Status of Transfusion and Transplantation Safety

Celso Bianco, MD

Advisory Committee on Blood Safety and Availability

DHHS

May 10, 2007

America's Blood® Centers
It's About *Life*.

America's Blood Centers (ABC)

- Founded in 1962, ABC is North America's largest network of community-based, not-for-profit blood centers
- 77 individually licensed blood programs (FDA or Health Canada) serving nearly 180 million people in 45 States and all of Canada
  - > 9 million blood donations at >600 collection sites
  - Over 2.5 million blood recipients at 3,500 hospitals
  - ABC Members collect half the U.S., and all of Canada's volunteer donor blood supply
- Members provide therapeutic and transfusion services, recruit marrow, cord and stem cell and tissue donors
- Several Members have Research Institutes

Questions from Dr. Holmberg

- What are areas of commonality with blood products, cord, progenitor cells and bone marrow, tissues and organs?
- What is the current state of safety in transfusion and transplantation?
- Is it sustainable? How to improve it in the future?
- Is there a need for a master strategy? Scope (rubric)?
- How to involve the stakeholders?
- What are the resources needed?

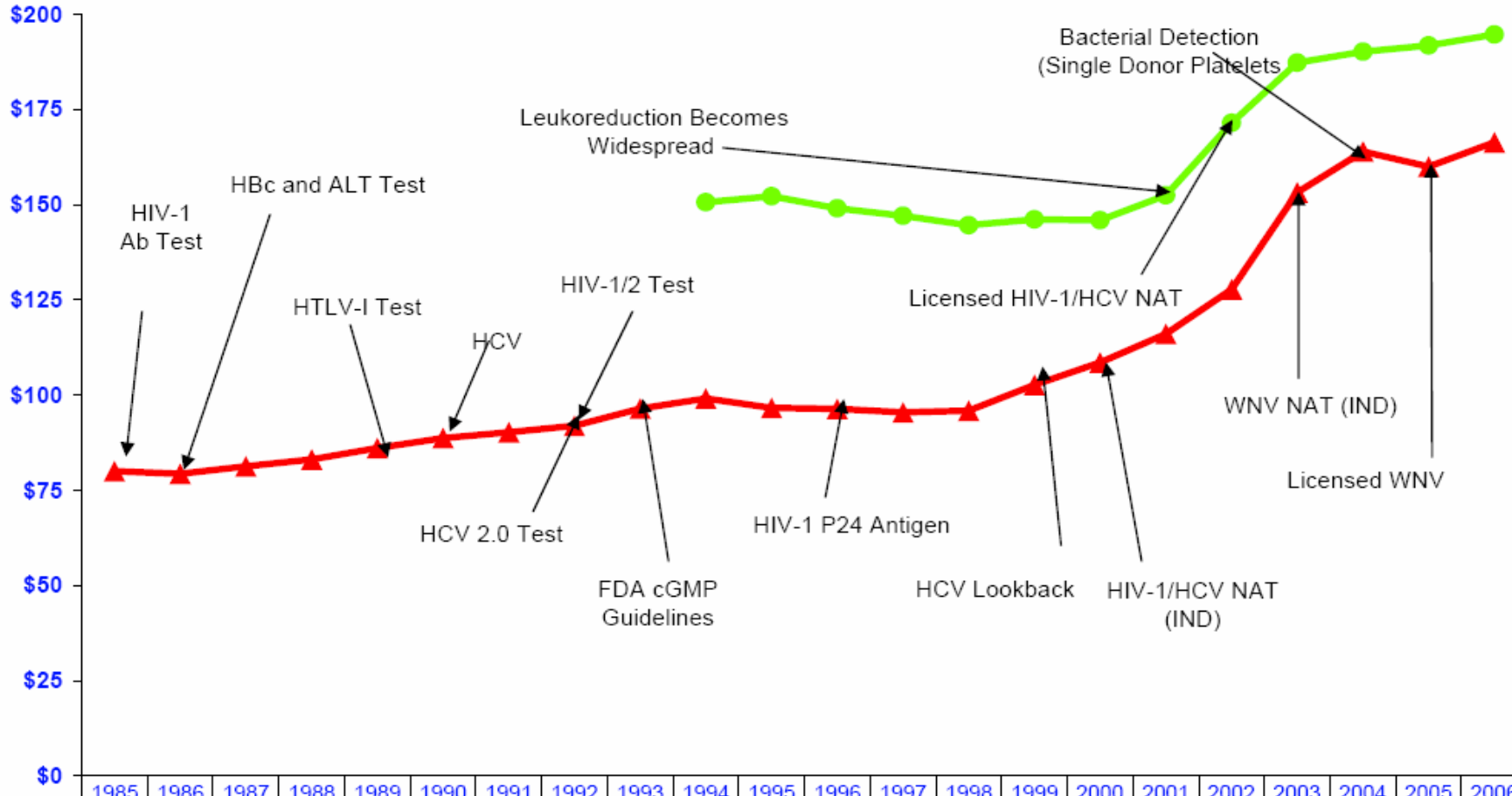
What is the current state of safety in transfusion and transplantation?

- Blood is safer than it has ever been; but can we sustain it?
  - Financial Resources
  - People
  - Investment in R&D, Innovation
  - Standards & Accreditation environment
  - Regulatory environment
  - Availability

Financial Resources

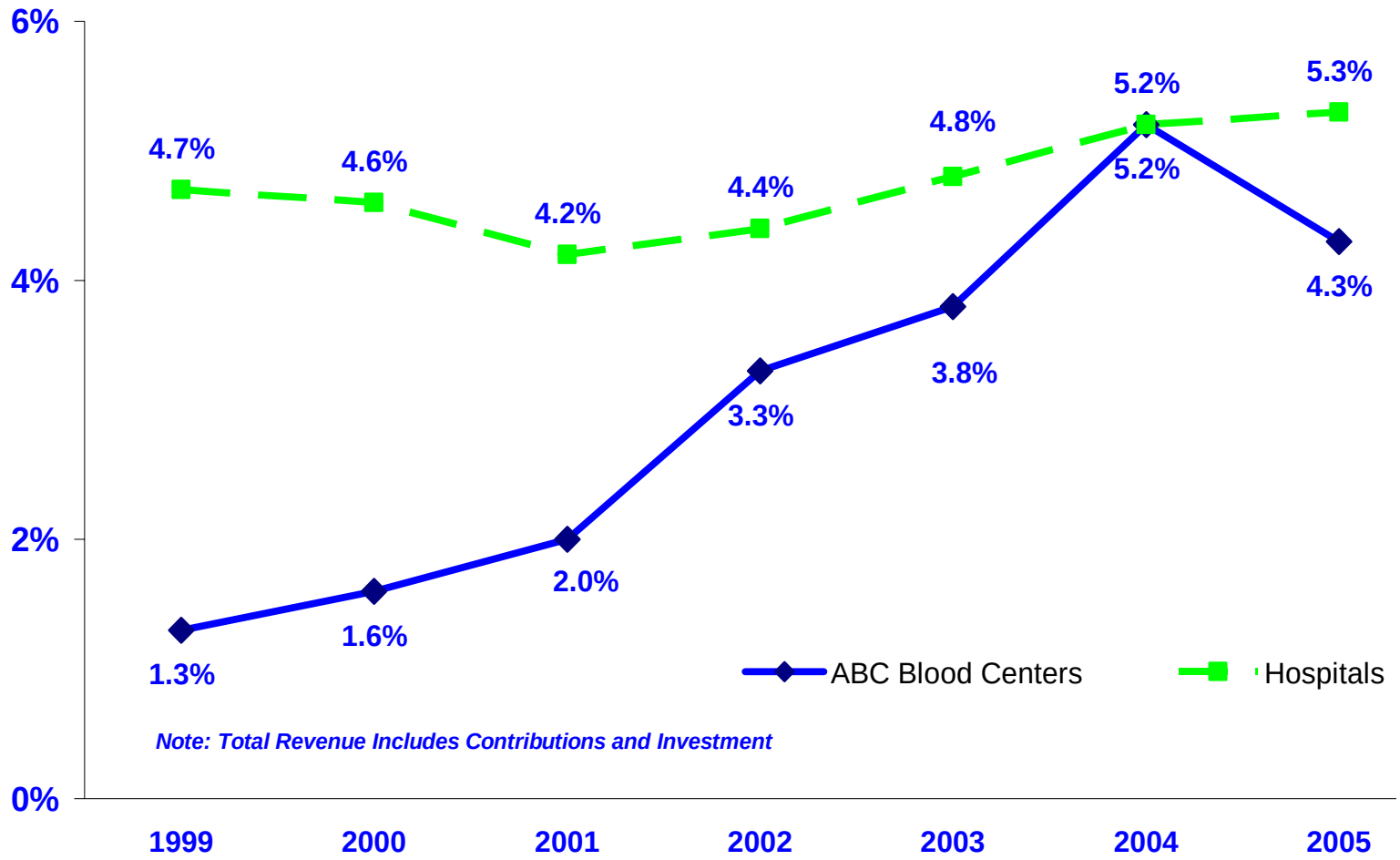
- **Blood collection and transfusion is a mature industry**
  - 15 million WB collections, flat between 2001 and 2004 (AABB/DHHS Survey)
  - ~2 million apheresis platelets, ↑5% 2001 to 2004
  - Little if any prospect for further growth
- **Manufacturers - less than 1% of revenue of J&J, Abbott, Chiron/Novartis, Roche comes from blood**
  - Profit margins for blood screening products is way below those of pharmaceuticals
- **Hospitals - less than 1% of hospital expense is blood**
  - 5-15% of patients are transfused
  - Blood is the highest expense in the laboratory budget, looking for savings
- **Blood centers – not-for-profit, low margins, low reserves**

America's Blood Centers
Safety Measures and Median Red Cell Service Fees
Adjusted for Inflation, 1985 - 2006



	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
RBCs	80	79	81	83	86	89	90	92	96	99	97	96	95	96	103	109	116	128	153	164	160	166
LR RBCs										151	152	149	147	145	146	146	153	172	187	190	192	195

Median Total Margins, ABC Blood Centers & Hospitals, 1999 - 2005



Note: Total Revenue Includes Contributions and Investment

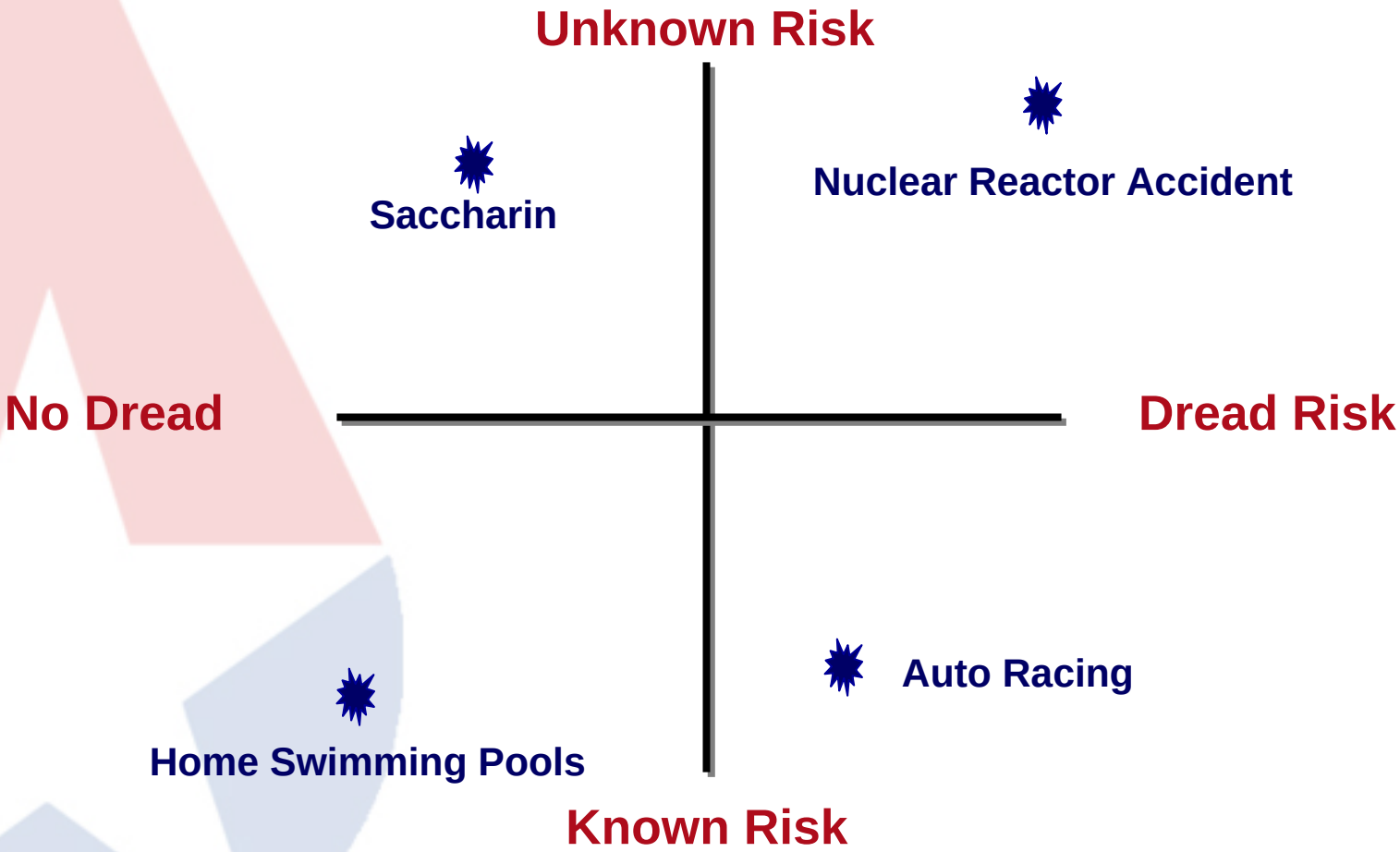
Blood Center Resources and People

- No new money, limited ability to pass on costs, limited ability to invest
- Current generation of leaders is aging
- Small number of training programs for physicians and PhDs entering the specialty
- Shortage of technicians and technologists, few training programs, SBB schools, etc.
- No resources or funding available for biovigilance or for physician education
- Limited internal resources to support R&D

Prospects for Innovation

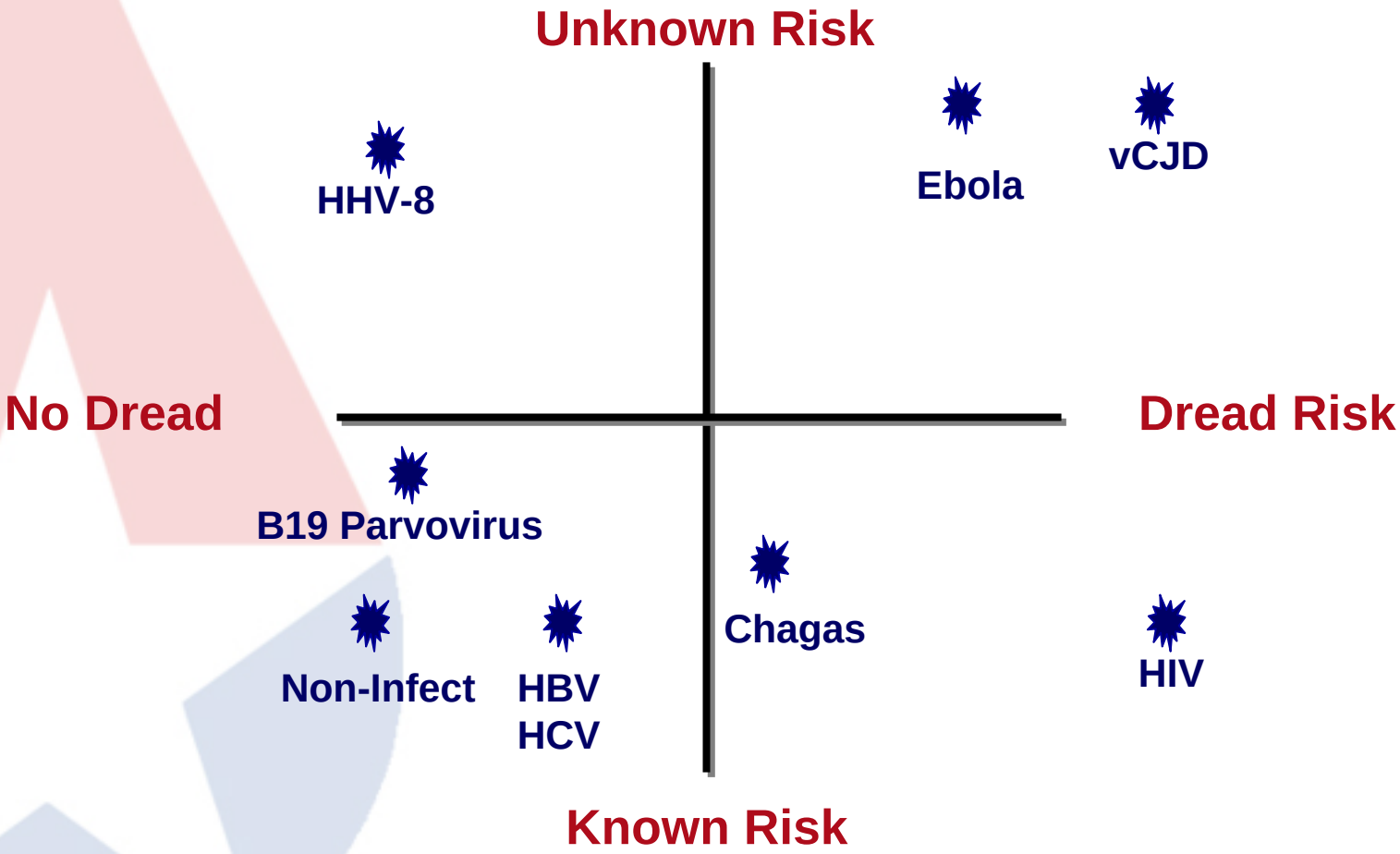
- Manufacturers of tests, equipment and software are few and shrinking – limited competition (higher prices, less innovation)
- Companies focused on the short term (limited R&D, test development only after commitment to mandate made by regulators)
- Little interest by venture capital limiting entry of biotechnology companies into the field (History of Oxygen Carriers and Pathogen Inactivation)

Perception of Risk



Slovic, P. Perception of Risk. Science 1987;206:280-285

Perception of Transfusion Risk

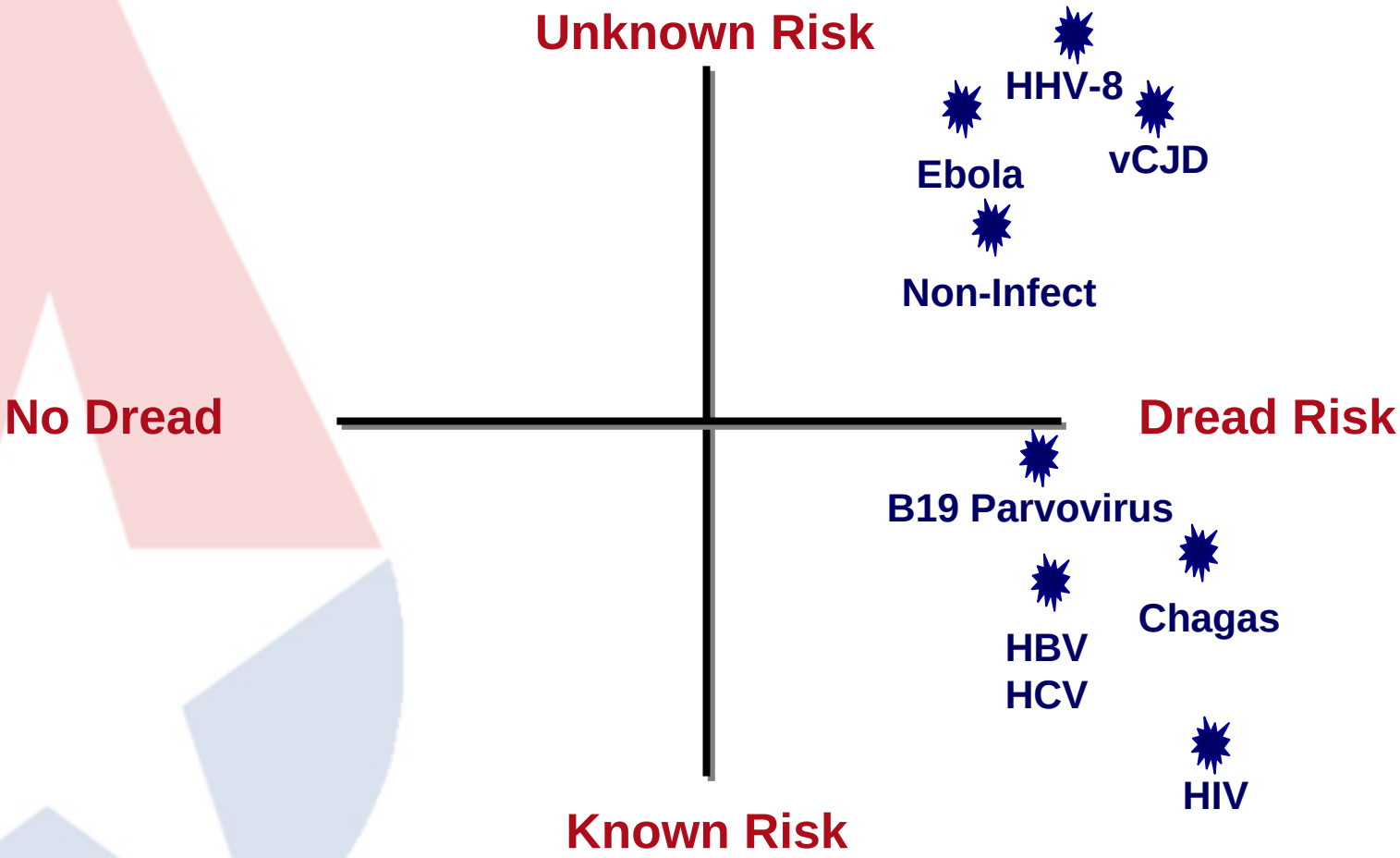


After Slovic, P. Perception of Risk. Science 1987;206:280-285

What is the current state of safety in transfusion and transplantation?

- There is an expectation of zero risk by the public and by recipient advocacy organizations
- The accreditation organizations and regulatory agencies react to these expectations
- Policy decisions are justified by the Precautionary Principle

Misperception of Transfusion Risk



After Slovic, P. Perception of Risk. Science 1987;206:280-285

Regulation & Standards

- Environment is risk averse because of *faux pas* (e.g. HIV, Vioxx, Salmonella in peanut butter, pet food)
- Regulators are terrified of making mistakes; no tolerance for risk leading to
  - Application of the Precautionary Principle (take action before data are available) without the balances of risk/benefit or cost/benefit
  - Strict regulatory measures attempting to prevent ***ALL*** risk (WNV, malaria, abbreviated donor history questionnaire, deferrals, reentry)
- Compliance issues affect safety:
  - We still screen donors with a second generation HCV assay – EU says we are not state-of-the-art

Regulation & Standards

- Regulatory agencies have gradually taken over territory from accrediting organizations – more practices are coded in guidance or regulation
- Accrediting organizations, in order to preserve their mission, attempt to preempt regulatory action
- Each is more strict than the other, generating inconsistencies
  - No screening of cadaveric donors for some agents because assays are not available or not licensed for that purpose
  - Discrepancy between requirements for ID-NAT for blood donors vs. HCT/Ps
  - Guidances for screening issued by accreditation organizations (bacterial detection, WNV, T. cruzi)

Regulations

- Dissociation between FDA priorities*/ and community priorities (*List derived from a recent presentation by an FDA officer)
  - Testing for syphilis antibodies
  - HCV lookback
  - Revised recommendations on deferral for vCJD risk
  - Reentry for NAT for HIV-1 and HCV
  - Collection of platelets by apheresis
  - Donor screening for Chagas' disease
  - Use of NAT for West Nile virus
  - Standards for leukocyte reduced products

Regulations

Priorities (cont.)

- Use of tests for human parvovirus B19
- Updating donor assessment for malaria risk
- Abbreviated UDHQ
- Validation of Computer Cross-Match
- Validation of BECS
- Donor reentry for reactive anti-HBc
- Management of donors reactive on HBV NAT
- Deferral of xenotransplantation product recipients

Back to the Questions from Dr. Holmberg

- What are areas of commonality with blood products, cord, progenitor cells and bone marrow, tissues and organs?
  - Donor recruitment (live or cadaveric donors)
  - Donor History, Donor Screening
  - Collection through needles or surgery
  - cGMP (GTP, GLP, etc.)
- Despite limited differences there are three (3) separate regulatory entities for tissues and organs:
  - Office of Blood Research and Review (Blood)
  - Office of Cellular, Tissue and Gene Therapies (HCT/Ps)
  - Health Resources and Services Administration (HRSA, Organ transplantation)

Back to the Questions

- Is there a need for a master strategy? Scope (rubric)? Yes!
  - Forum for development of common priorities involving regulators, regulated parties (manufacturers, clinicians) and product recipients – evidence based decision making
  - Focus on quality processes, not just products
  - Funding of operations research and discovery as with Canada and EU
  - Willingness to manage risks: the several parties need to share some risks in search of new technologies and new levels of safety
  - Applies to blood, tissue and organs

Back to the Questions

- How to involve the stakeholders?
  - Transparency through workshops, open meetings, discussion documents, dockets
  - Increased participation of experts at BPAC meetings
- What are the resources needed?
  - Increased appropriations for FDA with focus on evidence based regulation
  - Increased appropriations for CDC
  - Increased appropriations for NIH funded research in transfusion medicine and transplantation
  - Willingness and sweat

America's Blood® Centers
It's About *Life.*

Thank you!

cbianco@americasblood.org