



PLASMA PROTEIN
THERAPEUTICS
ASSOCIATION



INTERNATIONAL QUALITY
PLASMA PROGRAM

IQPP Certification Program Description

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Version 3.0

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1. Program Overview

1.1 Vision and Mission

PPTA's Voluntary Standards Program (VSP) provides global leadership for the plasma protein industry's goal of continuous improvement with a focus on safety and quality from the donor to the patient. The VSP will be transparent, credible, innovative, and responsive to stakeholder and industry needs.

1.2 Background

People around the world depend on therapies derived from human plasma proteins to treat bleeding disorders, primary immune deficiencies, Alpha-1 antitrypsin disease and certain neurological conditions. Plasma protein therapies are also used in emergency and surgical medicine. People who use these therapies and other immunoglobulins manufactured from human plasma rely on the generous donations made by committed individuals.

Safety of plasma protein therapies is the top priority of the plasma fractionation industry. The Plasma Protein Therapeutics Association (PPTA), on behalf of its industry members, supports efforts by regulatory authorities to establish minimum requirements to ensure the safety of these products.

PPTA has adopted voluntary standards that go beyond regulatory requirements and help define the regulations as they apply to plasma collection for further manufacture. These standards are in addition to formal regulatory requirements and are intended to promote the safety and quality of plasma protein therapies. The International Quality Plasma Protein (IQPP) voluntary standards were established to address collection, processing and testing of Source Plasma.

The IQPP program provides independent, third-party evaluation and recognition of a plasma center's adherence to global industry standards for Source Plasma collection. An independent, third-party auditor evaluates the center's adherence to the IQPP Standards. A center is certified only if it meets all of the requirements.

1.3 Control of the Program

Control of IQPP certification is important to maintain the quality and consistency of the certification program. Control and standardization of certification are achieved through four primary mechanisms:

- Adherence to established procedures for developing the IQPP Standards and related documents;
- Adherence to an established certification process;
- Qualified auditors; and
- Periodic audits with established provisions for timely correction of any deficiencies.

1.4 The Standards

The IQPP standards are developed in accordance with the PPTA Voluntary Standards Program Policies and Procedures.

2. Certification Process

IQPP certification provides recognition by PPTA that a center adheres to the IQPP VSP. Certification is based on the findings of an independent auditor's assessment of the center and its policies and procedures.

2.1 Eligibility

Certification is available to plasma collection centers worldwide that have been licensed by a competent national regulatory authority inspecting establishments based on, for example, FDA's Compliance Program Guidance Manual 7342.002 or PIC/S Guide to Inspection PI008-1. Centers in a country lacking a competent national regulatory authority are eligible for certification after they show that they have been inspected by an independent authority which has confirmed that the center meets the requirements of the PIC/S Guide to Inspection PI008-1.

The center shall be fully operational. There may be no current governmental regulatory restraints or sanctions from normal collection operations. Government actions resulting in the voluntary or involuntary discontinuation of collection and/or plasma release will result in withdrawal of IQPP certification. The center is not eligible to be re-certified until government approval to resume is obtained

2.2 General Rules

The following general rules apply to the IQPP certification process:

- PPTA must receive completed application form and payment for all applicable fees before any audits are scheduled.
- As new standards are developed, compliance will be confirmed at the next regularly scheduled audit following the implementation of the new Standard.
- Changes to the IQPP certification process, the IQPP Standards or the auditor qualifications are made under the procedures for change control, which require Global Plasma Board, IQPP Standards Working Group and/or PPTA management approval, as applicable.

3. Audits and Audit Reports

3.1 Types of Audits and Audit Frequencies

The IQPP Certification Program conducts four types of audits:

1. Center Audits - conducted for the purpose of initial certification or renewal of a center's certification/recertification. These audits are performed on a one to three-year cycle, determined by the outcome of the audit.

The initial IQPP certification date is based on the information provided on the initial application. Retroactive certification of this facility to the start-up date is requested or IQPP Certification is retroactive to the application receipt date.

2. Corporate Audits - conducted for the purpose of reviewing corporate policies and procedures in reference to the IQPP Standards. For companies with a separate corporate office from which policies and procedures regarding center operations are generated, the Corporate Audit will be performed. The Corporate audit may be performed on-site or as a desk audit (virtually), at the Company's discretion. These audits are performed on a six-month to two-year cycle, determined by the outcome of the audit.
3. Combined (Corporate/Center) Audits - conducted for the purpose of reviewing corporate and center policies and procedures in reference to the IQPP Standards and certification of the center. For companies that do not have a separate corporate office, the Corporate Audit will take place at a designated center and will be combined with the Center Audit. These audits are performed on a six month to two-year cycle, determined by the outcome of the audit.

4. Issue-Driven Audits – All centers may be subject to an issue-driven audit. These audits may occur at any time for the following reasons:
- a) center is placed on the Viral Marker Alert List,
 - b) center changes owners,
 - c) center relocates,
 - d) center receives an FDA Warning Letter, or
 - e) at PPTA’s discretion due to prior poor audit, formal complaints, etc.

3.2 Audit Process

The following figure provides an overview of the IQPP audit process.

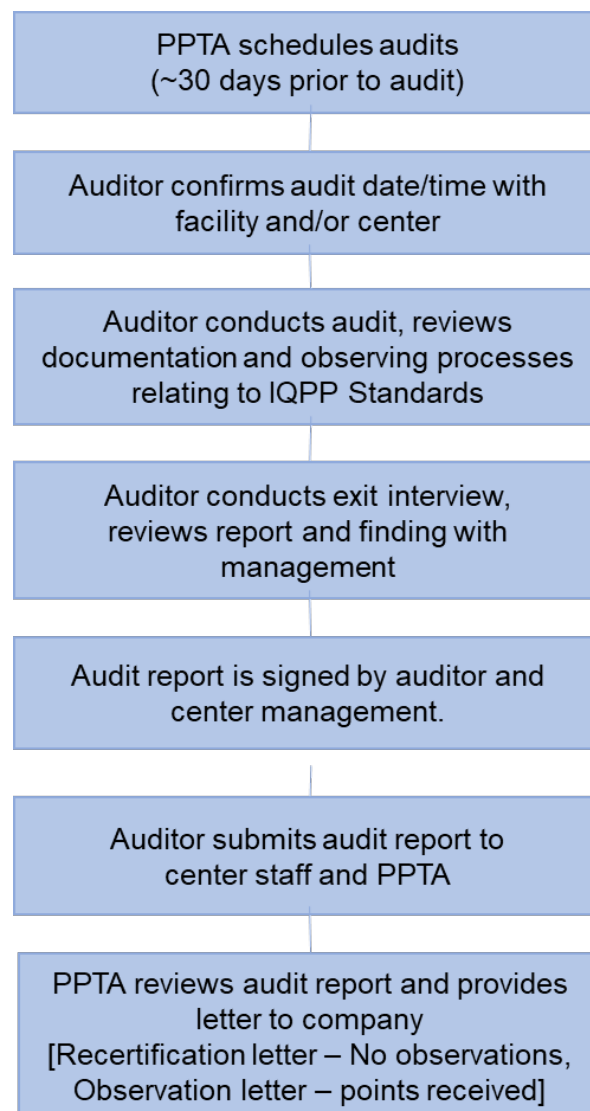


Figure 1, IQPP Audit Process

During the audit, the auditor will review documentation and observe the processes that occur at the center relating to the standards. The auditor will use the IQPP audit checklist to assess a center's compliance with the standards. At the conclusion of the audit, the auditor will review the IQPP audit checklist with the center's management. The auditor's report of the audit will then be sent to the PPTA IQPP Audit Manager for review.

3.3 Audit Findings / Certification Terms

IQPP audits are graded on an observation ranking system. All questions are assigned an observation level. Should a facility/center fail to comply with any question or questions on the audit checklist, the points associated with that question will be assigned and the final score will impact when the next audit will be scheduled to take place.

- Critical Observations are scored 50 points each.
- Major Observations are scored 10 points each.
- Minor Observations are scored 2 points each.

The following scoring guidelines will be used:

- 0 - 20 points - Next IQPP audit will take place in three (3) years.
- 21 - 50 points - Next IQPP audit will take place in two (2) years.
- 51 points or more - Issue-driven audit will take place in less than two years. The timing of the issue-driven audit will be determined at the discretion of PPTA staff in consultation with the auditor. The timing will be based on the nature of the audit observation(s) and the nature of the center or company's proposal for addressing the observation(s).

3.4 Auditor Recommendations

Based on the audit findings, an auditor's report to PPTA will result in one of three types of recommendations:

- For Certification/Recertification - the facility demonstrates compliance with the IQPP Standards.
- For Certification/Recertification, pending resolution of issues -- the facility demonstrates a need for improvement in its implementation of some aspects of the IQPP Standards.
- Recommend Re-audit within - the company or center demonstrates significant non-compliance with IQPP Standards.

3.5 Evaluation of Audit Reports

The IQPP Audit Manager reviews all audit reports and determines the validity of the auditors' observations. Figure 2 describes the review process for evaluating audit results.

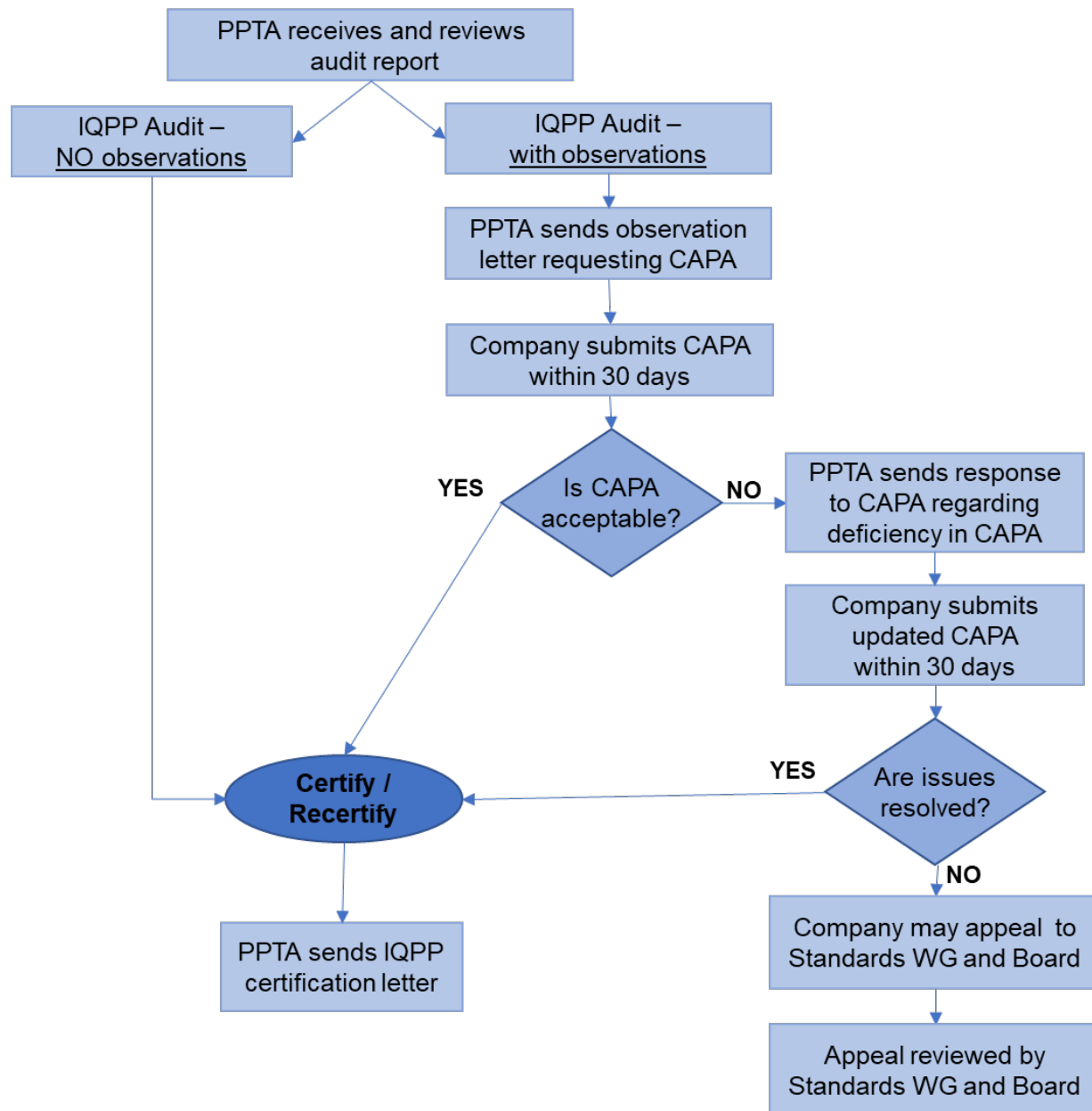


Figure 2, Process for Evaluating Audit Results

Following review and approval by PPTA, the outcome of the audit is communicated in writing to the company based on the auditor recommendations:

- “For Certification/Recertification” - a certification/recertification letter is issued.
- “Certification/Recertification, pending resolution of issues” - the Company is provided the opportunity to develop a Corrective and Preventative Action (CAPA) plan to correct the identified deficiencies. CAPA responses shall be submitted to PPTA no later than 30 days after receipt of the notification letter.
- “Recommend Re-audit within __days” - PPTA shall conduct an Issue-Driven Audit to assure the CAPAs were implemented and effective.

3.6 Corrective and Preventive Action Plan

PPTA will communicate to the Company in writing when a facility receives an audit recommendation of “Certification/Recertification, pending resolution of issues” or “Recommend Re-audit within __days. The Company will provide a Corrective and Preventive Action (CAPA) Plan to correct the identified deficiencies. CAPA responses shall be submitted to PPTA no later than 30 days after receipt of the notification letter.

Review of certification status may be escalated to the IQPP Standards Working Group by the IQPP Audit Manager in any situation where CAPAs to audit findings are not adequately resolved within 60 days of the center or company receiving the IQPP audit report.

3.7 Conflict Resolution

In the event a company does not agree with an audit report and PPTA review of that report, the company may enter into a dispute resolution process and appeal the decision to the IQPP Standards Working Group and Global Plasma Board of Directors.

3.7.1 Acceptable Bases for an Appeal

The following are accepted for appealing audit observation(s):

- a. One or more observations are factually inaccurate or incorrect; or
- b. The facility’s procedures, processes and/or practices do in fact meet the requirements of the standard.

The following are not acceptable bases for an appeal:

- a. The merits of an adopted PPTA Standard; or
- b. The findings of the PPTA Global Plasma Board under this provision.

3.7.2 Appeal Review

The IQPP Standards working group will consider each circumstance individually; identifying information will be blinded. Standards working group may uphold the company position, recommend acceptable CAPAs, or review the appropriate Standard for its applicability or interpretation. The company has 30 days to notify PPTA and to provide evidence that it has

made corrective and preventive action or that the company disputes the decision of the IQPP Standards Working Group. If so, the dispute is escalated to the PPTA Global Plasma Board.

3.7.3 Board Review

The Global Plasma Board shall review a dispute in a hearing. The hearing shall take place no later than 60 days after it receives an appeal notification or no later than 60 days after a dispute is escalated by the IQPP Standards Working Group. The company presenting the dispute shall have the right to present its argument to the Global Plasma Board during the hearing. All presentation materials shall be submitted to the Association at least ten (10) working days in advance of the hearing.

If the Global Plasma Board does not uphold the company position, the company has 15 days to provide evidence that it has corrected the observation or the IQPP certification will be revoked.

4. Independent Auditors

4.1 Auditor Qualifications

The PPTA auditor is essential to the IQPP certification process. Minimum qualifications for IQPP auditors are:

- Advanced degree from an accredited college or university, preferably in a scientific or engineering discipline;
- Minimum three years auditing experience, preferably in the pharmaceutical, biologics, or the blood/plasma industry;
- Professional certification by a recognized certifying organization is required (e.g., ASQ, ISO). These may include ISO Lead Assessor, Examiner for the National Baldrige Award, or a state award equivalent, certification by the Regulatory Affairs Professional Society.

4.2 Confidentiality and Conflict of Interest Agreements

As part of their agreement to perform IQPP audits on behalf of PPTA, auditors are required to execute a Confidentiality Agreement and a Conflict-of-Interest Agreement. These agreements specifically prevent the auditor from communicating, disclosing, or retaining copies of confidential information. The auditor is authorized to review documents and records associated with the IQPP Standards only. The auditor is also required to disclose any existing or potential conflict of interest to PPTA that may arise during the term of the auditor's consultancy.

4.3 Auditor Training

Prior to becoming a PPTA auditor, candidates shall receive training in the following:

- The IQPP VSP,
- The audit process,
- Documentation of audits.

PPTA will convene training workshops for auditors. These may be convened to introduce a new IQPP Standard or to ensure consistent interpretation of the current standards. These training programs will take place at a minimum of every other year. Attendance at these workshops is mandatory. Auditors are reimbursed for expenses incurred while participating in mandatory training, however they are not compensated for their time.

4.4 Auditor Continuing Education

To maintain one's qualification as an IQPP auditor, each auditor shall participate in at least one continuing education event every two years. These events may include:

- Industry or government workshops relevant to auditing, Quality Assurance, Quality Management, Good Manufacturing Practices, Validation, or government regulation;
- Completion of courses required for maintenance of a professional certification;
- Completion of one class at an additional advanced degree (Masters or Doctoral) level;

4.5 Auditor's Objectives

IQPP auditors have two very specific objectives:

- Assess a Company's adherence to the IQPP Standards and report this to the Association;
- Assist centers in interpretation of and adherence to the IQPP Standards, where appropriate.

5. Program Administration

Control and standardization of IQPP certification is important at the administrative level, as well as the audit level. Control and consistency at the administrative level is achieved through four primary mechanisms:

- a) a standardized administrative process;
- b) established rules which govern the administrative process;

- c) established authorities and responsibilities; and
- d) established procedures and document control system.

PPTA uses administrative procedures to manage certification programs. These procedures cover all aspects of administration of the IQPP Certification Program, from application to awarding of certification.

The following figure provides an overview of the process for coordinating audits.

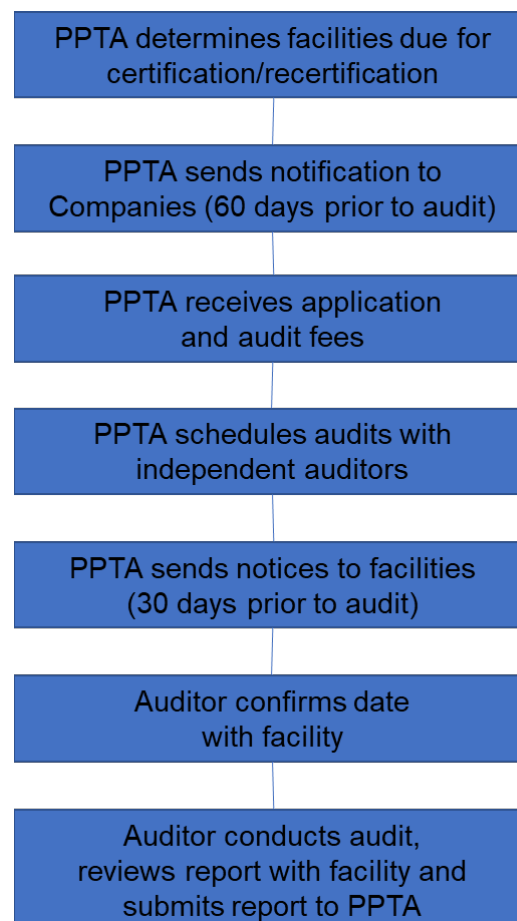


Figure 3, Process for Coordinating Audits

5.1 Center Relocation

For purposes of IQPP certification, a center is considered to be “relocated” when it moves from one physical address to another physical address and retains any portion of the Donor Recruitment Area that had been defined for the previous address, and the center retains the same FDA Registration number.

Companies shall notify the Association in writing of relocations at least 60 days prior to the date on which the center begins operation in its new location. The notification shall include:

- a. a completed Application for Recertification-Relocation Form,
- b. the new center address and contact information,
- c. the date on which the re-located center will begin operation,
- d. a statement that the center intends to continue to adhere to the requirements of the IQPP Standards, and
- e. a statement indicating whether the relocated center will retain any portion of the Donor Recruitment Area that had been defined for the center at its previous address.

A center that relocates will not be assigned a new PPTA ID number and will retain the certification anniversary date, and the history of viral marker data reported by the center at the previous address will be transferred to the re-located center for purposes of compliance with the IQPP VSP.

5.2 Center Move

A center that moves (relocates and does not retain any portion of the donor recruitment area of the center at its previous address) will be assigned a new PPTA ID number, and the history of viral marker data reported by the center at the previous address will not be transferred.

Companies shall notify the Association in writing of center moves at least 60 days prior to the date on which the center begins operation in its new location. The notification shall include:

- a. a completed Application for Certification,
- b. the new center address and contact information,
- c. the date on which the center will begin operation.

A center that moves will be subject to an IQPP Center Audit as soon as possible but no longer than three (3) months after that relocation, regardless of the certification anniversary date. Within 60 days of receipt of the notification, the Association shall schedule the audit; the audit shall not occur later than three months after the move.

The previous certification assigned to the center shall expire after the center has moved. Upon completion of a successful relocation audit, the center will be given a new certification anniversary date of the date on which the center began operation at its new location.

5.3 Company Mergers, Buy-outs, and Center Purchases

The company purchasing any IQPP-certified center(s) affected by company mergers, buy-outs or individual center purchases will be required to submit the PPTA Transition Plan to PPTA no

later than thirty (30) days prior to the sale is implemented, yet not until after the transaction has been made public. The PPTA ID number(s) and IQPP certification related to the center(s) will remain the same for centers that operate under the SOPs of member company as previously assigned and IQPP certification related to the center(s) will remain the same. Centers that open under new company ownership (non-member) may be assigned a new PPTA ID number and IQPP certification related to the center(s) will not be transferred.

PPTA may conduct a corporate audit, determined by PPTA with oversight by the IQPP Standards Working Group. A sampling of the centers affected may be subject to an IQPP audit should the SOPs change. Centers continuing to operate under the same SOPs will not be subject to a re-audit until the new SOPs are in place.

5.4 Center Closures

All IQPP-certified centers that cease operations for more than six (6) months and then reopen will be considered new centers and must follow the procedures outlined in Center Audits.

IQPP-certified centers that temporarily close (due to renovations, etc.) for a period of no longer than six (6) months may be subject to an issue-driven center audit within six (6) months of re-opening. IQPP-certified centers that temporarily close (due to renovations, etc.) for more than six (6) months will be required to apply for new IQPP certification.

If, however, the closure under these circumstances is due to regulatory censure the center shall be required to complete a successful issue-driven audit before recertification is granted.

5.5 Regulatory Censure

Should an IQPP-certified center undergo regulatory censure, (e.g., become subject to an FDA Consent Decree of Injunction or comparable regulatory action by another competent regulatory authority, be issued an FDA Warning Letter, or have their licensed revoked) IQPP status will be dealt with according to the following formula:

- Center closed.
- Consent Decree of Injunction or equivalent, or Warning Letter or equivalent; IQPP issue-driven audit will take place no later than 90 days subsequent to the company receiving a "cleared" status notification.

5.6 Government Regulatory Compliance

In the event that the center's government regulatory license is suspended or revoked, IQPP certification is automatically revoked.

If a center is issued an FDA warning letter or similar censure, or has its license revoked, the center or its parent shall communicate the action in writing to PPTA within three (3) working days.

5.7 Management Structure

Authority and responsibility for administrating the IQPP Certification Program is distributed in the management structure of the PPTA Global Plasma Division.

5.8 Governance Structure

The following governing bodies provide guidance for the IQPP Certification Program.

Governance Units	Comprised of	Responsibilities
Functional Working Group or Task Force	Member expert representatives or expert groups	Develop ideas for new standards; prepare drafts of new standards
Review Committee	IQPP Standards Working Group	Reviews issues appealed as a result of an IQPP audit; Reviews new standards and recommends standards to the Board
Board of Directors	PPTA Global Plasma	High-level policy and standards approval

5.9 Document Control

PPTA has a defined system for document control. Documents are numbered, indexed, and stored to provide traceability and easy retrieval. Confidential files are kept securely and archived after appropriate intervals.