The University of Iowa Dezii Translational Vision Research Group

TITLE: Protocol for Standard Operating Procedure (SOP)

SOP Number: D-GLO-PRO-001 Revision Number: 0

Effective Date: 08 Aug 2015

Author: _____ Date: _____

Reviewer: _____ Date: _____

QA Approval: _____ Date: _____

A. OBJECTIVE

Standard operating procedures (SOPs) are written procedures governing operations and are required for GMP compliance as given in 21 CFR 211. This document describes the process of writing, reviewing, approving, finalizing, revising, training on, retiring and archiving SOPs.

B. APPLICABILITY

This document applies to all personnel at The University of Iowa Dezii Translational Vision Research Group (DTVR).

C. REFERENCES

SOP D-GLO-TR-002	Competency Based Training Program
Form F-D-GLO-PRO-001	Change Control Form for Standard Operating Procedures (SOP) and Forms
Form F-D-GLO-PRO-002	SOP Annual Review Form
Form F-GLO-TR-001	Standard Operating Procedure Training Report

D. PROCEDURE

1. SOPs undergo a 4 stage finalization process:

   1.1. Stage 1 is writing the new SOP or revision. Writing a new or revised quiz may also be needed. After this stage is complete, the author will sign and date the SOP.

   1.2. Stage 2 is reviewing of the new SOP or revision. Review of a new or revised quiz may also be needed. After this stage is complete, the reviewer and QA approver will sign and date the SOP.

   1.3. Stage 3 is training on the new SOP or revision. The training stage is intended for reading the SOP and completing the quiz. Additional competency based training may be needed but is completed as a separate process as outlined in D-GLO-TR-002.

   1.4. Stage 4 is finalization of the new SOP or revision (after 80% of personnel have read the SOP). After this stage is complete, an effective date is assigned and the SOP is made via LabGuru.

2. SOPs should not be used for referenced until stage 4 when finalized. If an SOP is at stage 3, it may be referenced as a draft.

E. SOP FORMAT

1. Each SOP should have a header with the SOP title, number, revision number, and effective date on each page as well as the author signature and date, reviewer signature and date, and QA approval signature and date on the first page.

   1.1. Give a title to the SOP that describes the process or equipment.

1.1.1. For processes, titles incorporating words such as 'protocol' or 'method' should be used, as applicable.

1.1.1.1. A protocol is a plan of action that describes what is intended to be completed.

1.1.1.2. A method is a specific set of instructions that describe how a process is to be completed.

1.1.2. For equipment, titles incorporating words such as 'operation of', 'calibration of', 'preventive maintenance of' and 'qualification of' should be used, as applicable. Titles should also include the manufacturer and model number(s) of the equipment.

1.2. SOPs will be numbered with the convention D-DEP-CAT-XXX, where "D-" designates the SOP as being a part of the Quality System for the Dezii Translational Vision Research (DTVR) group, a cGMP entity within the Carver College of Medicine's Wynn Institute for Vision Research (WIVR). DEP is a two or three letter code for the designated department, CAT is a two or three letter code designating the category to which the SOP applies and XXX is a sequential numbering of the SOP.

1.2.1. Identify the department to which the SOP primarily applies. SOPs that are multi-departmental may be designated as global. The abbreviations of the departments within DTVR are as follows:

FAC	Facilities
GLO	Global
IT	Information Technologies
QA	Quality Assurance
QC	Quality Control
DEZ	Dezii Translational Vision Research

1.2.2. Identify the type of SOP in one of the following categories based on the purpose. The abbreviations of the categories are as follows:

1.2.2.1. Computerized Systems:

COM	Operations
CPM	Preventive Maintenance
CQV	Qualification/Verification

1.2.2.2. Equipment:

ECL	Calibration
EQP	Operations
EPM	Preventive Maintenance
EQV	Qualification/Verification

1.2.2.3. Processes:

PMP	Potent Materials
PQV	Qualification/Verification

PRO Operation/Procedures
PVL Validation

1.2.2.4. Safety:

SFT Safety

1.2.2.5. Training:

TR Training

1.3. SOP revision numbers will be sequential starting with revision 0 for the original document.

2. The body of the SOP should constitute parts, sections and subsections and may be referenced in these terms (e.g., part C, section 2, subsection 2.1, part C, step 2.1, section C.2.1, etc.). Each SOP should be formatted consistently. Use this SOP as an example.

2.1. Each part of the SOP will be designated alphabetically. The parts stating the OBJECTIVE, APPLICABILITY, 'PROCEDURE' and HISTORY are required for every SOP. The other parts are used only if necessary. Use this SOP as an example for the type of information under each part.

2.1.1. The part defining what the overall purpose of the SOP will be and why the SOP is needed is called OBJECTIVE. OBJECTIVE is always part A.

2.1.2. The part defining where and when the SOP must be followed and who is responsible for complying with the SOP is called APPLICABILITY. This part may also define where or when the SOP does not apply. APPLICABILITY is always part B.

2.1.3. The part that lists all applicable references used to write the SOP and references made in the SOP is called REFERENCES.

2.1.4. The part listing terminology used with specific meanings to minimize confusion is called DEFINITIONS. This part may be used to define acronyms and abbreviations.

2.1.5. The part that lists all chemicals and reagents needed to execute the SOP is called CHEMICALS AND REAGENTS, or MATERIALS AND MEDIA, as appropriate. For example, the SOP for the Western Blotting Protocol would have the transfer buffer and luminol listed under this part, among others.

2.1.6. The part listing all equipment referenced in the SOP needed to execute the SOP, not including any equipment listed in the title is called EQUIPMENT. For example, in a balance operation SOP, the weights used for a weight verification check of the balance would be listed in this part. The balance itself is not listed. The EQUIPMENT and MATERIALS AND MEDIA sections may be combined.

2.1.7. The part listing any special handling or safety requirements is called SPECIAL PRECAUTIONS.

2.1.8. The part giving additional information relating to the execution of the SOP is called GENERAL INFORMATION, BACKGROUND or the like.

2.1.9. The part describing in detail what is to be done is referred to as 'PROCEDURE'. This part may also be called by the name of the specific activity.

2.1.9.1. Use as many descriptors in the 'PROCEDURE' section as needed.

2.1.9.2. For equipment, acceptable alternatives to 'PROCEDURE' are SETUP OF …, VERIFICATION PROCEDURE, OPERATION OF …, MAINTENANCE OF… and the like.

2.1.9.3. For processes, acceptable alternatives to 'PROCEDURE' are RESPONSIBILITIES, ANALYSIS OF…, DEVELOPING A …, CHOOSING A …, SELECTING A … and the like.

2.1.10. The part listing all revisions to the SOP including a summary of what was revised and when the revision is effective is called HISTORY.

2.1.10.1. The first entry in this section will be the issue date of the original SOP. The revision will be listed as 0 and the change will be listed as "Original document".

2.1.10.2. Each subsequent revision will be entered with a summary of the major changes. For example if the SOP was revised to correct typographical and grammatical errors, the changes would be listed as correcting typographical errors without having to list each individual correction. Use this SOP as an example. Type in the effective dates from previous revisions. The current revision should have a hand written date entered.

2.2. SOP sections under each part will be numbered sequentially starting with 1. Do not use Roman numerals.

2.2.1. As possible, each section number should be a basic step in the procedure or equipment.

2.2.2. Subsections should be numbered with the section number a dot and then sequentially starting with 1. Further subsections should follow the same convention. These subsections should give all the necessary details to follow the procedure or run the equipment.

2.2.3. Sections and subsections may include tables or graphs as necessary to condense information or provide examples as long as they are appropriately labeled.

F. RESPONSIBILITIES

1. The author of a new SOP or a revision to an SOP may be any knowledgeable permanent personnel.

1.1. For revisions, the author should capture all changes on the Change Control Form for SOPs and Forms (F-D-GLO-PRO-001).

1.2. If there are many changes to the SOP, the change control form may read 'see attached' and a copy of the SOP marked with the changes will be included. In this case, the copy of the SOP with the noted changes must remain with the change control form.

1.3. The author should conduct the preliminary impact assessment.

1.4. For new SOPs a quiz will be created to assess the effectiveness of training on the SOP.

1.5. When an SOP is revised, the quiz will be reviewed and revised if needed.

2. When writing or revising a procedure the author will solicit input on the procedure from the individuals who will be subject to it and/or are experts on the subject matter. Where a procedure crosses departmental lines input will be solicited from other department heads, and individuals, as deemed appropriate by their supervisors. This process may be accomplished through one-on-one communication or through the Quality Meeting.

3. The reviewer should be the department supervisor or a subject matter expert.

3.1. The reviewer should check the new or revised SOP by running the procedure or equipment, when possible, to determine the accuracy of the instructions.

3.2. For revisions, the reviewer should check the change control form for accuracy. The change control form (or attached SOP with noted changes) should capture all changes.

3.3. The reviewer should also check for grammar and typographical errors.

3.4. The reviewer will check new quizzes for appropriate content and review existing quizzes for any necessary changes.

4. The Quality Assurance (QA) approver should check the SOP against regulatory documents for accuracy.

4.1. The QA approver should check the appropriateness of the SOP title and number, if necessary. The QA approver should also check references in the SOP for accuracy.

4.2. For revisions, the QA approver should sign the Change Control Form for SOPs and Forms (F-D-GLO-PRO-001) and verify the impact assessment. If the impact assessment is not accurate, the QA approver will change the impact assessment. The QA approver will notify necessary personnel of the impact assessment for equipment validation, LabGuru calibration Manager entries or other processes affected by the impact assessment.

4.3. The QA approver should also check for grammar and typographical errors.

4.4. The QA approver will verify each SOP has an associated quiz.

G. TRAINING

1. The author, reviewer and QA approver will be qualified to train on a new or revised SOP by signing the SOP. A copy of form F-D-GLO-TR-001 will be placed in each employee's training file to document their qualification.

2. Copies of newly drafted and revised SOPs will be distributed for training to each department supervisor, author or a qualified trainer as specified in D-GLO-TR-003.

    2.1. The department supervisor, Quality Manager, author and/or other designate will determine and identify individuals to be trained on the new or revised SOP.

        2.1.1. A review of LabGuru or other databases for the individuals previously trained on a revised SOP may ensure no individuals are missed.

        2.1.2. After this assessment, the distribution cover sheet for each department should be marked to indicate how many individuals will be trained on the SOP.

    2.2. For revised SOPs, a copy of the approved form F-D-GLO-PRO-001, including a marked up copy of the SOP if applicable, will be distributed.

    2.3. At the discretion of the Quality Manager or GMP Trainer, a training session for all of DTVR may be held on a new or revised SOP.

    2.4. At the discretion of a departmental supervisor, a training session may be held for individuals within a department on a new or revised SOP that directly affects the department.

    2.5. For an absent individual, training should be conducted on all new and revised SOPs over the absence period within 3 weeks of the return date.

3. Training will be captured on the Standard Operating Procedure Training Report (F-D-GLO-TR-001).

    3.1. The trainer will fill in the appropriate boxes for the SOP number, revision number and SOP title, mark the appropriate training application, training requirements and complete the trainer box.

    3.2. Each individual being trained will print their name, write their signature and enter the date into the appropriate box.

        3.2.1. Names of individuals may be entered into the ‘Print Name’ column by the trainer.

        3.2.2. The signature and date indicates the individual has read and understood the SOP.

    3.3. Form F-D-GLO-TR-001 should be turned into the GMP trainer or designate within 4 weeks of initial routing for a new or revised SOP(s).

        3.3.1. For individuals unable to sign the SOP Training Report form within the four week period (i.e. an employee is on an extended vacation), an individual training record will need to be signed.

        3.3.2. Until a training record is completed, individuals may not perform any tasks in reference to that SOP.

    3.4. The original form F-D-GLO-TR-001 is filed in the master binder. A copy of the form is placed in each individual’s training file.

4. Each SOP will have an associated quiz to assess the effectiveness of training.
   4.1. Quizzes for SOPs should pertain only to the SOP to assess effectiveness of training on the SOP.
      4.1.1. Quizzes should be appropriate in length to address the form and content of the SOP. For example, a typical procedural SOP would have at least five questions.
      4.1.2. The quiz format should be appropriate for the content of the SOP. Multiple choice and true/false questions are the default format.
      4.1.3. Questions should be based on the key elements of the SOP.
         4.1.3.1. Questions should be written to demonstrate a comprehension of what was read.
         4.1.3.2. Answers should be found in the SOP.

5. Obtain a copy of the quiz for each SOP from the QA. The author, reviewer and QA approver will need to take the quiz to finalize their training.
   5.1. For new and revised SOPs or group training, QA will provide a copy of the quiz to the trainer in each department as part of the distribution of the SOP for training.
      5.1.1. Quizzes may not need to be re-taken at every revision of an SOP depending upon the changes made to the SOP (e.g., an SOP revision used to correct typographical errors or changes made to the history section of an SOP).
      5.1.2. This information can be found on the change control form.
   5.2. The quizzes are open book.
   5.3. A passing grade is 80% or higher.
   5.4. If the employee fails, the test may be taken one additional time. If the employee fails a second time, the supervisor will complete the Remedial Training Report (F-GLO-TR-010) and determine an appropriate course of action.

6. When 80% or more of the individuals identified as needing training on the SOP are trained on the SOP an effective date may be assigned.

H. FINALIZATION

1. When the SOP is assigned an effective date, the SOP is considered final. QA will assign the effective date.
   1.1. The assigned effective date should be within 1 month of the new or revision submission date, when possible.
   1.2. The effective date should be several days in the future (up to a week in the future) to allow for distribution before the SOP becomes effective.

2. Once the SOP has been given an effective date, a review date will be assigned.

2.1. The review date is 2 years from the effective date.

2.2. The SOP must be reviewed by the author or subject matter expert and QA within 1 month of the review due date.

2.3. After 4 years (2 biennial reviews), if there are no changes, the SOP will be reviewed by a subject matter expert, a departmental reviewer and QA. All affected personnel will be retrained on the SOP. A new SOP Annual Review Form (F-D-GLO-PRO-002) will be placed with the master copy SOP.

I. DISTRIBUTION

1. Once the SOP is finalized, the document is considered the master SOP. Each page of the master SOP will be stamped in red ink as "Current New" on the right margin. For a revised SOP, the old master SOP and change control form will be retained by QA and archived in the Archived SOP binder. The "Current New" stamp on the old master SOP will be lined through with black.

2. All master SOPs and the SOP Master Index (containing the SOP number, title and revision number) will be maintained by QA and kept in protective plastic sleeves in labeled binders along with a SOP Annual Review Form (F-GLO-PRO-002) for each SOP. Master SOPs and the Master Index may only leave the area to be copied or read with permission from QA.

3. Official copies of the master SOPs and SOP Master Index may be requested individually by 3rd parties (including the FDA) or will be distributed as stamped official sets.

3.1. Stamped sets will be numbered, contain all SOPs and be kept in labeled binders.

3.2. A stamped official copy of the SOP Master Index will also be kept with the SOP binders in each area.

3.3. A master list of stamped sets (form F-D-QA-PRO-008) will be maintained by QA listing the set number, owner or department, room or location, date issued and date retired or returned.

4. All effective new and revised SOPs will be distributed individually as stamped official copies by QA into the appropriate sets from the master SOP. A stamped official copy of each affected page of the SOP Master Index will also be distributed.

5. Old revisions of the official stamped SOPs and SOP Indexes will be retrieved and returned to QA to be destroyed.

6. Form F-QA-PRO-007 will record the distribution, retrieval and destruction of official stamped copies of SOPs and SOP Index pages.

6.1. Fill in the complete title of each SOP to be distributed.

6.2. Replace '<NUMBER>' with the actual SOP number.

6.3. Record the revision number of the SOP distributed, retrieved and destroyed. Any discrepancies will be investigated.

6.4. Record the number of copies of each SOP that are distributed, retrieved and destroyed. The number of copies of each SOP that are distributed should be the same as the number of copies that are retrieved and destroyed. Any discrepancies should be noted in the comments section. Any discrepancies will be investigated.

6.5. Complete the signature and date for the distribution and retrieval of the official stamped copies of the SOPs listed.

6.6. The witness should verify the correct revision number of each SOP and the number of copies is correct before the SOPs are distributed. The witness should also verify the revision number of each SOP retrieved and that the number of copies has been correctly recorded.

7. Official stamped copies of old revisions of previous SOP revisions will be shredded.

8. Other copies of the master SOP, SOP Master Index, or stamped official copies are not allowed.

9. As part of the distribution process the new or revised SOP will be posted as a non-editable PDF on the Groupshare site. In the case of revised SOPs the superseded version will be deleted.

10. In a case where a master SOP is misplaced, printing of a “new master SOP” from Groupshare is allowed if “new master SOP” is noted on the front page of the newly printed master SOP.

J. REVISIONS

1. Effective SOPs may be revised at any time to reflect changes or clarifications to procedures or equipment. A change is instituted by filling out a Change Control Form for SOP and Forms (F-GLO-PRO-001). The change control form will list all changes, the reason for the change and a departmental review.

1.1. Any changes needed to a new SOP discovered during training (i.e. an SOP in stage 3, before an effective date is assigned) are not a revision and do not require a change control form.

1.2. Any changes needed to a revised SOP discovered during training (i.e. an SOP in stage 3, before an effective date is assigned) should have the changes added to the change control form.

1.3. Changes discovered during training on an SOP will need to be assessed to determine if a new copy needs to be distributed for additional training (e.g., typographical errors will not require more training but information added to the SOP would require redistribution and training).

2. Any submitted changes require an impact assessment as the changes may affect other SOPs, forms, quizzes, Calibration Manager entries and the validation status of equipment.

2.1. Changes to global SOPs will be submitted to all affected departments before revision to assess the impact to each department.

2.2. A review of other SOPs and forms that may be impacted will be made. Those SOPs and forms reviewed will be listed on the change control form. Affected SOPs and forms will be listed.

2.3. Assess if entries into Calman, other than for the new or revised SOP, are affected by the proposed changes. Record any affected entries to Calman on the appropriate line (e.g., if a revision to an SOP on equipment qualification, validation, calibration or preventive maintenance would add or delete activities, the Calman entries for that equipment would also need to be updated).

2.4. Assess if changes to the SOP will affect procedures or other functions (e.g., equipment cleaning procedures, facility procedures, etc.).

2.5. A review of the associated quiz will be assessed. If the quiz is revised in conjunction with revisions to the SOP, the quiz will need to be taken as part of training.

3. The change control form shall be submitted to QA for approval.

3.1. For extensive revisions to SOPs, the SOP may be copied and marked up with the changes and attached to the change control form. This marked up copy of the SOP must remain with the change control form. The copy of the SOP may be made only from the master SOP, SOP Master Index or stamped official copies unless otherwise authorized by QA.

3.2. If the SOP or form affects an IND product, the new revision and change control form will be reviewed and approved by the IND holder prior to QA approval.

4. When the change is approved, the SOP will be revised. The SOP will then be numbered with the new revision number and given back to the author of the change control form to be reviewed. If further changes are required, the document will be corrected and returned to the author.

5. When the new revision is finalized, the change control form will be filed by QA with the old master SOP and be retained by QA. The “Current New” stamp will be lined through with black. Calman will be updated with the revision number and review dates.

K. RETIRING

1. Retiring an SOP is performed by filling out a Change Control Form (F-D-GLO-PRO-001) for the SOP. Indicate on the form that the SOP is to be retired. Any retirement requires an impact assessment as the retirement may affect other SOPs, Calibration Manager entries and/or the validation status of equipment. The intent to retire global and multi-departmental SOPs will be submitted to all affected departments before retirement to assess the impact to each department. This can be accomplished through one-to-one communication or the Quality Meeting.

2. When the retirement is approved, the SOP will be retired. The retired master SOP will be filed and retained by QA as described in section I. The Master SOP Index will indicate the SOP was retired.

3. Quality Assurance will retrieve the previously distributed copies as described in section I.

4. Quality Assurance will delete the retired SOP from the Groupshare site.

L. HISTORY

Effective Date	Revision	Change
08 Aug 2015	0	Original document