

# **Analysis of US Source Plasma Infectious Disease Residual Risk compared to Recovered Plasma Residual Risk**

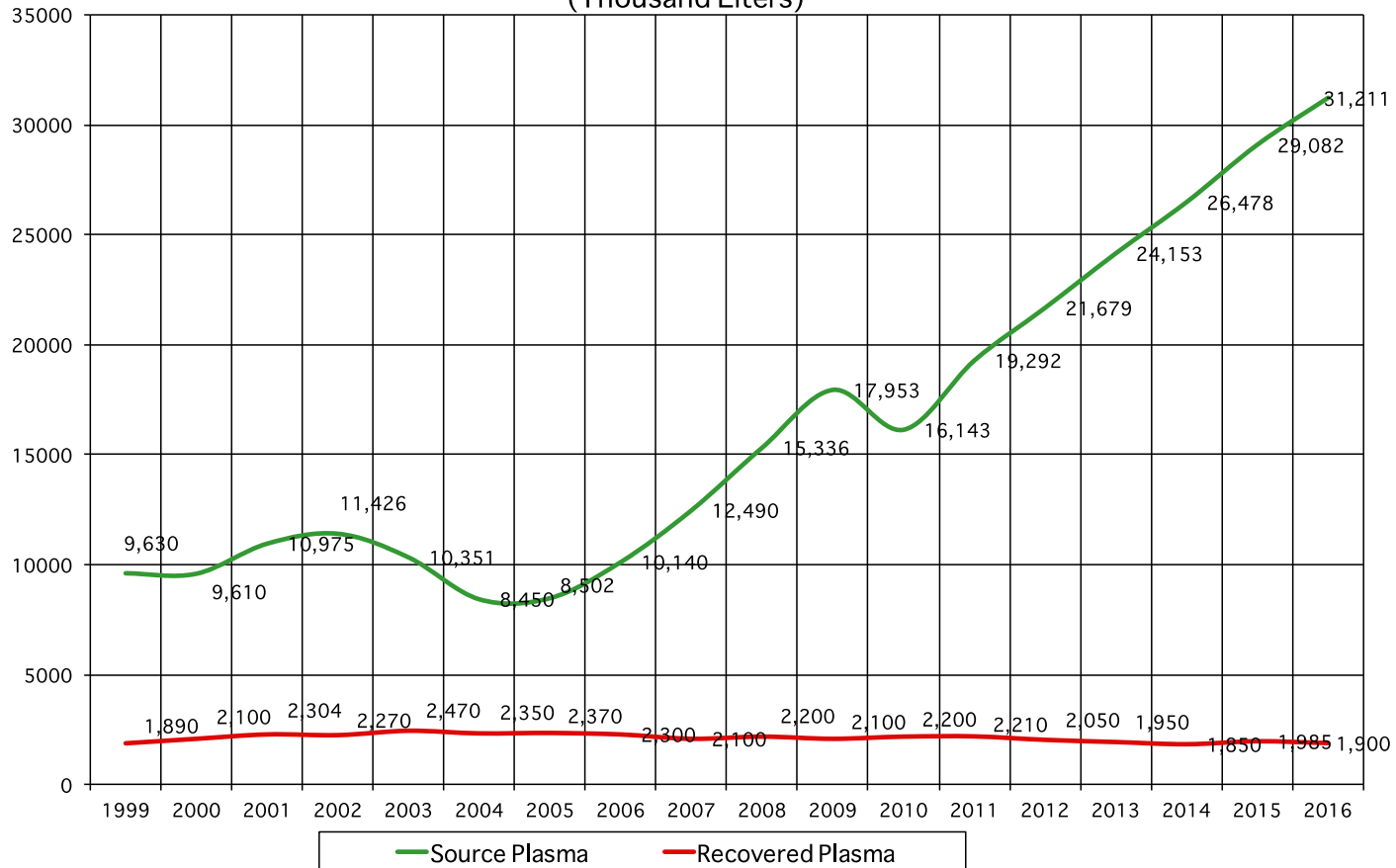
**IPFA/BCA Global Symposium on the Future  
for Blood and Plasma Donations**

***George Schreiber, ScD, PPTA Director, Epidemiology***

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Atlanta, Georgia

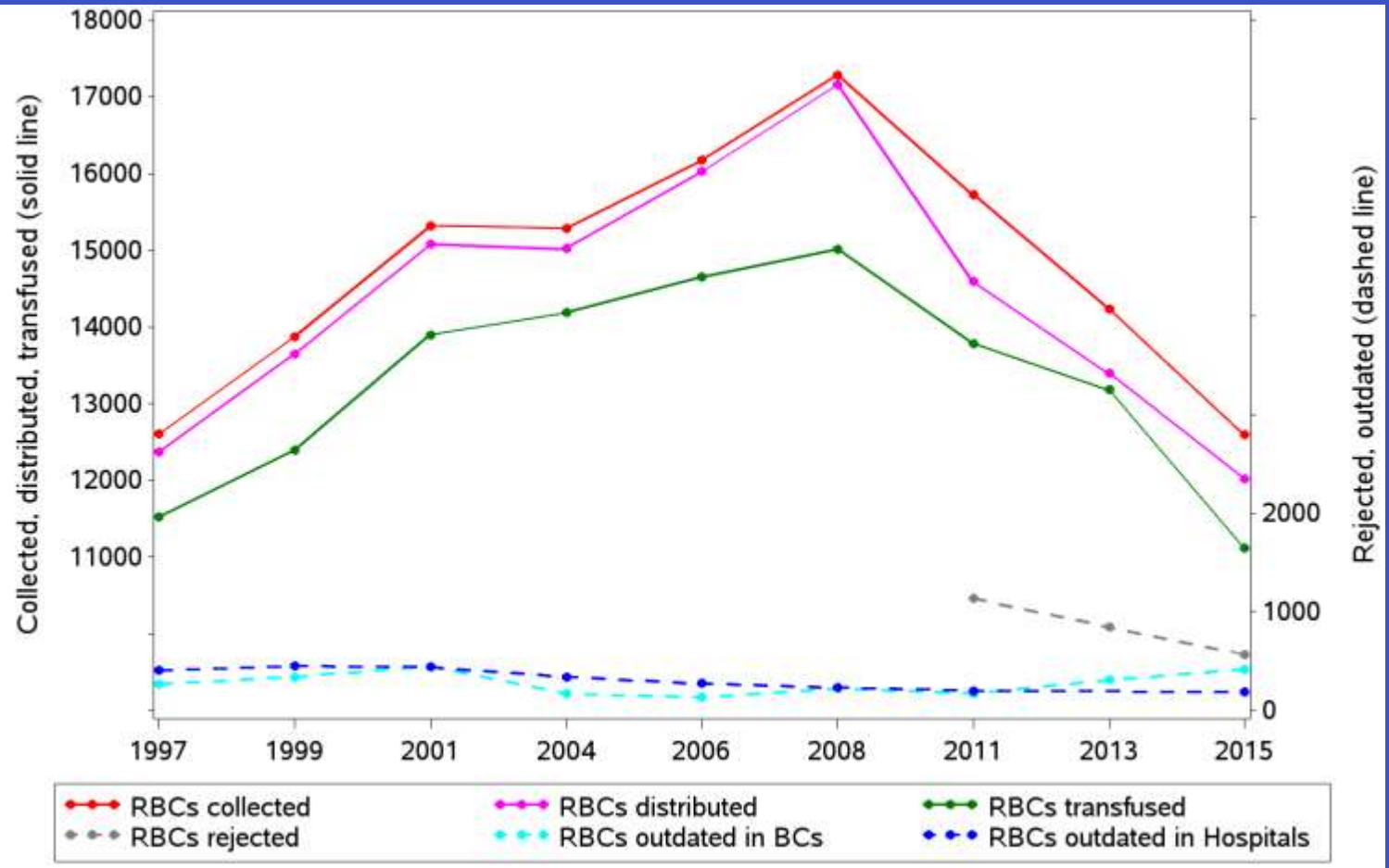
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PLASMA COLLECTIONS IN THE UNITED STATES FROM 1999 TO 2016  
(Thousand Liters)



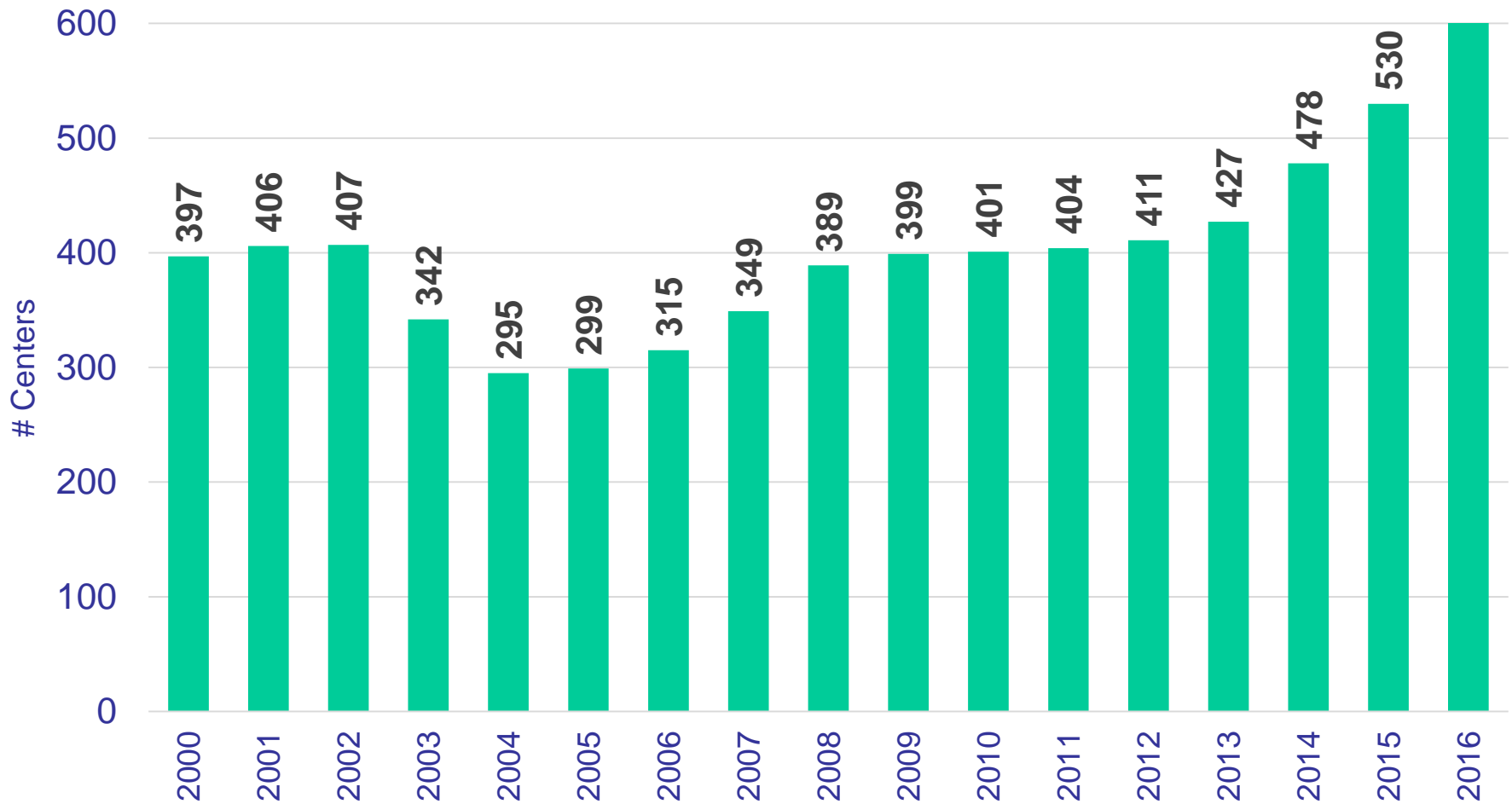
Source: MRB

# Trends in RBC collections, rejects, transfusion, blood center outdates

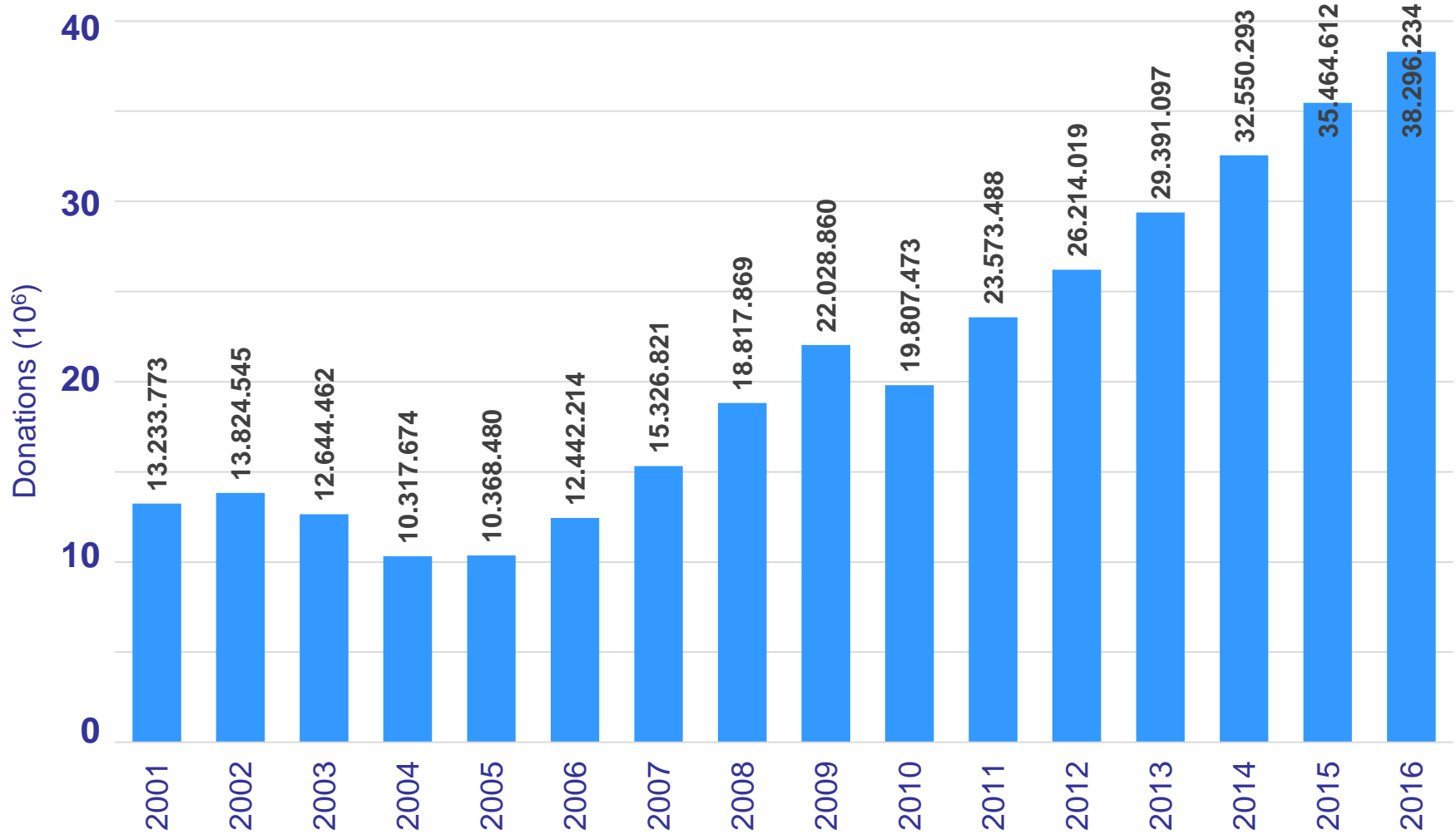


Source: Centers for Disease Control and Prevention

## Number of US Source Plasma Centers



# U.S. Source Plasma Donations, 2001-2016



## Important Plasma Quality Steps

### Donor Screening

- **Medical history and physical examination (protects donor health and reduces recipient risk)**

### Laboratory Testing

### Qualified Donors (Source Plasma)

### 60 Day Inventory Hold (Source Plasma)

### Residual Risk Assessments

### Epidemiological [viral marker] standards (Source Plasma)

Standards =  
Lowered  
Risk



Viral  
Marker  
Standard

- Center's viral marker rates compared to industry average
- Centers repeatedly exceeding Alert Limits subject to lose IQPP certification



Qualified  
Donor  
Standard

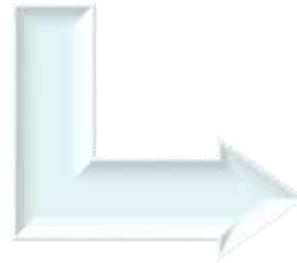
- New donors must pass 2 medical screenings and testing
- Reactivated donors (Qualified with  $\geq 6$  month lapse) must requalify
- One time donor infectious disease unites discarded

Standards  
Lowered  
Risk



Inventory  
Hold  
Standard

- Plasma held in inventory for at least 60 days after donation
- Allows for interdetection and destruction of plasma based on post-donation disqualifiers



NAT  
Testing  
Standard

- Requires NAT for HIV, HBV and HCV at minipool and at First Homogeneous Pool level
- Requires in-process testing for HAV and Parvovirus B19

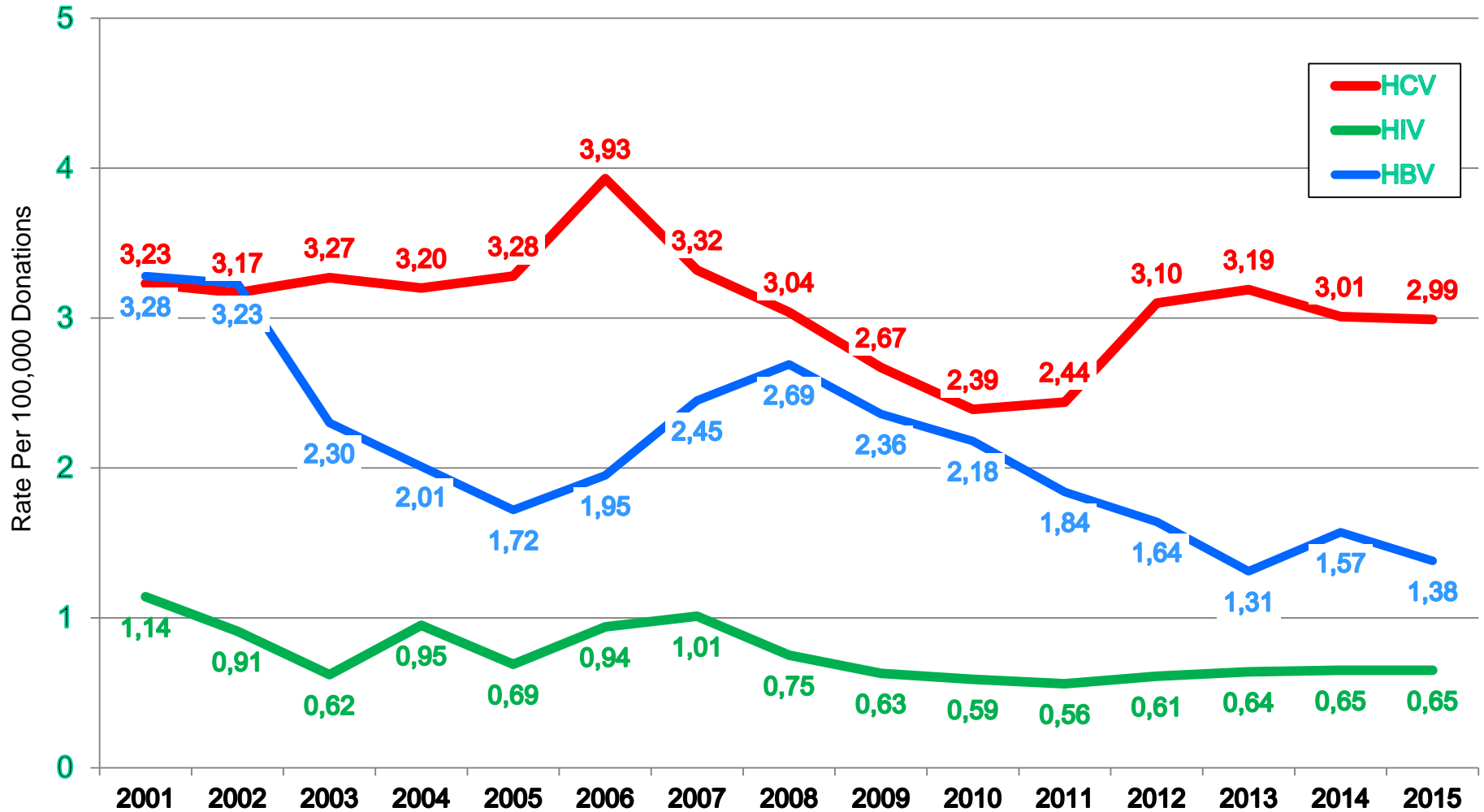


A statistically reliable system to ensure collection from quality Source Plasma collection centers, based on viral marker rates.

- In place for over a decade
- Serves as a guide for quality improvement
- Marker specific for HIV, HCV, and HBV
- Academic peer-reviewed
- Approach endorsed by FDA

- Alert Levels allow for identification of centers with higher than expected viral positivity rates.
- Allows for continuous epidemiological evaluation at individual plasma collection centers together with an annual update of the assessment.
- Reference rates based on overall industry averages for donors contributing to the pool, measured in a defined time period with the most appropriate testing technology.

# Qualified Donor Positivity Rates



# Residual Risk

Estimates of a potentially  
infectious unit being  
released for fractionation  
or transfusion

## Residual Risk of Viral Agent Entering the Manufacturing Pool

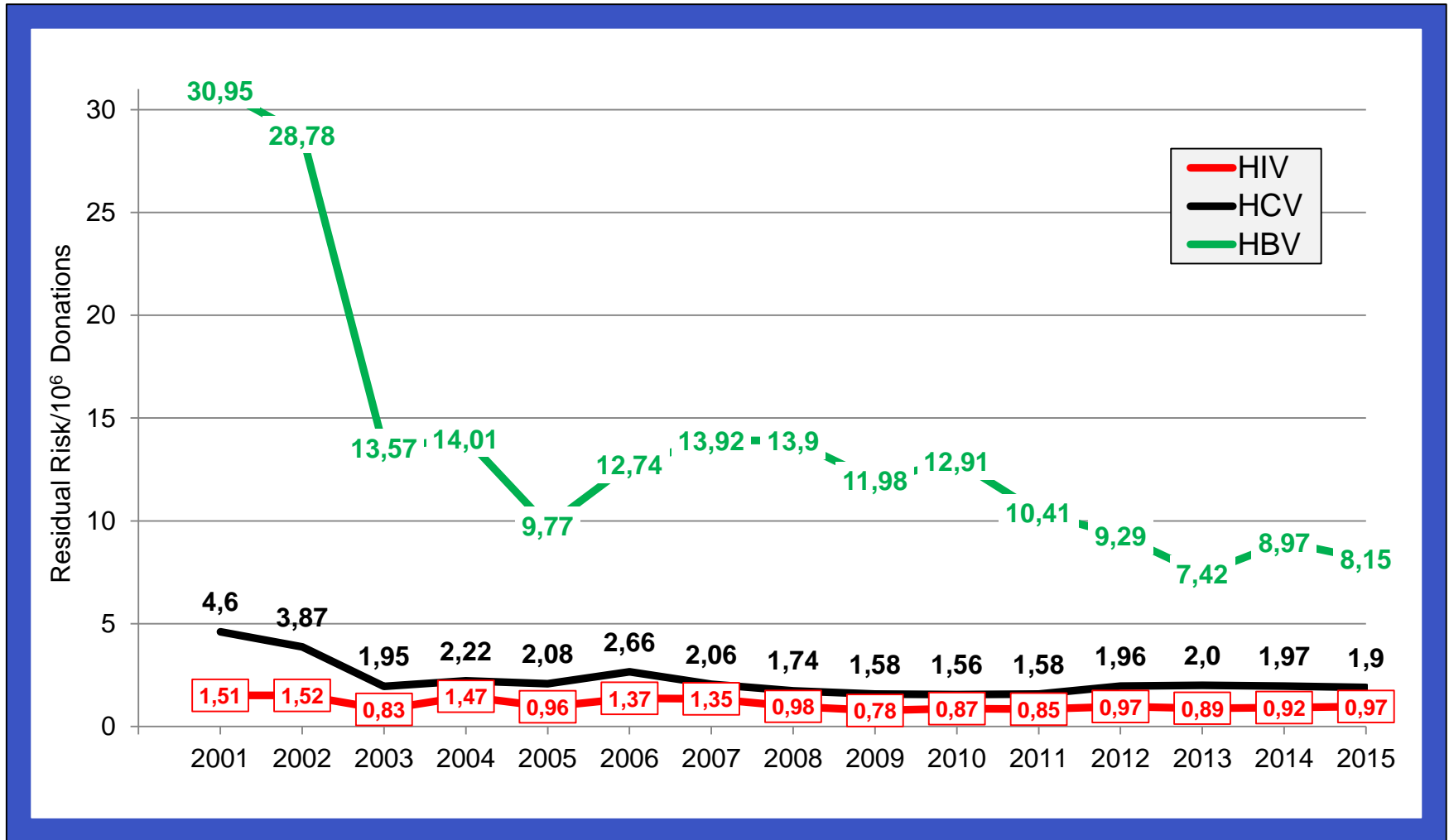
- The presence of certain viruses in asymptomatic donors who are negative on the screening tests (window period donations) constitutes the major risk of viruses entering the fractionation process.
- The Residual Risk is the *estimated probability of a potentially infectious plasma unit entering the manufacturing pool.* Accounts for Source Industry inventory hold.
- Used to assess the impact of Industry safety initiatives.
- Can be used to estimate pool viral load.
- The viruses of concern are: HCV, HIV, and HBV.

# Key Points to Remember

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- Residual Risk is risk of a **POTENTIALLY** contaminated unit entering manufacturing pool (applicable to both source and recovered plasma).
- Potentially contaminated units have detection levels below that of the NAT test.
- All manufactured plasma derived products have virus removed or inactivated.
- Residual risk of transmission is then reduced to zero.

# Source Plasma Residual Risk



## HIV, HCV and HBV Residual Risks (per 10<sup>6</sup> donations) for Source Qualified Donations and Recovered Repeat and All Donations

Virus	Source Plasma (2008) Qualified Donations	Recovered (2007-2008) Repeat Donations	Recovered (2007-2008) All Donations	Source Plasma <u>Qualified</u> Recovered
HIV *	0.98	0.54	0.68	1.4
HCV *	1.74	0.60	0.87	2.0

Virus	PPTA (2009-2011) Qualified Donations	Recovered (2009-2011) Repeat Donations	Recovered (2009-2011) All Donations	PPTA <u>Qualified</u> Recovered All
HBV **	12.0	0.83 1.19	1.22 1.74	9.84 WP 18.5 6.90 WP 26.5

\* Zou, et al., Transfusion 2010;50:1495-1504. \*\* Stramer, et al., Transfusion 2013; 53:2449-2458.



## Estimated Percentage of 6000 Liter – Plasma Pools Containing at Least One Potential WP Donation

	Source 7,500 Donations	Recovered 24,000 Donations
HCV	1.3%	2.1%
HIV	0.7%	1.6%
HBV	9.0%	2.9% 18.5 WP 4.2% 26.5 WP



## Viral Load in Manufacturing Pool

	Detection limit (96 minipool)	2015 Residual Risk	Chance of WP donation in pool	Maximum Viral Load 1 WP/pool (6000 donations)	Maximum Viral Load of WP donations
<b>HCV</b>	675 IU/mL	1.9	0.01	0.11 IU/mL	675 IU/mL
<b>HIV</b>	4420 IU/mL	0.97	0.005	0.74 IU/mL	4420 IU/mL
<b>HBV</b>	220 IU/mL	8.15	0.05	0.04 IU/mL	220 IU/mL

Effect of Viral Inactivation / Removal on Viral Load		
	Viral Load (IU/mL)	
	1 WP donation in pool	
	9 logs reduction	12 logs reduction
<b>HCV</b>	$1.1 / 10^{10}$	$1.1 / 10^{13}$
<b>HIV</b>	$7.4 / 10^{10}$	$7.4 / 10^{13}$
<b>HBV</b>	$4.0 / 10^{11}$	$4.0 / 10^{14}$

- Assuming one WP donation in the manufacturing pool, viral load reduction is complete.

**Demographic variations in infectious disease prevalence and incidence exist.**



**Viral removal and inactivation are key to ensuring the safety of fractionated plasma products.**



**Risk of a potentially infectious unit entering the plasma manufacturing pool is small. Viral inactivation and removal significantly reduces viral risk in finished plasma products.**

**Plasma derived products have never been safer as a result of the rigorous efforts of the industry to ensure quality donors, sensitive testing, and virus inactivation/removal technologies.**



**There has been no confirmed case of transmission of viral infection in more than two decades, attesting to the safety of plasma derived products.**

