1 PURPOSE
This procedure describes the processes followed by the Investigator and his/her key study personnel involved in the creation, management, review, and maintenance of files pertaining to the conduct of all human subject research.

2 GENERAL INSTRUCTIONS AND RESPONSIBILITIES
   a) The Investigator is responsible for ensuring that complete and precise data are collected, documented, and maintained throughout the course of an investigation involving human subjects.
   b) The Monitor is responsible for verifying that the files are complete, accurate, and securely maintained by the Sponsor and participating Investigators.
   c) The Sponsor is responsible for terminating the participation of, and discontinuing shipments of the investigational product to, any Investigator who has failed to maintain or make available required records or reports of the study.
   d) The Lead Principal Investigator of a multi-center study should maintain site-specific files for each participating investigator to best facilitate oversight of those sites and investigators.

3 SPECIFIC PROCEDURES
3.1 Creating the Trial Regulatory Master File (TMF)
   3.1.1. Prior to Study Initiation
   The Investigator or designee in charge of managing the regulatory documents should create a TMF that contains the following, as required:
   a) FDA Form 1571 (cover sheet for IND application submissions)
   b) FDA Form 1572 (Statement of Investigator for clinical studies under an IND)
c) Investigator Brochure (for drug/biologic studies) and/or an FDA approved package insert, or Investigational Plan and Report of Prior Investigations (medical device studies).

d) Signed protocol and amendments, if any (all versions).

e) Information given to study subject:
   • Informed consent form(s) (all versions)
   • Any other written information
   • Advertisements for subject recruitment

f) Financial disclosure information. Specific financial and contractual information should be retained in a separate secure file.

g) Dated, documented approval from the Institutional Review Boards (IRB) of record for the following:
   • Protocol and any amendments
   • CRF (if applicable)
   • Informed Consent Forms
   • Any other written information to be provided to subject(s)
   • Advertisement for subject recruitment (if used)
   • Any other documents given IRB approval

h) Committee composition or Federal Wide Assurance of IRB of record.

i) Regulatory authorities’ authorizations/approvals/notifications of protocol (where required), including any copies of all submission such as the Investigational New Drug (IND) submission, Investigational Device Exemption (IDE) submission, protocols, amendments, supplements, and other related correspondence.

j) Curriculum Vitae (CV) and/or other relevant documents evidencing qualifications of Investigator(s) and Sub-Investigator(s) e.g. medical license, CITI certification, etc.

k) Normal reference ranges for medical/laboratory/technical procedure(s) and test(s) included in the protocol.

l) For any medical/laboratory/technical procedures and/or tests, secure and file the following, as available:
   • Laboratory certification and accreditation (CLIA, CAP, state, etc.)
   • Lab Director’s CV and medical license
   • Established quality control and/or external quality assessment
   • Other validation

m) Sample of label(s) attached to investigational product container(s).

n) Instructions for handling of investigational product(s) and any other study-related labeling (if not included in protocol or Investigator Brochure).

o) Shipping records for:
   • Investigational product(s)
3.2 TMF Maintenance during Study Conduct

3.2.1 During the Ongoing Conduct of the Study

The Investigator, or designee such as the Regulatory Coordinator, should add documents, as required, “a” through “y” to the TMF, as evidence that all new and relevant information is documented as it becomes available.

a) Site Initiation Visit Report/Letter.
b) Investigator Brochure, FDA approved package insert, or Investigational Plan updates.
c) Any revision to:
   - 1571 and/or 1572
   - Protocol/amendment(s) and CRF
   - Informed consent form
   - Any other written information provided to subjects
   - Advertisement for subject recruitment (if used)
d) Dated, documented approval from the IRB of record, of revisions to the following:
   - Protocol amendment(s)
   - Informed consent form(s)
   - Any other written information to be provided to subject
   - Advertisement for subject recruitment
   - Any other documents given approval
e) Dated, documented evidence of continuing review and approval of study by the IRB.
f) Regulatory authorities’ authorizations/approvals/notifications where required for protocol amendment(s) and other documents including copies of all submission such as IND, IDE, amendments, supplements, and other related correspondence.
g) CVs, medical licenses and CITI certification for new Investigators and/or Sub-Investigators.
h) Updates of medical/laboratory/technical procedures/tests:
   - Laboratory Certification and Accreditation
   - Lab Director’s CV and medical license
   - Established quality control and/or external quality assessment
   - Updates to normal value ranges for medical/laboratory/technical procedure(s)/test(s) included in the protocol
   - Other validation

i) Documentation of investigational product(s) and study-related materials shipment.

j) Certificate(s) of analysis for new batches of investigational products.

k) Routine site monitoring visit reports.

l) Relevant sponsor/monitor communications other than site visits, such as:
   - Letters
   - Meeting notes
   - Notes of telephone calls
   - Newsletters
   - Memorandums
   - Email blasts

m) Sample of informed consent forms including original and all revised and updated versions.

n) Original signed, dated, and completed CRFs.

o) Original documentation of CRF corrections.

p) Copies of relevant source documents, if sent by or requested from the site, with subject identifiers redacted.

q) Notifications by originating Investigator to site of serious adverse events and related reports.

r) Notification by Sponsors and/or participating Investigators, if needed, to regulatory authorities and all IRB(s) of record of unexpected and serious adverse events of other safety information.

s) Notification by Sponsor to participating Investigators of safety information.

t) Interim or annual reports to IRB(s) of record and other authorities.

u) Subject Screening and Enrollment Logs.

v) Subject identification code list.

w) Investigational products accountability at the site.

x) Study Staff Signature Log and Delegation of Authority Log.

y) Record of retained subject body fluids/tissue samples (if any).
Investigator Standard Operating Procedures

3.3 TMF Closure after Study Completion/Termination

3.3.1 After Completion or Termination of the Study

The Investigator or designee should confirm that all documents listed above are in the TMF, along with the documents listed below:

a) Investigational product(s) accountability at site(s).
b) Documentation of investigational product destruction (if applicable).
c) Completed subject identification code list.
d) Information captured in CRFs, patient diaries, subject study files, etc.
e) Audit certificates and reports/FDA inspection reports.
f) Final study closeout monitoring report(s).
g) Treatment allocation and decoding documentation.
h) Final study report by Investigators to the IRB of record, and where applicable, to necessary regulatory authorities.
i) Clinical study report.

4 RECORDS RETENTION

a) All TMF contents, including those listed above in 3.3.1, will be maintained by the
Investigator for a minimum of two years after the conclusion of the study or FDA marketing
approval, or in accordance with the study contract, whichever is the longest (See
Attachment A).
b) After that period of time, files will be archived to a secure offsite location (see Attachments
B-D).
c) Archiving procedures must ensure that original records are available or can be provided
within a 48-hour period, if needed.

5 REFERENCES TO OTHER APPLICABLE SOPS

- 103 Sponsor-Investigator Responsibility and Delegation of Responsibility
- 201 Contacts and Submission for FDA
- 202 Reporting Requirements for FDA
- 401 Initiation Visit and Site Training
- 501 Communications
- 502 Investigational Product Inventory Management
- 504 Routine Monitoring Visits
- 505 Study Closeout Visit
- 603 Subject Screening and Enrollment
- 702 Clinical Research Data Management
Investigator Standard Operating Procedures

- 703 Use of Electronic Data Systems
- 801 Quality Assurance Audits
- 802 FDA Inspections

6 ATTACHMENTS
A. Summary of ICH Essential Documents
B. Recall-DMS Medical Collection & Supply Order Form
C. DMS Medical Customer CARE- Customer Order Form-Miami
D. Staff Instructions for Documenting Files for Recall America

7 APPLICABLE REGULATIONS AND GUIDELINES
- General Responsibilities of Sponsors (21 CFR 312.50)
- Review of Ongoing Investigations (21 CFR 312.56)
- Recordkeeping and Record Retention (21 CFR 312.57)
- Inspection of Sponsor’s Records and Reports (21 CFR 312.58)
- General Responsibilities of Investigators (21 CFR 312.60)
- Investigator Recordkeeping and Record Retention (21 CFR 312.62)
- Investigator Reports (21 CFR 312.64)
- Inspection of Investigator’s Records and Reports (21 CFR 312.68)
- General Responsibilities of Sponsors (21 CFR 812.40)
- Monitoring Investigations (21 CFR 812.46)
- General Responsibilities of Investigators (21 CFR 812.100)
- Records (21 CFR 812.140)
- Inspections (21 CFR 812.145)
- Reports (21 CFR 812.150)
- The Principles of ICH GCP (ICH E6, Sections 2.10 and 2.11)
- Records and Reports (ICH E6, Section 4.9)
- Progress Reports (ICH E6, Section 4.10)
- Safety Reporting (ICH E6, Section 4.11)
- Final Report(s) by Investigators (ICH E6, Section 4.13)
- Trial Management, Data Handling, and Record Keeping (ICH E6, Section 5.5)
- Record Access (ICH E6, Section 5.15)
- Clinical Trial/Study Reports (ICH E6, Section 5.22)
- Essential Documents for the Conduct of a Clinical Trial (ICH E6, Section 8.0)