Planning for reducing residual risk in blood transfusion

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Residual Risk

- Residual risk is the chance that an infected donation will escape detection.
- Risk estimates based on the incidence/window period model have been reported from many nations.

Residual Risk of TTI After Screening

- Window period (WP) of infections, account for 90% or more
- Virus epidemiology of the donor population
- Frequency of incidence in donors
- Failure to test
- Human error
- Non-conformity of software, equipment and reagents
- Variants of known agents
- New agents for which no test available
- Unknown agents
- Immunosilent donors

Blood Safety Procedures (Excluding Laboratory Testing)

- ***Production***
  1. Exclusion of donor groups/donor sites
  2. Elimination of donation incentives
  3. Donor education

4

Blood Safety Procedures (Excluding Laboratory Testing)

- ***At donation site prior to donation***

1. Self-exclusion in response to written material
2. Health history interview
3. Donor deferral registry
4. Confidential unit exclusion (CUE)

5

Blood Safety Procedures (Excluding Laboratory Testing)

- ***Post-donation***

1. Telephone call-back
2. Product retrieval
3. Recipient notification

6

Increasing the Sensitivity of test kits

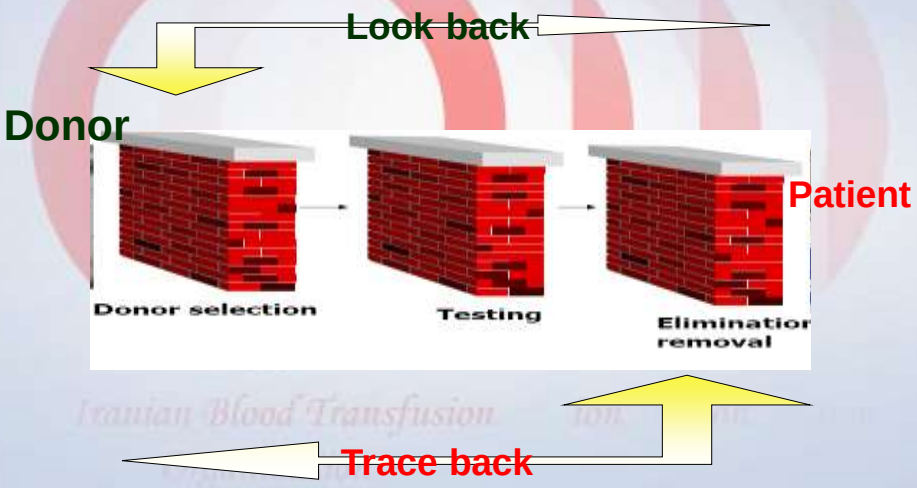
More sensitive Ab/Ag screening test kits, 2005

Donor selection & Blood Safety

- Exclusion of donor groups/ donors sits with high risk factors
- **100% Voluntary blood donors from 2007**
- Self-deferral procedure which is implemented nationwide since 1997, during which donors are asked not to donate blood if they had acquired immunodeficiency syndrome (AIDS)-related symptoms, HIV-related risk behaviors and history of jaundice or viral hepatitis.

Since 2002 the confidential unit exclusion (CUE) became mandatory and implemented in all blood centers

Establishment of look back from 2005

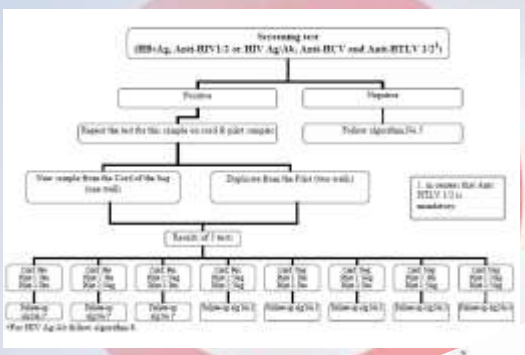


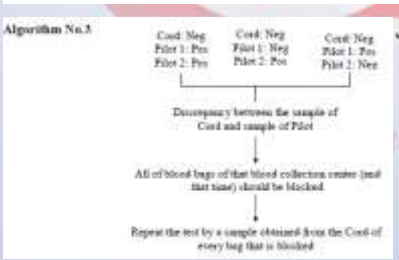
Donor selection & Blood Safety

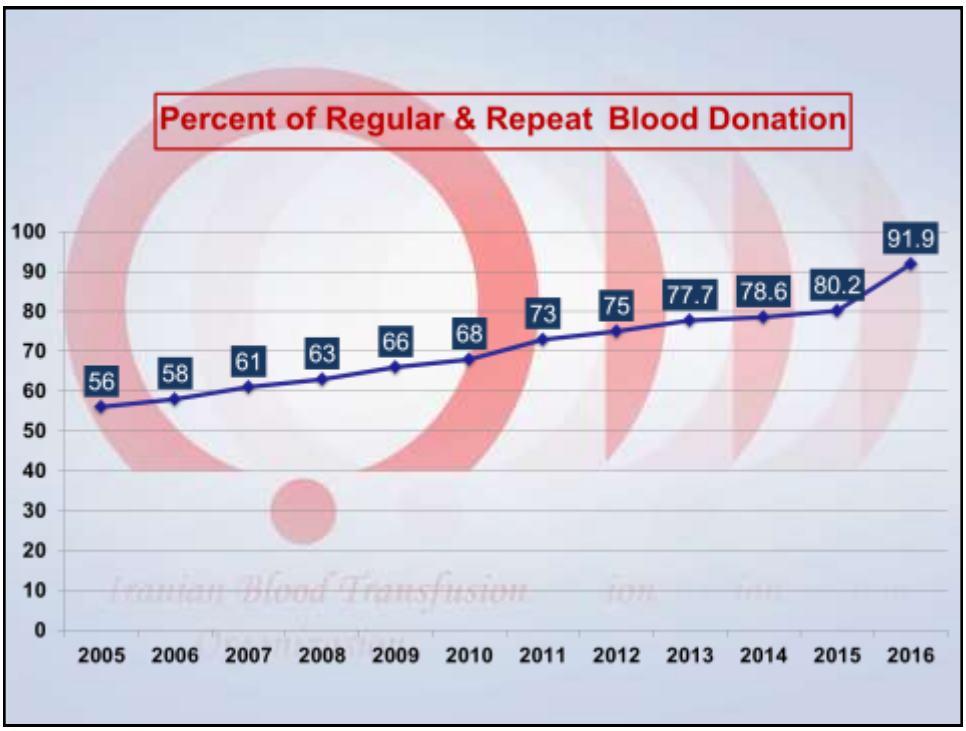
- **Donor notification of any abnormalities in post-donation laboratory tests**

- **Telephone call-back as a system established on beginning of 2010**

Error Management







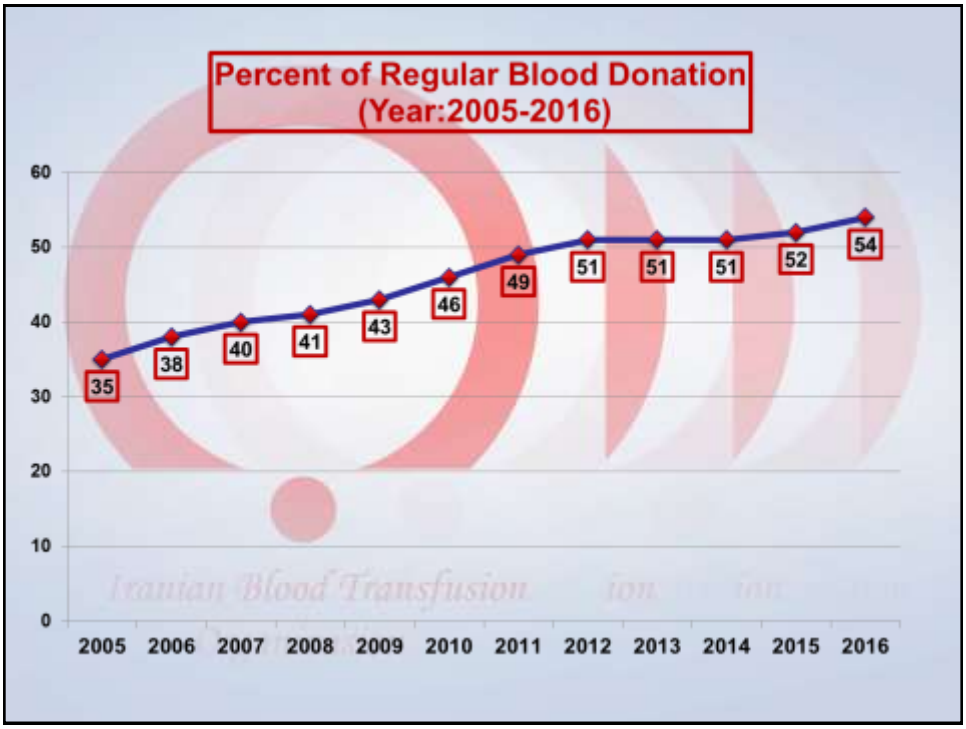


TABLE 4. Prevalence of HBV rate/10^5 donations in different donation status, age groups, and sex, 2006 to 2007

	2006				2007			
Markers	Donations	Positive	Prevalence/10^5 donations	95% CI	Donations	Positive	Prevalence/10^5 donations	95% CI
Status of donations								
Repeat	474,515	322	68	61-75	528,469	297	56	50-63
Lapsed	102,178	202	198	170-225	170,871	303	177	157-197
First time	579,136	5198	898	873-922	558,446	4445	796	773-820
Sex and age (years)								
Male								
<29	484,314	1860	384	367-401	524,698	1569	299	284-314
30-39	313,906	1538	490	466-514	338,116	1349	399	378-420
40-49	195,606	1308	669	633-705	219,488	1204	549	518-580
>50	775,25	594	766	705-828	85,756	522	609	557-661
Total	1,072,361	5300	494	481-508	1,168,058	4644	398	386-409
Female								
<29	32,752	106	324	262-385	35,030	80	228	178-278
30-39	21,770	95	436	349-524	22,796	84	368	290-447
40-49	18,576	109	587	477-697	20,355	98	481	386-577
>50	10,370	70	675	517-833	11,207	62	553	416-690
Total	83,468	380	455	410-501	89,388	324	362	323-402
Both male and female (years)								
<29	518,076	1966	379	363-396	559,728	1649	295	280-309
30-39	335,676	1633	486	463-510	360,912	1433	397	376-418
40-49	214,182	1417	662	627-696	239,843	1302	543	513-572
>50	87,895	664	755	698-813	96,963	584	602	554-651
Total	1,155,829	5680	491	479-504	1,257,446	4968	395	384-406

TABLE 5. Prevalence of HCV rate/10^5 donations in different donation status, age groups, and sex, 2006 to 2007

	2006				2007			
Markers	Donations	Positive	Prevalence/10^5 donations	95% CI	Donations	Positive	Prevalence/10^5 donations	95% CI
Status of donations								
Repeat	474,515	134	28	24-33	528,469	112	21	17-25
Lapsed	102,178	83	81	64-99	170,871	99	58	47-69
First time	579,136	1339	231	219-244	558,446	1348	241	229-254
Sex and age (years)								
Male								
<29	484,314	607	125	115-135	524,698	605	115	106-125
30-39	313,906	504	161	147-174	338,116	553	164	150-177
40-49	195,606	295	151	134-168	219,488	275	125	111-140
>50	77,525	114	147	120-174	85,756	118	138	113-162
Total	1,072,361	1520	142	135-149	1,168,058	1551	133	126-139
Female								
<29	32,752	7	21	5-37	35,030	10	29	11-46
30-39	21,770	15	69	34-104	22,796	8	35	11-59
40-49	18,576	15	81	40-122	20,355	10	49	19-80
>50	10,370	6	58	12-104	11,207	4	36	1-71
Total	83,468	43	52	36-67	89,388	32	36	23-48
Both male and female (years)								
<29	518,076	614	119	109-128	559,728	615	110	101-119
30-39	335,676	519	155	141-168	360,912	561	155	143-168
40-49	214,182	310	145	129-161	239,843	285	119	105-133
>50	87,895	120	137	112-161	96,963	122	126	103-148
Total	1,155,829	1563	135	128-142	1,257,446	1583	126	120-132

TABLE 6. Prevalence of HIV rate/10^5 donations in different donation status, age groups, and sex, 2006 to 2007

	2006				2007			
Markers	Donations	Positive	Prevalence/10^5 donations	95% CI	Donations	Positive	Prevalence/10^5 donations	95% CI
Status of donations								
Repeat	474,515	0	0.0	0.0-0.0	528,469	2	0.4	0.0-0.9
Lapsed	102,178	2	2.0	0.0-4.7	170,871	2	1.2	0.0-3.1
First time	579,136	39	6.7	4.8-8.7	558,446	51	9.1	6.4-11.9
Sex and age (years)								
Male								
<29	484,314	13	2.7	1.1-4.3	524,698	13	2.5	1.1-3.8
30-39	313,906	16	5.1	2.5-7.6	338,116	20	5.9	3.4-8.5
40-49	195,606	4	2.0	0.1-4.0	219,488	14	6.4	3.0-9.7
>50	77,525	0	0.0	0.0-0.0	85,756	4	4.7	0.2-9.2
Total	1,072,361	33	3.1	1.9-4.3	1,168,058	51	4.4	3.2-5.5
Female								
<29	32,752	1	3.1	0.0-9.1	35,030	2	5.7	0.0-13.5
30-39	21,770	4	18.4	0.3-36.4	22,796	1	4.4	0.0-13.0
40-49	18,576	1	5.4	0.0-16.0	20,355	1	4.9	0.0-14.5
>50	10,370	0	0.0	0.0-0.0	11,207	0	0.0	0.0-0.0
Total	83,468	6	7.2	1.5-12.9	89,388	4	4.5	0.2-8.8
Both male and female (years)								
<29	518,076	14	2.7	1.3-4.1	559,728	15	2.7	1.3-4.1
30-39	335,676	20	6.0	3.4-8.5	360,912	21	5.8	3.5-8.2
40-49	214,182	5	2.3	0.4-4.3	239,843	15	6.3	3.1-9.4
>50	87,895	0	0.0	0.0-0.0	96,963	4	4.1	0.2-8.0
Total	1,155,829	39	3.4	2.2-4.6	1,257,446	55	4.4	3.4-5.4

Test only for specified donors, 2007

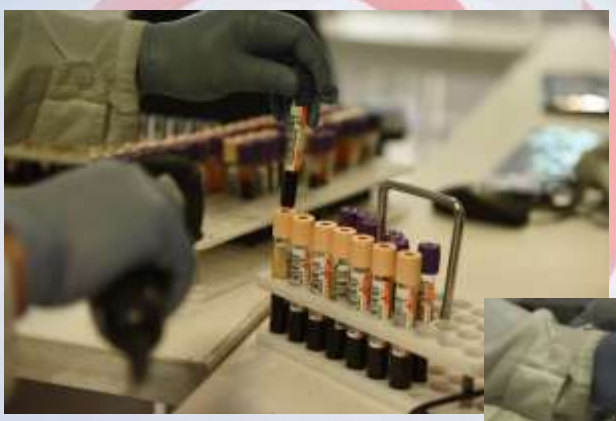
Decreased window period by NAT, Pilot study for establishment of NAT

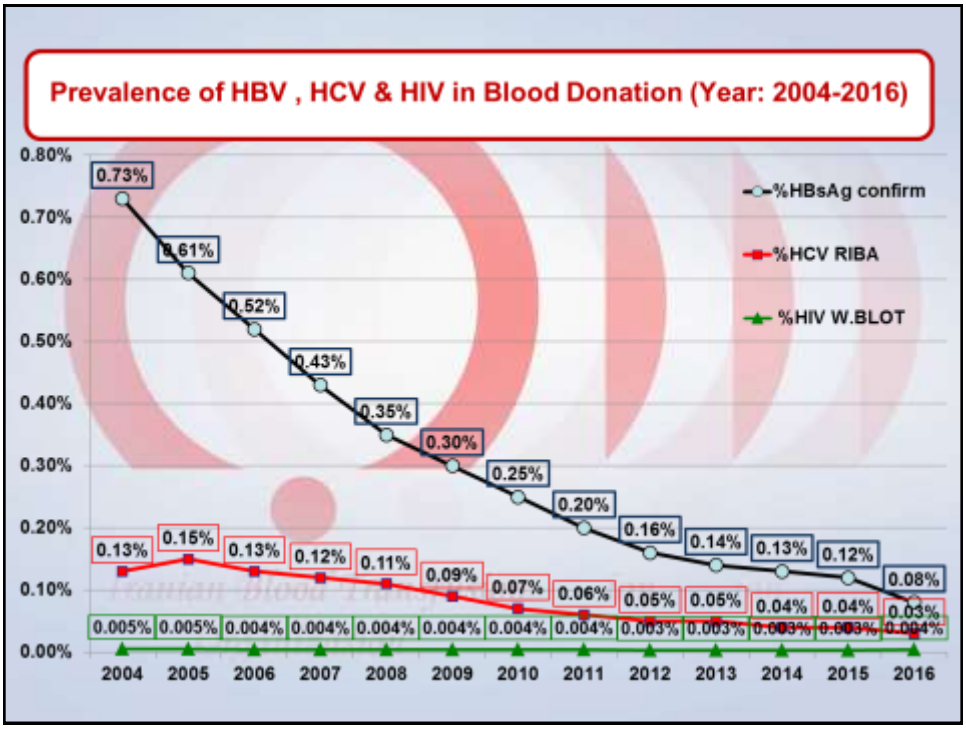
Screening the blood donations for HBV, HCV and HIV by NAT were performed during 2010-2012 in Tehran province (on more than 20% of blood donations in Iran) as a pilot study.

Results of Pilot Study

Screened Donations	HBV	HCV	HIV
479,572	13	1	0
Per 10^6	27	2	0

First time blood donor screening, 2016





Volume and number of recovered plasma units for fractionation and Prevalence of HBV DNA, HCV RNA and HIV RNA per 10^6 units in recovered plasma for contract fractionation, 2005-2015

Years	Volume of recovered plasma for contract fractionation/ Liter	Recovered plasma for contract fractionation / Units	HBV DNA Positive Sample/s	HCV RNA Positive Sample/s	Prevalence Positive Samples According Bleeding Date/10^6 Plasma Units During 2006-2015					
					HBV DNA	95% CI	HCV RNA	95% CI	HIV RNA	95% CI
2005	52404	278740	NA	NA	NA	NA	NA	---	NA	--
2006	44992	190680	4	0	20.9	8.1-53.9	0	0	0	--
2007	68732	348473	2	0	5.7	1.5-20.9	0	0	0	--
2008	89119	431632	4	0	9.5	3.6-23.8	0	0	0	--
2009	98821	404263	1	0	2.5	0.4-14.0	0	0	0	--
2010	107881	494753	2	3	4.0	1.1-14.7	6.1	2.1-17.8	0	--
2011	132293	712750	1	1	1.4	0.3-7.9	1.4	0.3-7.9	0	--
2012	149469	824889	1	2	1.2	0.2-6.9	2.4	0.7-8.8	0	--
2013	110216	594184	0	2	0	0	3.4	0.9-12.2	0	--
2014	176434	891857	0	0	0	0	0	0	0	--
2015	156236	820160	0	0	0	0	0	0	0	--
Total	1177745	5992381	15	8	2.6	1.5-4.1	1.4	0.7-2.6	0	--

Residual risk of TTIs

The magnitude of residual risk may differ within countries depending on:

- **sensitivity of screening assays**
- **levels of HBV, HCV and HIV endemicity**

Window period reduction by PCR

	Window period (days)		Reduction	
Virus	Serology	PCR	Days	%
HIV	16-22	11	11	50
HBV	56	31	25	45
HCV	70	4-11	59-66	84-94

Residual risk after NAT

Agent	NAT window period/ days	Residual risk Per million donation (NAT)
HIV	11	0.07-1.1
HCV	4-11	0.76-1.3
HBV	30-40	8.3-11.33

27

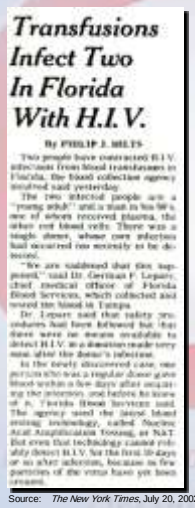
Residual Risk in US after establishment NAT

Based on window-period and incidence calculations, the current risk of HIV transmission by transfusion in the United States is approximately l in 1.5 million units,. the risk of HCV transmission is approximately 1 in 1.1 million units, and the risk of HBV transmission is approximately 1 in 800,000 to 1 in 1.2million units.

Risk of Dying in any 1 year

	Risk Estimate
• Playing soccer	1: 25 000
• Homicide	1: 100 000
• Train Accident	1: 100 000-1:1^6
• Lightning	1: 1 000 000

Risks of Blood Transfusion



Transfusions Infect Two In Florida With H.I.V.

By PHILIP J. HILTS

Source: *The New York Times*, July 20, 2002

METRO AND STATE NEWS

S.A. blood infects man with HIV

Experts say chances were one in millions, and supply is safe.

"Window of Infectivity" is still a problem

30

Risks of Blood Transfusion

- **HIV Transmission Through Transfusion --- Missouri and Colorado, 2008**
- ***Weekly* October 22, 2010 / 59(41);1335-1339**

Transmission of human immunodeficiency virus (HIV) through transfusion of contaminated blood components was documented in the United States in 1982 (*1*). Since then, the risk for transfusion-transmitted HIV infection has been almost eliminated by the use of questionnaires to exclude donors at higher risk for HIV infection and the use of highly sensitive laboratory screening tests to identify infected blood donations. The risk for acquiring HIV infection through blood transfusion today is estimated conservatively to be one in 1.5 million, based on 2007--2008 data (*2*). This report describes the first U.S. case of transfusion-transmitted HIV infection reported to CDC since 2002 (*3*). A blood center in Missouri discovered that blood components from a donation in November 2008 tested positive for HIV infection. A lookback investigation determined that this donor had last donated in June 2008, at which time he incorrectly reported no HIV risk factors and his donation tested negative for the presence of HIV. One of the two recipients of blood components from this donation, a patient undergoing kidney transplantation, was found to be HIV infected, and an investigation determined that the patient's infection was acquired from the donor's blood products. Even though such transmissions are rare, health-care providers should consider the possibility of transfusion-transmitted HIV in HIV-infected transfusion recipients

سه نسل در یک قاب