SOP Development

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New Procedure

- An SOP ensures a consistent product
- Concurrent with Process Development
- Validation or Equipment Qualification
- Other reasons:
  - New policies/procedures dictated by new regulation
  - SOPs or policies that have been “overlooked” (e.g. data entry/computer use, troubleshooting for equipment)
- Can be simple or complex

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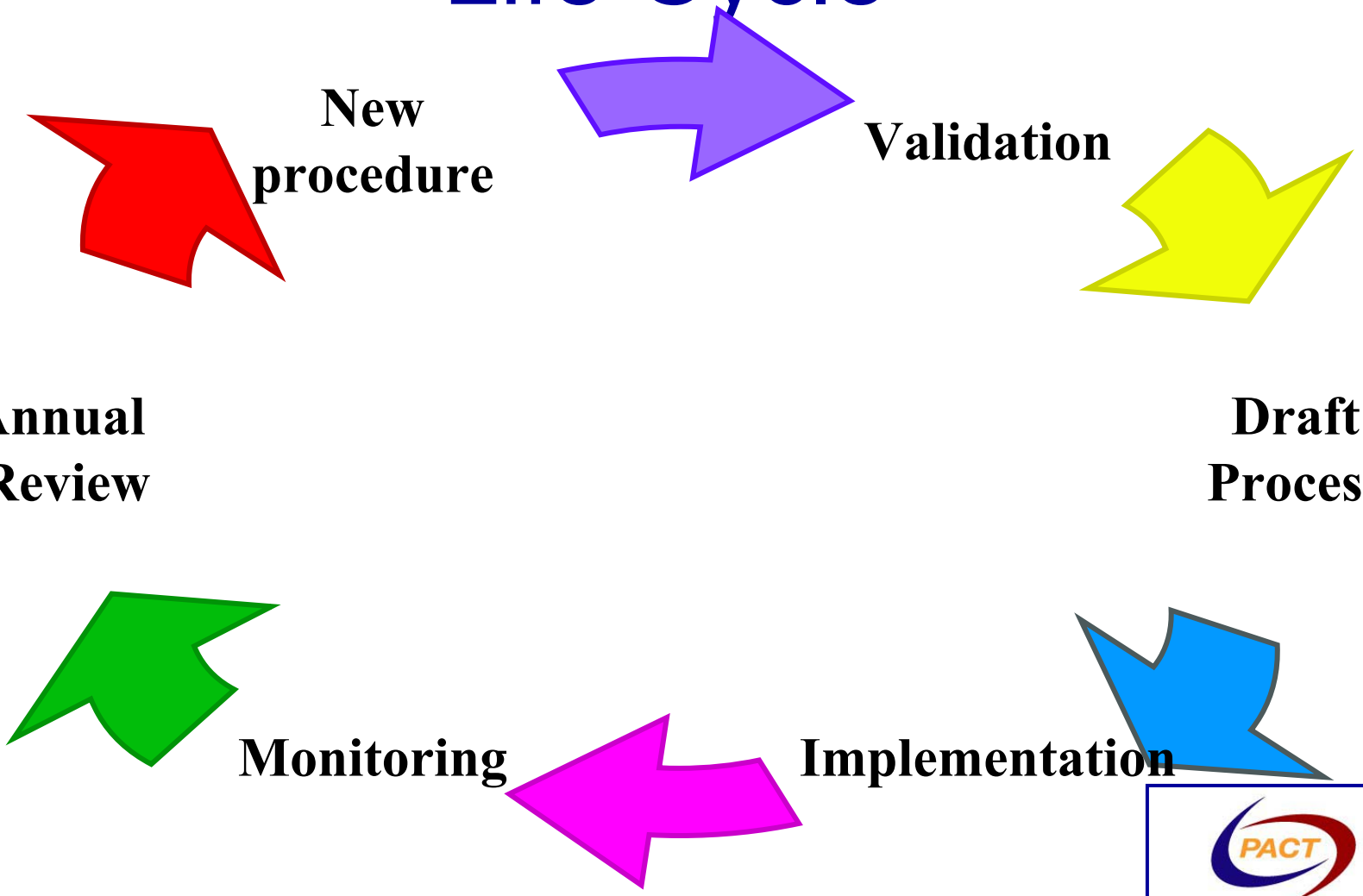
Life Cycle



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Regulatory requirements

- FDA
  - GTP 1271.180
  - GMP 211.100
- CAP LAB GEN GEN.20372
- FACT 2nd Ed. D5.100 – D5.800
- AABB Standards for Cellular Therapy, 1.2.3 – 1.2.5, 6.1

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Document Control Required Elements

- System for numbering/titling of SOPs
- Standardized format
- Training of staff
- Availability of SOPs at work site
- Revision status
- Archiving of obsolete (retired) SOPs
- Annual Review

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SOP Required Elements

- Purpose
- Materials
- Procedure/Process
- Expected endpoints
- References

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Sample Format

- Purpose
- Responsibility
- Definitions
- Safety, Warnings and Precautions
- Materials
- Process/procedure
- Acceptable Endpoints & Result Reporting
- Attachments
- References
- Revision History

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Additional Elements

Revision history

Revision	Change	Rationale	CFR/FACT Standards	Start Date	End Date
0	Creation	New procedure.	A2.220		
1	Address Change. Clarifications	Move from SHY hospital to Hillman Cancer Center. Addition of specific organisms that require quarantine.	D10.320, B6.170.	01/17/03	8/12/03
2	New Terminology, Revision Chart Modification	FACT standards, second edition; addition of the inclusive dates of use	D8.230, A3.000, D5.600	08/12/03	08/09/04
3	Addition of implementation date	FACT standards, second edition;	D5.225	08/09/04	06/20/05
4	Addition of GTP language	Required.	1271.260(a)(1)	06/20/05	

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Additional Elements

2007

☐ No revision necessary

Lab Supervisor_____Date_____

QA Manager_____Date_____

Lab Director_____Date_____

☐ Revision necessary, SOP revised & archived

Lab Supervisor_____Date_____

QA Manager_____Date_____

Lab Director_____Date_____

☐ In document control ☐ Staff review initiated

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Additional Elements

- Standards chart

CFR	FACT	PADH	CAP	AABB
1271.260(a)(1)	D10.320 B6.170	N/A	N/A	5.13.2 2)

CFR	FACT	PADH	CAP	AABB
N/A	D2.600	N/A	N/A	10.3

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Document Template

SOP that states your format

- Sections and subsections
- Style: font type and size, bolding, italics, uppercase letters

- Include a numbering system for sections within the document for easy reference (e.g. outline numbering, alpha/numeric combination, Roman numerals)
- Must include at the minimum, an adequate amount of instruction to perform the task at hand. This can be accomplished by:
  - Using the manufacturer's instruction sheet or manual
  - Using a friend's SOP as a starting point
  - Modifying an existing SOP to meet the needs of the new manufacturing process

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Validation Plan

- Validation plan must be written prior to initiation of the validation process
- Should contain a detailed explanation of how the validation process will proceed and what the acceptable endpoints are.
- Should specify in broad terms how the procedure is run.
- Sometimes you'll need a few practice runs to iron out the wrinkles and really solidify your document prior to beginning the actual validation. This is the time to perfect your SOP.

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Draft process

- Initiate the validation process
- Draft copy of the SOP on site, preferably with two techs working on the SOP.
- Make comments and notes on draft copy, review with author of the SOP
- Have a tech who has not performed the procedure follow the SOP to clarify any difficult passages.

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Implementation

- Have Director or other ultimate approval of the procedure.
- Supervisors or other personnel responsible for the procedure are to review the SOP in depth with their staff.
- Tech staff should be familiar with the SOP and have signed off that they have read the procedure.
- Techs who will be performing the procedure must be trained and determined to be competent prior to implementation of the SOP.

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Monitoring of Procedure

- Periodic monitoring of the new procedure will provide insight into how the procedure is actually being performed.
- Methods for assessing the procedure:
  - Audit the procedure by observing several technologists perform the procedure. This is different from competency. You want to make sure that the procedure is adequate, not the technologist.
  - Ask for input from the technologists. Often they will have plenty of comments about inadequate procedure when questioned, but are unlikely to volunteer this type of information.
  - Have a person who has not been trained on the procedure perform a mock procedure.

Annual Review

- Two ways to handle it:
  - Single once-a-year review
  - Rolling

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Annual Review (2)

- Performed in multiple steps
  - Review of the procedure by a supervisor, QA Manager or staff member
    - Prints out current copy of the SOP
    - Suggests modifications or clarifications
    - If a major format change has been initiated, this will be performed electronically in a draft SOP
    - Initials and dates
  - Review by the Director or designee
    - Approves/disapproves suggestions
    - Makes additional modifications
    - Returns to staff for change of electronic copy
  - Staff revises electronic copy, assigns date approved
  - Director signs/dates approval and goes to implementation route

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Document Control

- The AABB Cell Therapy Standards specify that a master list of SOPs be maintained. This makes using the system of numbering and titling simple

1-Jan-05	05-05-R0	AcT Diff Equipment	Procedure for AcT Diff 2 IQAP
1-Jan-05	05-06-R0	AcT Diff Equipment	Procedure for AcT Diff 2 Maintenance
11-Mar-05	05-07-R0	PACT Procedure Man	Procedure for PACT Sample Notification and Shipment
11-Mar-05	05-08-R0	PACT Procedure Man	Procedure for PACT Bone Marrow Isolex CD34 Selection Validation
24-Apr-05	05-09-R0	Procedure Manual	Procedure for NMDP Form 180 Calculations
3-Jun-05	05-10-R0	Procedure Manual	Procedure for Medical Exception

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Electronic Document Control

- Several methods:
  - Word document
  - Excel spreadsheet
  - Electronic database
    - Access
    - Commercial products

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Take Home Message…

- Good SOP development is essential for maintaining consistency in your processing
- Document control is critical when you are faced with increasing numbers of documents due to regulations

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