Quality Management

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Goals of Quality Management

- Significantly reduce errors
- Ensure credibility of outcomes
- Improve patient safety and quality of processes
- Emphasize measures to investigate, detect, assess, correct, and prevent errors

Quality Medical and Laboratory Practice in Cellular Therapy
Elements of a QM Plan

• Structural Requirements
• Assessment and Reporting
• Information and Document Control
The Quality Management Program can be related to the institutional program in several ways, including:
**Quality Management Plan**

A written document that describes the systems in place to implement the quality management program.

**Policies**

Documents that define the scope of an organization, explain how the goals of the organization will be achieved, and/or serve as a means by which authority can be delegated.

**Procedures**

Documents that describe in detail the process or chronological steps taken to accomplish specific tasks; a procedure is more specific than a policy.

**Supporting Documentation**

Worksheets, forms, and templates through which performance of a procedure is documented.
# QM Plan vs Policies vs Procedures

<table>
<thead>
<tr>
<th>Quality Management Plan</th>
<th>Policies</th>
<th>Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Example:</td>
<td></td>
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<tr>
<td>The Clinical Program enters into written agreements with third parties whose services impact the clinical care of the recipient or donor.</td>
<td>Written agreements must be audited annually for compliance with contractual requirements.</td>
<td>1. Review contractual requirements 2. Request documentation from third-party 3. Reconcile documentation with requirements</td>
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</table>
The QM Plan in Perspective

QM Plan

- Organizational Chart
- Outcome Analysis
- Critical Processes, Policies, and Procedures
- Document Control
- Positive Microbial Cultures
- Written Agreements
- Audits
- Incidents
- Validation
- Product/Unit Tracking and Tracing
- Personnel Requirements
- Validation
- Quality Assurance
- Qualification
- Continuous Operations
- Validation

External Threats

Internal Weaknesses
Suggested Steps to Establishing a QM Plan

• Assess existing materials
• Address missing elements
• Conduct final assessment with FACT Inspection Checklist
• Obtain final approval of the QM Plan
Common Questions

• “Where do we begin?
  - Identify what you already have
  - Follow the order of the Standards
• How do we integrate with:
  - “Main institution’s QM Plan?”
  - “Distinct facilities?”
The Quality Management Plan shall provide:

1. Sufficient summarization of the elements of the Quality Management Program

2. Reference to applicable policies and procedures
A Procedure for preparation, approval, implementation, review, and revising all procedures

A standardized format for policies and procedures, including worksheets, reports, and forms

### Purpose
Establish a standardized method of creating, approving, implementing, cataloguing, maintaining, reviewing, and revising policies and procedures.

### Scope
All Cellular Therapy Product Institute personnel.

### Implementation

#### A. Policies
- Policies must be written in a standard format (see Template PDM-1):
  1. Document type
  2. Subject category
  3. Policy Number (See Procedure 2.1.1)
  4. Policy Name
  5. Date of implementation
  6. Issuer name
  7. Responsible party
  8. Revision Number
  9. Date of most recent review

#### B. Text Heading
- Purpose (required)
- Scope (required)
- Definitions (optional)
- Policy (required)
- References (required)

#### C. Footer
  1. Page number
  2. Signature of QM Supervisor and Program Director

A system of numbering and/or titling of individual procedures, policies, worksheets, and forms
Critical Processes, Policies, and Procedures

• Each critical process, policy, and procedure remains accurate, operational, and relevant
  • Development
  • Approval
  • Validation
  • Implementation
  • Review
  • Revision
  • Archival
Document Control

• Critical documents used in the manufacturing process are current and protected

• Similar to process control, but specific to documents
  • SOPs
  • Worksheets
  • Forms
  • Labels

• Make sure the specific types of documents are listed in the QM Plan!
<table>
<thead>
<tr>
<th>Role</th>
<th>Responsibilities</th>
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<tr>
<td>Director</td>
<td>• Authority over and responsibility for ensuring that the QM Program is effectively established and maintained.</td>
</tr>
<tr>
<td>Quality Manager</td>
<td>• Responsible for establishing, maintaining, and reporting on activities and performance of the QM Program</td>
</tr>
<tr>
<td>All Personnel</td>
<td>• Responsible for participating in the QM Program</td>
</tr>
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</table>
Organizational Chart and Description of Interactions

• Integration, cohesiveness, and objectivity throughout the entire life cycle of a cellular therapy product or cord blood unit

• Break down barriers
  • Physical space
  • Functions
  • Timing and chain of custody
  • Leadership
  • Third parties
  • Conflicts of interest
Quality Management Program Meetings

- Clinical Program
- Collection Facility
- Other Services
- Cell Processing Laboratory
Personnel Requirements

Position-specific Requirements
- Qualifications
- Job description

Training
- Orientation
- Training plan

Continued Assessment
- Competency
- Continuing education
Personnel

• Documentation of personnel qualifications and ownership of processes
• Investments in personnel that increase quality:
  • Education
  • Self-improvement
  • Empowerment
  • Job satisfaction
Written Agreements

- Third parties whose services impact the cellular therapy product or cord blood unit understand and comply with requirements
  - Reference Standards in agreements
  - Does not include suppliers (use vendor qualification)
  - Only applies to agreements that impact products or units
  - Include general description of process if no written agreements are currently used – commonly cited!
Outcome Analysis

• Therapeutic outcomes can indicate the quality of a cellular therapy program’s processes.

• Use the data to analyze the *entire* program:
  • Analyze the data on an ongoing basis
  • Share the analysis with all aspects of the program or bank
  • Required and suggested criteria for product efficacy/clinical outcome in applicable Standards and Accreditation Manuals
  • Entities only involved with collection and/or processing must make genuine effort to obtain the data from clinical programs
Outcome Analysis

• Collection of Patient Outcome Data
• Evaluation of Data
• Distribution of Data
• Reanalyze

For more information on Outcome Analysis, please see several educational opportunities available in the FACT store at www.factwebsite.org/store.
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<th>Audit</th>
<th>Validation</th>
<th>Qualification</th>
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<tr>
<td><strong>Definition:</strong></td>
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<td>Documented, systematic evaluation to determine whether approved policies or procedures have been properly implemented and are being followed.</td>
<td>Confirmation by examination and provision of objective evidence that particular requirements can consistently be fulfilled.</td>
<td>The establishment of confidence that equipment and reagents function consistently within established limits.</td>
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<td><strong>Example:</strong></td>
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<td>Audit of documentation of proper donor eligibility and determination.</td>
<td>Review viability and sterility of products prior to processing to validate the effectiveness of the apheresis procedure.</td>
<td>Prospective qualification of new controlled rate freezer to confirm the freezing program meets predetermined freezing parameters.</td>
</tr>
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</table>
Performance vs Outcome Metrics

- Performance metrics: measure how personnel comply with policies and procedures, for example:
  - Completion of all donor evaluation steps
  - Inclusion of all requirements on chemotherapy order
  - Regular standardization and calibration of processing equipment

- Outcome metrics: measure success of therapy, for example:
  - Days to engraftment
  - Length of hospital stay
  - Survival
Positive Microbial Culture Results

• A major role of a Quality Management Plan is to assess regulatory affairs and ensure requirements are met
• One of the concerns of the US FDA is the use of products with positive microbial cultures
  • Will not be allowed for licensed products, but could be allowed for products under IND
  • Must notify the recipient and all facilities of the positive culture, an investigation is completed, and the incident is reported to the regulatory authority
  • Requires extensive teamwork between collection sites, processing facilities, cord blood banks (if applicable), and clinical programs
Errors, Accidents, Adverse Events, Biological Product Deviations, & Complaints
Information & Document Control

- Process for product tracking
- Actions to take when operations are interrupted
Tracking and Tracing

- Enable investigation of issues, document chain of custody, and maintain information needed for further action
  - Tracking: to follow a process from beginning to end
  - Tracing: to follow the history of a process, product, or service by review of documents
Continuous Operations

• Be prepared for situations that may interrupt typical operations
  • Policy or procedure is required that addresses emergencies and disasters
  • Programs must also have a plan for the management of interruptions that do not rise to the disaster level
• Program is required to describe actions to take when an interruption presents, including:
  • Who needs to be contacted
  • How to prioritize cases
  • Key personnel to be involved in identifying alternative steps to continue functions
Case Study: Investigation of Poor Engraftment

Results

• Collection procedure validated to achieve target cell counts at time of implementation

Validation Study

• Apheresis machine undergoes Operational Qualification (OQ) to ensure it is still functioning appropriately

Qualification

• Personnel compliance with collection procedure audited to ensure all necessary steps are followed

Audit

Clinical Program reports outcome analysis results: poor engraftment likely due to low cell counts

Audit identified noncompliance with collection procedure
Case Study: Clinical Program Infection Control

Personnel
Capable and empowered to generate new ideas to improve current processes related to infection control

Processes
Thoroughly developed, reviewed, and documented to be effective at preventing infection

Documents
Protected and controlled to always instruct personnel to follow current infection control procedures – not outdated ones!
Thank You