Owner Group Name and Plasma Collection Center Address	Center Code/NDDR and Center Status	First and Last Collection Dates, Last Ship Date	QA Test Lab (Serology), Name, Address, and FDA License No	Audit by or on behalf of MA applicant	Inspections by competent Authority. Name and frequency	Certification by other organization (FDA/CLIA)
Talecris Plasma Resources, Inc. 3511-A Desiard St. Monroe, LA 71203	PMLA 0352 Active	6 /26/1998	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 5/1/2005 PPTA/IQPP: biennial German Auth: ** NRW German Insp: 7/18/2006	1757 19D0464163
Nabi Biopharmaceuticals 2301 N. University Dr., Ste 103 Pembroke Pines, FL 33024	PPFL 0596 Active	12/1 /1999	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 4/1/2005 PPTA/IQPP: biennial German Auth: ** HS German Insp: 3/22/2007	1687 10D0672151
PlasmaCare Enterprises 1221 London Blvd Portsmouth, VA 23704	PQVA (1) 0691 Inactive	1 /2 /2003 2 /28/2007 6 /20/2007	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 8/1/2005 PPTA/IQPP: biennial German Auth: ** NRW German Insp: 7/8/2005	1756 49D1006965
Talecris Plasma Resources, Inc. 1902 N. Sheridan Peoria, IL 61604	PRIL (1) 0694 Active	6 /26/1998	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 1/1/2007 PPTA/IQPP: biennial German Auth: ** NRW German Insp: 2/12/2007	1757 14D0896569
PlasmaCare Enterprises 1600 5th Av. Pittsburgh, PA 15219	PTPA (1) 0361 Inactive	6 /26/1998 2 /28/2007 6 /18/2007	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 1/1/2007 PPTA/IQPP: biennial German Auth: ** NRW German Insp: 4/13/2004	1756 39D0178225
Talecris Plasma Resources, Inc. 1211 7th Ave. Phenix City, AL 36867	PXAL 0462 Active	8 /9 /2005	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 10/1/2005 PPTA/IQPP: biennial German Auth: ** NRW German Insp: 4/5/2006	1757 01D1043152

[1] Center Status was changed during the year

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ZLB Bioplasma, Inc dba ZLB Plasma Services 1601 Washington Av., Ste. 200 Racine, WI 53403	RCWI 0588 Active	6 /26/1998	ZLB Bioplasma, Inc.-Knoxville Central Testing Laboratory 9320 Park West Blvd Knoxville, TN 37923 FDA Lic. No: 1639	Talecris QO - Annual	FDA Insp: 8/1/2007 PPTA/IQPP: biennial German Auth: ** HS German Insp: 2/20/2007	1639 52D0672160
Talecris Plasma Resources, Inc. 502 5th St, SW Roanoke, VA 24016	RGVA 0365 Active	6 /26/1998	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 7/1/2005 PPTA/IQPP: biennial German Auth: ** NRW German Insp: 8/13/2007	1757 49D0231494
Advanced BioServices, LLC 19255 Vanowen St. Reseda, CA 91335	RSCA (1) 0535 Active	9 /10/2007	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 7/10/2006 PPTA/IQPP: biennial German Auth: ** EMEA German Insp: 3/1/2007	1714 05D0883848
Life Sera 423 Wakara Way, #208 Salt Lake City, UT 84108	SHUT 0547 Active	6 /26/1998	LifeSera Testing Laboratory 780 Park North Bl., #100 Clarkston, GA 30021 FDA Lic. No: 1730	Talecris QO - Annual	FDA Insp: 4/1/2006 PPTA/IQPP: biennial German Auth: ** HS German Insp: 6/23/2006	1730 46D0922251
Nabi Biopharmaceuticals 409 Adams Ave. Scranton, PA 18510	SJPA 0589 Active	8 /18/2003	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 11/1/2006 PPTA/IQPP: biennial German Auth: ** HS German Insp: 6/19/2006	1687 39D0672167
ZLB Bioplasma, Inc dba ZLB Plasma Services 3655 Fredericksburg Rd., #107 San Antonio, TX 78201	SNTX 0632 Active	6 /26/1998	ZLB Bioplasma, Inc.-Knoxville Central Testing Laboratory 9320 Park West Blvd Knoxville, TN 37923 FDA Lic. No: 1639	Talecris QO - Annual	FDA Insp: 2/1/2006 PPTA/IQPP: biennial German Auth: ** HS German Insp: 3/21/2007	1639 45D0670035

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ZLB Bioplasma, Inc dba ZLB Plasma Services 2978 S. State St. S. Salt Lake City, UT 84115	SYUT 0427 Active	6 /26/1998	ZLB Bioplasma, Inc.-Knoxville Central Testing Laboratory 9320 Park West Blvd Knoxville, TN 37923 FDA Lic. No: 1639	Talecris QO - Annual	FDA Insp: 9/1/2003 PPTA/IQPP: biennial German Auth: ** HS German Insp: 8/1/2006	1639 46D0862929
Nabi Biopharmaceuticals 711 Broadway St. San Antonio, TX 78215	SZTX 0394 Active	1 /1 /2002	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 6/1/2006 PPTA/IQPP: biennial German Auth: ** HS German Insp: 8/18/2006	1687 45D0862926
Talecris Plasma Resources, Inc. 3201 10th Ave., Ste E Tuscaloosa, AL 35401	TCAL 0784 Active	7 /14/2003	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 1/1/2006 PPTA/IQPP: biennial German Auth: ** NRW German Insp: 7/19/2006	1757 01D0682097
Talecris Plasma Resources, Inc. 230 Clayton St. Montgomery, AL 36104	TGAL 0814 Active	12/2 /2005	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 3/29/2007 PPTA/IQPP: biennial German Auth: ** N/A German Insp:	1757 01D1048402
ZLB Bioplasma, Inc dba ZLB Plasma Services 824 S. Cheyenne Av. Tulsa, OK 74119-1408	TLOK 0592 Active	6 /1 /1999	ZLB Bioplasma, Inc.-Knoxville Central Testing Laboratory 9320 Park West Blvd Knoxville, TN 37923 FDA Lic. No: 1639	Talecris QO - Annual	FDA Insp: 6/1/2005 PPTA/IQPP: biennial German Auth: ** HS German Insp: 7/11/2006	1639 37D0672172
International BioResources 1912 Civic Center Dr. N. Las Vegas, NV 89030	VGNV (1) 0373 Active	3 /19/2007 12/24/2005 2 /23/2006	ZLB Bioplasma, Inc.-Knoxville Central Testing Laboratory 9320 Park West Blvd Knoxville, TN 37923 FDA Lic. No: 1639	Talecris QO - Annual	FDA Insp: 5/1/2006 PPTA/IQPP: biennial German Auth: ** NRW German Insp: 11/8/2004	1655 29D1008463

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PlasmaCare Enterprises 3840 E. Main St. Whitehall, OH 43213	WHOH [1] 0803 Inactive	11/10/2004 2 /28/2007 6 /18/2007	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 11/1/2005 PPTA/IQPP: biennial German Auth: ** NRW German Insp: 4/7/2006	1756 36D1022167
Interstate Blood Bank, Inc. 665 Carey Ave. Wilkes-Barre, PA 18702	WPPA 0483 Active	10/4 /2005	Interstate Blood Bank, Inc.-Memphis 5700 Pleasant View Rd. Memphis, TN 38134 FDA Lic. No: 173	Talecris QO - Annual	FDA Insp: 4/1/07 PPTA/IQPP: biennial German Auth: ** NRW German Insp: 4/13/2006	444 39D0922008
Talecris Plasma Resources, Inc. 2770 Grand Ave. Waukegan, IL 60085	WUIL 0838 Active	10/25/2005	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 2/1/2004 PPTA/IQPP: biennial German Auth: ** NRW German Insp: 4/10/2006	1757 14D1007657
PlasmaCare Enterprises 1116 Main St. Cincinnati, OH 45202	WWOH [1] 0693 Inactive	6 /26/1998 2 /28/2007 4 /26/2007	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 5/1/2005 PPTA/IQPP: biennial German Auth: ** NRW German Insp: 4/19/2004	1756 36D0346026
PlasmaCare Enterprises 502 N. Capitol Av. Indianapolis, IN 46204	YAIN [1] 0339 Inactive	6 /26/1998 2 /28/2007 4 /29/2007	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 4/1/2006 PPTA/IQPP: biennial German Auth: ** NRW German Insp: 6/15/2006	1756 15D0353369
Nabi Biopharmaceuticals 444 Martin Luther King Bl. Youngstown, OH 44502	YTOH 0595 Active	6 /26/1998	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 1/1/2007 PPTA/IQPP: biennial German Auth: ** HS German Insp: 6/21/2006	1687 36D0672178

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ZLB Bioplasma, Inc dba ZLB Plasma Services 1000 E. Broadway Rd. Tempe, AZ 85282	YZAZ 0591 Active	9 /9 /1998	ZLB Bioplasma, Inc.-Knoxville Central Testing Laboratory 9320 Park West Blvd Knoxville, TN 37923 FDA Lic. No: 1639	Talecris QO - Annual	FDA Insp: 1/1/2005 PPTA/IQPP: biennial German Auth: ** HS German Insp: 3/22/2007	1639 03D0672170
ZLB Bioplasma, Inc dba ZLB Plasma Services 2701 Morgan Ave., Ste 400 Corpus Christi, TX 78405	ZCTX 0403 Active	3 /14/2005	ZLB Bioplasma, Inc.-Knoxville Central Testing Laboratory 9320 Park West Blvd Knoxville, TN 37923 FDA Lic. No: 1639	Talecris QO - Annual	FDA Insp: 11/1/2006 PPTA/IQPP: biennial German Auth: ** HS German Insp: 6/5/2007	1639 45D0862927
ZLB Bioplasma, Inc dba ZLB Plasma Services 3815 Rossville Blvd. Chattanooga, TN 37407	ZHTN 0307 Active	6 /27/2005	ZLB Bioplasma, Inc.-Knoxville Central Testing Laboratory 9320 Park West Blvd Knoxville, TN 37923 FDA Lic. No: 1639	Talecris QO - Annual	FDA Insp: 8/1/2004 PPTA/IQPP: biennial German Auth: ** HS German Insp: 6/23/2006	1639 44D0310207
ZLB Bioplasma, Inc dba ZLB Plasma Services 9621 E. Sprague Ave. Spokane, WA 99206	ZSWA 0422 Active	3 /14/2005	ZLB Bioplasma, Inc.-Knoxville Central Testing Laboratory 9320 Park West Blvd Knoxville, TN 37923 FDA Lic. No: 1639	Talecris QO - Annual	FDA Insp: 7/1/2005 PPTA/IQPP: biennial German Auth: ** HS German Insp: 6/22/2005	1639 50D0862935
ZLB Bioplasma, Inc dba ZLB Plasma Services 8725 Marbach Rd., # 275 San Antonio, TX 78227	ZXTX 0626 Active	6 /26/1998	ZLB Bioplasma, Inc.-Knoxville Central Testing Laboratory 9320 Park West Blvd Knoxville, TN 37923 FDA Lic. No: 1639	Talecris QO - Annual	FDA Insp: 4/1/2006 PPTA/IQPP: biennial German Auth: ** HS German Insp: 7/28/2006	1639 45D0669924
Talecris Plasma Resources, Inc. 2118 S. Zarzamora Blvd., Ste 448 San Antonio, TX 78207	ZZTX 0959 Active	2 /27/2006	South Texas Blood/Tissue Ctr 6211 IH 10 West San Antonio, TX 78201 FDA Lic. No: 0678-001	Talecris QO - Annual	FDA Insp: 5/14/2007 PPTA/IQPP: biennial German Auth: ** RP-D German Insp: 8/16/2007	1757 45D1051323
Centers: 108						

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Talecris Biotherapeutics, Inc. T.18.05-04
Clayton, NC

Product: Plasma

Procedure for Approval of Plasma Suppliers

Number of Pages
(including cover page)

3

Original is signed

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Name and Rank Date

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Name and Rank Date

Valid From: 21 Jun 2004

Routine Actions Taken For Plasma Suppliers Which Are To Be Approved:

- New plasma suppliers must go through the following sequence of events to be approved as a supplier of Source Plasma:
  - Upon notification by Plasma Operations, Quality Operations (QO) will schedule and perform an inspection for approval of the physical facilities, procedures, and records prior to acceptance of plasma.
  - Suppliers found to be unacceptable during inspection for approval will be brought to the immediate attention of Plasma Operations and Quality Management. If agreement between the unacceptable supplier, Plasma Operations and Quality is reached for the actions to be taken to correct the discrepancies, the supplier may then be approved. A follow-up inspection may be required before approval.
  - Quality Operations will obtain and retain on file a copy of the following documents:
    - US FDA Establishment and Product License
    - US FDA approval letters to collect hyperimmune plasma if applicable
    - CLIA certification[1]
    - PPTA international Quality Plasma Program (iQPP) certification[2]
    - Viral marker data submitted by the plasma collection facility
  - Suppliers may have to meet additional criteria specified to meet certain national authority requirements (e.g. EU Competent Authority Approval).
  - Approved suppliers will be added to the Supplier Quality Information Database that contains the list of plasma centers.

Routine Actions Taken For Plasma Suppliers Which Are On The Approved List:

- All plasma centers will be audited annually unless the overall conclusion of the previous audit requires an early re-audit, or if the center meets the criteria for an extended audit interval as described as follows:
  - Extended Audit Frequency - Plasma center audits may be scheduled by the Audit Manager not more than twenty-four months from the previous audit if the following criteria are satisfied:
    - Quality systems at the corporate office have been audited and are found to be in compliance.
    - The center has a history (NLT 2 consecutive years) of satisfactory compliance.
    - There have been no major changes in management, quality systems, processes or SOPs.

[1] CLIA is the Clinical Laboratory Improvement Amendments enforced by the U.S Department of Health and Human Services, Health Care Finance Administration (HCFA).

[2] PPTA is a plasma industry association that has established an international Quality Plasma Program with specific criteria for compliance and performance which all plasma centers must meet.

    - The center has a history (NLT 2 consecutive years) of supplying satisfactory product.
- If during a Plasma Operations and/or Quality inspection, a previously approved supplier is considered unacceptable due to lack of adherence to procedures and/or Federal Regulations, Plasma Operations and Quality will evaluate the discrepancies. If agreement between Plasma Operations, Quality, and the supplier cannot provide corrective action suitable to Plasma Operations and Quality, the approved list will be amended to delete the supplier until acceptable.
- Plasma centers must be regularly inspected and found acceptable by the US FDA.
    - US FDA suspensions, license revocations, and unlicensed or unaccredited plasma centers will result in the supplier being deleted from the approved list.
- Plasma centers must be inspected and certified every two years by PPTA to maintain iQPP certification.
    - Each plasma center must submit viral marker data for evaluation and continuation of iQPP certification.
- Plasma centers must be inspected and found acceptable by HCFA every two years to maintain CLIA certification.
- Plasma centers must be inspected and found acceptable by other federal, state, local, or international authorities where required.
    - An EU competent authority must regularly inspect and approve plasma centers supplying Source Plasma for further manufacture into plasma-derivatives to be marketed in Europe.
- The plasma manufacturing plant will be notified of supplier status changes.

Product: Plasma

Remuneration of Donors

Plasmapheresis donor remuneration is widely accepted in the United States, which is the country of collection for all plasma supplied to Talecris. Plasmapheresis donors receive a nominal reimbursement that covers travel expenses, time at the collection center and other inconvenience costs incurred while participating in the plasmapheresis program. The reimbursement is made directly to the donor by the plasmapheresis centers. The average amount of this reimbursement in the United States plasma collection industry is 25 to 30 US dollars per unit of normal Source Plasma. Donors have the option of directing the reimbursement for specific causes such as child's savings, family vacation or for community or charitable purposes.

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Name and Rank Date

Valid from: 23 Jun 2005

Plasma Donor

Epidemiology at the Plasmapheresis Centers

Number of Pages
(including cover page)

33

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Name and Rank Date

Valid from: 14 Dec 2007

Table of Contents

1. PPTA Viral Marker Standard

The Viral Marker Standard for Source Plasma collection in the United States is part of the international Quality Plasma Program (iQPP) administered by PPTA. The standard is designed to provide a mechanism to ensure that plasmapheresis centers are not collecting from a high-risk population for bloodborne infections.

All iQPP certified facilities must participate in the PPTA Viral Marker Standard program. Each center must submit viral marker data to PPTA on a monthly schedule where it is compiled and analyzed every six months for adherence to the current standard. All iQPP certified centers must have qualified viral marker rates for HBV, HIV, HCV and a composite of the three markers at or below the PPTA source's viral marker alert limits to maintain their iQPP certification.

The viral marker alert limits are based on the observed qualified donor prevalence rate and Poisson Distribution that describes the probabilities of random occurrences. The iQPP Viral Marker Standards are presented in the tables that assess the relative probability of any number of confirmed positive qualified donors based on the number of total donations at each center. This approach enables each center to be assessed with the same periodicity using its own plasma donation volume. The use of probabilities as a standard setting tool allows comparisons of all plasmapheresis centers regardless of the number of total donations for a given time period.

The PPTA viral marker alert limits for HBV, HIV, HCV and a composite of the three markers are provided in Tables 1 through 4. The PPTA has set the viral marker alert limits based on the number of confirmed positive qualified donors (not applicant donors) since only plasma from qualified donors is used during the manufacture of final container product. Currently, there are no PPTA standards for applicant donors. The alert limits are set at a probability of 0.005 for the individual viral markers and 0.01 for the viral marker rate standard composite. The alert limits mean that a center would fail to meet the established standard if it had more positive donors than would be expected at 99.5 or 99% confidence (individual and composite rates respectively) based on the number of donations for a given period of time.

If a plasmapheresis center exceeds the viral marker alert limits PPTA has established, PPTA will notify the center of its status. The center has 30 days following notification to submit a corrective action plan. The center will have six months following submission of their corrective action plan to demonstrate viral marker rates below the standard.

2. Viral Marker Data Collection by Plasmapheresis Center

Appendix A contains a summary of the viral marker rates for each plasma center by owner group for both applicant and qualified donors for the year 2006. The following viral marker data is provided.

- Talecris assigned plasma center code
- Total donations collected
- Total applicant donors
- Confirmed positive applicant donors
- Confirmed positive qualified donors
- Confirmed positive applicant donors per total applicant donors
- Confirmed positive qualified donors per 100,000 donations

For each viral marker test, data are provided for both confirmed positive applicant and qualified donors.

3. Incidence of Confirmed Positive Seroconversions in Donors

The viral marker test data provided for each plasmapheresis center includes the number of confirmed positive donations and the incident rate calculations for each viral marker for both applicant and qualified donors.

The first calculation indicates the number of confirmed positive applicant donors per total applicant donors at each plasma center for the indicated marker. The calculation is performed as follows.

(# confirmed positive applicant donors / # total applicant donors)

The second calculation indicates the number of confirmed positive qualified donors per 100,000 donations at each plasma center for the indicated marker. The calculation is performed as follows.

(# confirmed positive qualified donors / # total donations) x 100,000

During 2006 all plasma centers demonstrated acceptable performance. A systematic monthly review of the serological and NAT test results was conducted to ensure an adequate selection of donors with respect to infection risk. The summary of epidemiology data is presented in Appendix A. In addition, for all iQPP certified plasma centers, serology data obtained for qualified donors is presented in 6-month intervals to show that these centers are in compliance with the iQPP Standards. Appendix B provides details on parameter values relating to the qualified donor estimated infection rates. According to PPTA Guidelines, the plasma centers exceeding the Viral Marker Alert Limit will have six months following submission of CAPA, to demonstrate a viral marker

rate below the Alert Limit, before the potential withdrawal of the iQPP Certification. In all cases presented in this report, plasma centers were able to comply.

4. Estimation of Residual Risk

Results from the 2006 epidemiology data analysis show that the risk of major bloodborne infectious diseases among qualified plasma donors to Talecris is currently at a very low level. All plasmapheresis centers supplying plasma to Talecris have acceptable viral marker rates according to the PPTA Viral Marker Standards and maintain iQPP certification current.

Incidence and risk of transfusion-transmitted infections is monitored for all plasma centers to decrease the risk of post transfusion infections.

The risk of transfusion-transmitted infection (or "residual risk") refers to the chance that an infected donation escapes detection because of a laboratory test's window period (i.e., the time between infection and detection of the virus by that test). The probability of residual contamination of a unit of plasma after testing was determined by using the incidence/window period model, which is based on the incidence of infection in qualified donors and the window period for each laboratory test. The viral markers evaluated were HIV, HCV and HBV.

After a person has been infected with HIV, HCV or HBV, there is a Window Period (WP) before which Serology or NAT testing will record a positive result. Residual risk (RR) is the probability that a particular donated unit of plasma has been donated during the WP. Viral Infection Rate (IR) is also a factor in determining RR. The formula for calculating RR is as follows:

$$RR = IR \times WP$$

Probability Rates for bloodborne pathogens were calculated based on 4,428,892 total plasma donations collected in 2006 from qualified donors at centers supplying plasma to Talecris. The NAT window period was taken from previously published sources.[1,2,3] The HBV WP from presumed infectivity was estimated at 49 days.[3] Window periods for HIV was estimated at 9 days, for HCV at 7.4 days.[4]

Infection rate values presented in the table below are estimated based on the Talecris analysis of monthly viral marker data supplied by the approved plasma centers in 2006. HIV, HCV and HBV infection rates are very low and equal 1.17, 5.2 and 1.74,

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[1] Glynn, Kleinman, Wright and Busch, 2002, "International Application of the Incidence Rate/Window Period Model", Transfusion, V42: 967-72.

[2] M.Bush, S.Glynne, S.Stramer et al. 2005. "A new strategy for estimated risks of transfusion-transmitted viral infections" Transfusion Vol 45: 254-263.

[3] G. Schreiber 2006. Global Epidemiology. International Plasma Protein Congress, 2006 Prague.

[4] B.Wang, M.J.Higgins, S.Kleinman et al. Transfusion, 2004, Vol 44 :1243-1251.

respectively. Residual Risk of infectious unit not to be detected by the approved assays during the assay window period is 0.029 for HIV, 0.0105 for HCV and 0.23 for HBV. These numbers correspond very well with the reference rates estimated by PPTA based on the overall industry averages for the US Source Plasma qualified donors.

Table 1 - Residual Risk from Qualified Donors

	Positive Test Results	NAT Window Period (days)	Infection Rate per 100,000 Donations	Residual Risk per 100,000 Donations	Residual Risk per 100,000 Donations. PPTA Source[a]
HIV	52	9	1.17	0.029	0.083
HCV	229	7.4	5.2	0.0105	0.195
HBV	67	49	1.74	0.23	0.136
[a] G. Schreiber 2006. Global Epidemiology. International Plasma Protein Congress, 2006 Prague					

Based on a production pool of 4750 units, the probability of any given production pool including an infected unit that has been donated in the window period is calculated in the table below. The assumption made is that there is a constant IR and random distribution of positive viral tests.

There is a very low estimated probability of a potentially infectious unit entering the plasma manufacturing pool. The residual risk was calculated before the viral inactivation steps. Viral inactivation and removal steps introduced into the manufacturing process substantially minimize the residual risk in final plasma derived products.

Table 2 - Probability of Production Pool Infection

NAT/Serological Test	Probability of Production Pool Infection
HIV	0.0013
HCV	0.0049
HBV	0.0109

PPTA Viral Marker Alert Limits

Table 3 - Virus Type = HBV[5] Confirmed Positives by Serology

Total Number Of Donations		Maximum Number Of 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

Table 4 - Virus type = HIV[6] Confirmed Positives by Serology

Total Number Of Donations		Maximum Number Of Positive Donors
From	To	
0	10699	1
10700	35199	2
35200	70599	3
70600	113899	4
113900	162999	5

[5] 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.

[6] 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.

PPTA Viral Marker Alert Limits

Table 5 - Virus type = HCV[7] Confirmed Positives by Serology

Total Number Of Donations		Maximum Number Of 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

[7] 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.

PPTA Viral Marker Alert Limits

Table 6 - Virus type = Composite[8] Confirmed Positives by Serology (HBV, HCV and HIV combined)

Total Number Of Donations		Maximum Number Of 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

[8] 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.

APPENDIX A

Epidemiology Data Report for First Time Donors - VMT Data for 2006

ABSK		HIV			HCV			HBV		
Assigned Plasma Center Code	Total No. of Donors tested in the given period (A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
		HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
JHTN	1428	3	0	210.08	51	4	3851.54	1	0	70.03
RSCA	1284	4	1	389.41	20	0	1557.63	0	0	0.00
Total	2712	7	1	294.99	71	4	2765.49	1	0	36.87

Epidemiology Data Report for First Time Donors - VMT Data for 2006

BLPS		HIV			HCV			HBV		
Assigned Plasma Center Code	Total No. of Donors tested in the given period (A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
		HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
BBAL	278	1	0	359.71	8	0	2877.70	2	0	719.42
FRND	2419	1	0	41.34	2	0	82.68	0	0	0.00
FYAR	1795	2	0	111.42	19	0	1058.50	0	0	0.00
JSMS	1017	4	0	393.31	17	0	1671.58	1	1	196.66
MLAL	114	0	0	0.00	3	0	2631.58	0	0	0.00
ODTX	555	0	0	0.00	2	0	360.36	0	0	0.00
Total	6178	8	0	129.49	51	0	825.51	3	1	64.75

Epidemiology Data Report for First Time Donors - VMT Data for 2006

DCI		HIV			HCV			HBV		
Assigned Plasma Center Code	Total No. of Donors tested in the given period (A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
		HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
BGKY	591	0	0	0.00	10	1	1861.25	0	0	0.00
BNTX	1018	0	0	0.00	5	0	491.16	0	0	0.00
CDIL	936	3	0	320.51	7	1	854.70	1	0	106.84
CJTX	946	2	0	211.42	3	0	317.12	0	0	0.00
DIMN	908	1	0	110.13	5	0	550.66	1	0	110.13
FSAZ	794	2	0	251.89	7	0	881.61	0	0	0.00
GINC	1043	4	0	383.51	11	0	1054.65	1	0	95.88
JEFL	1081	2	0	185.01	19	0	1757.63	8	0	740.06
LUTX	2348	0	0	0.00	28	2	1277.68	5	0	212.95
PLME	531	0	0	0.00	7	0	1318.27	0	0	0.00
TKAR	1058	3	0	283.55	31	0	2930.06	4	0	378.07
WGNC	970	1	0	103.09	36	2	3917.53	3	0	309.28
Total	12224	18	0	147.25	169	6	1431.61	23	0	188.15

Epidemiology Data Report for First Time Donors - VMT Data for 2006

IBBI		HIV			HCV			HBV		
Assigned Plasma Center Code	Total No. of Donors tested in the given period (A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
		HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
ASNC	980	0	0	0.00	25	0	2551.02	0	0	0.00
IMMO	1100	0	0	0.00	10	0	909.09	0	0	0.00
ITTN	805	1	0	124.22	9	0	1118.01	0	0	0.00
JNTN	1470	1	0	68.03	21	0	1428.57	4	0	272.11
JQTN	1953	2	0	102.41	51	3	2764.98	2	0	102.41
KVTN	1010	0	0	0.00	29	1	2970.30	1	0	99.01
MVMI	1126	0	0	0.00	10	0	888.10	0	0	0.00
MZWI	1222	1	0	81.83	8	0	654.66	2	0	163.67
OKKY	859	0	0	0.00	13	0	1513.39	1	0	116.41
WPPA	879	1	0	113.77	24	1	2844.14	3	0	341.30
Total	11404	6	0	52.61	200	5	1797.61	13	0	114.00

Epidemiology Data Report for First Time Donors - VMT Data for 2006

IBR		HIV			HCV			HBV		
Assigned Plasma Center Code	Total No. of Donors tested in the given period (A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
		HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
FWTX	1846	1	0	54.17	42	0	2275.19	1	0	54.17
Total	1846	1	0	54.17	42	0	2275.19	1	0	54.17

Epidemiology Data Report for First Time Donors - VMT Data for 2006

LSER		HIV			HCV			HBV		
Assigned Plasma Center Code	Total No. of Donors tested in the given period (A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
		HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
COSC	1643	2	0	121.73	8	0	486.91	0	0	0.00
CSSC	1957	2	0	102.20	13	0	664.28	2	0	102.20
CTNC	1602	4	0	249.69	13	0	811.49	0	0	0.00
JPFL	1325	3	0	226.42	22	1	1735.85	0	0	0.00
MBAL	1317	2	0	151.86	16	0	1214.88	0	0	0.00
MTLA	734	4	0	544.96	7	0	953.68	4	0	544.96
PEFL	2207	2	0	90.62	10	1	498.41	0	0	0.00
SHUT	1798	0	0	0.00	1	0	55.62	0	0	0.00
Total	12583	19	0	151.00	90	2	731.15	6	0	47.68

Epidemiology Data Report for First Time Donors - VMT Data for 2006

NABI		HIV			HCV			HBV		
Assigned Plasma Center Code	Total No. of Donors tested in the given period (A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
		HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
FMFL	1439	2	0	138.99	57	0	3961.08	2	0	138.99
GVFL	1349	3	0	222.39	27	1	2075.61	3	0	222.39
JANC	2372	1	0	42.16	14	0	590.22	2	0	84.32
LNNE	2254	1	0	44.37	35	0	1552.80	3	0	133.10
NRVA	2609	11	0	421.62	57	0	2184.75	4	0	153.32
PPFL	2029	5	0	246.43	51	1	2562.84	6	0	295.71
SJPA	1118	1	0	89.45	36	0	3220.04	0	0	0.00
SZTX	3248	3	0	92.36	51	0	1570.20	6	0	184.73
YTOH	1457	2	0	137.27	39	1	2745.37	1	0	68.63
Total	17875	29	0	162.24	367	3	2069.93	27	0	151.05

Epidemiology Data Report for First Time Donors - VMT Data for 2006

PLCR		HIV			HCV			HBV		
Assigned Plasma Center Code	Total No. of Donors tested in the given period (A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
		HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
CZOH	1302	2	0	153.61	50	0	3840.25	4	0	307.22
HHAL	715	5	0	699.30	33	2	4895.10	5	0	699.30
HPVA	706	2	0	283.29	15	1	2266.29	1	1	283.29
JTIL	512	3	0	585.94	14	0	2734.38	3	0	585.94
MHIN	1804	7	0	388.03	23	0	1274.94	2	0	110.86
MKPA	495	0	0	0.00	20	2	4444.44	2	0	404.04
MYWI	1954	6	0	307.06	41	1	2149.44	5	0	255.89
PIOH	1225	0	0	0.00	17	2	1551.02	5	0	408.16
PQVA	814	4	0	491.40	18	0	2211.30	3	0	368.55
PTPA	1328	6	0	451.81	39	0	2936.75	0	0	0.00
WHOH	1334	1	1	149.93	21	1	1649.18	1	0	74.96
WWOH	1338	4	0	298.95	40	6	3437.97	1	1	149.48
YAIN	1835	7	1	435.97	45	1	2506.81	2	1	163.49
Total	15362	47	2	318.97	376	16	2551.75	34	3	240.85

Epidemiology Data Report for First Time Donors - VMT Data for 2006

TPRE		HIV			HCV			HBV		
Assigned Plasma Center Code	Total No. of Donors tested in the given period (A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
		HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
ADIN	1733	1	0	57.70	25	0	1442.59	0	0	0.00
AFGA	1189	3	0	252.31	16	0	1345.67	5	0	420.52
BRLA	2132	3	0	140.71	44	0	2063.79	6	0	281.43
DWTX	504	0	0	0.00	0	0	0.00	0	0	0.00
EATX	1987	0	0	0.00	21	2	1157.52	2	0	100.65
EBTX	562	0	0	0.00	6	0	1067.62	2	0	355.87
EGOR	1999	0	0	0.00	29	0	1450.73	3	0	150.08
ELTX	2719	2	0	73.56	35	0	1287.24	0	0	0.00
FHTX	2057	0	0	0.00	44	0	2139.04	2	0	97.23
GLAZ	2282	3	0	131.46	33	0	1446.10	0	0	0.00
GOOR	1746	0	0	0.00	32	2	1947.31	1	0	57.27
IIWI	1280	1	0	78.13	5	0	390.63	4	0	312.50
KLTX	1294	0	0	0.00	0	0	0.00	0	0	0.00
KPCO	2405	1	0	41.58	28	0	1164.24	1	0	41.58
LDKY	1416	3	0	211.86	16	0	1129.94	2	0	141.24
LPTX	2430	0	0	0.00	26	1	1111.11	2	0	82.30
LQLA	2157	12	0	556.33	64	0	2967.08	4	0	185.44
OFOK	1154	1	0	86.66	25	0	2166.38	0	0	0.00
PCCO	1486	1	0	67.29	36	0	2422.61	0	0	0.00

Epidemiology Data Report for First Time Donors - VMT Data for 2006

TPRE		HIV			HCV			HBV		
Assigned Plasma Center Code	Total No. of Donors tested in the given period (A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
		HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
PMLA	2635	6	0	227.70	51	1	1973.43	8	0	303.61
PRIL	1224	2	0	163.40	18	1	1552.29	1	0	81.70
PXAL	2544	4	1	196.54	52	0	2044.03	6	0	235.85
RGVA	1957	2	0	102.20	48	0	2452.73	0	0	0.00
TCAL	2079	0	0	0.00	42	1	2068.30	1	0	48.10
TGAL	807	4	0	495.66	16	1	2106.57	2	0	247.83
WUIL	1336	2	0	149.70	27	0	2020.96	0	0	0.00
ZZTX	1047	1	0	95.51	36	0	3438.40	1	0	95.51
Total	46161	52	1	114.82	775	9	1698.40	53	0	114.82

Epidemiology Data Report for First Time Donors - VMT Data for 2006

ZLBP		HIV			HCV			HBV		
Assigned Plasma Center Code	Total No. of Donors tested in the given period (A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
		HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
ABTX	1460	0	0	0.00	48	1	3356.16	3	0	205.48
ALNM	2768	3	0	108.38	68	0	2456.65	1	0	36.13
AUCO	3574	11	0	307.78	104	0	2909.90	3	0	83.94
BXWI	1014	1	0	98.62	19	0	1873.77	0	0	0.00
CNTN	2074	2	0	96.43	17	0	819.67	2	0	96.43
CQNC	2904	9	0	309.92	97	0	3340.22	10	0	344.35
CRSC	1822	4	0	219.54	44	0	2414.93	3	0	164.65
DBTX	1919	8	0	416.88	70	0	3647.73	13	1	729.55
EZCO	2175	0	0	0.00	26	1	1241.38	1	0	45.98
FCCO	2565	0	0	0.00	23	0	896.69	1	0	38.99
GEOR	2971	2	0	67.32	58	2	2019.52	3	0	100.98
GPTX	2334	2	0	85.69	39	0	1670.95	5	0	214.22
KCMO	2651	5	0	188.61	54	0	2036.97	10	0	377.22
LEKY	1741	5	0	287.19	42	0	2412.41	2	1	172.31
LSMI	2462	0	0	0.00	40	1	1665.31	2	0	81.23
LWKS	1888	0	0	0.00	16	0	847.46	0	0	0.00
MDOR	1588	1	0	62.97	33	2	2204.03	1	0	62.97
MNKS	2344	0	0	0.00	7	0	298.63	0	0	0.00
MSTN	2376	5	0	210.44	40	0	1683.50	8	0	336.70

Epidemiology Data Report for First Time Donors - VMT Data for 2006

ZLBP		HIV			HCV			HBV		
Assigned Plasma Center Code	Total No. of Donors tested in the given period (A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
		HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
NMOK	2090	2	0	95.69	24	0	1148.33	6	0	287.08
OHNE	1245	1	0	80.32	25	0	2008.03	1	0	80.32
OPMI	2766	10	0	361.53	59	0	2133.04	13	0	469.99
OZOK	2462	6	0	243.70	62	0	2518.28	2	0	81.23
RCWI	1378	0	0	0.00	27	1	2031.93	1	0	72.57
SNTX	2165	2	0	92.38	52	0	2401.85	3	0	138.57
SYUT	3384	0	0	0.00	45	1	1359.34	4	0	118.20
TLOK	1693	3	0	177.20	61	2	3721.20	7	0	413.47
TSAZ	1470	0	0	0.00	41	0	2789.12	0	0	0.00
YZAZ	2515	0	0	0.00	45	0	1789.26	1	0	39.76
ZCTX	1483	4	0	269.72	66	0	4450.44	1	0	67.43
ZHTN	2545	2	0	78.59	68	0	2671.91	6	0	235.76
ZPWA	2677	1	0	37.36	61	0	2278.67	2	0	74.71
ZSWA	1892	1	0	52.85	18	0	951.37	0	0	0.00
ZXTX	2001	2	0	99.95	34	1	1749.13	2	0	99.95
Total	74396	92	0	123.66	1533	12	2076.72	117	2	159.95

APPENDIX B

Epidemiology Data Report for Repeat Donors - VMT Data for 2006

ABSK				HIV			HCV			HBV		
Assigned Plasma Center Code	No. of Donors tested in the given period (A)	No. of Donations in the given calendar year (B)	Donor Frequency (B/A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
				HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
JHTN	7,674	34201	4.46	0	2	26.06	0	27	351.84	0	0	0.00
RSCA	8,813	44087	5.00	0	0	0.00	0	0	0.00	0	0	0.00
Total	16,487	78288		0	2	12.13	0	27	163.77	0	0	0.00

Epidemiology Data Report for Repeat Donors - VMT Data for 2006

BLPS				HIV			HCV			HBV		
Assigned Plasma Center Code	No. of Donors tested in the given period (A)	No. of Donations in the given calendar year (B)	Donor Frequency (B/A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
				HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
BBAL	854	9846	11.53	0	0	0.00	0	0	0.00	0	0	0.00
FRND	3,673	60685	16.52	0	0	0.00	1	0	27.23	0	0	0.00
FYAR	2,345	37244	15.88	0	0	0.00	0	0	0.00	2	0	85.29
JSMS	500	29894	59.79	0	2	400.00	1	1	400.00	0	3	600.00
MLAL	209	1908	9.13	0	0	0.00	0	0	0.00	0	0	0.00
ODTX	1,387	50059	36.09	0	0	0.00	0	1	72.10	0	1	72.10
Total	8,968	189636		0	2	22.30	2	2	44.60	2	4	66.90

Epidemiology Data Report for Repeat Donors - VMT Data for 2006

DCI				HIV			HCV			HBV		
Assigned Plasma Center Code	No. of Donors tested in the given period (A)	No. of Donations in the given calendar year (B)	Donor Frequency (B/A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
				HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
BGKY	1,309	28138	21.50	0	0	0.00	0	2	152.79	0	0	0.00
BNTX	1,455	23924	16.44	0	0	0.00	0	0	0.00	0	0	0.00
CDIL	1,427	21690	15.20	0	0	0.00	0	0	0.00	0	0	0.00
CJTX	1,566	26932	17.20	0	0	0.00	0	0	0.00	0	0	0.00
DIMN	1,710	34757	20.33	0	0	0.00	0	1	58.48	0	0	0.00
FSAZ	1,198	18750	15.65	0	0	0.00	0	0	0.00	0	0	0.00
GINC	1,722	32689	18.98	0	0	0.00	0	0	0.00	0	1	58.07
JEFL	1,799	36192	20.12	2	1	166.76	1	2	166.76	0	0	0.00
LUTX	3,614	62808	17.38	0	0	0.00	0	1	27.67	0	0	0.00
PLME	953	23368	24.52	0	0	0.00	0	1	104.93	0	0	0.00
TKAR	1,749	35780	20.46	0	0	0.00	2	4	343.05	1	0	57.18
WGNC	1,275	22874	17.94	0	0	0.00	0	0	0.00	1	0	78.43
Total	19,777	367902		2	1	15.17	3	11	70.79	2	1	15.17

Epidemiology Data Report for Repeat Donors - VMT Data for 2006

IBBI				HIV			HCV			HBV		
Assigned Plasma Center Code	No. of Donors tested in the given period (A)	No. of Donations in the given calendar year (B)	Donor Frequency (B/A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
				HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
ASNC	1,358	18604	13.70	0	0	0.00	0	0	0.00	0	0	0.00
IMMO	1,443	14522	10.06	0	0	0.00	1	0	69.30	0	0	0.00
ITTN	1,055	5912	5.60	0	0	0.00	2	0	189.57	0	0	0.00
JNTN	2,010	25080	12.48	4	0	199.00	1	0	49.75	1	0	49.75
JQTN	2,550	26050	10.22	0	2	78.43	1	4	196.08	0	0	0.00
KVTN	1,320	13922	10.55	0	0	0.00	0	2	151.52	0	0	0.00
MVMI	1,551	20010	12.90	0	0	0.00	0	0	0.00	0	0	0.00
MZWI	1,656	19966	12.06	0	0	0.00	0	0	0.00	0	0	0.00
OKKY	1,144	12663	11.07	0	0	0.00	0	4	349.65	0	0	0.00
WPPA	1,266	20367	16.09	1	0	78.99	1	2	236.97	0	0	0.00
Total	15,353	177096		5	2	45.59	6	12	117.24	1	0	6.51

Epidemiology Data Report for Repeat Donors - VMT Data for 2006

IBR				HIV			HCV			HBV		
Assigned Plasma Center Code	No. of Donors tested in the given period (A)	No. of Donations in the given calendar year (B)	Donor Frequency (B/A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
				HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
FWTX	1,974	29707	15.05	0	0	0.00	0	3	151.98	0	1	50.66
Total	1,974	29707		0	0	0.00	0	3	151.98	0	1	50.66

Epidemiology Data Report for Repeat Donors - VMT Data for 2006

LSER				HIV			HCV			HBV		
Assigned Plasma Center Code	No. of Donors tested in the given period (A)	No. of Donations in the given calendar year (B)	Donor Frequency (B/A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
				HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
COSC	2,630	14828	5.64	0	0	0.00	0	0	0.00	0	0	0.00
CSSC	2,696	14780	5.48	0	0	0.00	0	0	0.00	0	0	0.00
CTNC	3,337	20188	6.05	0	0	0.00	0	1	29.97	0	0	0.00
JPFL	2,383	13734	5.76	0	0	0.00	2	0	83.93	0	0	0.00
MBAL	2,134	12793	5.99	0	0	0.00	0	0	0.00	0	0	0.00
MTLA	701	4530	6.46	0	0	0.00	1	0	142.65	0	0	0.00
PEFL	3,540	20093	5.68	0	0	0.00	0	0	0.00	0	0	0.00
SHUT	4,198	24547	5.85	0	0	0.00	0	0	0.00	0	0	0.00
Total	21,619	125493		0	0	0.00	3	1	18.50	0	0	0.00

Epidemiology Data Report for Repeat Donors - VMT Data for 2006

NABI				HIV			HCV			HBV		
Assigned Plasma Center Code	No. of Donors tested in the given period (A)	No. of Donations in the given calendar year (B)	Donor Frequency (B/A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
				HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
FMFL	2,133	28560	13.39	0	1	46.88	6	6	562.59	0	1	46.88
GVFL	2,553	48518	19.00	0	2	78.34	1	1	78.34	0	0	0.00
JANC	3,216	39196	12.19	0	0	0.00	0	0	0.00	0	0	0.00
LNNE	4,333	65172	15.04	1	0	23.08	3	4	161.55	2	1	69.24
NRVA	3,922	63797	16.27	1	1	50.99	3	4	178.48	1	0	25.50
PPFL	2,526	39443	15.61	0	0	0.00	3	3	237.53	1	0	39.59
SJPA	2,146	45214	21.07	0	0	0.00	7	7	652.38	0	0	0.00
SZTX	4,815	72712	15.10	0	1	20.77	7	2	186.92	3	0	62.31
YTOH	2,813	54731	19.46	0	1	35.55	6	5	391.04	0	0	0.00
Total	28,457	457343		2	6	28.11	36	32	238.96	7	2	31.63

Epidemiology Data Report for Repeat Donors - VMT Data for 2006

PLCR				HIV			HCV			HBV		
Assigned Plasma Center Code	No. of Donors tested in the given period (A)	No. of Donations in the given calendar year (B)	Donor Frequency (B/A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
				HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
CZOH	1,765	37823	21.43	0	0	0.00	2	2	226.63	0	0	0.00
HHAL	1,540	37113	24.10	1	1	129.87	0	1	64.94	2	1	194.81
HPVA	1,819	20110	11.06	0	0	0.00	0	0	0.00	0	2	109.95
JTIL	850	16564	19.49	0	0	0.00	0	0	0.00	0	0	0.00
MHIN	2,414	40029	16.58	0	0	0.00	0	4	165.70	0	1	41.43
MKPA	838	16470	19.65	0	0	0.00	0	0	0.00	0	0	0.00
MYWI	3,151	80346	25.50	0	0	0.00	0	0	0.00	1	1	63.47
PIOH	1,832	32517	17.75	0	0	0.00	0	1	54.59	1	2	163.76
PQVA	1,272	26981	21.21	1	0	78.62	0	4	314.47	0	2	157.23
PTPA	2,504	58201	23.24	0	1	39.94	0	4	159.74	1	1	79.87
WHOH	1,819	35473	19.50	0	0	0.00	0	3	164.93	0	0	0.00
WWOH	2,386	56947	23.87	0	1	41.91	0	3	125.73	3	4	293.38
YAIN	2,950	52935	17.94	2	1	101.69	2	0	67.80	0	1	33.90
Total	25,140	511509		4	4	31.82	4	22	103.42	8	15	91.49

Epidemiology Data Report for Repeat Donors - VMT Data for 2006

TPRE				HIV			HCV			HBV		
Assigned Plasma Center Code	No. of Donors tested in the given period (A)	No. of Donations in the given calendar year (B)	Donor Frequency (B/A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
				HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
ADIN	1,912	41649	21.78	0	0	0.00	0	0	0.00	0	1	52.30
AFGA	898	14435	16.07	0	1	111.36	0	0	0.00	0	1	111.36
BRLA	2,190	35227	16.09	1	0	45.66	0	3	136.99	1	0	45.66
DWTX	763	24777	32.47	0	0	0.00	0	1	131.06	0	0	0.00
EATX	2,140	48802	22.80	0	0	0.00	0	2	93.46	0	0	0.00
EBTX	461	12109	26.27	0	1	216.92	0	0	0.00	0	0	0.00
EGOR	2,230	45725	20.50	0	0	0.00	0	3	134.53	0	1	44.84
ELTX	2,907	83249	28.64	1	0	34.40	0	6	206.40	2	0	68.80
FHTX	1,882	35560	18.89	0	1	53.13	0	1	53.13	0	1	53.13
GLAZ	2,505	46493	18.56	0	0	0.00	0	2	79.84	1	0	39.92
GOOR	1,995	46049	23.08	0	0	0.00	1	2	150.38	0	0	0.00
IIWI	1,317	17924	13.61	0	0	0.00	0	0	0.00	0	1	75.93
KLTX	1,158	13974	12.07	0	0	0.00	0	0	0.00	0	0	0.00
KPCO	2,531	49375	19.51	0	0	0.00	0	2	79.02	1	1	79.02
LDKY	1,169	18704	16.00	0	0	0.00	0	2	171.09	0	0	0.00
LPTX	2,598	50788	19.55	0	0	0.00	1	2	115.47	0	0	0.00
LQLA	2,122	35922	16.93	0	0	0.00	0	5	235.63	1	0	47.13
OFOK	1,106	14861	13.44	0	0	0.00	0	1	90.42	1	0	90.42
PCCO	1,890	50588	26.77	0	0	0.00	0	0	0.00	1	0	52.91
PMLA	2,801	56640	20.22	1	1	71.40	0	1	35.70	3	1	142.81

Epidemiology Data Report for Repeat Donors - VMT Data for 2006

TPRE				HIV			HCV			HBV		
Assigned Plasma Center Code	No. of Donors tested in the given period (A)	No. of Donations in the given calendar year (B)	Donor Frequency (B/A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
				HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
PRIL	1,385	29875	21.57	0	0	0.00	0	0	0.00	0	0	0.00
PXAL	2,446	49230	20.13	1	1	81.77	0	2	81.77	1	2	122.65
RGVA	2,202	47063	21.37	1	0	45.41	1	3	181.65	1	2	136.24
TCAL	2,120	42759	20.17	0	1	47.17	0	3	141.51	0	0	0.00
TGAL	768	12103	15.76	0	0	0.00	0	0	0.00	4	0	520.83
WUIL	1,198	22897	19.11	0	0	0.00	0	1	83.47	0	0	0.00
ZZTX	832	16424	19.74	0	0	0.00	1	3	480.77	0	1	120.19
Total	47,526	963202		5	6	23.15	4	45	103.10	17	12	61.02

Epidemiology Data Report for Repeat Donors - VMT Data for 2006

ZLBP				HIV			HCV			HBV		
Assigned Plasma Center Code	No. of Donors tested in the given period (A)	No. of Donations in the given calendar year (B)	Donor Frequency (B/A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
				HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
ABTX	2,564	40066	15.63	0	0	0.00	6	11	663.03	1	0	39.00
ALNM	3,724	47284	12.70	1	0	26.85	8	4	322.23	0	0	0.00
AUCO	4,937	72601	14.71	2	0	40.51	8	2	202.55	2	0	40.51
BXWI	1,613	30176	18.71	1	0	62.00	1	0	62.00	1	0	62.00
CNTN	2,843	38499	13.54	0	0	0.00	4	1	175.87	0	0	0.00
CQNC	4,742	92058	19.41	1	1	42.18	9	2	231.97	1	1	42.18
CRSC	2,636	39345	14.93	1	0	37.94	5	0	189.68	0	1	37.94
DBTX	3,193	62390	19.54	3	3	187.91	3	2	156.59	1	0	31.32
EZCO	3,056	43166	14.13	0	0	0.00	3	1	130.89	0	0	0.00
FCCO	3,394	37781	11.13	0	0	0.00	0	0	0.00	0	0	0.00
GEOR	4,411	65988	14.96	0	0	0.00	5	5	226.71	1	2	68.01
GPTX	3,599	64276	17.86	0	0	0.00	4	0	111.14	0	0	0.00
KCMO	4,083	83366	20.42	2	1	73.48	5	2	171.44	1	1	48.98
LEKY	3,181	61352	19.29	0	0	0.00	1	0	31.44	2	1	94.31
LSMI	3,729	68202	18.29	0	1	26.82	3	3	160.90	1	0	26.82
LWKS	2,750	36232	13.18	0	0	0.00	2	1	109.09	1	0	36.36
MDOR	2,824	50131	17.75	0	0	0.00	7	2	318.70	0	1	35.41
MNKS	3,217	35729	11.11	1	0	31.08	0	0	0.00	0	0	0.00
MSTN	3,403	62048	18.23	1	2	88.16	3	1	117.54	1	1	58.77
NMOK	3,010	34697	11.53	0	0	0.00	3	2	166.11	2	0	66.45

Epidemiology Data Report for Repeat Donors - VMT Data for 2006

ZLBP				HIV			HCV			HBV		
Assigned Plasma Center Code	No. of Donors tested in the given period (A)	No. of Donations in the given calendar year (B)	Donor Frequency (B/A)	No. of Positive Donors		HIV Rate per 100,000 Donors (C+D)/A x 100,000	No. of Positive Donors		HCV Rate per 100,000 Donors (E+F)/A x 100,000	No. of Positive Donors		HBV Rate per 100,000 Donors (G+H)/A x 100,000
				HIV 1/2 Antibody (C)	HIV NAT Only (D)		HCV Antibody (E)	HCV NAT Only (F)		HBsAg (G)	HBV NAT Only (H)	
OHNE	2,773	53283	19.21	0	0	0.00	3	2	180.31	2	0	72.12
OPMI	4,349	84374	19.40	3	4	160.96	7	3	229.94	3	7	229.94
OZOK	4,301	81113	18.86	1	1	46.50	7	3	232.50	0	1	23.25
RCWI	2,163	45097	20.85	0	2	92.46	1	1	92.46	0	1	46.23
SNTX	3,726	70027	18.79	0	0	0.00	7	11	483.09	0	2	53.68
SYUT	4,800	77217	16.09	0	0	0.00	4	9	270.83	1	1	41.67
TLOK	2,658	44387	16.70	0	0	0.00	10	4	526.71	3	1	150.49
TSAZ	2,189	33190	15.16	0	0	0.00	0	4	182.73	1	0	45.68
YZAZ	3,725	52993	14.23	1	0	26.85	1	0	26.85	2	0	53.69
ZCTX	2,658	49271	18.54	1	1	75.24	10	3	489.09	2	0	75.24
ZHTN	3,823	49857	13.04	1	0	26.16	11	6	444.68	0	1	26.16
ZPWA	3,753	60068	16.01	0	0	0.00	6	2	213.16	1	1	53.29
ZSWA	2,899	48852	16.85	0	0	0.00	2	3	172.47	1	0	34.49
ZXTX	3,161	47580	15.05	0	1	31.64	4	3	221.45	0	0	0.00
Total	113,887	1862696		20	17	32.49	153	93	216.00	31	23	47.42

Talecris Biotherapeutics, Inc.
Clayton, NC

T.18.16-10US

Plasma Donor

Test Site(s)

Number of Pages
(including cover page)

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Original is signed

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Name and Rank Date

_____ _____

Name and Rank Date

Valid from: 28 Nov 2007

1. Test Sites

Tables 1 and 2 list the test laboratories that perform viral marker testing of individual donations and NAT testing of minipools of plasma donations. The Raleigh Test Laboratory (RTL) creates minipools and performs HBV, HCV, HIV-1 and Parvovirus B19 testing. National Genetics Institute (NGI) serves as an alternate test site for HCV, HIV-1, HBV and Parvovirus B19 testing of minipools.

Plasma test laboratories must be licensed by US FDA and CLIA (Clinical Laboratory Improvement Amendment)[1]. The laboratories are inspected on a routine basis by the US FDA. Audits of the test laboratories are performed annually by Quality Operations. The laboratories only use US FDA licensed test kits from US FDA licensed test kit manufacturers. Both the use of the test laboratories by a collection organization and the laboratories' use of US FDA licensed test kits are subject to review by Talecris.

2. Test Methods

Information on the test methods are presented in Chapter 2.2.2 *Testing of Plasma Donations and Pools for Infectious Agents*.

[1] The requirements set forth by CLIA require that laboratories performing moderate and high complexity tests on samples from plasma donors must be certified by the Health Care Finance Administration (HCFA), a part of the US Department of Health and Human Services. The test facilities are inspected on behalf of HCFA to determine compliance with the CLIA regulations.

Table 1 - Information on the Viral Marker Plasma Donation Testing Laboratories

Organization Responsible for Viral Marker Testing	Address	US FDA Approval Status		
		US FDA License Number	Inspection Date	Final Outcome
ZLB Bioplasma, Inc.	9320 Park West Blvd. Knoxville, TN 37923, USA	1639	Jan 2005	Satisfactory
BioLife Plasma Services, L.P.	BioLife Lab - Hoover 2197 Parkway Lake Dr. Hoover, AL 35244, USA	1640	Apr 2007	Satisfactory
Life Sera	780 Park North Blvd., #100 Clarkston, GA 30021, USA	1704	Mar 2007	Satisfactory
South Texas Blood and Tissue Center	South Texas Blood Bank 6211 IH 10 West San Antonio, TX 78201, USA	0678-001	Jan 2007	Satisfactory
Nabi Biopharmaceuticals	5900 Park of Commerce Blvd. NW Boca Raton, FL 33487, USA	1687	Aug 2005	Satisfactory
Interstate Blood Bank, Inc.	5700 Pleasant View Rd. Memphis, TN 38134, USA	173	Jan 2006	Satisfactory

Table 2 - Information on the Plasma Donation NAT Testing Laboratories

Organization Responsible for NAT Testing	Address	US FDA Approval Status		
		US FDA License Number	Inspection Date	Final Outcome
Talecris Raleigh Test Laboratory	1200 New Hope Rd. Raleigh, NC 27610, USA	1716	Mar 2006	Satisfactory
National Genetics Institute	2440 S. Sepulveda Blvd. Suite 130 Los Angeles, CA 90064, USA	1582	Aug 2005	Satisfactory

Plasma Pool

Test Site(s)

Number of Pages
(including cover page)

3

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Name and Rank Date

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Name and Rank Date

Valid from: 28 Nov 2007

1. Test Sites

All plasma manufacturing pools processed at the Clayton, NC fractionation facility are tested at sites under the control and license of Talecris. Tables 1 and 2 list the test laboratories and their inspection status. Plasma manufacturing pool viral marker testing is performed at the Clayton, NC fractionation facility while NAT testing is performed at the Raleigh Test Laboratory (Talecris four letter code RTTL).

National Genetics Institute serves as an alternate/back-up testing laboratory to perform HCV, HBV, HIV-1 and Parvovirus B19 NAT testing as necessary.

2. Test Methods and Validation

Information on the test methods and validation data are presented in Chapter 2.2.2 *Testing of Plasma Donations and Pools for Infectious Agents*.

Table 1 - Information on the Plasma Manufacturing Pool Test Laboratories

Address	US FDA Approval Status		
	US FDA License Number	Inspection Date	Final Outcome
Organization Responsible for Viral Marker Testing: Clayton Fractionation Facility			
Talecris Biotherapeutics, Inc. 8368 U.S. Hwy 70 West Clayton, NC 27520, USA	1716	Jan 2007	Satisfactory
Organization Responsible for NAT Testing: Raleigh Test Laboratory			
Talecris Biotherapeutics, Inc. Raleigh Test Laboratory 1200 New Hope Rd. Raleigh, NC 27610, USA	1716	Mar 2006	Satisfactory

Table 2 - Information on the Alternative/Back-Up NAT Plasma Manufacturing Pool Test Laboratory

Address	US FDA Approval Status		
	US FDA License Number	Inspection Date	Final Outcome
Organization Responsible for NAT Testing: National Genetics Institute			
2440 S. Sepulveda Blvd. Suite 130 Los Angeles, CA 90064, USA	1582	Aug 2005	Satisfactory

Plasma Donor

Qualification of Donor

Donor Qualification, Examination and Interview

Number of Pages
(including cover page)

3

Original is signed

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Name and Rank Date

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Name and Rank Date

Valid from: 30 Jun 2004

1. Definition of Applicant and Qualified Donors

The qualification of a Source Plasma donor involves a well documented, scheduled series of steps, including routine physical examination, testing and interviews by the medical supervisor and designated trained staff as outlined below. The PPTA Qualified Donor Voluntary Standard is implemented at all PPTA iQPP certified centers. iQPP certification for all plasma centers is required. The standard provides a mechanism to allow for the identification and removal of "window period" plasma units by requiring further testing and screening to qualify new "Applicant" Source Plasma donors.

1.1 Applicant Donor

All individuals presenting themselves who have not been previously qualified as a donor within the past six months.

1.2 Qualified Donors

All individuals who have been qualified for continued donations by successfully passing two donor screenings and viral testing events within a six-month period.

2. Nature of the Examination and Interview of Donors

2.1.1 Examinations

- Each Donation

  Weight
  Temperature
  Pulse
  Blood pressure
  Hematocrit
  Total plasma protein

- Every Four Months

  Total serum protein and serum protein electrophoresis

  Serological test for Syphilis

- Initial Applicant Donation and Annually

  Urine glucose and protein

  Physical examination which includes: Blood pressure, visual examination of eyes, ears, nose, throat and skin, testing of reflexes, stethoscope examination of heart and lungs, palpation of the abdomen while in supine position for enlarged organs, and the neck palpated for the presence of enlarged glands. Further examination is carried out if any initial findings warrant.

2.1.2 Interviews

- Each Donation

  Donor is asked questions which cover AIDS risks and behavior, hepatitis risks, CJD risks, hospitalization(s), medications taken, recent illness, and activities requiring deferral such as recent tooth extraction, jail time within the past 12 months, body piercing, etc. During questioning, the donor's demeanor and general state of health is observed. Women are asked about present or recent pregnancy.

- Applicant Donations

  Donor is asked by the plasma center medical supervisor in a confidential setting if they understand the concept of high-risk behavior, or if they have any questions about the donor educational material which has been presented to them. Donor is given the opportunity to self-exclude.

- Applicant Donations and Annually

  Donor's medical history is reviewed by the medical supervisor. This includes questioning about prescribed medications such as Accutane, Tegison, Proscar, having spent three or more months cumulatively in the UK from 1980 to 1996, human pituitary-derived growth hormone and dura mater and/or corneal transplants, and use of bovine insulin since 1980. The donor is asked if there is any family history of CJD.

Plasma Donor

Donor Exclusion Criteria

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Valid from: 23 Oct 2006

1. Donor Exclusion Criteria

US Regulation 21CFR640.63(b)(3) states that each donor must be certified to be in good health on the initial donation and 21CFR640.63(c) states that the donor is to be in good health on the day of donation. To ensure viral safety for recipients with respect to major pathogenic agents, persons in the following categories will be excluded, either permanently or temporarily as indicated, from acting as donors:

1.1 Permanent Exclusion Criteria

1. Donors with clinical or laboratory evidence of infectious disease, e.g., infection with hepatitis virus, HIV-1 or HIV-2
2. Past or present intravenous drug abusers
3. Men who have had a sexual relationship, even one time, with another man since 1977
4. Donors who have engaged in sex for money or drugs even one time since 1977
5. Donors with hemophilia or other clotting factor defects who have received clotting factor preparations
6. Donors who are confirmed to be syphilis positive are not acceptable for Talecris
7. Donors who have been diagnosed with vCJD or any other form of CJD
8. Donors at increased risk for CJD
    - Donors are considered to have an increased risk for CJD if they have received a dura mater transplant, or human pituitary-derived growth hormone
    - Donors with one or more blood relatives diagnosed with CJD are also considered to be at increased risk of CJD
9. Donors at potential risk for CJD
    - Donors who have spent three months or more cumulatively in the UK from the beginning of 1980 through the end of 1996
    - Donors who have spent 5 years or more cumulatively in France from 1980 to the present
    - Donors who have received a transfusion of blood or blood components in the UK between 1980 and the present

- Former or current US military personnel, civilian military personnel and their dependents as follows:
  - Individuals who resided at US military bases in Northern Europe (Germany, Belgium and the Netherlands) for 6 months or more, from 1980 through 1990 or,
  - Individuals who resided at US military bases elsewhere in Europe (Greece, Turkey, Spain, Portugal and Italy) for 6 months or more, from 1980 through 1996

10. Donors who have injected bovine insulin since 1980

1.2 Temporary (12 month deferral) Exclusion Criteria

1. Donors who are close contacts of those with hepatitis
2. Sexual partners of any of those in categories 1 to 5 under Permanent Exclusion Criteria during the preceding 12 months
3. Donors who have been in jail more than 3 consecutive days within the past 12 months
4. Donors who have had unsterile body piercing or tattoos within the past 12 months
5. Donors who have received blood products or a blood transfusion other than from autologous donations within the past 12 months

Plasma Donor

System to Trace Each Donation

System to Trace and Lookback Procedure

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Valid from: 13 Nov 2007

1. System to Trace Each Donation

Talecris confirms that each batch of final production can be traced to the individual plasma donations used for its manufacture and vice versa. Standard Operating Procedures have been in place to provide assurance that the integrity of contract arrangements between Talecris plasma suppliers is maintained to safeguard donation/product identity.

At the collection site, each unit of plasma is assigned a unique identifying number which is applied to the unit, any sample, and all documentation which accompanies the plasma unit to Talecris. The same unique identifying number of the plasma unit is placed in the donor's file. All documentation relating to the collection of plasma is maintained for at least 33 years to facilitate traceability of any plasma unit.

Talecris assigns a unique number to each plasma manufacturing pool and a record of the plasma donation numbers assigned to each pool is maintained. Prior to production, a check of the donation numbers assigned to each pool is conducted to provide assurance that all plasma units identified through the post-donation information and lookback process have been removed. Documentation integrity is maintained throughout the plasma fractionation and purification process all the way to plasma-derivative final container lot numbers to allow for tracing back to the single plasma donations.

2. Lookback Procedure for Viral Marker and NAT Tests

The lookback procedure is initiated when the plasma center receives notification from any test laboratory of a positive/reactive viral marker or NAT test result which impacts the status of the donor. Appropriate actions must be taken regarding the donated plasma unit(s) and units donated prior to receipt of a positive/reactive viral marker or NAT test results from the associated donor. Plasma center personnel initiate a series of actions to document both the deferral status of the donor, whether temporary or permanent, and the disposition of the plasma unit(s) impacted by the test result. All of the actions taken are appropriately recorded in the donor record file and in other controlled plasma center documentation and are checked for verification prior to final disposition of the plasma unit(s).

In accordance with T.18.01, *General Specification for Source Plasma*, plasma centers are required to notify Talecris within 3 days of receipt of lookback information concerning a plasma donor. The plasma center must complete the required notification form and submit it to the Talecris fractionation facility. The notification form documents outstanding plasma units and requests the units be destroyed. The notification form is used to identify each unit that is determined to be unacceptable for further manufacture including lookback units that must be traced and removed. Required information includes the plasma center identification (name and address), reason for notification and all data on the plasma units that need to be located and removed from inventory. All information received from the plasma center is verified.

All incoming plasma notifications are received, logged by the Plasma Receiving Department and reviewed by Quality Operations (QO). All lookback units that have not been processed are identified and marked for removal and destruction. All data reported by the plasma supplier is entered into the validated Talecris database containing all information received from the plasma centers regarding lookback information associated plasma units from a donor.

As part of the QO approval process for a staged plasma pool, QO verifies all received notifications have been documented in the validated notification database. This database is part of the PUV (Plasma Unit Verification) system that 100% scans each unit staged and processed in a manufacturing pool. As the PUV system scans units assigned to a manufacturing pool, a prompt for unit removal is signaled each time a lookback or post donation unit is scanned. As prompted by the electronic system, the lookback or post donation reported unit is removed and scanned to a biohazard waste bin. All destruction information is captured electronically and automatically updated in the notification database. Both Plasma Receiving and QO reconcile notification units listed on the "Pool Unit Removal" report to physical units removed and discarded.

In case plasma units associated with received post donation information (PDI) have already been processed, the reason for notification of the questionable plasma units is further evaluated by the Quality unit. The need for further action is determined in accordance with approved procedures based on the potential impact of the reason for the notification. If it is determined the reason for the notification could potentially affect the quality or safety of final products a lot trace would be initiated and the appropriate actions determined in accordance with current regulations and guidelines (e.g. Directives 2002/98/EC, 2004/33/EC, 2005/61/EC & 2005/62/EC, CPMP/BWP/269/95 rev. 3, Annex 14 to the EU GMP Guide, US CFR, FDA guidance documents, etc.). If warranted, appropriate actions might include quarantining the manufacturing pool and all intermediates/products manufactured from the pool, notification of relevant authorities and consignees or recall of distributed final product.

In instances where lookback plasma units have been processed prior to receipt of notification no further action is required on the processed product. Lookback plasma units have all negative viral marker and NAT testing documented. The lookback plasma units are recorded and included in the batch trace information so that a comprehensive viral risk assessment is conducted for the associated final container batches.

Once the final disposition of all units identified on the notification is complete with all plasma units accounted for, the notification form is considered "closed". QO performs an audit of each closed notification received from the plasma center. The audit includes checking each unit listed on a notification to verify each unit has been completely dispositioned. All destruction information associated with reported units is captured electronically from the PUV system and automatically updates the notification database.

Table 1 specifies the actions taken when a reactive/positive viral marker or NAT test result notification is received from the test laboratory. Lookback periods are specified not to exceed 3 years according to the Talecris specified plasma expiration date. Talecris will not fractionate plasma that is older than 3 years from the date of collection. Consequently, lookback periods longer than 3 years are not required by Talecris.

Table 1 - Actions on Unacceptable Plasma and Donors (Viral Marker and NAT Tests)

Test Results	Action on Index Donation	Action on Prior Donations	Action on Subsequent Donations	Action on the Plasma Donor
HBsAg or HBV by NAT	Destroy[1]	Destroy[1]	Destroy[1] Lookback units NLT 6 months[2] from the last negative donation, not to exceed 3 years	Permanent Deferral (Enter into the National Donor Deferral Registry)
Household contact or Sexual Partner	Destroy[1]	Destroy[1]	Destroy[1] Lookback units NLT 6 months[2] from date of notification	Temporary Deferral 12 months from the date of notification
Anti-HCV or HCV by NAT	Destroy[1]	Destroy[1]	Destroy[1] Lookback units NLT 6 months[2] from the last negative donation, not to exceed 3 years	Permanent Deferral (Enter into the National Donor Deferral Registry)
Household contact or Sexual Partner	Destroy[1]	Destroy[1]	Destroy[1] Lookback units NLT 6 months[2] from date of notification	Temporary Deferral 12 months from the date of notification
Anti-HIV-1/2	Destroy[1]	Destroy[1]	Destroy[1] Lookback units NLT 6 months from the last negative donation, not to exceed 3 years	Permanent Deferral (Enter into the National Donor Deferral Registry)
Sexual Partner	Destroy[1]	Destroy[1]	Destroy[1] Lookback units NLT 6 months from date of notification	Temporary Deferral 12 months from the date of notification
HIV-1 by NAT	Destroy[1]	Destroy[1]	Destroy[1] Lookback units NLT 3 months from the last negative donation, not to exceed 3 years	Permanent Deferral (Enter into the National Donor Deferral Registry)
Sexual Partner	Destroy[1]	Destroy[1]	Destroy[1] Lookback units NLT 3 months from date of notification	Temporary Deferral 12 months from the date of notification
Parvovirus B19 by NAT	Destroy[1]	No Action	No Action	No Action

[1] The option to divert plasma units from Talecris is allowed. The plasma is unacceptable for further manufacture into plasma derivatives by Talecris.
[2] The information presented is in harmonization with the lookback requirements defined by CPMP/BWP/269/95. Actual lookback periods may be longer in accordance with US FDA requirements.

Compliance Standards for Plasma

Plasma Collected in the USA

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Valid from: 28 Nov 2007

Talecris accepts single donor Plasma (Human) for further manufacture into plasma derivatives. Plasma collected in the USA by plasmapheresis meets the following requirements:

I. Source Plasma as defined in the United States Code of Federal Regulations (US CFR) Title 21 Part 640 – Subpart G – Source Plasma

All plasma collection facilities supplying plasma to Talecris for use in the manufacture of plasma-derivatives must be licensed by the US FDA and are inspected on a routine basis by the US FDA. Plasma centers must also be licensed and inspected for compliance with the Clinical Laboratory Improvement Amendments of 1988 (CLIA regulations) and comply with any applicable state or local regulatory agency requirements. Audits of the collection facilities are performed annually by Talecris unless the requirements for an extended audit frequency have been met. Plasma centers must also be inspected and determined to meet iQPP standards established by PPTA (Plasma Protein Therapeutics Association).

Quality aspects for plasma are addressed in the General Specification – Source Plasma. Quality aspects addressed in the specification include the following:

I. Meeting the required specifications for collection

II. Meeting the required specifications for plasma donor and donation testing

III. Meeting the required plasma storage and transport conditions

IV. Meeting the record retention requirements, and other procedural requirements

V. Requirement to maintain viral marker rates is also specified

VI. Requirement to notify Talecris in the event of: significant changes in the process, serious failure to meet regulations, post-donation information

VII. Requirement to confirm licensing status of product and facility, allowance for audits by Talecris Quality Operations, agreement to forward results of FDA inspections to Talecris, agreement to be certified in the PPTA international Quality Plasma Program (iQPP)

Plasma collected in the USA by plasmapheresis complies with the applicable requirements as published in the following:

21 CFR §600 Biological Products
21 CFR §606 Current Good Manufacturing Practice for Blood and Blood Components
21 CFR §610 General Biological Products Standards

21 CFR §640	Additional Standards for Human Blood and Blood Products
21 CFR §210	Current Good Manufacturing Practice in Manufacturing, Processing Packing, or Holding of Drugs; General
21 CFR §211	Current Good Manufacturing Practice for Finished Pharmaceuticals
21 CFR §803	Medical Device Reporting
42 CFR §493	Clinical Laboratory Improvement Amendments of 1988 (CLIA)

All plasma suppliers are required to follow all applicable *Recommendations and Guidelines* published by FDA Departments of Health and Human Services.

Talecris Biotherapeutics, Inc.
Clayton, NC

T.18.01-05

Plasma

Specification

Source Plasma

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Valid from:19 June 2007

1. Purpose

To provide and describe the requirements specified by Talecris Biotherapeutics, Inc. for the procurement of source plasma intended for manufacture of therapeutic biological products, both domestic and foreign. This specification is intended to assure that incoming plasma meets all requirements, in addition to established domestic and international regulations and standards for source plasma.

2. Scope

These requirements are applicable to all source plasma purchased by Talecris.

3. General Requirements

3.1 Quality Operations (QO) Compliance

3.1.1 Plasma Supplier Approval

All plasma intended for use must be collected by approved suppliers and collection facilities, and tested by approved laboratories using approved test kits.

3.1.2 Supplier Files

All supplier information is maintained by QO Compliance. Copies of the following documents must be current and updates provided by the supplier, when applicable.

- FDA approved ELA, PLA or BLA
- CLIA registration certificate for the facility
- Individual state licenses, as required
- iQPP certification for the collection facility
- FDA approved SOP[1] manual
- Viral Marker Rates - provided no less than quarterly
- FDA written approval to collect hyperimmune plasma, if shipped to Talecris.
- The supplier must notify the Plasma Operations Account Manager of any changes in the following, at the corporate level, or at an individual facility:
  - Facility address or location, phone and fax numbers
  - Hours of operation
  - Management or medical supervisory personnel:
    - Lab Director
    - Medical Director
    - Physician Substitute
    - Center Director, Manager or Assistant Manager

[1] Standard Operating Procedure

- Quality Assurance Specialist
- Regional Manager

- The supplier must notify Plasma Operations Account Manager prior to any changes in the following.
  - Tests performed
  - Methods/reagents/equipment or procedures used
  - Plasma types collected
  - Facility address
- Quality Compliance Audits - QO Compliance group will conduct audits of all facilities on a periodic basis, not less than (NLT) once every 24 months.
- Epidemiology Data - In accordance with current regulatory requirements and with some consideration given to the PPTA Viral Marker Standard, epidemiology data (viral marker serological and NAT), compiled monthly, must be provided for each facility collecting source plasma. The data is required to be reported monthly for the entire year (January 1 through December 31) for each collection center supplying plasma to Talecris at any point in a given year regardless of duration of supply during the year. This is necessary to meet regulatory requirements for an epidemiological profile to be established and reported for each individual center supplying plasma to the manufacturing facility.
  - Failure on the part of any collection facility to meet PPTA (iQPP) Standards will result in the removal of the collection facility from the approved supplier list.
  - Data must be submitted by the end of the month following the close of each quarter (i.e., Q1 due by 4/30, Q2 due by 7/31, Q3 due by 10/31 and Q4 due by 1/31).
  - Definitions are provided below:
    1) "First time tested donor" - person whose blood/plasma is tested for the first time for viral markers without evidence of prior testing. The first time tested donor population represents a subset of applicant donors ("applicant donors" that are tested for the first time in the given system).
    2) "Repeat tested donor" - person whose blood/plasma has been tested previously for viral markers in the given system. This includes "applicant donors" tested for the second time, "applicant donors" re-qualifying after 6 months or more and "qualified donors".
    3) "Qualified donor" - an individual who has provided a plasma sample at a specified plasma center, at least twice in a 6-month period, and all screening requirements have been met for both a) questions and tests and for b) the donor and the plasma sample according to the iQPP Qualified Donor Standard.
    4) Total number "First time tested donors" - the total number of unique/ individual donors present at a center at any time during the entire reporting calendar year (Jan. 1 to Dec. 31) who are tested for the first time for viral markers without evidence of prior testing. Do not count the same donor as

identified by the unique donor ID more than once in a given year. These data should be provided when the December epidemiology data are reported and is to be a comprehensive annual count. When reporting January through November epidemiology data, simply NA this box for each center.

5) Total number "Repeat tested donors" - the total number of unique/ individual donors present at a center at any time during the entire reporting calendar year (Jan. 1 to Dec. 31) who have been tested previously for viral markers in the given system. Do not count the same donor as identified by the unique donor ID more than once in a given year. These data should be provided when the December epidemiology data are reported as is to be a comprehensive annual count. When reporting January through November epidemiology data, simply NA this box for each center.
6) Total number donations from "Repeat tested donors" - the total number of donations collected from "repeat tested donors" during the entire reporting calendar year (Jan. 1 to Dec. 31). These data should be provided when the December epidemiology data are reported and is to be a comprehensive annual count. When reporting January through November epidemiology data, simply NA this box for each center.
7) Donation frequency - applies only to the "repeat tested donors". This should be calculated as the total number of donations from "repeat tested donors" divided by the total number of "repeat tested donors" for the entire reporting calendar year (Jan. 1 through Dec. 31) for each center. These data should be provided when the December epidemiology data is reported. When reporting January through November epidemiology data, simply NA this box for each center.
8) Confirmed seropositive - donors testing repeat reactive with a serological screening test (HBsAg, anti-HIV-1/2, anti-HCV) and who are subsequently confirmed positive by a supplementary method (Western Blot, RIBA, etc.). Do not count the same donor more than once in a given year.
9) NAT only positive: confirmed positive in a NAT assay for a specific virus (HIV-1, HCV or HBV), and not found repeat reactive for that virus in serological screening i.e., window period cases. NAT only positives may or may not be subsequently confirmed by serological testing. Do not count the same donor more than once in a given year.

- All plasma suppliers must have a QA program in place, which is consistent with the current CBER document entitled "Guideline for Quality Assurance in Blood Establishments".
- Deviations from Specifications
  - Any proposed deviation to specification must be submitted in writing to the Plasma Operations Account Manager **prior** to implementation. Plasma

Operations will initiate any required change control, on which QO disposition will be documented.

3.2 Regulatory Affairs

The supplier must notify the Plasma Operations Account Manager, no longer than three working days from discovery, in the event that any of the following occur, at the corporate level, or at an individual facility.

- Any fatal donor reaction, as defined in 21 CFR 640.73.
- Any FDA or other regulatory inspection results that may affect the approval status of any facility.
- Any regulatory action (i.e., warning letter, injunction, suspension) that would adversely affect, or bring into question, the quality of product produced for Talecris.

The supplier must notify the Plasma Operations Account Manager and Clayton Plasma Receiving, and QO within one working day of notification for product seizure or recall.

The supplier must notify Plasma Receiving within three working days of any lookback notification.

The supplier must notify Plasma Receiving in a timely manner (e.g., as soon as investigation and unit trace are completed) of any Post Donation Information notifications (examples, but not limited to, tattoos, body piercings, high risk, etc.).

Regulatory actions may result in the removal of a facility from approved supplier list.

3.3 Plasma Operations

Supplier agreements - Each supplier group will sign a written statement agreeing to meet the specifications.

The Supplier will communicate directly all concerns, questions and changes to the Plasma Operations Account Manager assigned to the supplier group, and in turn, the Account Manager will disseminate, within Talecris, all communications to and from the Supplier.

3.4 Documents and Records, Requirements as Defined in 21 CFR 640.72, and in Addition

Copies of this specification are sent to Plasma Operations Account Managers with each revision. From the date the specification is approved, the effectivity date will be stamped one month in advance and sent to plasma suppliers to conduct training.

All facility documents and records pertaining to the collection, processing, QA/QC, storage, shipment and testing of plasma intended for manufacture by Talecris must be available for review for a minimum of 33 years.

Each facility collecting or testing Source Plasma will be assigned a unique four-digit facility identification code. All documentation and records accompanying plasma units shipped to Talecris must be clearly identified with the facility identification code.

If original documents are required, but are unavailable, a copy may be substituted as long as it is stamped with the statement "This is a true and accurate copy of the original." Verification must be provided to assure that all copies are accurate, legible and accounted for.

3.5 European Product

Product intended for shipment to Europe must be collected and tested by EU approved facilities.

EU requirements are as follows:

- Inspection and approval by a European Competent Authority
- Listed on the GMP certificate

4. Donor Suitability

Requirements as defined in 21 CFR 640.61, 640.62, 640.63, 640.65(b) and 640.71 must be met, and in addition:

- Applicant donor procedures and policies must be in effect in accordance with the iQPP Qualified Donor Standard.
- Donors must be at least 18 years old. Donors older than 65 may donate if an acceptable physical examination and medical history is acquired annually.
- Normal Source Plasma, collected from donors who have been re-entered through FDA approved re-entry programs, is not acceptable for delivery to or use by Talecris (except Anti-D plasma, refer to Talecris Anti-D plasma specification for requirements. No other plasma type, including NX, may be shipped to Talecris from re-entered donors).
- Donors participating in an Anti-D stimulation program are not allowed to contribute to any other plasma type (NX, TX, HX, AX, RX) shipped to Talecris. Only Anti-D plasma may be shipped from donors participating in an Anti-D stimulation program.

5. Plasma Collection

Requirements defined in 21 CFR 640.62, 640.64, 640.65, 640.66 and 640.71 must be met, and in addition:

- Plasma identification systems and labels, plasma collection containers, anticoagulant, supplies and equipment, sample tubes and all packaging and shipping materials used must be approved in writing, prior to use, by Plasma Operations, Technical Services.
- Only plasma collected in approved bottles are allowed to ship to Talecris.
- Each collection facility must adhere to PPTA (iQPP) and PPTA voluntary standards.
- A FDA approved nomogram must be used.
- Plasma Identification:
  - A unique Control Number/Bleed Number must be assigned to one specific unit of plasma and all associated samples, which must be traceable to an individual donor and donation.
  - The Source Plasma Label applied to the unit of plasma must also contain the facility identification code, name, address and US license number of the collection facility, or minimally, the address of the plasma supplier corporate office.
  - Material Numbers:
    - Talecris will determine and provide the appropriate material number(s) for use by the collection facility.
    - In the event that it is ever necessary to change a material number on plasma already received or in transit to Talecris, the plasma supplier will communicate this change to the Plasma Operations Account Manager.
    - In the event that it is necessary to change a material number on plasma that is in storage at a supplier's facility, the supplier will be notified by the Plasma Operations Account Manager and requested to correct the shipping documents for the affected plasma, prior to shipment.

6. Plasma Processing

Requirements defined in 21 CFR 640.68, 640.69(d), 640.70, 640.71 and 640.72 must be met, and in addition:

- All plasma units must be placed in the freezer within one hour of collection and maintained at -20 C or colder.
- All plasma units must be evaluated for unacceptably high hemoglobin concentration using the Hemoglobin Comparator, following the instructions for use printed on the card. Plasma units with unacceptably high hemoglobin concentrations must not be shipped to Talecris.
- Plasma intended for the recovery of proteins that are labile in plasma is frozen currently by cooling rapidly in a chamber at -30°C or below as soon as possible and at the latest within 24 hours of collection. As of January 1, 2008 plasma will be frozen in conditions validated to ensure that a temperature of -25°C or below is attained at the core of each plasma unit within 12 hours of placing in the freezer apparatus and within 24 hours of collection.

7. Plasma Packing

Plasma must remain frozen during packing procedures.

8. Plasma Storage

Requirements defined in 21 CFR 640.71, 640.76 and the EP Monograph for Human Plasma for Fractionation must be met, and in addition:

- Hyperimmune plasma, designated as Salvaged Plasma, must be relabeled as Normal X plasma. Talecris will not accept salvaged hyperimmune plasma. Note: Anti-D plasma cannot be relabeled as Normal X plasma nor shipped as salvaged.

9. Plasma Shipping

Requirements defined in 21 CFR 640.71 and 640.76, and in addition:

- Plasma Aging - Plasma must not be older than 24 months when shipped to Talecris.
- Plasma that falls into one of the following categories is unacceptable for shipment to Talecris:
  - units with reactive or positive test results
  - prior and/or subsequent units from temporary or permanently deferred donors
  - hemolyzed units, units with red spots in or on the plasma containers
  - lipemic units
  - units with frozen plasma on the outside of the container
  - broken, torn or contaminated units
  - untested, or units with incomplete testing
  - orphan units
  - units collected from donors re-entered through a FDA approved donor re-entry program (except Anti-D plasma, refer to Talecris Anti-D plasma specification for requirements)
  - recovered plasma
  - unlabeled or mislabeled units, or units with torn or unreadable labels
  - units tested by a non-approved laboratory, or by non-approved test methods, reagents or equipment
  - units collected at non-approved facilities or by non approved owner groups
  - units having errors that breech traceability, such as units that cannot be traced back to an individual donor
  - units with <200 mL/bottle
  - parvo elevated units
  - plasma shipped to Talecris out of collection sequence
  - unit(s) with prior notification to supplier of unacceptable status by Talecris
- Quarantine Plasma Shipments
  - Quarantined plasma shipments must be pre-approved by CBER.

- Quarantined plasma shipments must be pre-approved by Talecris. Notification, in writing, including documentation of CBER approval, must be provided to the Plasma Operations Account Manager and written approval received from Talecris prior to shipment.
- Source Plasma - Salvaged
  - Salvaged Plasma shipments must be pre-approved by Talecris. Notification, in writing, must be provided to the Plasma Operations Account Manager and written approval received from Talecris prior to shipment.
- A documentation packet must accompany each shipment of plasma and must be QA approved.
- Transport/Carriers
  - All carriers used to transport Source Plasma must be pre-approved by Talecris.
  - The temperature of the transport trailer must be -25 C or colder prior to loading the plasma shipment.

10. Testing Requirements

Testing requirements as described in 21 CFR 640.67 and 640.71 must be met, and in addition plasma intended for use by Talecris must meet the following criteria.

Test Type	Test Requirements
HBsAg[a,d]	Non-reactive[c]
Anti-HIV-1/2[a,d]	Non-reactive[c]
Anti-HCV[a,d]	Non-reactive[c]
Syphilis[d,h]	Negative or Non-reactive[c] for donor
Atypical Antibody[b,d,e,f]	Negative or Non-detectable (<1:1)
HCV NAT[d]	Negative[c]
HIV-1 NAT[a,d]	Negative[c]
HBV NAT[d,g]	Negative[c]
Parvovirus B19 NAT[i]	Non-Elevated

[a] Most current version or generation available of a FDA approved test method must be used.
[b] Test reagents for atypical antibody screening tests must include specific anti-D antibody. Detection of other atypical antibodies is not required, except anti-C for Rho-D plasma.
[c] Some manufacturer package inserts use the terms "negative" and "non-reactive" interchangeably.
[d] Prior to use, the test kit manufacturer, test kit methodology and testing facility must be approved by Talecris.
[e] Test not performed on anti-D specialty plasma.
[f] Test applicant or qualified donors. Testing must be performed and acceptable prior to sending units from donor.
[g] Under an approved IND or FDA approved.
[h] Donor test performed every 4 months.
[i] Parvo elevated units are unacceptable to ship to Talecris.

Testing must be performed by a testing facility that meets all regulatory and licensing requirements and has been pre-approved by Talecris. The Director of Plasma Operations

will approve one of the eligible viral marker testing labs for each plasma supplier. The Director will also approve any switch of viral marker testing laboratories prior to change.

10.1 Notification for Destruction of Plasma

- Notification to Plasma Receiving must be made:
  - within three working days upon receipt of a reactive or positive test result for a donor from whom prior or subsequent units have been shipped to Talecris (lookbacks).
  - within one working day of notification of Post Donation Information resulting in product recalls or seizure concerning units shipped to Talecris.
  - within a timely manner for Post Donation Information not resulting in a seizure or recall (example: tattoo, body piercing, high risk).

11. Reference(s)

21 CFR 210 - Current Good Manufacturing Practice in Manufacturing, Processing, Packing or Holding of Drugs; General

21 CFR 211 - Good Manufacturing Practice for Finished Pharmaceuticals

21 CFR 606 - Current Good Manufacturing Practice for Blood and Blood Components

21 CFR 640 - Additional Standards for Human Blood and Blood Products, Plasma and Source Plasma

42 CFR 493 - CLIA regulations

EU Pharmacopoeia Monograph for Human Plasma for Fractionation

Revision to Annex 14 to EU Guide to GMP: Manufacture of products derived from human blood or plasma.

All current FDA guidance documents relating to collecting, testing, processing, storing or transporting Source Plasma

iQPP Viral Marker Standards, Qualified Donor Standard and NAT Testing Standard.

EMEA/CHMP/BWP/3794/03 Guideline on the Scientific Data Requirements for A Plasma Mater File (PMF)

EMEA/CHMP/BWP/125/04 Guideline on the Epidemiological Data on Blood Transmissible Infections

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Plasma Donor

Test Specification for the Plasma Donation

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Valid from: 09 Jul 2004

Test	Specification
Hepatitis B Surface Antigen	Non-Reactive
HCV Antibody	Negative
HIV-1/2 Antibody	Negative
HCV by NAT[1]	Negative
HIV-1 by NAT[1]	Negative
HBV by NAT[1]	Negative
Parvovirus B19 by NAT[1]	Non-Elevated
[1] Test is performed on "mini-pools" of plasma donation samples.	

Plasma Donor

Test Procedure

Test Information for the Plasma Donation

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Valid from: 28 Nov 2007

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1. Test Method Information

The test methods used to perform viral marker and NAT testing on each plasma donation are listed in Tables 1 and 2.

Table 1 - Viral Marker Testing of Individual Donations

Parameter	Test Method/ Name of Test Kit	Manufacturer	US License Number	Test Site
HBsAg	AUSZYME® MONOCLONAL	Abbott Laboratories	US License No. 0043	Interstate Blood Bank Life Sera ZLB Bioplasma
HBsAg	ABBOTT PRISM® HBsAg	Abbott Laboratories	US License No. 0043	ZLB Bioplasma, Inc. Test Lab BioLife Lab - Hoover LifeSera Test Lab South Texas Blood Bank Interstate Blood Bank, Inc. Nabi Biopharmaceuticals
Anti-HCV	ABBOTT HCV EIA 2.0	Abbott Laboratories	US License No. 0043	Interstate Blood Bank Life Sera South Texas Blood Bank ZLB Bioplasma
Anti-HCV	ABBOTT PRISM® Anti-HCV	Abbott Laboratories	US License No. 0043	Life Sera, Inc. South Texas Blood Bank BioLife Lab - Hoover ZLB Bioplasma Interstate Blood Bank, Inc. Nabi Biopharmaceuticals
Anti-HIV-1/2	HIVAB™ HIV-1/HIV-2 (rDNA) EIA	Abbott Laboratories	US License No. 0043	Interstate Blood Bank Life Sera South Texas Blood Bank ZLB Bioplasma
HBsAg	Genetic Systems™ HBsAg EIA 3.0	Bio-Rad Laboratories	US License No. 1109	BioLife Lab - Hoover
Anti-HCV	ORTHO® HCV Version 3.0 ELISA Test System	Ortho-Clinical Diagnostics, Inc.	US License No. 1236	BioLife Lab - Hoover
Anti-HIV-1/2	Genetic Systems™ HIV-1/HIV-2 *Plus O* EIA	Bio-Rad Laboratories	US License No. 1109	BioLife Lab - Hoover

2. Summary of Information on the Validation of and the Procedure for Plasma Donation Viral Marker Test Methods

Each viral marker test laboratory contracts directly with the plasma collection organizations and is licensed to perform viral marker testing in accordance with US FDA regulations. These facilities are inspected and approved by US FDA, and audited by Quality Operations. The facilities use only US FDA licensed test kits from licensed test kit manufacturers. All contract test laboratories performing viral marker testing for Talecris are certified to perform testing under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), a program under the responsibility of the US Department of Health and Human Services.

In order for a laboratory to obtain and maintain CLIA certification, each laboratory must have validation data on file for each test kit/methodology used for viral marker testing. Both US FDA and CLIA inspectors review validation information prior to approving a contract test laboratory to perform viral marker testing. CLIA site inspections occur every two years prior to the expiration of CLIA certification. The requirements for validation are stated in 42 CFR 493.1213 *Establishment and Verification of Method Performance Specifications*. Each laboratory must verify or establish, for each method, the performance specifications for the following performance characteristics: accuracy, precision, analytical sensitivity and specificity, and any other applicable performance characteristic. Validations must be performed for new methods or devices introduced prior to reporting test results. Each laboratory must have documentation of the verification or establishment of all applicable test performance specifications. In addition, the laboratory must include positive and negative external controls with each run of samples to indirectly assess the accuracy and precision of test results.

Tests are carried out in accordance with the manufacturers' directions for use. If a plasma donation sample tests reactive/positive during the initial testing, that plasma donation sample is repeat tested in duplicate. If neither of the repeat tests are reactive/positive, the sample is considered nonreactive/negative for the specific viral marker. If the plasma donation sample is reactive/positive in either of the repeat tests, the sample is considered repeatable reactive. The plasma donation is eliminated from manufacture and the lookback procedure is initiated. The plasma donor is permanently deferred and not eligible to donate plasma again for Talecris. Supplementary/confirmatory testing is performed for donor notification purposes only. This supplementary testing has no impact on plasma donor and donation suitability for Talecris.

Table 2 - NAT Testing of Mini-Pools

Parameter	Test Method/ Name of Test Kit	Manufacturer	US License Number	Test Site
HCV by NAT	Roche COBAS AmpliScreen™ HCV Test	Roche Diagnostics	US License No. 1636	Talecris Raleigh, NC
HIV-1 by NAT	Roche COBAS AmpliScreen™ HIV-1 Test	Roche Diagnostics	US License No. 1636	Talecris Raleigh, NC
HBV by NAT	Roche COBAS AmpliScreen™ HBV Test	Roche Diagnostics	US License No. 1636	Talecris Raleigh, NC
Parvovirus B19 by NAT	Digene SHARP Signal™ System Assay	NA[a]	NA[a]	Talecris Raleigh, NC
Parvovirus B19 by NAT	Parvovirus B19 Fluorogenic Donation Qualification Assay, version 1 (B19 FDQA, v1)	NA[a]	NA[a]	Talecris Raleigh, NC
HCV by NAT	NGI UltraQual™ HCV RT-PCR Assay	NA[b]	US License No. 1582[b]	National Genetics Institute
HIV-1 by NAT	NGI UltraQual™ HIV RT-PCR Assay	NA[b]	US License No. 1582[b]	National Genetics Institute
HBV by NAT	NGI UltraQual™ HBV PCR Assay	NA[b]	NA[b]	National Genetics Institute
Parvovirus B19 by NAT	NGI Parvovirus SuperCycle Assay	NA[c]	NA[c]	National Genetics Institute

[a] Testing of donations for Parvovirus B19 is not a required test and is performed as an in-process control according to the PPTA voluntary standard. The Digene SHARP Signal™ System Assay and the B19 FDQA, v1 are in-house test methods developed by Talecris and the testing is performed under the authority of Talecris. These tests are not distributed.

[b] The NGI UltraQual™ HCV, HIV and HBV assays are in-house test methods developed by NGI and performed as a testing service under the authority and license of NGI. The tests are not distributed.

[c] Testing of donations for Parvovirus B19 is not a required test and is performed as an in-process control according to the PPTA voluntary standard. The NGI Parvovirus SuperCycle PCR Test is an in-house test method developed by NGI and the testing is performed under the authority of NGI. The test is not distributed.

3. Summary of Information on the Validation of Raleigh Test Laboratory (RTL) Plasma Donation NAT Testing Methods

The HCV, HIV-1, HBV and Parvovirus B19 NAT tests are validated. Validation studies were performed in accordance with the ICH Harmonized Tripartite Guideline on the Validation of Analytical Procedures and the European Directorate for the Quality of Medicines (EDQM) document PA/PH/OMCL (98) 22, DEF *Validation Of Nucleic Acid Amplification Technology (NAT) For The Detection Of Hepatitis C Virus (HCV) RNA In Plasma Pools* and PA/PH/OMCL (03) 38, DEF *Guideline for Validation of Nucleic Acid Amplification Techniques (NAT) for Quantitation of B19 Virus DNA in Plasma Pools*, as well as in accordance with the E.P. general chapter 2.6.21, *Nucleic Acid Amplification Techniques*.

Additional information in the form of full validation reports for the Talecris in-house B19 NAT tests is provided in section 2.2.2b.

The Roche COBAS AmpliScreen™ HCV kit, v2.0 is used at RTL. The multi-prep test procedure is performed on minipools of 96 plasma donation samples. The HCV in-house standard was used in the validation. The standard was calibrated against the WHO International Standard, at a titer of 5.75×10^7 IU/mL. Roche has determined that the COBAS AmpliScreen™ HCV test, v2.0 can detect HCV RNA at levels as low as 50 IU/mL with a 95% test positive rate. Test specificity was addressed by testing 100 plasma pools. The validation requirement that no positive results be obtained was successfully achieved. Cross-contamination concerns were addressed by testing a panel of alternating non-reactive pools and pools spiked with HCV at a titer of 57.5×10^4 IU/mL. Robustness of assay performance was demonstrated by the ability of the test to accurately detect negative and high-titer HCV positive samples arranged in an alternating pattern. Validation of the high speed centrifugation step in the multiprep sample preparation method was addressed by detecting HCV spiked at varying concentrations into plasma pools tested and found negative for antibodies to HCV. The centrifugation speed was set at the lower limit as defined by the standard operating procedure. The acceptance criteria for the detection of HCV at 95% overall was met. Analytical sensitivity validation was performed for the standard specimen processing procedure of the Roche COBAS AmpliScreen™ HCV kit, v2.0 which is used to deconstruct positive minipools and identify individual positive plasma donations. The HCV in-house standard was used in the study. Roche has determined that the COBAS AmpliScreen™ HCV test using the standard specimen processing procedure can detect HCV RNA levels as low as 41.9 IU/mL with a 95% test positive rate. For the purposes of this study, 100 IU/mL was used to meet the requirements set forth by EMEA/CPMP/BWP/390/97. The accuracy of the targeted 100 IU/mL value was assessed by testing plasma pools spiked with the in-house standard to a titer of 100 IU/mL. The acceptance criteria that positive samples must be detected at a 95% test positive rate and that no positive results be obtained from negative diluent samples was achieved.

The Roche COBAS AmpliScreen™ HIV-1 kit, v1.5 is used at RTL. The multi-prep test procedure is performed on minipools of 96 plasma donation samples. The HIV-1 in-house standard was used in the studies. The standard was calibrated against the WHO International Standard and can be considered to have a potency of 3.55×10^6 IU/mL. The standard has a titer of 1.02×10^6 gEq/mL. The previous HIV-1 NAT test method (Roche AmpliScreen™ HIV-1 microwell plate test) was shown to detect HIV-1 RNA at 20 gEq/mL with a 95% test positive rate. This value was used in the COBAS AmpliScreen™ validation studies to show comparability between the Roche AmpliScreen™ HIV-1 microwell plate test and the Roche COBAS AmpliScreen™ HIV-1 test. Test specificity was addressed by testing 100 plasma pools. The validation requirement that no positive results be obtained was successfully achieved. Cross-contamination concerns were addressed by testing a panel of alternating non-reactive pools and pools spiked with HIV-1 at a titer of 1.02×10^4 gEq/mL. Robustness of assay

performance was demonstrated by the ability of the test to accurately detect negative and high-titer HIV-1 positive samples arranged in an alternating pattern. Validation of the high speed centrifugation step in the multiprep sample preparation method was addressed by detecting HIV-1 spiked at varying concentrations into plasma pools tested and found negative for antibodies to HIV. The centrifugation speed was set at the lower limit as defined by the standard operating procedure. The acceptance criteria for the detection of HIV-1 at 95% overall was met. Analytical sensitivity validation was performed for the standard specimen processing procedure of the Roche COBAS AmpliScreen™ HIV-1 kit, v1.5 which is used to deconstruct positive minipools and identify individual positive plasma donations. The HIV-1 in-house standard was used in the study. Roche has determined that the COBAS AmpliScreen™ HIV-1 test using the standard specimen processing procedure can detect HIV-1 RNA levels as low as 150.3 IU/mL with a 95% test positive rate. Guidelines established by EDQM recommend at least 20 negative plasma pools spiked with HIV-1 RNA to a final concentration of 3 times the 95% cut off value (451 IU/mL) should be tested and found positive. The accuracy of the targeted 451 IU/mL value was assessed by testing plasma pools spiked with the in-house standard to a titer of 451 IU/mL. The acceptance criteria that positive samples must be detected at a 95% test positive rate and that no positive results be obtained from negative diluent samples was achieved.

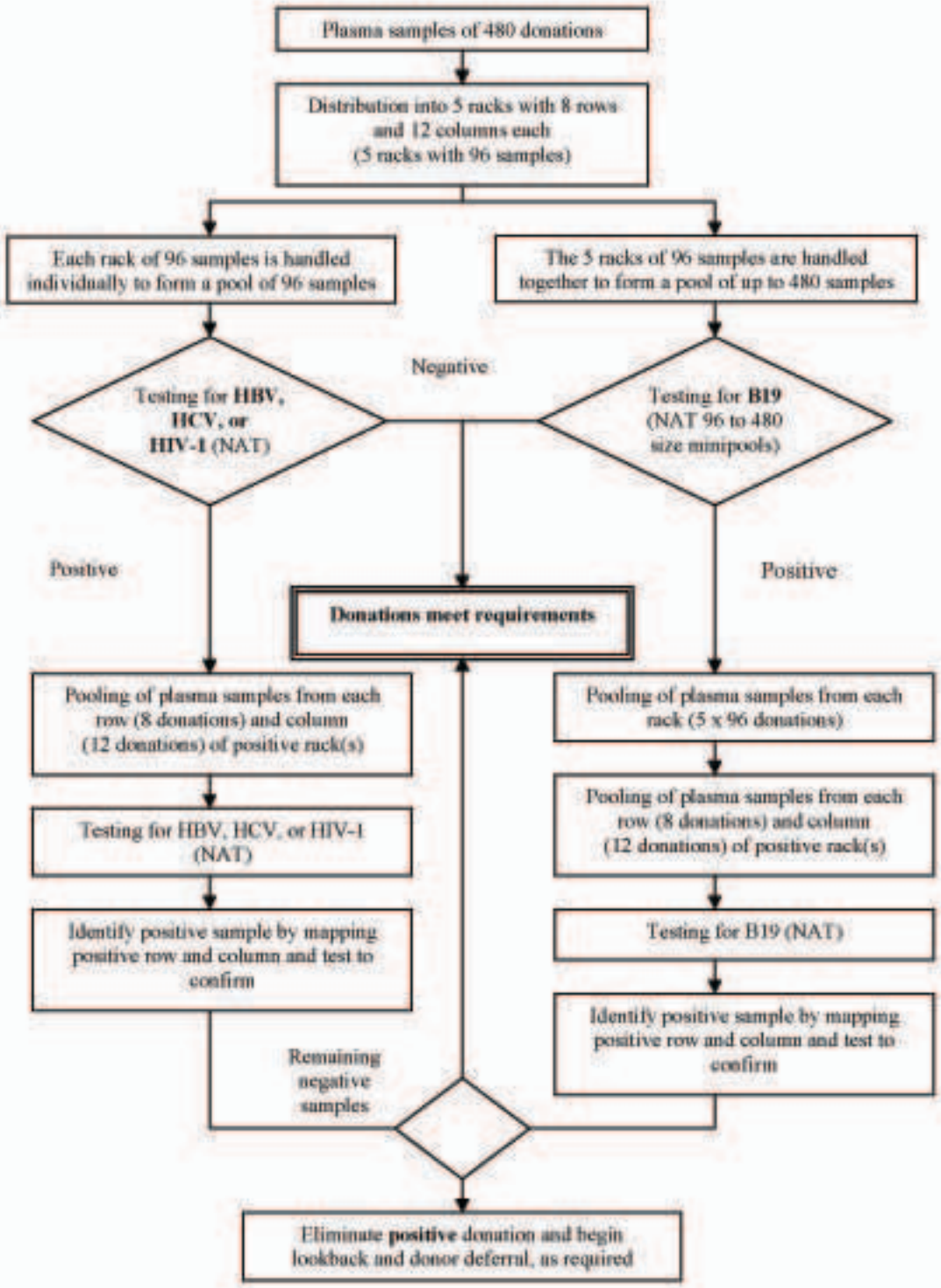
The Roche COBAS AmpliScreen™ HBV kit is used at RTL. The multi-prep test procedure is performed on minipools of 96 plasma donation samples. The HBV in-house standard was used in the studies. The standard consists of an HBV positive plasma donation, calibrated against the WHO international standard at a titer of 7.64×10^8 IU/mL. The COBAS AmpliScreen™ HBV test, can detect HBV DNA at levels as low as 6 IU/mL with a 95% test positive rate. Test specificity was addressed by testing 100 plasma pools. The validation requirement that no positive results be obtained was successfully achieved. Cross-contamination concerns were addressed by testing a panel of alternating non-reactive pools and pools spiked with HBV at a titer of 7.64×10^6 IU/mL. Robustness of assay performance was demonstrated by the ability of the test to accurately detect negative and high-titer HBV positive samples arranged in an alternating pattern. Analytical sensitivity validation was performed for the standard specimen processing procedure of the Roche COBAS AmpliScreen™ HBV kit which is used to deconstruct positive minipools and identify individual positive plasma donations. The HBV in-house standard was used in the study. Roche has determined that the COBAS AmpliScreen™ HBV test using the standard specimen processing procedure can detect HBV DNA levels as low as 13 IU/mL with a 95% test positive rate. Guidelines established by EDQM recommend at least 20 negative plasma pools spiked with HBV DNA to a final concentration of 3 times the 95% cut off value (39 IU/mL) should be tested and found positive. The accuracy of the targeted 39 IU/mL value was assessed by testing plasma pools spiked with the in-house standard to a titer of 39 IU/mL. The acceptance criteria that positive samples must be detected at a 95% test positive rate and that no positive results be obtained from negative diluent samples was achieved.

4. RTL Plasma Donation NAT Minipool Strategy

Talecris performs Nucleic Acid Amplification Technology (NAT) on mini-pools of plasma donations to avoid the loss of complete manufacturing pools and to reduce the viral load in plasma pools challenging the manufacturing process. The size of the mini-pools and the sensitivity of the NAT tests used to perform donation testing allow identification and removal of single plasma units testing positive by NAT. The Raleigh Test Laboratory uses validated automated pipetting instruments to create mini-pools of 96 plasma donations for HCV, HIV-1, HBV and to create mini-pools of 96 to 480 plasma donations for Parvovirus B19 testing by NAT. A summary scheme of the current RTL strategy of mini-pool testing is provided in Figure 1.

National Genetics Institute (NGI) serves as an alternate test site for HCV, HIV-1, HBV and Parvovirus B19 testing of minipools. The NGI HCV, HIV-1, HBV and Parvovirus B19 NAT tests are validated to test minipools of up to 512 plasma donations.

Figure 1 - RTL Plasma Donation NAT Minipool Scheme



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Plasma Pool

Specification

Test Specification for the Plasma Manufacturing Pool

Number of Pages
(including cover page)

2

Original is signed

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Name and Rank Date

Valid from: 18 Oct 2006

Test	Specification
HBsAg	Non-Reactive
Anti-HIV-1/HIV-2	Negative
HCV by NAT	Negative
HIV-1 by NAT	Negative
HBV by NAT	Negative
Parvovirus B19 by NAT	Non-Elevated ($\leq 1 \times 10^3$ IU of Parvovirus B19 DNA/mL)

Plasma Pool

Test Procedure

Number of Pages
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3

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Valid from: 05 Dec 2007

1. Test Method Information

The test methods performed on each plasma manufacturing pool processed at the Clayton, NC fractionation facility are listed in Table 1.

Table 1 - Test Methods

Parameter	Test Method/ Name of Test Kit	Manufacturer	US License Number	Test Site
HBsAg	Abbott Auszyme® Monoclonal	Abbott Laboratories	US License No. 0043	Talecris Clayton, NC
Anti-HIV-1/2	Abbott HIVAB™ HIV-1/HIV-2 (rDNA) EIA	Abbott Laboratories	US License No. 0043	Talecris Clayton, NC
HCV by NAT	Roche COBAS AmpliScreen™ HCV Test	Roche Diagnostics	US License No. 1636	Talecris Raleigh, NC
HIV-1 by NAT	Roche COBAS AmpliScreen™ HIV-1 Test	Roche Diagnostics	US License No. 1636	Talecris Raleigh, NC
HBV by NAT	Roche COBAS AmpliScreen™ HBV Test	Roche Diagnostics	US License No. 1636	Talecris Raleigh, NC
Parvovirus B19 by NAT	Digene SHARP Signal™ System Assay	NA[a]	NA[a]	Talecris Raleigh, NC
Parvovirus B19 by NAT	Parvo B19 Fluorogenic Donation Qualification Assay version 1 (B19 FDQA, v1)	NA[b]	NA[b]	Talecris Raleigh, NC
HCV by NAT	NGI UltraQual™ HCV RT-PCR Assay	NA[b]	US License No. 1582[b]	National Genetics Institute[c] (NGI)
HBV by NAT	NGI UltraQual™ HBV PCR Assay	NA[b]	NA	NGI
HIV-1 by NAT	NGI UltraQual™ HIV-1 RT-PCR Assay	NA[b]	US License No. 1582[b]	NGI
Parvovirus B19 by NAT	NGI Parvovirus SuperCycle Assay	NA[d]	NA[d]	NGI

[a] The Digene SHARP Signal™ System Assay and the B19 FDQA, v1 are in-house test methods developed by Talecris and the testing is performed under the authority of Talecris. The tests are performed as an in-process control and the kits are not distributed.

[b] The NGI UltraQual™ HCV, HBV and HIV-1 assays are in-house test methods developed by NGI and performed as a testing service under the authority and license of NGI. The tests are not distributed.

[c] National Genetics Institute serves as an alternate/back-up manufacturing pool testing laboratory to perform HCV, HBV, HIV-1 and Parvovirus B19 NAT as necessary. No Talecris plasma manufacturing pools are tested by NGI at this time.

[d] The NGI Parvovirus SuperCycle Assay is an in-house test method developed by NGI and the testing is performed under the authority of NGI. The test is performed as an in-process control and the test kit is not distributed.

2. Validation of Viral Marker Test Methods

Validation reports for Viral Marker plasma manufacturing pool test methods are presented in Chapter 2.2.2.a, *Viral Marker Testing of the Plasma Pool*. The ICH Harmonized Tripartite Guideline on the Validation of Analytical Procedures was used for the validation of the Viral Marker test methods. The validation of the viral marker tests for the plasma manufacturing pool were carried out in accordance with the two BWP guidelines (made effective as of April 2007) *Guideline on Validation of Immunoassay for the Detection of Antibody to Human Immunodeficiency Virus (Anti-HIV) in Plasma Pools*, (EMEA/CHMP/BWP/298388/2005) and *Guideline on Validation of Immunoassay for the Detection of Hepatitis B Virus Surface Antigen (HBsAg) in Plasma Pools*, (EMEA/CHMP/BWP/298390/2005).

3. Validation of NAT Test Methods

Validation reports for NAT plasma manufacturing pool test methods are presented in Chapter 2.2.2.b, *NAT Testing of the Plasma Pool*. The ICH Harmonized Tripartite Guideline on the Validation of Analytical Procedures and the EDQM document PA/PH/OMCL (98) 22, DEF *Validation of Nucleic Acid Amplification Technology (NAT) For The Detection of Hepatitis C Virus (HCV) RNA In Plasma Pools* and PA/PH/OMCL (03) 38, DEF *Guideline for Validation of Nucleic Acid Amplification Techniques (NAT) for Quantitation of B19 Virus in DNA in Plasma Pools*, were used for the validation of the NAT test methods.

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Validation Report of Test Methods/Other Methods Revision 1

Determination of Hepatitis B Surface Antigen (HBsAg) in Plasma or Plasma Derived Products by EIA

Number of Pages
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Table of Contents

Table 1: Summary of Assay Characteristics and Acceptance Criteria for Validation of the procedure "Determination of Hepatitis B Surface Antigen (HBsAg) in Plasma or Plasma Derived Products by EIA"

Characteristic	Validation Design	Statistics to Report	Actual Results			
Precision (Repeatability)	Absorbance determined for 3 plasma pools (unspiked), 3 plasma pools (spiked), kit controls, and kit negative control spiked	Mean, Standard Deviation, % CV		Operator 1		
				Mean	SD	% CV
			Kit Negative Control	0.004	0.005	147.5
			Kit Positive Control	0.872	0.054	6.2
			Plasma Pool 1, unspiked	0.003	0.005	139.9
			Plasma Pool 2, unspiked	0.004	0.005	124.9
			Plasma Pool 3, unspiked	0.006	0.005	81.1
			Plasma Pool 4, spiked	0.041	0.010	23.1
			Plasma Pool 5, spiked	0.035	0.006	18.0
			Plasma Pool 6, spiked	0.038	0.010	26.0
			Kit Negative Control, spiked	0.079	0.046	5.3
				Operator 2		
				Mean	SD	% CV
			Kit Negative Control	0.007	0.004	49.2
			Kit Positive Control	0.924	0.071	7.1
			Plasma Pool 1, unspiked	0.005	0.003	50.1
			Plasma Pool 2, unspiked	0.007	0.008	105.4
			Plasma Pool 3, unspiked	0.0063	0.005	157.1
			Plasma Pool 4, spiked	0.034	0.018	54.4
			Plasma Pool 5, spiked	0.034	0.020	57.0
			Plasma Pool 6, spiked	0.033	0.014	40.5
			Kit Negative Control, spiked	0.060	0.052	86.6
Precision (Intermediate)	Retrospective Data from 100 negative pools, kit negative control, and kit positive control	Mean, Standard Deviation, % CV		Mean	SD	% CV
			Pool	0.007	0.006	91.1
			Negative Control	0.005	0.004	80.3
			Positive Control	0.835	0.124	13.1
Specificity	Comparison of kit positive control to kit negative control	Fold-Difference		Operator 1	Operator 2	
			Original Validation Data	218-fold	132-fold	
			Retrospective Pool Data	167-fold (multiple operators)		
Detection Limit	Comparison of kit negative control to cutoff	Fold-Difference		Operator 1	Operator 2	
			Original Validation Data	7-fold	5-fold	
			Retrospective Pool Data	6-fold (multiple operators)		

Summary

The purpose of this study is to validate the method for determination of Hepatitis B surface antigen in plasma pools. This method is described in the procedure "Determination of Hepatitis B Surface Antigen (HBsAg) in Plasma or Plasma Derived Products by EIA". It is an *in vitro* enzyme immunoassay (EIA) for the detection of Hepatitis B surface antigen.

Introduction

The purpose of this document is to describe the characteristics evaluated in order to validate the method "Determination of Hepatitis B Surface Antigen (HBsAg) in Plasma or Plasma Derived Products by EIA" and to report the results of the validation study in order to determine the suitability of the method for the determination of Hepatitis B surface antigen in plasma pools.

Principle

In this method, the Abbott AUSZYME® Monoclonal immunoassay, beads, coated with mouse monclonal antibody to Hepatitis B surface antigen (anti-HBs), are incubated with plasma samples. Any HBsAg present in the plasma sample is bound to the solid phase antibody. The antibody-antigen complex on the bead reacts with added enzyme-conjugate. The amount of antigen present in the sample is directly proportional to the absorbance of the sample at 492 nm.

Validation Testing Facility

Bayer Corporation
Quality Assurance
8368 U.S. 70 West
Clayton, North Carolina 27520
(919) 553-5011

Description of Products Being Tested

Plasma pools were created using 20 or more individual units.

Sensitivity panel consisting of 17 samples of negative recalcified plasma spiked with varying amounts of human HBsAg ranging from 0 ng/mL to 3.999 ng/mL. The panel was supplied by Abbott Diagnostics (Abbott Park, IL).

A combination of sensitivity panel samples A (3.674 ng/mL of HBsAg), E (3.999 ng/mL of HBsAg), J (2.040 ng/mL of HBsAg), and K (1.904 ng/mL of HBsAg) were used to spike samples at a ratio of 1:10. The positive sensitivity panel samples were used in order to provide a means

of quantitation to spike response. The average of samples A, E, J, and K is 2.9 ng/mL. Negative samples (plasma pools and kit negative control) were spiked with a 1:10 dilution of this combined positive material.

Validation Design

Precision (Repeatability): Three plasma pool samples (unspiked), three plasma pool samples [spiked (9 parts plasma and one part 2.9 ng/mL HBsAg)], the kit controls, and the kit negative control [spiked (9 parts kit negative control and one part 2.9 ng/mL HBsAg)] were tested by each of two operators on three separate days.

Precision (Intermediate): One-hundred negative plasma pools and their respective kit controls (positive and negative) were tested by multiple operators over a period of approximately 6 months.

Specificity: Specificity was addressed by comparing the kit negative control to the kit positive control. In addition, kit negative and positive controls were compared from the retrospective data from the testing of 100 negative pools.

Detection Limit: The lower limit of detection is set by the cutoff value, which is defined by the kit manufacturer (Abbott). Since this is not a quantitative test, a numerical value cannot be placed on this response level. However, as part of the commercial antibody panel, samples designated as weakly positive were included in the study, to assess the sensitivity of the assay. In addition, a comparison was made between the cutoff value and the kit negative control absorbances from both the original validation and the retrospective pool data.

Comparison of EIA Method to RIA Method: A comparison between the EIA method and the RIA method was done by testing the Abbott sensitivity panel by both the EIA and the RIA methods. The testing was performed three times each by two operators.

Discussion of Experimental Results

Precision (Repeatability) was determined by analyzing three plasma pool samples (unspiked), three plasma pools (spiked), negative and positive kit controls, and kit negative control (spiked). All samples for each lot were analyzed by each of two operators on three separate days (Tables 2-3). The data is summarized in Table 4. All positive and negative kit controls were within kit specifications. The high % c.v.'s (coefficient of variation) for the negative kit control and the plasma pool samples reflect the low absorbance values. Only the kit positive control had a % c.v. of less than 10%. Its absorbance value was approximately 0.9. The highest absorbance value for the plasma pool samples and the kit negative control was 0.041 (spiked plasma pool sample 4; operator 1).

Precision (Intermediate) was determined by evaluating retrospective data from 100 pools that tested negative for HBsAg and the kit controls (negative and positive) that were included with each determination. The % c.v. was approximately 15% for the positive control (Table 5). For both the negative control and the 100 plasma pool samples, the % c.v. was 80% to 90%. The higher %c.v. is reflective of the extremely low absorbance values for the negative control (0.005) and the pool samples (0.007).

Specificity of the assay was demonstrated by the ratio of the mean of the positive control values to the mean of the negative control values, as summarized in Table 6. The positive control was 218-fold higher than the negative control for Operator 1 and 132-fold higher for Operator 2. In addition, the positive and negative control samples were compared from the 100 retrospective pool tests (Table 5). In the retrospective study, the positive control was 167-fold higher than the negative control. Both sets of data show that there is ample spread between the positive and negative samples to yield confidence in assigning a sample as either reactive or nonreactive.

Detection Limit was assessed by determining the reactivity of the sensitivity panel. Each of the panel members had varying amounts of HBsAg ranging from 0.000 ng/mL to 3.999 ng/mL. The data in Table 7 show that the panel was consistently reactive (100% of the replicates were positive) at the 0.784 ng/mL level (or greater) of HBsAg (samples B, C, N, K, J, A, and E). Sample S contained 0.485 ng/mL and tested reactive 100% of the time. However, sample R contained 0.730 ng/mL and tested reactive 92% of the time; sample P contained 0.525ng/mL of HBsAg and tested reactive 75% of the time. The difference among samples is that R and P have antigen *ad* subtype while S has antigen of the *ay* subtype. In this assay, the subtype detection limit is slightly different resulting in an assay that is more sensitive for the *ay* subtype of the HBsAg than the *ad* subtype. The sensitivity samples were provided and quantitated by Abbott Diagnostics. This level establishes the overall detection limit of the assay for plasma pools at 0.784 ng/mL.

Also, detection limit was assessed by comparing the cutoff value to the kit negative control.. The data from the original validation show that the cutoff value is approximately 5- to 7-fold higher than the negative control (Table 6). For the retrospective 100 negative pools, the cutoff value is 6-fold higher than the negative control (Table 5).

Comparison of the EIA method to the RIA method was done by determining the reactivity of the Abbott sensitivity panel by both methods. As shown in Table 8, EIA demonstrates greater sensitvity than RIA. The EIA method shows reactivity 100% of the time at 0.784ng/mL HBsAg while 3.674 ng/mL HBsAg is needed for the RIA to give reactivity 100% of the time.

Conclusions

Validation of the method CQAB 08-090 "Determination of HBsAg in Plasma or Plasma Derived Products by EIA" for plasma pools was accomplished by running a series of experiments that assessed the following characteristics: Precision, Specificity and Detection Limit. "Determination of HBsAg in Plasma or Plasma Derived Products by EIA" in plasma pools, CQAB 08-090, is considered validated and suitable for its intended purposes.

References

1. CQAP 202 "Validation of Analytical Methods", Revision 3.
2. ICH Harmonized Tripartite Guideline on Validation of Analytical Procedures", May 1997

Attachments

Table 1:	Summary of Assay Characteristics and Acceptance Criteria for Validation of the procedure "Determination of Hepatitis B Surface Antigen (HBsAg) in Plasma or Plasma Derived Products by EIA"
Table 2:	Operator 1: Absorbance Values for Samples Assayed Day 1, Day 2, and Day 3
Table 3:	Operator 2: Absorbance Values for Samples Assayed Day 1, Day 2, and Day 3
Table 4:	Precision (Repeatability): Statistical Summary of Original Validation Data
Table 5:	Precision (Intermediate), Specificity and Detection Limit: Statistical Summary of Retrospective Data and Comparison of Controls
Table 6:	Specificity and Detection Limit: Comparison of Positive and Negative Controls
Table 7:	Detection Limit: Raw Data for Sensitivity Panels
Table 8:	Comparison of EIA and RIA Methods
Appendix 1:	Pool Data for Retrospective Study

Table 2: Operator 1: Absorbance Values for Samples Assayed Day 1, Day 2, and Day 3

Sample		Day 1	Day 2	Day 3
Kit Negative Control:	Well 1	0.011	0.004	-0.006
	Well 2	-0.001	0.004	0.011
	Well 3	0.002	0.006	0.002
Mean		0.004	0.005	0.002
Kit Positive Control2:	Well 1	0.892	0.839	0.819
	Well 2	0.968	0.876	0.836
Mean		0.930	0.858	0.828
Plasma Pool 1(unspiked)	Well 1	0.000	0.003	-0.001
	Well 2	0.011	0.004	0.001
	Well 3	0.011	-0.001	0.002
Mean		0.007	0.002	0.001
Plasma Pool 2 (unspiked)	Well 1	0.014	0.002	-0.003
	Well 2	0.007	0.001	0.001
	Well 3	0.005	0.006	0.002
Mean		0.009	0.003	0.012
Plasma Pool 3 (unspiked)	Well 1	0.002	0.016	0.009
	Well 2	0.003	0.008	0.006
	Well 3	0.001	0.010	0.001
Mean		0.002	0.011	0.005
Plasma Pool 4 (spiked)	Well 1	0.046	0.042	0.034
	Well 2	0.046	0.045	0.029
	Well 3	0.059	0.036	0.029
Mean		0.050	0.041	0.031
Plasma Pool 5 (spiked)	Well 1	0.033	0.038	0.041
	Well 2	0.028	0.033	0.044
	Well 3	0.036	0.039	0.024
Mean		0.032	0.037	0.036
Plasma Pool 6 (spiked)	Well 1	0.042	0.050	0.026
	Well 2	0.036	0.054	0.026
	Well 3	0.042	0.038	0.030
Mean		0.040	0.047	0.027
Kit Negative Control (spiked)	Well 1	0.111	0.103	0.017
	Well 2	0.103	0.121	0.017
	Well 3	0.103	0.114	0.020
Mean		0.106	0.113	0.018
Cutoff Value[a]		0.029	0.030	0.027

[a] Cutoff Value = Negative Control Mean + 0.025

Table 3: Operator 2: Absorbance Values for Samples Assayed Day 1, Day 2, and Day 3

Sample		Day 1	Day 2	Day 3
Kit Negative Control:	Well 1	0.008	0.013	0.003
	Well 2	0.012	0.004	0.003
	Well 3	0.008	0.008	0.007
Mean		0.009	0.008	0.004
Kit Positive Control:	Well 1	0.993	0.925	0.819
	Well 2	0.958	0.989	0.861
Mean		0.976	0.957	0.840
Plasma Pool 1 (unspiked)	Well 1	0.009	0.005	0.009
	Well 2	0.005	0.002	0.004
	Well 3	0.004	0.002	0.007
Mean		0.006	0.003	0.007
Plasma Pool 2 (unspiked)	Well 1	0.008	-0.001	0.002
	Well 2	0.006	0.005	0.013
	Well 3	0.015	-0.003	0.020
Mean		0.010	0.000	0.012
Plasma Pool 3 (unspiked)	Well 1	0.000	0.002	0.000
	Well 2	0.015	-0.002	0.007
	Well 3	-0.001	0.003	0.007
Mean		0.005	0.001	0.005
Plasma Pool 4 (spiked)	Well 1	0.041	0.047	0.009
	Well 2	0.042	0.053	0.012
	Well 3	0.055	0.032	0.012
Mean		0.046	0.044	0.011
Plasma Pool 5 (spiked)	Well 1	0.044	0.031	0.025
	Well 2	0.074	0.029	0.013
	Well 3	0.048	0.037	0.009
Mean		0.055	0.032	0.016
Plasma Pool 6 (spiked)	Well 1	0.037	0.054	0.019
	Well 2	0.043	0.031	0.018
	Well 3	0.042	0.042	0.015
Mean		0.041	0.042	0.017
Kit Negative Control (spiked)	Well 1	0.128	0.014	0.019
	Well 2	0.119	0.021	0.026
	Well 3	0.131	0.059	0.019
Mean		0.126	0.031	0.021
Cutoff Value*		0.034	0.033	0.029

* Cutoff Value = Negative Control Mean + 0.025

Table 4. Precision (Repeatability): Statistical Summary of Original Validation Data [a]

	Operator 1			Operator 2		
Sample	**Mean**	**S.D.**	**% c.v.**	**Mean**	**S.D**	**% c.v.**
Kit Negative Control	0.004	0.005	147.5	0.007	0.004	49.2
Kit Positive Control	0.872	0.054	6.2	0.924	0.071	7.7
Plasma Pool 1 (unspiked)	0.003	0.005	139.9	0.005	0.003	50.5
Plasma Pool 2 (unspiked)	0.004	0.005	124.9	0.007	0.008	105.4
Plasma Pool 3 (unspiked)	0.006	0.005	81.1	0.003	0.005	157.1
Plasma Pool 4 (spiked)	0.041	0.010	23.8	0.034	0.018	54.4
Plasma Pool 5 (spiked)	0.035	0.006	18.0	0.034	0.020	57.0
Plasma Pool 6 (spiked)	0.038	0.010	26.0	0.033	0.014	40.5
Kit Negative Control (spiked)	0.079	0.046	58.4	0.060	0.052	86.6
Cutoff Value[b]	0.029	0.002	5.3	0.032	0.003	8.3

[a] Summary of data from Tables 2-3

[b] Cutoff Value = Negative Control Mean + 0.025

Table 5. Precision (Intermediate), Specificity and Detection Limit: Statistical Summary of Retrospective Data and Comparison of Controls[a]

Sample	Mean	S.D	% c.v.
Kit Negative Control	0.005	0.004	80.3
Kit Positive Control	0.835	0.124	14.9
Plasma Pool	0.007	0.006	91.1
Cutoff Value[b]	0.030	0.004	13.1

Ratio: Negative/Positive	0.599
Fold Difference: Positive/ Negative	167-fold
Fold Difference: Positive/Cutoff	28-fold
Fold Difference: Cutoff/Negative	6-fold

[a] Individual pool and control data is in Appendix A
[b] Cutoff Value = Negative Control Mean + 0.025