

QUALITY STANDARDS OF EXCELLENCE, ASSURANCE AND LEADERSHIP

Public Review Draft 1, Proposed Revision to Version 2.0 of the QSEAL NAT Testing Standard

In accordance with the procedures for developing PPTA Voluntary Standards, this document is hereby issued for public review, from November 16, 2026 until January 15, 2027. This is a proposed revision to Version 2.0.

We encourage your early review and look forward to your feedback. Members of the public are asked to send your feedback to Matt Baalke at mbaalke@pptaglobal.org by January 15, 2027.

After the close of the comment period, all comments received in relation to the draft will be considered. If resolution to the comments results in substantive changes to the draft, another comment period may be initiated.

If resolution to the comments results in no or minor changes, the draft will be implemented as part of the QSEAL Voluntary Standards Program. Adequate notice will be provided prior to the implementation period for any PPTA Standard.

QSEAL NAT Testing Standard

QSEAL

Version 3.0

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.

The Nucleic Acid Amplification Technology (NAT) Testing Standard was established to decrease the possibility of viruses entering the first homogenous plasma pool. In particular, it allows for the detection of units reactive for Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), and Hepatitis A Virus (HAV); and any unit of plasma that would lead to a plasma pool exceeding 10^4 IU/ml of Parvovirus B19 (B19V) much earlier after an infection than serological testing technologies, thereby limiting the window period. Early detection increases safety by reducing the chance of viruses entering the first homogenous plasma pool. Furthermore, the potential viral load in all donations released is below the limit of detection of a sensitive NAT assay.

2. Scope

This standard applies to all units of plasma that are released for manufacturing, including both source and recovered plasma, regardless of whether toll fractionation or company-owned fractionation is being performed.

3. Requirements

3.1. Qualification of Donations

3.1.1. Before assembling the first homogenous plasma pool, Plasma donations shall be tested for viral nucleic acid of the target viruses, HIV, HBV, HCV, HAV and B19V using Nucleic acid Amplification Technology ("NAT").

Minipool testing for HIV, HBV, HCV and HAV shall be resolved to the individual donation, as shall any unit of plasma with a high titer that would lead to a plasma pool exceeding 10^4 IU/ml B19V.

3.1.2. The manufacturer shall ensure that ALL donations are tested for HIV, HBV, HCV, HAV and B19V using test kits licensed/approved by national and/or international regulatory authorities and have validated test assays in compliance with applicable national and/or international requirements.

Where testing is performed, or contracted to be performed, by either the manufacturer or collector, the manufacturer or collector shall report reactive results for HIV, HBV, HCV, HAV and any unit of plasma with a high titer that would lead to a plasma pool exceeding 10^4 IU/ml B19V to each other per an established written procedure and/or agreement.

3.1.3. No unit of plasma that receives a positive NAT test result for HIV, HBV, HCV or HAV, and no unit of plasma with a high titer that would lead to a plasma pool exceeding 10^4 IU/ml B19V, shall be used in manufacturing.

3.1.4. The plasma release facility should have a written, approved system whereby any such unit shall be destroyed or segregated from units that have not been tested or that have received negative test results.

3.2. Qualification of First Homogenous Plasma Pools

3.2.1. NAT testing for HIV, HCV, HBV, HAV and B19V shall be performed at the first homogenous plasma pool level using test kits licensed/approved by national and/or international regulatory authorities and have laboratory validated test assays in compliance with applicable national and/or international requirements.

3.2.2. If a first homogenous plasma pool NAT test is confirmed positive for HIV, HBV, HCV or HAV, the pool, or material derived from it, shall not be used in manufacturing and shall be destroyed or designated “not for human use.”

3.2.3. The manufacturer shall have in place a written, approved system to ensure that, as soon as possible, any such pool, or material derived from it, shall be destroyed or designated “not for human use”, e.g. manufacturing into reagent material.

3.2.4. If a first homogenous plasma pool exceeds 10^4 IU/ml for B19V, the pool, or material derived from it, shall not be used in manufacturing and shall be destroyed or designated “not for human use.”

3.2.5. The manufacturer shall have in place a written, approved system to ensure that, as soon as possible, any such pool, or material derived from it, shall be destroyed or designated “not for human use”, e.g. manufacturing into reagent material.

3.3. Laboratory Compliance

3.3.1. The testing laboratory shall have a system and features to assure compliance with the QSEAL NAT Testing Standard, including:

a. An active Good Manufacturing Practice (GMP) license issued by the National Competent Authority (NCA).
b. A Quality Management System based on GMP.
c. Systems and procedures to ensure that NAT specimen identity is retained at all times and that the specimens are stored at appropriate temperatures.
d. A written, approved training program including NAT training as appropriate.
e. Quality agreements and/or specifications are in place between the manufacturer and NAT testing laboratory.
f. A written, approved procedure to link each NAT result to its individual donation and donor. Manual data transfer processes should be avoided whenever possible (e.g. for positive test result reporting). Where manual transfer is necessary, it should be safeguarded through a four-eyes principle under GMP.
g. The minipooling process shall ensure that the identity of each individual donation in any pool is adequately documented.
h. There shall be written, approved specifications and procedures to ensure that minipools for NAT testing will retain traceability and will be kept at appropriate temperatures.
i. The manufacturer shall have in place a written, approved specification to report to the collector reactive results for HIV, HBV, HCV and HAV, and any unit of plasma with a high titer that would lead to a plasma pool exceeding 10^4 IU/ml of B19V.

3.3.2. There shall be written, approved specifications and procedures pertaining to an appropriate environment for pooling donation samples, which include provisions for unidirectional flow, segregation, and adequate & organized space.

3.3.3. There shall be written approved specifications in place to prevent, monitor and remedy cross contamination events.

3.3.4. Testing QC Measures

a. Test assays and working standards shall be calibrated against or traceable to an applicable international standard, when available, or other well-characterized, commonly accepted reagents.
b. There shall be a written, approved procedure that describes the Out-of-Specification (OOS) testing process when a laboratory test result falls outside the predefined acceptance criteria and shall follow applicable national and/or international requirements.
c. There shall be a reagent QC/monitoring program in place to include:
   - Traceability
   - Functional QC

- Specific reagent QC to address overall reagent quality

d. The testing laboratory shall participate in an external assessment, such as proficiency testing for HIV, HBV, HCV, HAV, B19V on a scheduled routine basis, in the last 3 years minimum.

3.3.5. Compliance with the quality elements of this standard should be verified with initial and regular internal and supplier quality assessments.

Revision History

Document	Description of Changes	Revision #	Date Approved

QSEAL NAT Testing Standard	**Introduction** • Added "*HAV and B19V*" where HIV, HBV, and HCV are referenced. **Scope** • Removed exemption from toll fractionation. • Added to include both source and recovered plasma, regardless of whether toll fractionation or company-owned fractionation is being performed. **3.1.1.** • Added "*HAV and B19V*" where HIV, HBV, and HCV are referenced. • Removed Note for testing of plasma donations for HAV and Parvovirus B19 as being encouraged. **3.1.2.** • Added "*HAV and B19V*" where HIV, HBV, and HCV are referenced. • Added reference to "*national and/or international regulatory authorities*". • Added "*applicable*" national and/"*or*" international requirements. • Added reference "*or contracted to be performed*" by "*either*" the manufacturer "*or collector*", the manufacturer "*or collector*". • Added reference "*results above manufacturer's single donation testing limit for B19V, ensuring ≤10^4 IU/ml of B19V in manufacturing pool,) to the collector each other per an established written procedure and/or agreement.*" • Removed section regarding where testing is performed by the plasma collector. **3.1.3.** • Separated from section 3.1.2. • Added "*B19V*". **3.1.4.** • Separated from section 3.1.2. • Added reference "*The plasma release facility should have a written, approved system whereby*". **3.2.1.** • Added "*HAV and B19V*" where HIV, HBV, and HCV are referenced. • Added reference "*test kits licensed/ approved by national and/or international regulatory authorities and have laboratory*". **3.2.2** • Removed and reassigned with new section 3.2.2. • Added "*and shall be destroyed or designated "not for human use."*. **3.2.3.** New section **3.2.4.** New section **3.2.5.**	3.0	11/02/2026

	• Replaced section 3.2.4. • Added "*as soon as possible*". • Removed reference "*first homogenous plasma pools do not exceed 104 IU/ml Parvovirus DNA.*" And "*that exceeds this limit shall be used in manufacturing*". • Added Any "*such*" pool, or material derived from it, "*shall be destroyed or designated "not for human use" e.g. manufacturing into reagent material.*". **3.3.** New Section **3.3.1.** New Section **3.3.2.** New Section **3.3.3.** New Section **3.3.4.** New Section **3.3.5.** New Section		