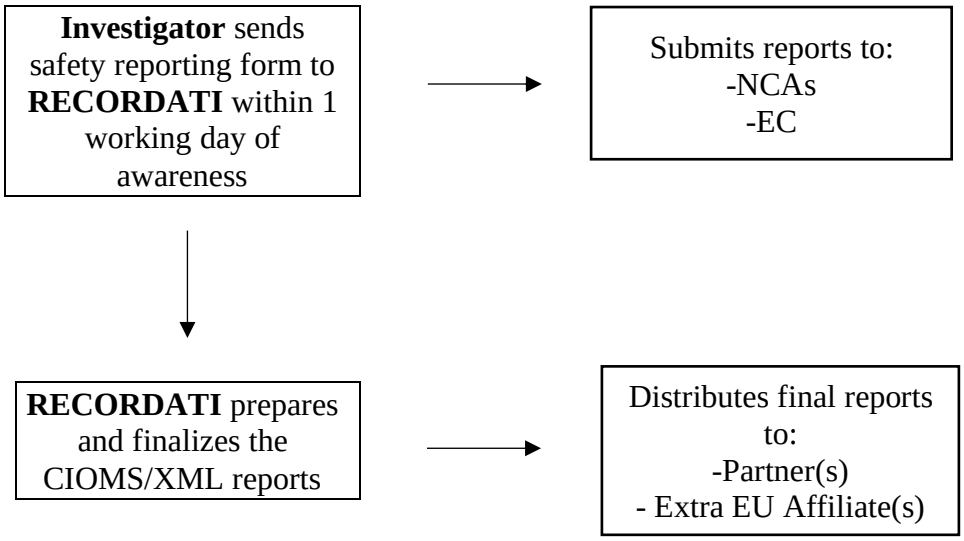
Valid Non-Serious ADR related to suspect drug in the concerned trial (domestic) within **90 calendar days**.

Note: Observational studies follow Module VI of GVP submission requirement.

A flowchart describing the safety information exchange process is reported in the section 7.

7 PROCESS FLOW FOR ADRs

Process flow for ADRs



8 PERIODIC UPDATES

Recordati HQ PVU is responsible for the periodic review of the safety profile of the study drug (Lercanidipine). The Investigator will provide any necessary and relevant update on the safety of the product involved in the study (Lercanidipine) to ensure this process.

9 PERIODIC REPORTING

Recordati HQ PVU is responsible for the preparation of periodic reports related to Lercanidipine product.

10 RECONCILIATION OF SAFETY DATA

On a monthly basis, a reconciliation of all the collected safety exchanged during the previous month will be performed between the Investigator and Recordati HQ PVU. To this end, FRM 01-C_SOP-PV60 will be used.

The **Investigator** will send to Recordati PVU, at the e-mail ICSR-RecordatiHQ@recordati.it, a list of all the managed safety reports handled in the reconciliated period and extrapolated by the clinical study database/clinical tracker.
Recordati HQ PVU will compare the list sent by the Investigator with the cases contained in the Recordati Global Safety Database (ARGUS). In the event of a discrepancy, the Investigator must immediately provide a copy of any missing report to Recordati.

In addition, the Investigator must provide detailed explanation for the discrepancy, indicate the corrective action that was taken or planned and justify that such corrective action is appropriate to avoid a similar discrepancy in the future.

The end of the study, intended as the last day treatment of the last patient, will be clearly communicated by the Sponsor/Investigator. As soon as possible, the Investigator will send via e-mail the final LL of all ADRs (serious and non-serious ADRs) to Recordati for the final reconciliation.

11 PROCESSING OF PERSONAL DATA

Personal data, included those contained in the training material and in safety information collected in the study, shall be processed in accordance with the applicable data protection laws.

12 ARCHIVING

All study related documents are filed by Recordati during the project.
Recordati HQ PVU will archive all the safety related documents in the processed case reports in ARGUS and in ad hoc folder stored in Recordati Safety Area of the Recordati SharePoint, as applicable.
A local archive could be maintained by the Investigator as well.
All study related documents are exchanged between the Sponsor and Recordati for archiving purposes at the end of the project.

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ADDENDUM 1: TASKS RESPONSIBILITIES

The table below describes each party's responsibilities

TASK	*INVESTIGATOR*	*RECORDATI HQ PVU*
Maintain the Trial database	*x*	
Maintain the Safety database		*x*
Completion of (e-)CRF/tracking and Safety reporting forms, including INVESTIGATOR causality assessment	*x*	
Safety forms (ADR, Incident, Pregnancy, Special situation) transmission to RECORDATI	*x*	
Pregnancy/Special Situations processing		*x*
Data entry (incl. QC) into safety database, narrative writing and medical assessment and validation for each version medical review.		*x*
Query addressing to the investigators		*x*
Answer to queries	*x*	
Notification of ADR/Incident to CA/C-IEC	*x*	
Preparation of ADR/Incident reconciliation file	*x*	*x*
Archiving of documents	*x*	*x*

* X = Responsible of the Task

Attachment 1: example of email for sending Safety forms from the Investigator to Recordati HQ PVU

Specify members of the team to be copied:
Study code: *specify code*
Study title: specify title

Dear Team

Please find attached an *(initial/follow-up) / (serious/non-serious) safety report* and/or source documentation that has been received on *dd-mmm-yyyy* with DAY 0 *dd-mmm-yyyy* and related to the following event:

Principal Investigator/Site:
Country:
Site Number:
Subject ID:
SAE and SAE/device deficiency/incident Term:
SAE and SAE/device deficiency/incident Criteria:
Relationship to study drug:
Onset Date:
Date of first study drug administration:
End Date:
Outcome:
Reporter's causality: ☐ No
☐ Yes

Reporting:
For Medicinal product ☐ 15 calendar days (serious) ☐ 90 calendar days (non-serious)

The following confirmation will be sent to the site:
"We confirmed that the English translation of the source safety data has been reviewed under our responsibility".

Please let me know if you have any additional queries, or any questions. Kind regards,

Signature

Certificate Of Completion

Envelope Id: B95C9E16-1D79-821D-805F-FEAF12F8E072
Status: Completed
Subject: Complete with Docusign: DSMP_Lercanidipine_ISS-000157.docx
Source Envelope:
Document Pages: 12
Signatures: 2
Envelope Originator:
Certificate Pages: 5
Initials: 0
Benedetta Pagani
AutoNav: Enabled
pagani.b@recordati.it
EnvelopeId Stamping: Disabled
IP Address: 91.230.96.104
Time Zone: (UTC) Dublin, Edinburgh, Lisbon, London

Record Tracking

Status: Original
22-May-2026 | 08:44
Holder: Benedetta Pagani
pagani.b@recordati.it
Location: DocuSign

Signer Events	Signature	Timestamp
Caterina Carollo caterina.carollo@unipa.it Security Level: Email, Account Authentication (Required), Logged in	Firmato da: Caterina Carollo Nome firmatario: Caterina Carollo Motivo per la firma: Approvo il documento Ora firma: 26-mag-2026 | 17:14:42 BST 7982FD7E88874DC78653EC4419C179AC Signature Adoption: Pre-selected Style Signature ID: 7982FD7E-8887-4DC7-8653-EC4419C179AC Using IP Address: 37.180.44.255 With Signing Authentication via Docusign password With Signing Reasons (on each tab): Approvo il documento	Sent: 22-May-2026 | 08:51 Viewed: 26-May-2026 | 17:12 Signed: 26-May-2026 | 17:14
Electronic Record and Signature Disclosure: Accepted: 26-May-2026 | 17:12 ID: 026c38fd-d6a6-46b6-a6b0-19e23841e36f		
Cecilia Maffei Maffei.C@recordati.it Deputy QPPV & QPPV Office Lead Recordati S.p.A. Security Level: Email, Account Authentication (Required), Logged in	Signed by: Cecilia Maffei Signer Name: Cecilia Maffei Signing Reason: I approve this document Signing Time: 22-May-2026 | 10:06:10 BST 2D361C6F054B4C7FB390744BBD2A6497 Signature Adoption: Pre-selected Style Signature ID: 2D361C6F-054B-4C7F-B390-744BBD2A6497 Using IP Address: 91.230.96.104 With Signing Authentication via Docusign password With Signing Reasons (on each tab): I approve this document	Sent: 22-May-2026 | 08:51 Viewed: 22-May-2026 | 10:05 Signed: 22-May-2026 | 10:06
Electronic Record and Signature Disclosure: Accepted: 14-Jan-2026 | 16:34 ID: 37d79937-a8f7-4f6b-99f9-17916d7c4736		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp
Certified Delivery Events	**Status**	**Timestamp**
Carbon Copy Events	**Status**	**Timestamp**
Witness Events	**Signature**	**Timestamp**
Notary Events	**Signature**	**Timestamp**
Envelope Summary Events	**Status**	**Timestamps**
Envelope Sent	Hashed/Encrypted	22-May-2026 | 08:51
Certified Delivered	Security Checked	22-May-2026 | 10:05
Signing Complete	Security Checked	22-May-2026 | 10:06
Completed	Security Checked	26-May-2026 | 17:14
Payment Events	**Status**	**Timestamps**
Electronic Record and Signature Disclosure		

ELECTRONIC RECORD AND SIGNATURE DISCLOSURE

From time to time, Recordati S.p.A. (we, us or Company) may be required by law to provide to you certain written notices or disclosures. Described below are the terms and conditions for providing to you such notices and disclosures electronically through the DocuSign system. Please read the information below carefully and thoroughly, and if you can access this information electronically to your satisfaction and agree to this Electronic Record and Signature Disclosure (ERSD), please confirm your agreement by selecting the check-box next to 'I agree to use electronic records and signatures' before clicking 'CONTINUE' within the DocuSign system.

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Withdrawing your consent

If you decide to receive notices and disclosures from us electronically, you may at any time change your mind and tell us that thereafter you want to receive required notices and disclosures only in paper format. How you must inform us of your decision to receive future notices and disclosure in paper format and withdraw your consent to receive notices and disclosures electronically is described below.

Consequences of changing your mind

If you elect to receive required notices and disclosures only in paper format, it will slow the speed at which we can complete certain steps in transactions with you and delivering services to you because we will need first to send the required notices or disclosures to you in paper format, and then wait until we receive back from you your acknowledgment of your receipt of such paper notices or disclosures. Further, you will no longer be able to use the DocuSign system to receive required notices and consents electronically from us or to sign electronically documents from us.

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Unless you tell us otherwise in accordance with the procedures described herein, we will provide electronically to you through the DocuSign system all required notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you during the course of our relationship with you. To reduce the chance of you inadvertently not receiving any notice or disclosure, we prefer to provide all of the required notices and disclosures to you by the same method and to the same address that you have given us. Thus, you can receive all the disclosures and notices electronically or in paper format through the paper mail delivery system. If you do not agree with this process, please let us know as described below. Please also see the paragraph immediately above that describes the consequences of your electing not to receive delivery of the notices and disclosures electronically from us.

How to contact Recordati S.p.A.:

You may contact us to let us know of your changes as to how we may contact you electronically, to request paper copies of certain information from us, and to withdraw your prior consent to receive notices and disclosures electronically as follows:
To contact us by email send messages to: frigoli.c@recordati.it

To advise Recordati S.p.A. of your new email address

To let us know of a change in your email address where we should send notices and disclosures electronically to you, you must send an email message to us at frigoli.c@recordati.it and in the body of such request you must state: your previous email address, your new email address. We do not require any other information from you to change your email address.

If you created a DocuSign account, you may update it with your new email address through your account preferences.

To request paper copies from Recordati S.p.A.

To request delivery from us of paper copies of the notices and disclosures previously provided by us to you electronically, you must send us an email to frigoli.c@recordati.it and in the body of such request you must state your email address, full name, mailing address, and telephone number. Not Applicable

To withdraw your consent with Recordati S.p.A.

To inform us that you no longer wish to receive future notices and disclosures in electronic format you may:

i. decline to sign a document from within your signing session, and on the subsequent page, select the check-box indicating you wish to withdraw your consent, or you may;

ii. send us an email to frigoli.c@recordati.it and in the body of such request you must state your email, full name, mailing address, and telephone number. We do not need any other information from you to withdraw consent.. The consequences of your withdrawing consent for online documents will be that transactions may take a longer time to process..

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The minimum system requirements for using the DocuSign system may change over time. The current system requirements are found here: https://support.docusign.com/guides/signer-guide-signing-system-requirements.

Acknowledging your access and consent to receive and sign documents electronically

To confirm to us that you can access this information electronically, which will be similar to other electronic notices and disclosures that we will provide to you, please confirm that you have read this ERSD, and (i) that you are able to print on paper or electronically save this ERSD for your future reference and access; or (ii) that you are able to email this ERSD to an email address where you will be able to print on paper or save it for your future reference and access. Further, if you consent to receiving notices and disclosures exclusively in electronic format as described herein, then select the check-box next to 'I agree to use electronic records and signatures' before clicking 'CONTINUE' within the DocuSign system.

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- You can print on paper this Electronic Record and Signature Disclosure, or save or send this Electronic Record and Disclosure to a location where you can print it, for future reference and access; and
- Until or unless you notify Recordati S.p.A. as described above, you consent to receive exclusively through electronic means all notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you by Recordati S.p.A. during the course of your relationship with Recordati S.p.A..