Public Review Draft 1, Proposed Revision to Version 4.1 of the IQPP Viral Marker Standard

November 9, 2021

In accordance with the procedures for developing PPTA Voluntary Standards, this document is hereby issued for a sixty-day public review, from November 9, 2021 until January 8, 2022. Members of the public are asked to **send any comments, using the enclosed comment form, to Sonia Balboni at sbalboni@pptaglobal.org, by January 8, 2022.**

We encourage your early review and feedback. After the close of the comment period, all comments received in relation to the proposed revision will be considered. All commenters will receive written notification of the resolution to their comment(s). If resolution to the comments results in substantive changes to the draft(s), another comment period may be initiated. If resolution to the comments results in no or minor changes, the draft(s) will be implemented as a revision to an IQPP standard. Adequate notice will be provided prior to the implementation period for any amendment.

Public Review Draft 1, Proposed Revision to Version 4.1 of theIQPP Viral Marker Standard

1. Introduction

The IQPP Viral Marker Standard ("Standard") is based on the industry wide Qualified Donor viral marker rates for HIV, HBV and HCV and on the plasma center number of collections. It includes viral marker confirmed positive donations by serology or NAT.

This Standard is part of a series of standards that comprise the PPTA IQPP Voluntary Standards Program. For more information about the program, visit www.pptaglobal.org.

2. Scope

This standard applies to facilities that collect Source Plasma.

3. Purpose

The purpose of this standard is to provide a quality control measure to ensure that plasma centers have viral marker rates that meet defined industry parameters. The standard serves as a guide for quality improvement assessment and improvement of the viral marker rate for donors within the catchment area of a center.

4. Requirements

4.1. Data Collection

4.1.1. All IQPP certified plasma centers ("centers") shall participate in the PPTA viral marker data collection program, using the IQPP Instructions for Viral Marker Data Reporting. Monthly serology and NAT viral marker test results and other information shall be submitted within three months after the bleed month. These data shall be submitted to PPTA by the 20th day of each month.

4.1.2. If viral marker data have not been reported to PPTA within 30 days of the due date, a letter shall be sent to the Corporate Board Member or Company Contact via expedited mail informing them that IQPP certification could be revoked if viral marker data are not reported within 72 hours.

4.1.3. The number of Qualified Donor confirmed positive viral marker test results by serology or NAT for HIV, HCV, HBV, and a composite of the three markers for each center shall be at or below the PPTA published Viral Marker Alert Limits (the "VM Alert Limit," see Appendix I).

4.2. SOPs and CAPA

4.2.1 All companies shall have a mechanism for compliance with the requirements in the standard and for training relevant staff in applying the mechanism.

4.2.2 All companies shall have a mechanism for developing CAPAs should the center exceed the Viral Marker Alert Limits. This mechanism shall include provisions for investigation, performance of root cause analysis, involvement of appropriate staff and records.

4.2.3 For centers undergoing a CAPA relating to compliance with the requirements in the Viral Marker Standard, relevant staff shall be given training relating to the CAPA.

4.3. Data Evaluation

4.3.1. See the timeline in Annex A. It describes the normal events in the data collection and standard administration process. Centers submit data to PPTA on a monthly basis in six-month intervals ("Data Collection Periods"). PPTA evaluates a center's six-month data in April and October of each year. The April evaluation covers the immediately preceding Data Collection Period of July 1 through December 31. The October evaluation covers the Data Collection Period from January 1 through June 30.

4.3.2. PPTA shall notify the corporate office of a center in writing if it is found that the center exceeded the VM Alert Limit during a six-month Data Collection Period. This notification shall occur no later than the last day of the month during which the data are evaluated (on April 30 or October 31). The company shall have 30 days from notification to submit a corrective and preventive action plan (CAPA) to PPTA. The center shall then demonstrate a viral marker rate at or below the VM Alert Limit during the next six-month Data Collection Period (the "CAPA Evaluation Period" identified in Annex A). If the rate is not demonstrated, then the center's IQPP certification will be revoked.

> NOTE: For new centers, data will be evaluated for the first Data Collection Period in which the center operates. However, if the center does not collect plasma for the full six months of that Data Collection Period, the center's IQPP certification will not be revoked if the center does not demonstrate the requisite viral marker rate during the applicable CAPA Evaluation Period.

4.3.3. If a center is on the alert list for a six-month Data Collection period, the center may request to implement a CAPA earlier than the CAPA Implementation Period prescribed in the timeline in Annex A. This early review will examine the center's viral marker data for any six-month period, as long as it begins on a date following the end of the Data Collection Period for which the center was most recently out-of-range. In order to initiate the early review, the center must send a written request, including its CAPA, to PPTA before the desired early review period begins.

In this circumstance, if the data submitted for a center for the alternate CAPA Evaluation Period are out of range, PPTA shall respond in writing with a revocation notice within ten

business days after the out-of-range center has submitted the full and correct set of data to PPTA for the given alternate CAPA Evaluation Period.

4.3.4 If a center is already on the alert list for one Data Collection Period, and it chooses not to request an early review of its CAPA, then the CAPA implementation period will take place according to the schedule indicated in the Annex A timeline. However, the center may still choose to ask PPTA to review the center's data for the CAPA Implementation Period early, as long as the company submits a request to PPTA in writing by the end of the CAPA Implementation Period.

In this circumstance, if the data submitted for a center for the given CAPA Implementation Period would result in a revocation of certification, PPTA shall respond in writing with a revocation notice within ten business days after the out-of-range center has submitted the full and correct set of data to PPTA for the given CAPA Implementation Period.

5. Viral Marker Rates

5.1. Viral Marker Alert Limits

The viral marker alert limits are based on Poisson distribution probability tables. These tables assess the relative probability of having a number of confirmed positive donors based on any given number of total donations and the industry wide average viral marker positivity rates for Qualified Donors. Thus, each center can be assessed with the same periodicity using its own collection volume. The use of probabilities as a standard setting tool permits fair comparisons of all centers regardless of the number of total collections for a given period. Appendix I contains the PPTA viral marker alert limits confirmed positive by serology & NAT for HCV, HIV and HBV. It also includes a composite table of the three markers.

5.2. Probability and Reference Rates

The Alert Limits are set at a probability of 0.01 for the viral marker rate standard composite and a probability of 0.005 for the individual viral markers. This means that a center would fall outside the Standard if it had more positive donors than would be expected 99% or 99.5% of the time for a center based on their number of donations for a given period. The actual number of positive donors that would put a center outside the Standard will depend on two factors: the number of donations at a center for a given period and the reference rate.

The reference rates are the overall industry average viral marker positivity rates that serve as the basis for establishing the VM Alert Limit tables. The industry viral marker prevalence for Qualified Donors measured during the data collection year of January through December 2000 is the basis for the standard for HCV and HIV. The industry viral marker prevalence for Qualified Donors measured during the data collection year of January through December 2001 is the basis for the standard for HBV. The composite is derived from the sum of the HIV, HCV and HBV reference rates.

6. Inspection

During the IQPP Corporate Audit, the auditor shall request the company's SOPs that relate to the Standard. They shall then review the procedures for compliance to the Standard.

6.2 During the IQPP Plasma Center Audit, the auditor shall confirm, through a six- month sample, that the data in the Donor Record file and the reactive data at the center are consistent with the Viral Marker data reported by the center.

> NOTE – For an initial certification audit, a full six-month sample of data may not be available.

If a center has been placed on the Viral Marker Alert List since the previous IQPP audit, the auditor shall confirm that there is a copy of the CAPA on file accessible at the center and that it has been implemented. The auditor shall review the plasma center's SOPs that relate to the Standard (if applicable) and ensure the center is following the SOPs.

7. Loss of Certification

7.1.1. If the out-of-range center does not demonstrate improvement in accordance with subclause 4.3, IQPP certification shall be revoked.

7.1.2. IQPP certification shall be revoked from any center exceeding acceptable limits at least three times in a three-year period.

7.1.3. IQPP certification may be revoked if data are not reported to PPTA within thirty (30) days of the due date, in accordance with Section 4.1 of this Standard.

7.1.4. If certification is revoked due to non-compliance with the requirements of this Standard, companies shall be informed of their rights to dispute the decision in accordance with the International Quality Plasma Program Certification Program Description.

8. Re-certification following Revocation or Voluntary Withdrawal

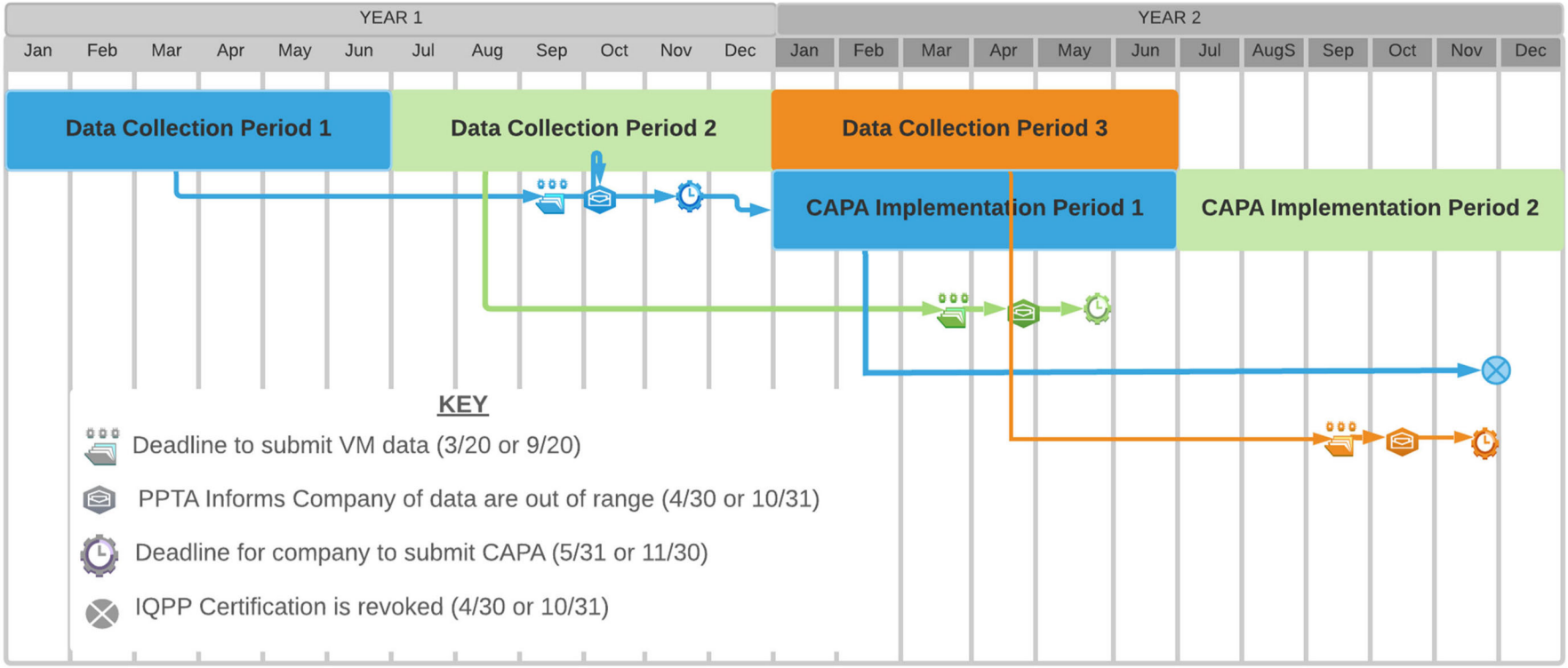
A center that has voluntarily withdrawn its certification or lost its certification due to non-compliance with the Standard may choose to apply for a new certification. In this case:

a) As part of its application, the center shall submit viral marker data collected during a six-month period that may begin as early as the day after the Data Collection Period that resulted in the center's losing its certification. The center must submit to PPTA a CAPA that was implemented at the beginning of the six-month period for which the center is providing recertification data. Viral marker data submitted as part of the application shall be at or below the VM Alert Limits;

b) The center shall undergo a successful IQPP audit before re-certification is granted; and

c) The beginning date for any re-certification granted will be retroactive to the date on which the previous certification was revoked, but may not exceed one year from the date of revocation.

ANNEX A
Timeline for Viral Marker Standard



APPENDIX I

PPTA Viral Marker Alert Limits
Virus type = Composite Confirmed Positives by Serology or NAT
(HBV, HCV and HIV combined)

Alert limits are based on observed qualified donor prevalence (reference rate) of 8 per 100,000 donations and will be applied for a given six-month period.

TOTAL NUMBER OF DONATIONS		MAXIMUM NUMBER OF CONFIRMED POSITIVE DONORS
FROM	TO	
0	1856	1
1857	5450	2
5451	10290	3
10291	15988	4
15989	22316	5
22317	29127	6
29128	36326	7
36327	43843	8
43844	51627	9
51628	59640	10
59641	67852	11
67853	76238	12
76239	84779	13
84780	93459	14
93460	102263	15
102264	111182	16
111183	120000	17

Last Revision: January 2003
Reviewed Annually

PPTA Viral Marker Alert Limits
Virus type = HCV Confirmed Positives by Serology or NAT

Alert limits are based on observed qualified donor prevalence (reference rate) of 4 per 100,000 donations and will be applied for a given six-month period.

TOTAL NUMBER OF DONATIONS		MAXIMUM NUMBER OF CONFIRMED POSITIVE DONORS
FROM	TO	
0	2699	1
2700	8799	2
8800	17699	3
17700	28499	4
28500	40799	5
40800	54199	6
54200	68599	7
68600	83699	8
83700	99399	9
99400	115699	10
115700	132499	11
132500	149599	12
149600	167199	13
167200	184999	14

Last Revision: January 2003
Reviewed Annually

PPTA Viral Marker Alert Limits
Virus type = HIV Confirmed Positives by Serology or NAT

Alert limits are based on observed qualified donor prevalence (reference rate) of 1 per 100,000 donations and will be applied for a given six-month period.

TOTAL NUMBER OF DONATIONS		MAXIMUM NUMBER OF CONFIRMED POSITIVE DONORS
FROM	TO	
0	10699	1
10,700	35199	2
35,200	70599	3
70,600	113899	4
113,900	162999	5

Last Revision: January 2003
Reviewed Annually

PPTA Viral Marker Alert Limits
Virus type = HBV Confirmed Positives by Serology or NAT

Alert limits are based on observed qualified donor prevalence (reference rate) of 3 per 100,000 donations and will be applied for a given six-month period.

TOTAL NUMBER OF DONATIONS		MAXIMUM NUMBER OF CONFIRMED POSITIVE DONORS
FROM	TO	
0	3449	1
3450	11262	2
11263	22406	3
22407	35930	4
35931	51230	5
51231	67911	6
67912	85703	7
85704	104413	8
104414	120000	9

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