Annual Statistics

- **Volunteer Blood Donations:**
  - ~ 8 million blood donors
  - ~ 14 million units donated
  - ~ 1.9 blood components / unit

- **Transfusions:**
  - ~ 4 million patients
  - ~ 4-5 units / transfusion (highly variable)

- **Paid Plasma Donations:**
  - ~ 12 million units of plasma
    - utilized for plasma fractionation
    and plasma derivative production
Landmarks: HIV & the Blood Supply

- **Late 1982**: AIDS-like illnesses in hemophiliacs and blood recipients first reported
- **March 1983**: FDA memorandum:
  - Education of donors regarding persons at increased risk of AIDS
  - Specific donor history questions to detect possible AIDS symptoms or exposure to patients with AIDS
- **1983-1984**: HIV-1 discovered (HTLV-III/LAV)
Landmarks:
HIV & the Blood Supply

□ **December 1984**, FDA memorandum:
  - Educational materials to inform donors who should refrain from donating blood
  - History questions
  - Confidential Self-Exclusion

□ **March 1985**: HIV-1 Antibody EIA test


□ **June 1992**: HIV-2 antibody test required
  (anti-HIV-1/2 combination EIA)

□ **March 1996**: HIV-1 p24 Ag test licensed for blood donor screening

□ **July 1996**: HIV-1, group O -- first case in U.S
**New Test Implementation and Declining Risk of Viral Infections from Transfusion**

Source: Kathryn C. Zoon, Ph.D.
Director, CBER FDA
5th Annual FDA and the Changing Paradigm for Blood Regulation - Jan 16-18, 2002

Based on data provided by Michael P. Busch, M.D.
Layers of Safety

- Voluntary Donations vs. Donation Incentives
- Donor Education
- Self-Exclusion in Response to Written Material
- On-site Donor Deferral Registry ("Precheck")
- Health History Interview
Layers of Safety

- Confidential Unit Exclusion (CUE)

- Telephone Callback
  - Postdonation Information
  - CUE

- Donor Deferral Registry: Central Facility

- Laboratory Testing

- Viral Inactivation (plasma derivatives)
Donor Education

- Information on blood safety, AIDS epidemiology, and high-risk activities
- A language appropriate for each donor
- Culturally sensitive educational format
- Opportunity at each visit for the donor to:
  - Consider the information
  - Make an informed and private decision about whether to donate
- Focus is on behavior, not on stereotypes
Donor Education

- includes a description of HIV-associated clinical signs and symptoms:
  - unexplained weight loss
  - night sweats
  - blue or purple spots typical of Kaposi’s sarcoma on or under the skin, or on mucous membranes
  - swollen lymph nodes lasting more than one month
  - persistent white spots or unusual blemishes in the mouth
  - temperature > 100.5° F for more than 10 days
  - persistent cough and shortness of breath
  - persistent diarrhea

- donors may self-defer if these conditions are present
Donor Education

- **"Window period"**: time interval early in infection during which tests for HIV may be negative although infection may still be transmitted.

- **Blood Testing**:
  - sample will be tested for HIV (and other organisms)
  - donor notified if test is positive
  - positive tests: donor permanently deferred

- **Donor Deferral Registries**:
  - confidential list

- **Alternative Testing Sites**
Health History Interview

- Direct Questions on High Risk Behavior:
  - clinical or laboratory evidence of HIV infection
  - men who have had sex with another man even one time since 1977
  - past or present injecting drug use
  - hemophilia or clotting disorder requiring clotting factor concentrates
  - engaging in sex for money or drugs since 1977
  - sex with any of the above during past 12 months
  - syphilis or gonorrhea during past 12 months
  - receiving a transfusion of whole blood, a blood component, or a clotting factor concentrate within the past 12 months
Fig. 1. TA-AIDS cases by year of transfusion, 1978 through 1991. The solid portion of the bars shows cases reported from June 1, 1981 through June 30, 1992, with transfusion(s) in a single year. The cross-hatched portion shows additional cases diagnosed but not yet reported, estimated by adjusting for the delay between diagnosis and report.

Figure 2. Projected risk of HIV-1 infection per unit of transfused between January 1978 and December 1984 (left ordinate). This curve also represents the time distribution of the projected 2135 infected recipients by year of transfusion (right ordinate). Busch MP, et al. Transfusion 31:4-11, 1992
## Prevalence and Incidence Rates
(per hundred thousand)

(Dodd R, *Emily Cooley Lecture*, AABB 53rd Annual Meeting November 2000.)

<table>
<thead>
<tr>
<th></th>
<th>Donor Prevalence</th>
<th>Population Prevalence</th>
<th>Donor Incidence</th>
<th>Population Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
<td>1760</td>
<td>4900</td>
<td>4.5</td>
<td>111.4</td>
</tr>
<tr>
<td>HCV</td>
<td>348</td>
<td>1800</td>
<td>2.2</td>
<td>13.4</td>
</tr>
<tr>
<td>HIV</td>
<td>12</td>
<td>136</td>
<td>1.7</td>
<td>15.0</td>
</tr>
</tbody>
</table>
## Risk Estimates of Transfusion-Transmitted HIV Infection

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Period of Study</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient</td>
<td>1985-1991</td>
<td>1:60,000</td>
</tr>
<tr>
<td>Seroconversion(^1)</td>
<td>(11,532 pts)</td>
<td>(120,301 units)</td>
</tr>
<tr>
<td>PCR / Viral Culture(^2)</td>
<td>1987-1992</td>
<td>1:160,000</td>
</tr>
<tr>
<td></td>
<td>(200,000 units)</td>
<td></td>
</tr>
</tbody>
</table>


## Risk Estimates of Transfusion-Transmitted HIV Infection

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Period of Study</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence x</td>
<td>1992-1993</td>
<td>1:450,000</td>
</tr>
<tr>
<td>Window Period Model</td>
<td></td>
<td>to</td>
</tr>
<tr>
<td>Model(^3)</td>
<td></td>
<td>1:660,000</td>
</tr>
<tr>
<td>Incidence x</td>
<td>1991-1993</td>
<td>1:493,000</td>
</tr>
<tr>
<td>Window Period Model</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model (REDS)(^4)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


1996 Transfusion Risks*

<table>
<thead>
<tr>
<th></th>
<th>point estimate</th>
<th>95% C.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>1:676,000</td>
<td>[1:202,000 - 1:2,778,000]</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1:63,000</td>
<td>[1:31,000 - 1:147,000]</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>1:103,000</td>
<td>[1:28,000 - 1:288,000]</td>
</tr>
<tr>
<td>HTLV I/I</td>
<td>1:641,000</td>
<td>[1:256,000 - 1:2,000,000]</td>
</tr>
</tbody>
</table>

*per unit of blood that is negative in laboratory testing

HIV-1 p24 Antigen Testing

March 15, 1996 - March 27, 1999:
-- ~ 45,000,000 units screened for HIV Ag

-- many false positive test results even with neutralization testing

-- only 5 HIV Ag (+), HIV Ab (-) donor

-- rate of HIV Ag (+), HIV Ab (-) donors: 1 : 9,000,000
## Current Transfusion Risks*
*(with minipool HIV/HCV NAT)*

<table>
<thead>
<tr>
<th></th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>1 : 2,135,000</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>1 : 1,935,000</td>
</tr>
</tbody>
</table>

(Dodd RY, Notari EP, Stramer SL. Transfusion 2002; 42: 975-979.)

<table>
<thead>
<tr>
<th></th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>1 : 1,800,000</td>
</tr>
<tr>
<td>HCV</td>
<td>1 : 1,600,000</td>
</tr>
</tbody>
</table>

(Busch MP, Kleinman SH, Nemo GJ. JAMA 2003; 289: 959-962.)

*per unit of blood that is negative in laboratory testing
Pathogen Inactivation

- Cerus Corporation:
  1. **Psoralen S-59 & UVA**: (targets Nucleic Acid)
     -- FFP & platelets (SDP, RDP conc.)
     -- inactivation of **enveloped** and **nonenveloped viruses**, **bacteria**, **protozoa**
     -- **leukocytes** (including T-cells): inhibition of proliferation and cytokine synthesis.
     -- S-59 photodegrades during inactivation process: residual S-59 & free photoproducts are "quenched" by passive adsorption.
     -- **Phase 3 trials** -- platelets
     -- **Phase 2 trials** -- FFP