



QSEAL Intermediates Purchased from an External Supplier Standard

**Version 2.0
Approved June 13, 2013**



Background

The QSEAL Intermediates Purchased from an External Supplier Standard is part of a series of standards that comprise the Plasma Protein Therapeutics Association (PPTA) QSEAL Standards Program. PPTA's Voluntary Standards Program 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.

This voluntary QSEAL Standard was developed by the PPTA QSEAL Standards Committee, and was approved by the PPTA Global Board of Directors on June 13, 2013. The current version of this standard supersedes the previous version in its entirety.

For questions about this PPTA Voluntary Standard contact QSEAL@pptaglobal.org. For more information about the QSEAL Standards Program or PPTA, visit www.pptaglobal.org.

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1. Introduction

Safety of plasma protein therapies is the top priority of the plasma fractionation industry. PPTA has adopted Voluntary Standards and other criteria that apply to the collection and fractionation of plasma for plasma protein therapies. 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 address collecting, processing and testing of Source Plasma. The Quality Standards of Excellence, Assurance and Leadership (QSEAL) program addresses the manufacture and fractionation of plasma protein therapies, regardless of the source of plasma. QSEAL certification provides recognition of a company's adherence to the voluntary standards to address product safety during the manufacture of life-saving plasma protein therapies.

This PPTA Voluntary standard is an industry initiative to further promote the consistency, quality and traceability of intermediate products being incorporated into final therapeutics by its member companies. While many of the elements described herein are required through current good manufacturing practice or through regulation, the standard significantly harmonizes processes and improves the traceability of the intermediate products, particularly those that are not subject to Competent Authority oversight throughout their production. The standard restricts products that may be of unverifiable or inconsistent quality or documentation from entering the manufacturing chain. For QSEAL certified manufacturers adherence to this standard will be verified through the QSEAL audit process.

2. Scope

This standard applies to the use of intermediates in manufacturing plasma protein therapies. The standard is not applicable to intermediates transferred between subsidiaries or other legal entities under a common corporate ownership.

This QSEAL Standard is not applicable for toll fractionation (i.e., where plasma from a specific country is only manufactured under contract into final products that are delivered for distribution in that country). If products (or intermediates used for manufacture of such products) are intended to be marketed outside the jurisdiction where the plasma was collected, this standard will apply.



3. REQUIREMENTS

3.1. THERE SHALL BE A CONTRACT BETWEEN EACH SUPPLIER AND EACH PURCHASER OF THE INTERMEDIATE THAT STIPULATES QUALITY REQUIREMENTS WHICH ARE FURTHER VERIFIED THROUGH INITIAL AND SUBSEQUENT REGULAR QUALITY ASSESSMENTS, E.G. AUDITS.

3.2. INTERMEDIATES SHALL BE MANUFACTURED FROM POOLS OF PLASMA THAT COMPLY WITH ALL APPLICABLE PPTA VOLUNTARY INDUSTRY STANDARDS/SPECIFICATIONS VALID AT THE TIME OF POOLING.

3.3. THE MANUFACTURER OF THE PLASMA POOL(S) MUST PROVIDE ADEQUATE DOCUMENTATION OF STARTING MATERIAL, E.G. THE PLASMA MASTER FILE, TO MEET THE REQUIREMENTS LAID DOWN IN ITEM 3.2 ABOVE.

3.4. THE CURRENT OWNER OF THE INTERMEDIATE SHALL DEMONSTRATE THAT THE PRIOR MANUFACTURING PROCESSES USED TO PRODUCE THE INTERMEDIATE ARE ABLE TO CONSISTENTLY PROVIDE INTERMEDIATES FULFILLING THE MUTUALLY AGREED SPECIFICATIONS. THIS SHALL BE CERTIFIED BY THE SUPPLIER AND VERIFIED THROUGH THE REGULAR QUALITY ASSESSMENT BY THE CURRENT OWNER OF THE INTERMEDIATE.

3.5. IF IN THE THERAPEUTIC PRODUCT LICENSE APPLICATION OR IN THE REGISTRATION DOSSIER A CLAIM WAS MADE FOR A VIRAL REMOVAL/INACTIVATION STEP DURING THE MANUFACTURING PROCESS OF THE INTERMEDIATE, THE CURRENT OWNER OF THE INTERMEDIATE SHALL ASSURE THAT THE CLAIM IS VALID.

3.6. THE CURRENT OWNER OF THE INTERMEDIATE SHALL HAVE A RECORD OF EACH PREVIOUS OWNER OF THE INTERMEDIATE WITH A LINK TO THE PREVIOUS PROCESSES OF THE INTERMEDIATE.

3.7. TEMPERATURE OF STORAGE AND SHIPPING OF THE INTERMEDIATE SHALL COMPLY WITH THE AGREED SPECIFICATIONS BETWEEN THE SUPPLIER AND THE BUYER AND SHALL BE CERTIFIED BY THE SUPPLIER FOR ALL PREVIOUS TRANSACTIONS AND CERTIFIED AND VERIFIED FOR THE MOST RECENT TRANSACTION.

3.8. EACH INTERMEDIATE SHALL BE ACCOMPANIED BY A RELEASE CERTIFICATE FROM THE MANUFACTURER'S QA/QC DEPARTMENT.

3.9. SAMPLES OF THE FIRST HOMOGENEOUS PLASMA POOL(S) SHALL ACCOMPANY THE PRODUCT AT EVERY TRANSFER OF OWNERSHIP AND THEIR



INCLUSION SHALL BE SPECIFIED WITHIN THE CONTRACT, UNLESS POOL TESTING CERTIFICATION IS ACCEPTED BY THE BUYER.

3.10. THE MANUFACTURER SHALL HAVE A SYSTEM IN PLACE TO ENSURE THAT, IF A SUPPLIER BECOMES AWARE OF A NOTIFIABLE EVENT, THE SUPPLIER SHALL INFORM THE MANUFACTURER OF THE NONCONFORMANCE AS SOON AS POSSIBLE BUT NOT TO EXCEED FIVE (5) WORKING DAYS.

THIS REPORTING REQUIREMENT SHALL BE FOLLOWED THROUGHOUT THE ENTIRE CHAIN OF MANUFACTURERS/OWNERS OF INTERMEDIATES UP TO THE FINAL THERAPEUTIC PRODUCT. CONFIRMATION OF RECEIPT OF NOTIFICATION BY THE NEXT OWNER SHALL BE RECEIVED BY THE NOTIFYING PARTY.

BACKUP INFORMATION TO SUPPORT A RISK ASSESSMENT SHALL BE PROVIDED AS REQUESTED.

3.11. MATERIAL SOLD FOR REAGENT USE ONLY SHALL BE LABELLED AS SUCH. ALL DOCUMENTATION SHALL REFERENCE THAT THE MATERIAL IS DEEMED FOR REAGENT USE ONLY AND THAT IT WILL NOT BE USED FOR MANUFACTURE OF THERAPEUTIC PRODUCTS.

3.12. THERE SHALL BE A MAXIMUM OF 3 TRANSACTIONS (NO MORE THAN 4 OWNERS) FROM THE PLASMA POOL TO THERAPEUTIC PRODUCT.

4. Definitions

4.1. Owner: Legal owner having physical possession of the intermediate.

4.2. Quality Assessment: Objective qualification, by a systematic approach, of the ability of the supplier of the intermediate to meet the requirements of the purchaser as defined by specifications.

4.3. First homogeneous plasma pool: As defined by the Eu. Ph. Monograph on Plasma for Fractionation. The first homogeneous plasma pool represents the quality control check point at which the quality of the plasma is approved for manufacture.

4.4. Intermediate: A plasma derived material which must undergo further manufacturing steps before it becomes a final therapeutic product.



4.5. Notifiable Event:

- a) Inclusion of a plasma unit from a donor with probable or confirmed vCJD or similar emergent pathogen-caused diseases transmitted by blood or plasma for which there is no test and no cure; or
- b) Inadvertent inclusion of any reactive unit in a plasma pool from which the intermediate was derived; or
- c) A manufacturing, transportation or storage event that would render the intermediate not meeting the requirements of the specifications.

NOTE: This standard will apply to any intermediates manufactured from plasma pools created subsequent to the implementation date of this standard.