



Seroconversion Panels

Improving test kit quality

Teaching us about early infection with
HIV, HCV and HBV

Darmstadt, Germany

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Seroconversion Panels

- What are they?
- Where do they come from?
- How were they found?
- Why are they useful?
- What are they for?

Whole Blood Collections



- **13 million U.S. collections annually**
- **8.7 million donors**
- **1.5 donations/year**
- **About 450 mls/collection, 200 mls plasma**

Source Plasma Collections



- 13 million U.S. collections annually
- 400 centers
- 750,000 donors
- 17 donations/year
- 500 – 880 mls/collection



*Portland Biologicals
Thanks You for your
Plasma Donations*

Who can ever forget and not be touched by the horrific pictures of "America under Attack." Once again, it is our soldiers who will be called upon to defend our freedom and our way of life. We, at home, can do our part and help support our armed forces by donating plasma. They need us now... more than ever.

**Please help. "Where it pays to care...
earn up to \$185/month"**

Did you know... that your plasma can save lives everyday? Plasma is used by our armed forces:



to treat shock due to trauma or hemorrhage (gunshot)
to treat fluid loss due to severe burns
in cardiovascular surgery

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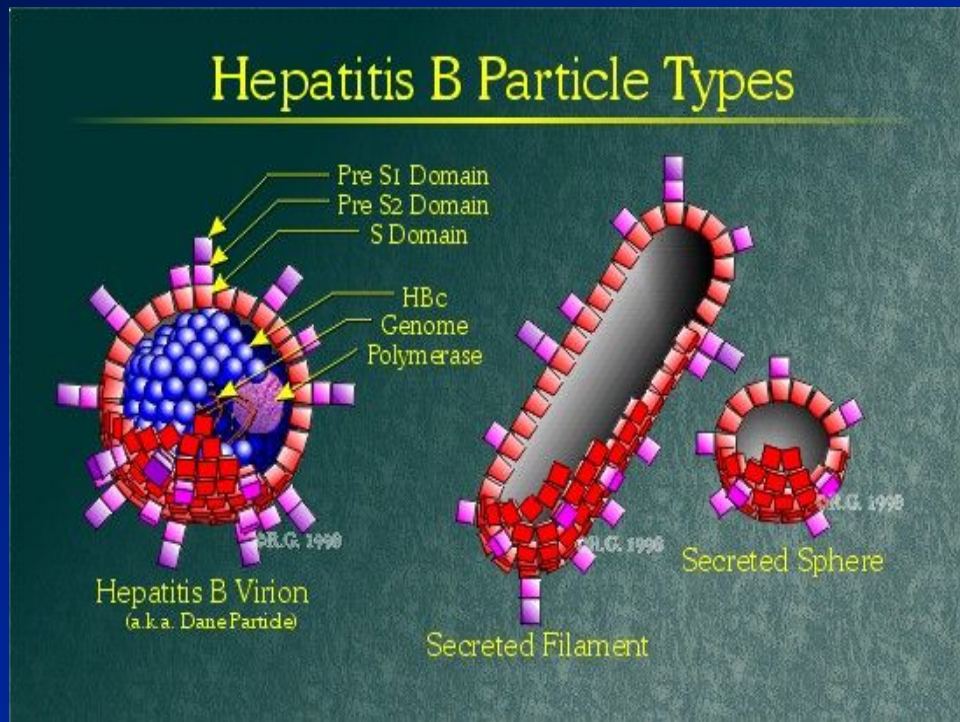
GOD BLESS AMERICA



Uses for Whole Blood and Plasma

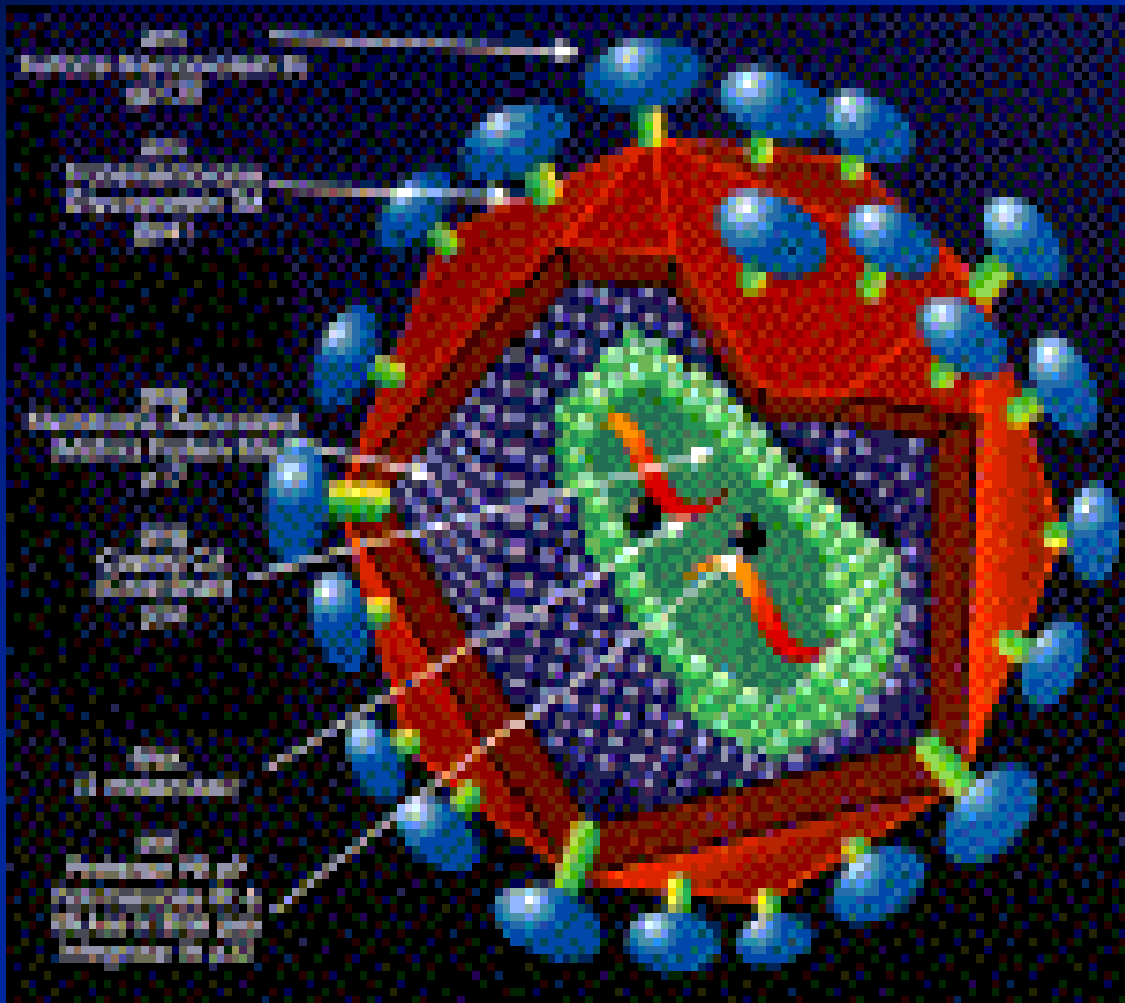
- Whole Blood uses
 - Transfusion of red cells, platelets, plasma
 - Recovered plasma for further manufacture
- Plasma uses
 - Source plasma for manufacture into therapeutics like FVIII, IVIG, albumin
 - Specialty plasma for use in vaccines and other therapeutics
 - Plasma and serum for use in test kits

Hepatitis B Virus Screening



- Hepatitis B surface antigen
- Testing developed in 1972
- Significant improvement in blood product safety
- HBV DNA 1999

Human Immunodeficiency Virus



- New disease reported in 1982
- First anti-HIV tests U.S. licensed 1985
- HIV 1/2 "combo" Ab test U.S. 1992
- HIVAg (p24, viral protein) 1996
- HIV Ag/Ab tests 1998
- HIV RNA 1999

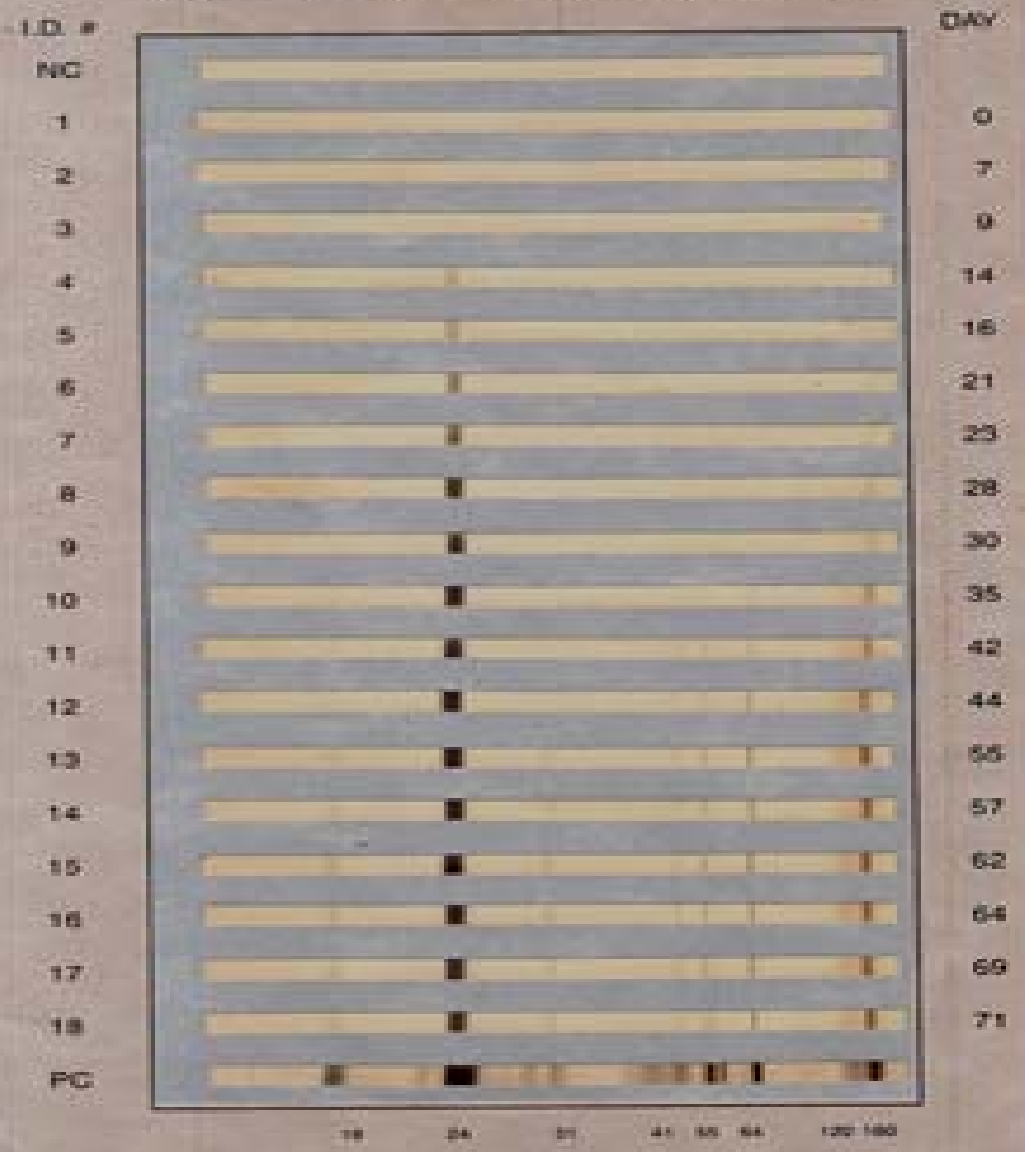


Seroconversion Panel

A serial collection of samples taken over time from a single donor while markers of an infection are emerging

Anti-HIV 1 Seroconversion Panel C

from an asymptomatic seroconverting plasma donor



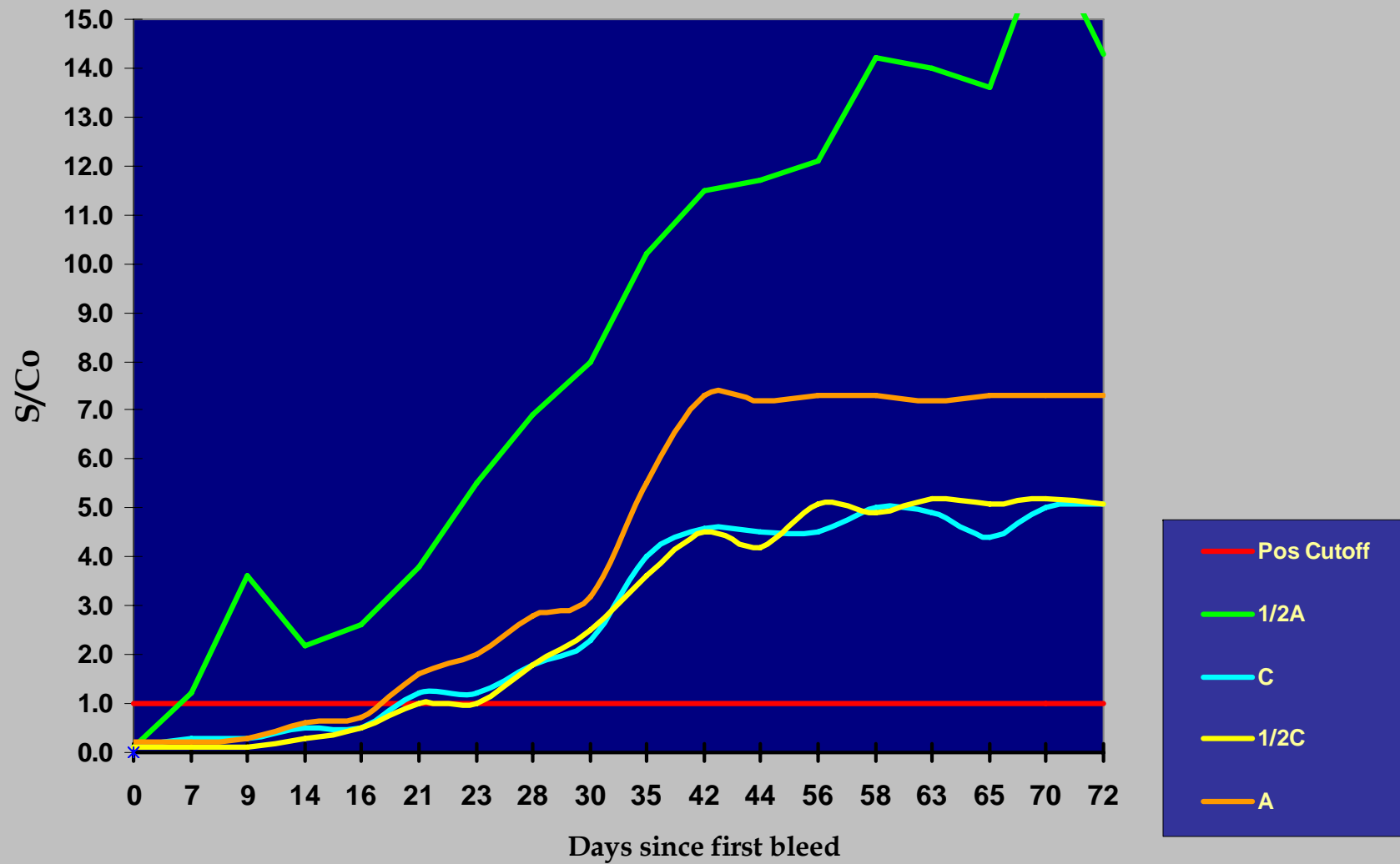
HIV-1 Seroconversion Panel C (PRB903)

Data Sheet

----- U.S. FDA-Licensed Anti-HIV EIA Tests, results expressed as s/co -----

| Member I.D. # | Bleed Dates | Days Since 1st Bleed | 1988 | 1992 | 1988 | 1992 | 1988 | 1992 |
|------------------|----------------|-------------------------|----------------------|----------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| | | | Abbott HIV BBI | Abbott HIV BBI | Gen. Sys. HIV BBI | Gen. Sys. HIV BBI | Org. Tek. HIV BBI | Org. Tek. HIV BBI |
| PRB903-01 | 16-Jul-85 | 0 | 0.4 | 0.2 | 0.3 | 0.1 | 0.4 | 0.4 |
| PRB903-02 | 23-Jul-85 | 7 | 0.3 | 0.2 | 0.1 | 0.3 | 0.5 | 0.4 |
| PRB903-03 | 25-Jul-85 | 9 | 0.3 | 0.3 | 0.2 | 0.3 | 0.7 | 0.4 |
| PRB903-04 | 30-Jul-85 | 14 | 0.5 | 0.6 | 0.4 | 0.5 | 1.0 | 1.0 |
| PRB903-05 | 01-Aug-85 | 16 | 0.5 | 0.7 | 0.8 | 0.5 | 1.2 | 1.2 |
| PRB903-06 | 06-Aug-85 | 21 | 0.9 | 1.6 | 0.8 | 1.2 | 1.6 | 2.1 |
| PRB903-07 | 08-Aug-85 | 23 | 0.9 | 2.0 | 0.8 | 1.2 | 2.0 | 2.3 |
| PRB903-08 | 13-Aug-85 | 28 | 1.0 | 2.8 | 1.1 | 1.8 | 2.2 | 3.2 |
| PRB903-09 | 15-Aug-85 | 30 | 1.8 | 3.2 | 2.0 | 2.3 | 2.3 | 3.6 |
| PRB903-10 | 20-Aug-85 | 35 | 4.7 | 5.5 | 2.6 | 4.0 | 2.7 | 4.5 |
| PRB903-11 | 27-Aug-85 | 42 | 6.3 | 7.3 | 3.3 | 4.6 | 3.0 | 4.7 |
| PRB903-12 | 29-Aug-85 | 44 | 6.4 | 7.2 | 3.3 | 4.5 | 2.7 | 4.8 |
| PRB903-13 | 10-Sep-85 | 56 | 7.1 | 7.3 | 3.3 | 4.5 | 2.9 | 5.3 |
| PRB903-14 | 12-Sep-85 | 58 | 6.7 | 7.3 | 3.7 | 5.0 | 2.9 | 5.1 |
| PRB903-15 | 17-Sep-85 | 63 | 6.0 | 7.2 | 3.0 | 4.9 | 3.0 | 5.1 |
| PRB903-16 | 19-Sep-85 | 65 | 7.5 | 7.3 | 2.8 | 4.4 | 3.0 | 5.4 |
| PRB903-17 | 24-Sep-85 | 70 | 7.4 | 7.3 | 4.1 | 5.0 | 3.0 | 5.5 |
| PRB903-18 | 26-Sep-85 | 72 | 8.8 | 7.3 | 3.7 | 5.1 | 2.9 | 5.2 |

PRB903-Panel C HIV1 and HIV 1/2 Assay Performance



Boston Biomedica, Inc.
HIV-1 Seroconversion Panel AQ (PRB941)
Data Sheet

----- U.S. FDA-Licensed Anti-HIV EIA Tests, results expressed as s/co -----

| Member I.D. # | Bleed Dates | Days Since 1st Bleed | Abbott | Abbott | Gen. Sys. | Gen. Sys. | Org. Tek. |
|-------------------|----------------|-------------------------|------------|----------------|------------|----------------|------------|
| | | | HIV BBI | HIV 1/2 BBI | HIV BBI | HIV 1/2 BBI | HIV BBI |
| PRB941-01 | 22 JUL 96 | 0 | 0.2 | 0.1 | 0.3 | 0.2 | 0.3 |
| PRB941-02 | 26 JUL 96 | 4 | 0.2 | 0.1 | 0.3 | 0.2 | 0.3 |
| PRB941-03 | 31 JUL 96 | 9 | 0.2 | 0.2 | 0.3 | 0.3 | 0.3 |
| PRB941-04 | 09 AUG 96 | 18 | 0.9 | 15.9 | 0.8 | 0.3 | 0.4 |
| PRB941-05 | 12 AUG 96 | 21 | 2.1 | 11.3 | 2.1 | 0.4 | 0.6 |
| PRB941-06 | 16 AUG 96 | 25 | 2.5 | 6.7 | 3.5 | 2.0 | 0.9 |
| Run Date: | | | 26 DEC 96 | 24 DEC 96 | 08 JAN 97 | 30 SEP 97 | 11 JAN 97 |
| Kit Lot #: | | | 23168M301 | 22404M101 | 191NX1 | 091PP1-10 | 160051 |
| Exp. Date: | | | 12 FEB 97 | 01 APR 97 | 28 FEB 97 | 19 MAR 98 | 15 JAN 98 |
| Product #: | | | 3A11 | 3A77 | 0218 | 32542 | 59605 |

----- HIV Antigen Tests, results expressed as s/co -----

| Member I.D. # | Abbott | Coulter | Innogenetics | Org. Tek. | Roche PCR HIV RNA |
|-------------------|-----------|-----------|--------------|-----------|----------------------|
| | BBI | BBI | BBI | BBI | BBI |
| PRB941-01 | 0.3 | 0.0 | 0.3 | 0.0 | BLD |
| PRB941-02 | 0.4 | 0.0 | 0.3 | 0.1 | 3 x 10 ³ |
| PRB941-03 | 0.5 | 1.4 | 1.5 | 0.4 | 5 x 10 ⁴ |
| PRB941-04 | 0.9 | 2.3 | 2.2 | 0.7 | 7 x 10 ⁴ |
| PRB941-05 | 0.4 | 0.2 | 0.4 | 0.1 | 1 x 10 ⁴ |
| PRB941-06 | 0.3 | 0.1 | 0.3 | 0.1 | 9 x 10 ² |
| Run Date: | 08 JAN 97 | 26 DEC 96 | 17 DEC 97 | 08 JAN 97 | 22 JAN 97 |
| Kit Lot #: | 21456M301 | 2066D036 | 70329734 | D02116 | 88106 |
| Exp. Date: | 13 JUN 97 | 18 MAR 97 | 31 MAR 98 | 07 MAR 97 | 30 APR 97 |
| Product #: | 2A81 | 933180 | K-1048 | 59464 | 83088 |



----- INTERNATIONAL Anti-HIV 1/2 Test Kits -----

| Member I.D. # | Days Since 1st Bleed | Abbott 3rd Gen. Plus | Abbott AxSYM | Abbott PRISM | Behring Enzygnost | Biotest HIV 1/2 | Boeh. Mann. Enzymun Gen 3 | Diag. Past. Genscreen |
|------------------|-------------------------|-------------------------|-----------------|-----------------|----------------------|--------------------|------------------------------|--------------------------|
| | | RL19 s/co | RL19 s/co | RL23 s/co | RL23 s/co | RL29 s/co | BBI s/co | RL29 s/co |
| PRB941-01 | 0 | 0.4 | 0.3 | 0.2 | 0.2 | 0.4 | 0.2 | 0.2 |
| PRB941-02 | 4 | 0.4 | 0.4 | 0.3 | 0.1 | 0.4 | 0.2 | 0.3 |
| PRB941-03 | 9 | 0.4 | 0.5 | 0.5 | 0.1 | 0.3 | 0.2 | 0.4 |
| PRB941-04 | 18 | 6.6 | 5.0 | 6.2 | 5.9 | >7.8 | 0.4 | 1.5 |
| PRB941-05 | 21 | 5.8 | 4.9 | 5.8 | 6.0 | >7.8 | 2.2 | 9.3 |
| PRB941-06 | 25 | 4.7 | 4.8 | 5.5 | 5.4 | >7.8 | 7.5 | >14.9 |
| Run Date: | | 05 MAY 97 | 13 MAR 97 | 06 MAR 97 | 20 MAR 97 | 05 MAR 97 | 17 JAN 97 | 03 MAR 97 |
| Kit Lot #: | | 27448HP00 | 27237 LU 03 | 23286HP00 | 28811 | 110076 | 190583-01 | 6L107U |
| Exp. Date: | | 11 SEP 97 | 17 SEP 97 | 19 JUL 97 | 11 MAY 97 | 01 APR 97 | 30 SEP 97 | 15 AUG 97 |
| Product #: | | 7A84 | 9A44 | 4A27 | OQFK12/13 | 807004 | 1557319 | 72276 |

| Member I.D. # | Murex ICE HIV 1.0.2 | Org. Tek. Uniform II Plus | Ortho Capture | Roche DAGS | Fujirebio Serodia | In-House IgA | In-House IgM |
|------------------|------------------------|------------------------------|------------------|---------------|-----------------------------|-----------------|-----------------|
| | RL19 s/co | RL23 s/co | RL29 s/co | RL23 s/co | RL23 Result ² | RL12 s/co | RL12 s/co |
| PRB941-01 | 0.3 | 0.4 | 0.0 | 0.0 | -/- | 0.4 | 0.3 |
| PRB941-02 | 0.3 | 0.4 | 0.0 | 0.1 | -/- | 0.4 | 0.3 |
| PRB941-03 | 0.3 | 0.5 | 0.1 | 0.1 | -/- | 0.4 | 0.8 |
| PRB941-04 | 9.0 | 2.5 | >11.5 | 0.3 | +/- | 2.1 | 4.3 |
| PRB941-05 | >11.0 | 3.7 | >11.5 | 2.2 | +/- | 2.3 | 4.5 |
| PRB941-06 | >11.0 | 5.8 | >11.5 | 9.2 | +/- | 1.9 | 2.9 |
| Run Date: | 01 MAY 97 | 29 APR 97 | 28 FEB 97 | 14 APR 97 | 20 NOV 97 | 25 MAR 97 | 25 MAR 97 |
| Kit Lot #: | BP F046 210 | 97042301 | HVK 102-2 | E1740 | TP70805 | NA | NA |
| Exp. Date: | 28 SEP 97 | 28 MAR 98 | 17 MAY 97 | 31 JAN 98 | 31 AUG 98 | NA | NA |
| Product #: | 00A 1/A2/A3 | 80495 | 932360 | 756059 | 576063 | In-House | In-House |

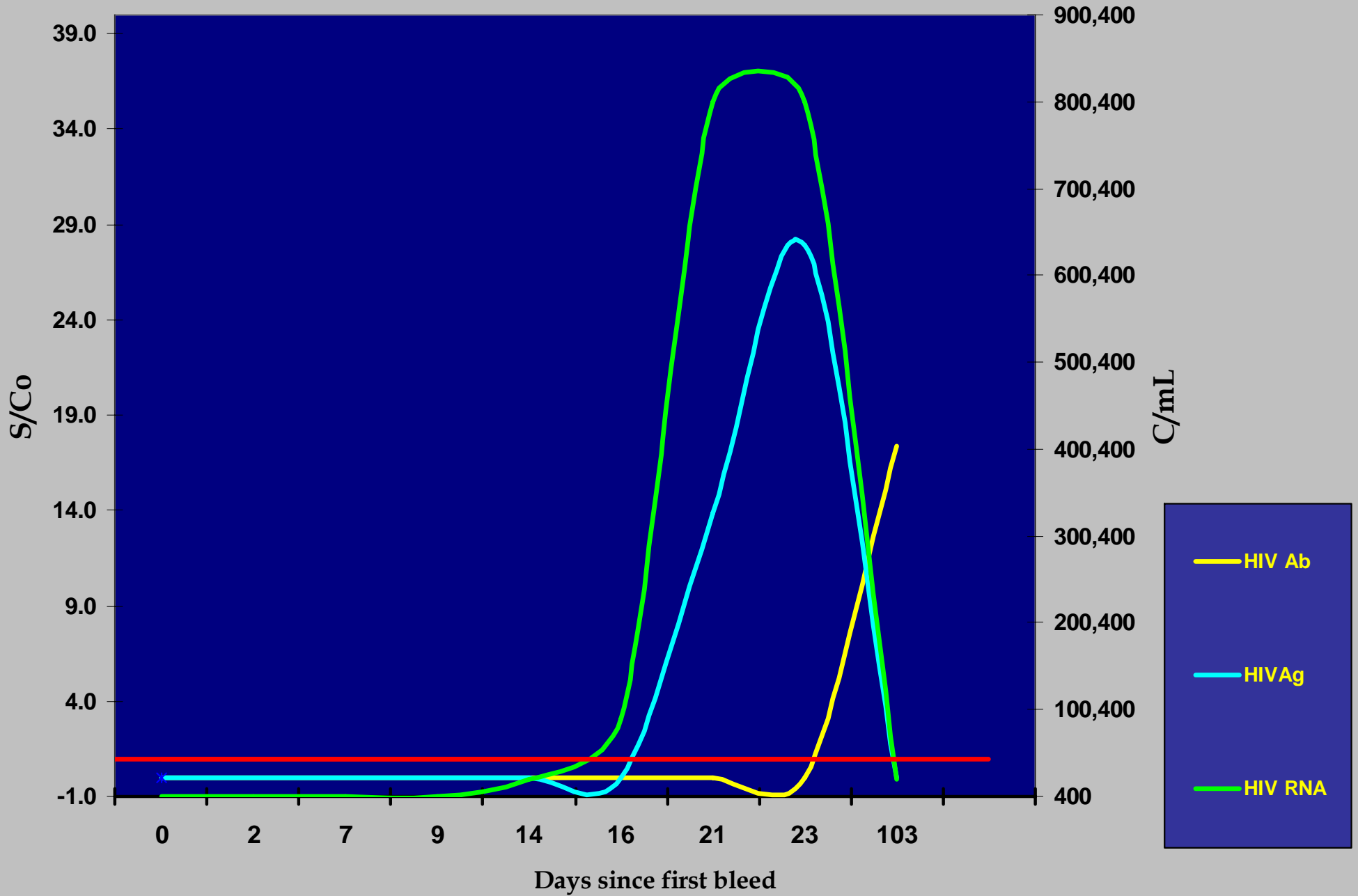
²Results for this particle agglutination assay are expressed for HIV-1/HIV-2 respectively.

Lessons from Seroconversion Panels

Uses in test kit development

- Demonstrate improvements in sensitivity.
- Monitor and compare the sensitivity among tests over time.
- Evaluate tests for one marker in the natural presence and absence of others.

HIV Seroconversion: PRB939

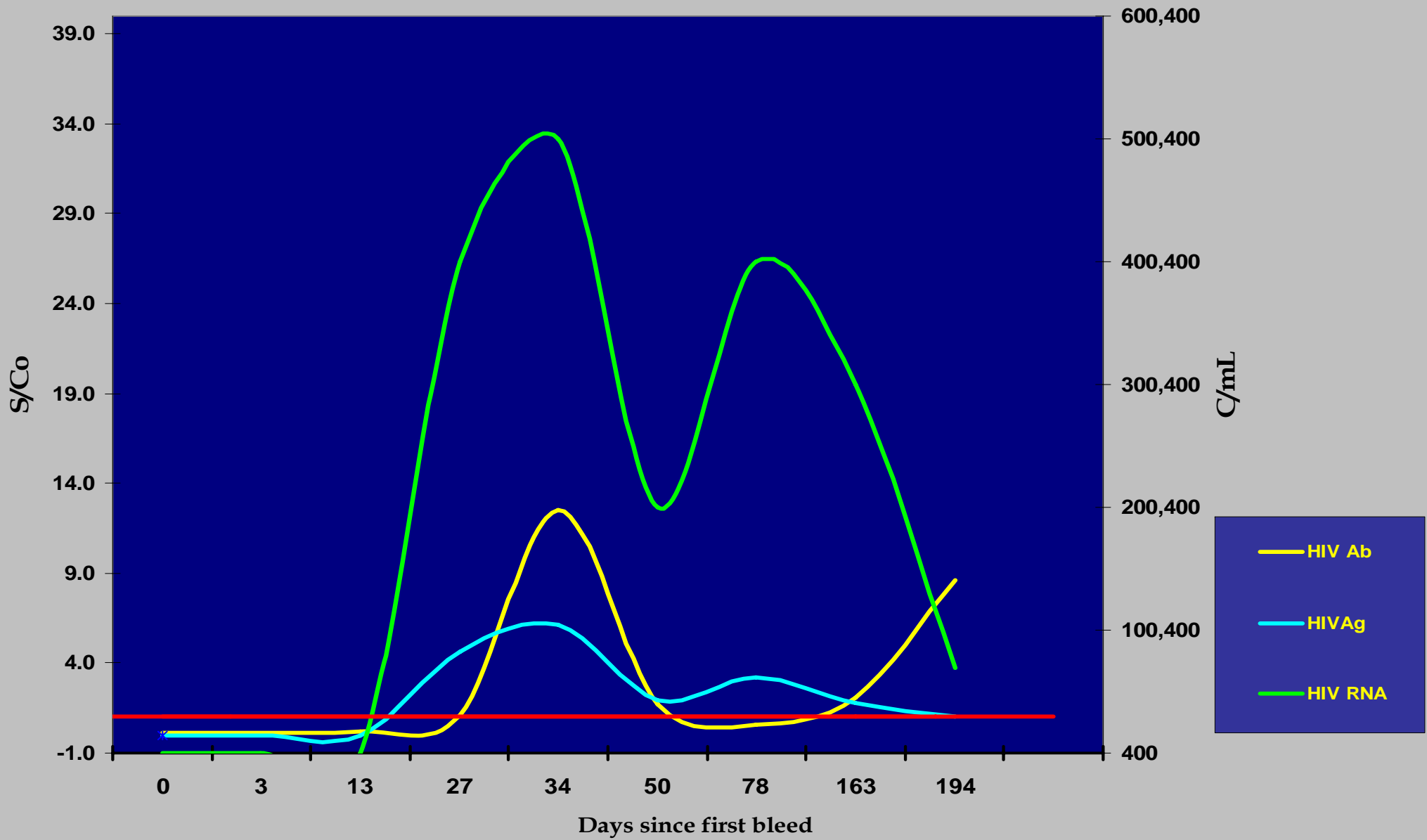


Lessons from Seroconversion Panels

Clinical/Blood Bank/Plasma uses

- Determine window periods, implement safeguards.
- Study viral replication and viral dynamics in the host.
- Correlate clinical stage with viral marker evolution.
- Identify outliers.

HIV Seroconversion: PRB932



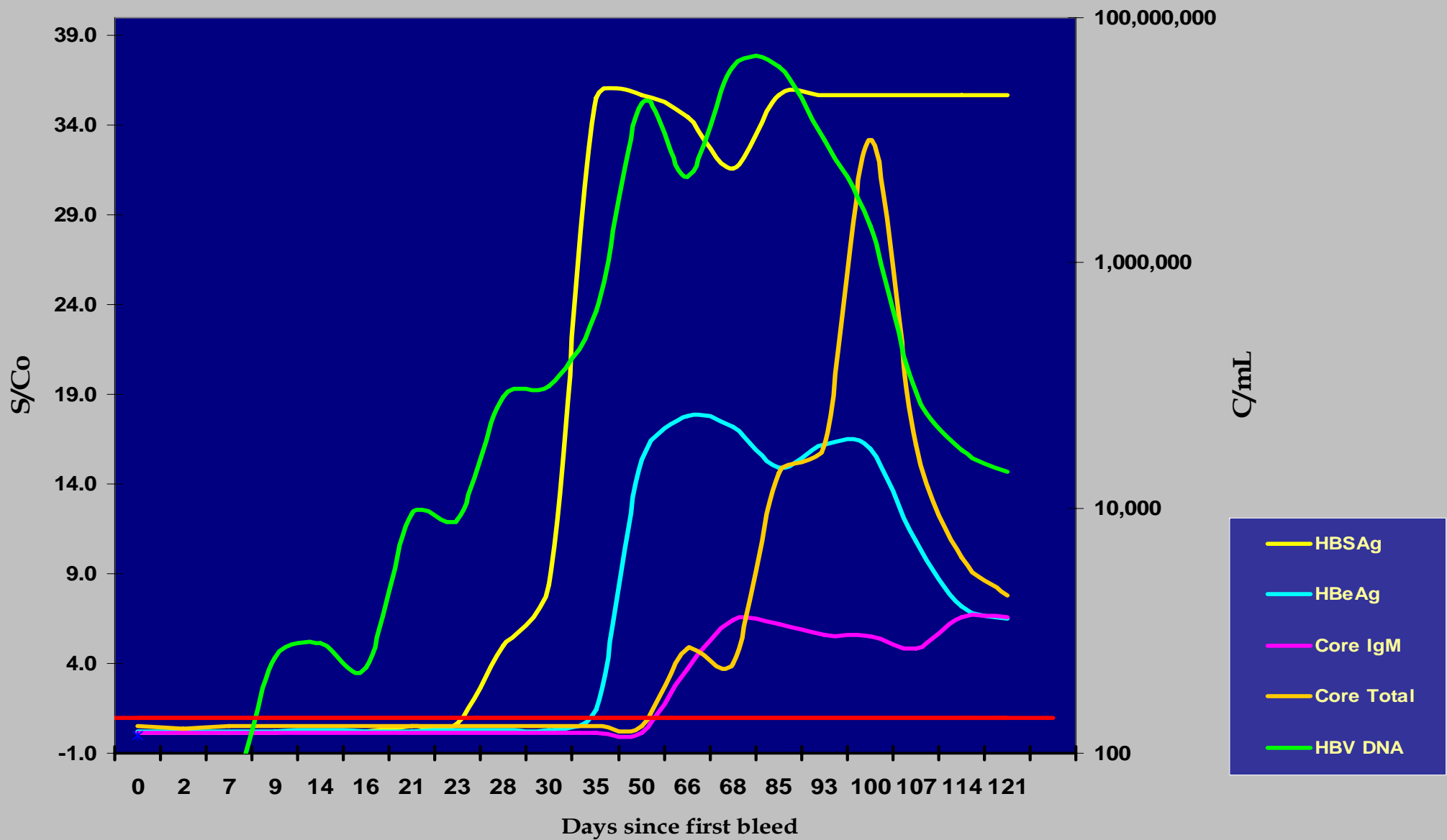
Seroconversion Panel contributions, continued

- Window Period
 - Changes every time a more sensitive test comes along
- Evolution of viral markers
 - As new markers are found, the analytical picture becomes more complex, and more useful

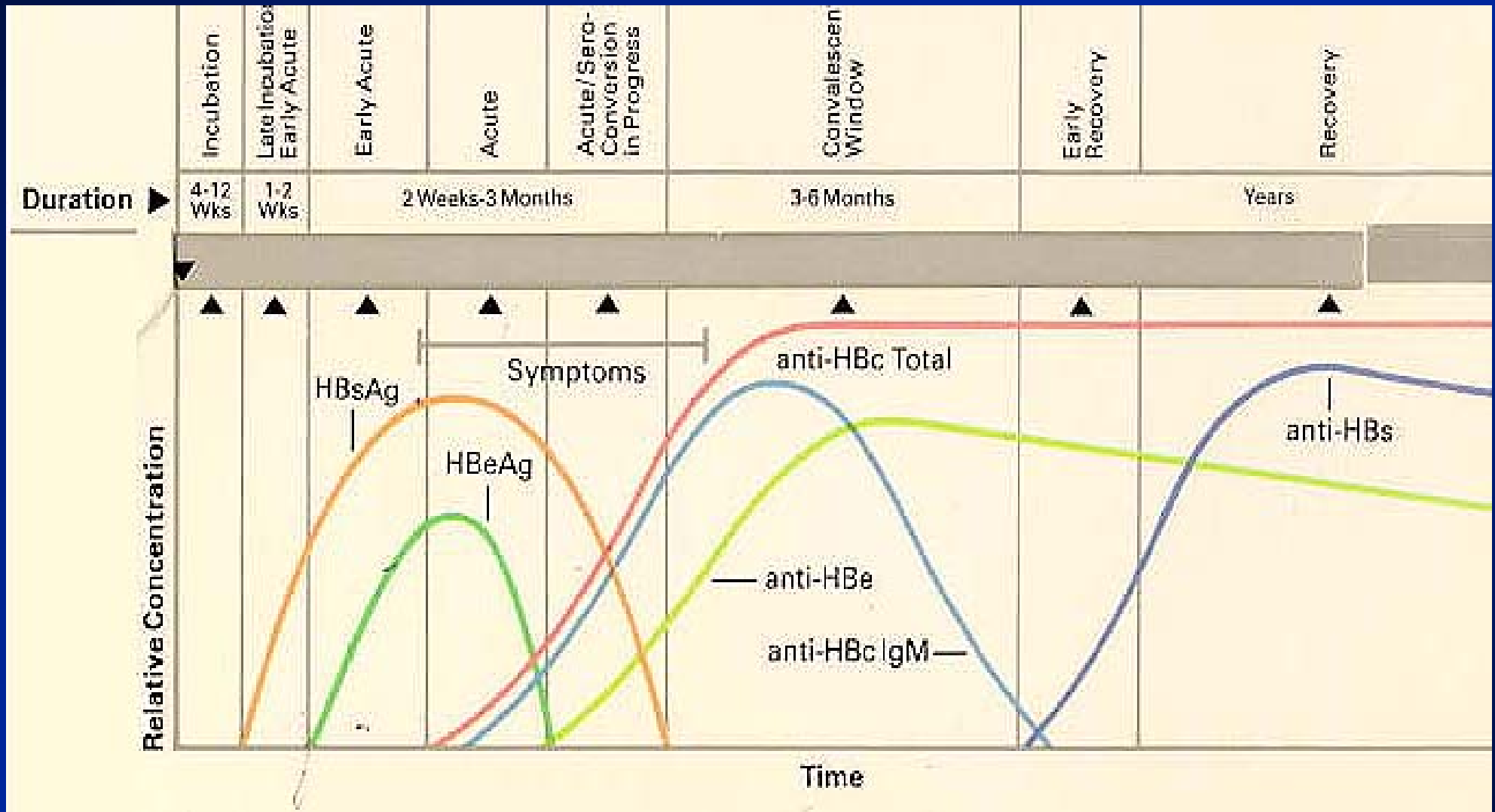
Window Period

| Virus | Window Period (WP) | WP with Minipool | WP with Single Donor |
|--------------|---------------------------|-------------------------|-----------------------------|
| HIV | 22 days | 13 days | 9 days |
| HCV | 70 days | 10 days | 7 days |
| HBV | 45 days | 30 days | 20 days |

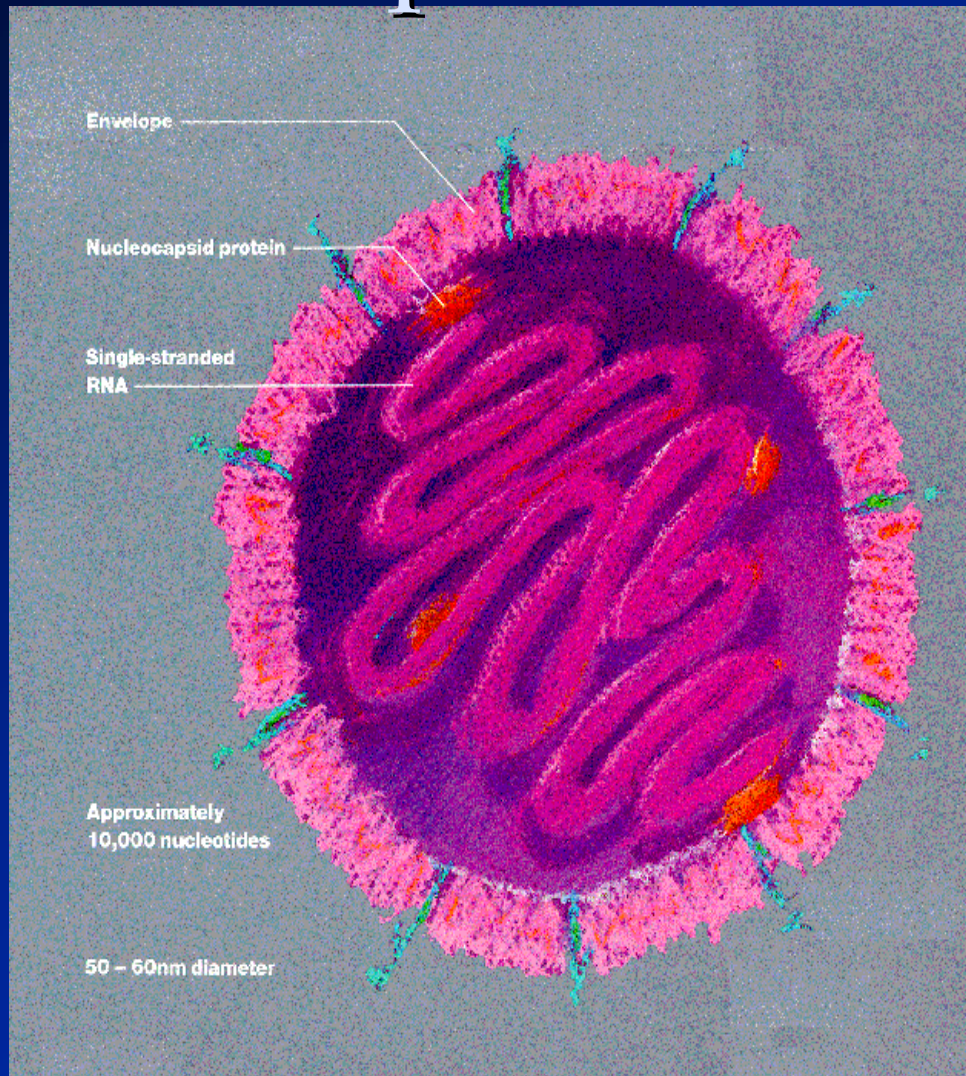
Hepatitis B Seroconversion: PHM935A



Hepatitis B Diagnostic Profile

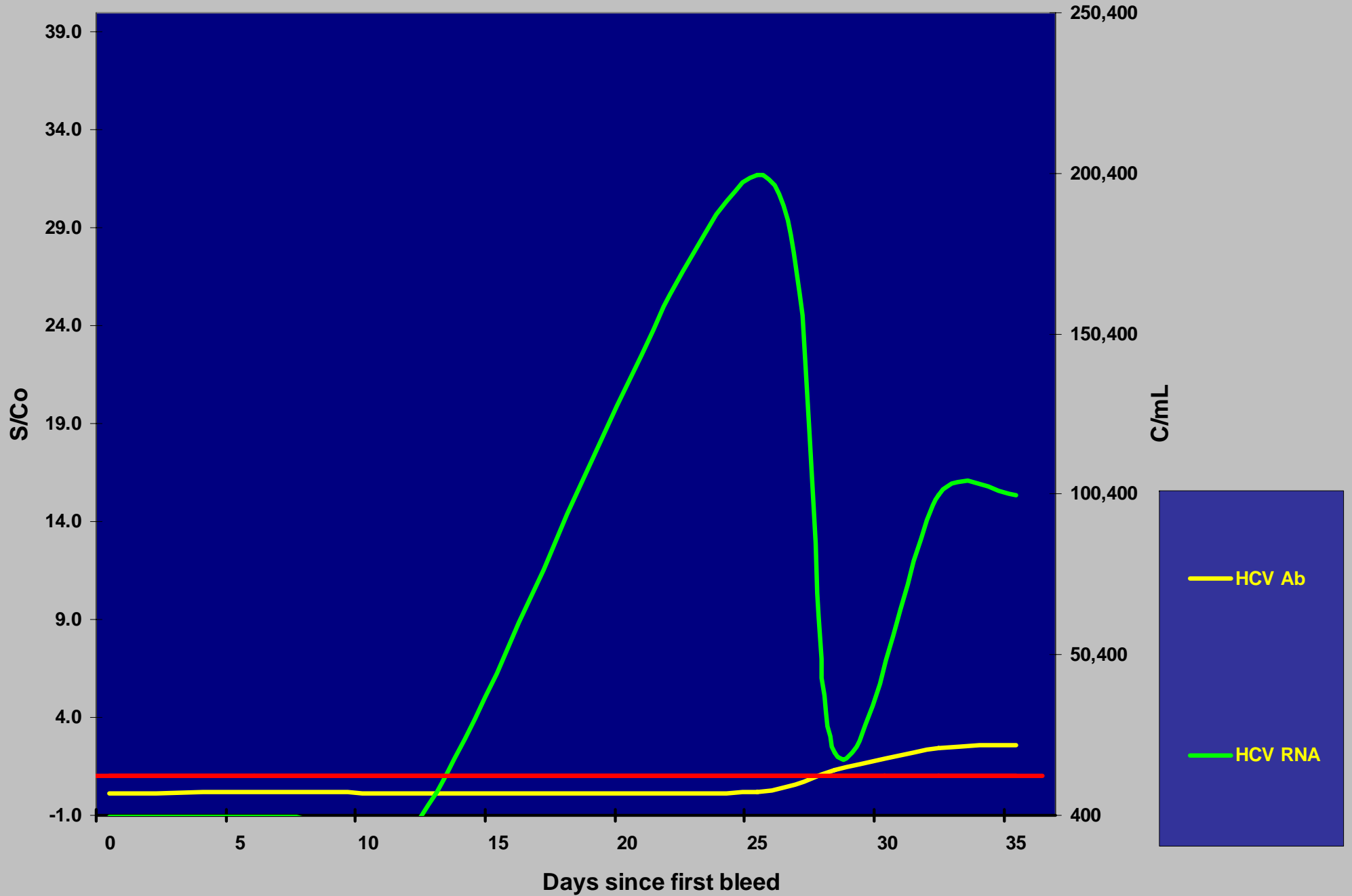


Hepatitis C Virus



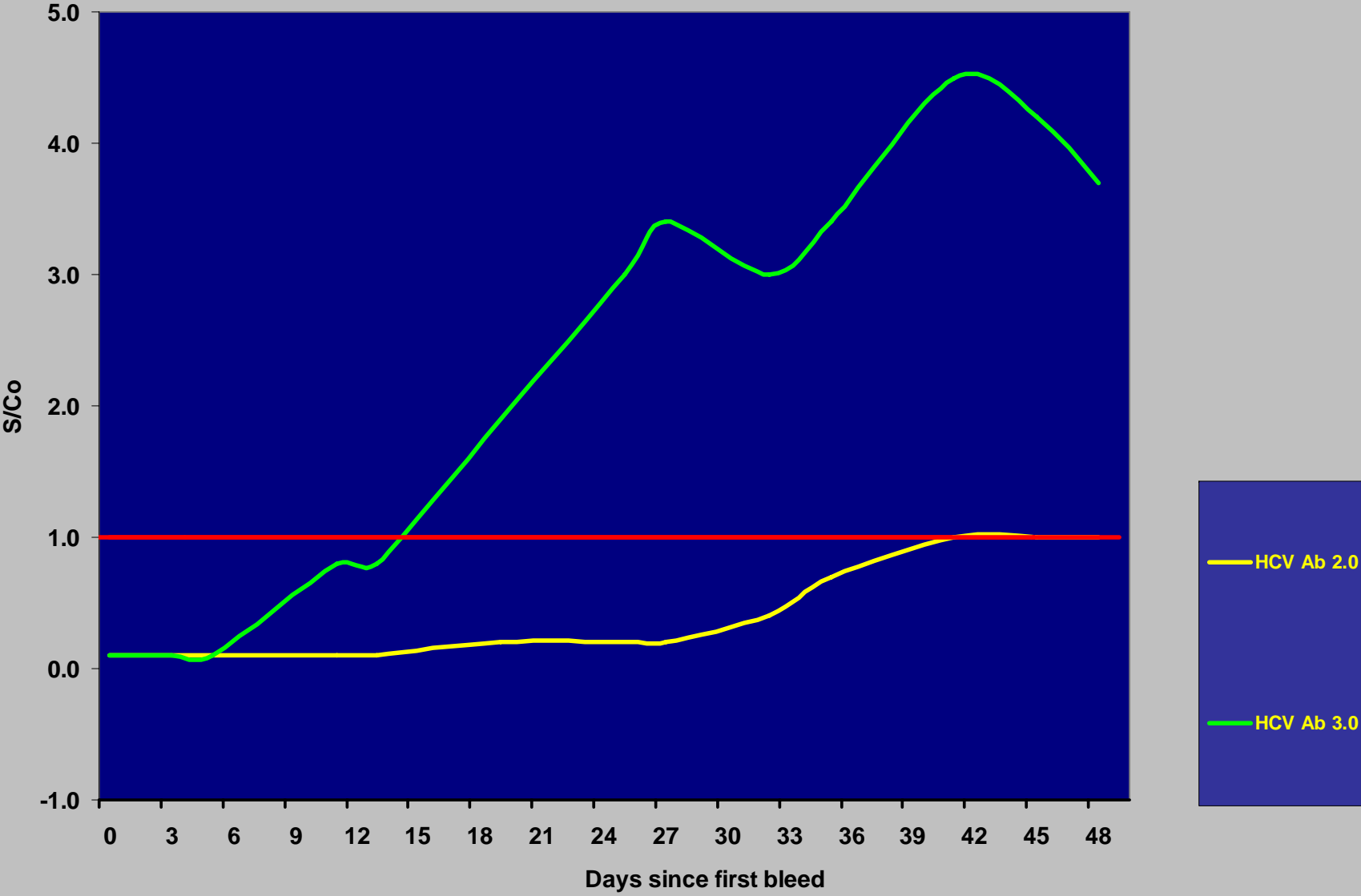
- Formerly categorized as Hepatitis non-A , non-B
- First generation HCV antibody assays implemented 1990
- Second generation 1993
- Third generation 1997
- HCV Nucleic Acid Testing (NAT) 1999

HCV Seroconversion : PHV919



Hepatitis C Seroconversion: PHV908

Performance of Second and Third Generation Assays



Seroconversion Panels

- have proven to be a “gold standard” for sensitivity of HIV test kits, especially for antibody tests
- have played a major role in improving the safety of the blood supply
- have provided important information on the “window period” for viral infection, and other aspects of viral dynamics