American Red Cross

Pathogen Inactivation and Blood Safety in the US

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Conflict of Interest

The American Red Cross is participating in a clinical trial of the Intercept pathogen inactivation process under IDE in Puerto Rico

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

The Safety of the Blood Supply — Time to Raise the Bar

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April 22, 2015. Available at nejm.org

Summary

- US blood collectors are facing unprecedented competitive challenges with commoditization of blood products and diminished reserve to address safety challenges
- Unlike other countries, risk-based decision making by *individual blood operators* is currently not feasible due to the competitive environment
- The US blood industry cannot develop and implement additional safety advances in the current economic situation without mandated implementation and clear, immediate reimbursement mechanisms
- There is a need for timely and decisive actions from all stakeholders to protect patients
- Additional mandated layers of safety are needed, including pathogen inactivation technologies

The US Blood System

- American Red Cross
- Blood Systems Inc
- One Blood
- New York Blood Center

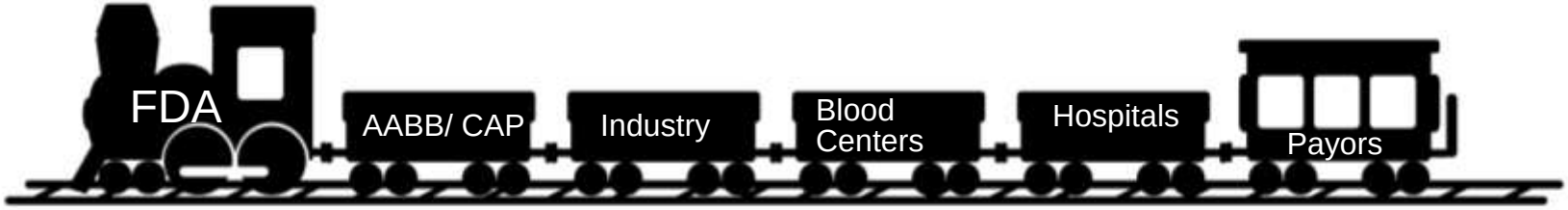
~50% of the blood supply

~ 67 independent blood centers

~ 200 hospital self collectors

- All are “not-for-profit”
- Regulated by the US Food and Drug Administration
- Blood is paid for through individual hospital contracts in a competitive market environment
- Safety is paid for out of blood operators margins

Blood Safety is a Joint Responsibility



- All participants share a joint responsibility in ensuring the safety of the US blood supply
- No single group or agency has a comprehensive ability to assure blood safety
- With changes over the prior decade, it is now unclear whether the US has an effective decision making process for blood safety

US Blood Policy

THE SECRETARY OF HEALTH AND HUMAN SERVICES

WASHINGTON, D.C. 20201

CHARTER

ADVISORY COMMITTEE ON BLOOD AND TISSUE SAFETY AND AVAILABILITY

DESCRIPTION OF DUTIES

The Committee will provide advice on a range of policy issues to include: (1) identification of public health issues through surveillance of blood and tissue safety issues with national biovigilance data tools; (2) identification of public health issues that affect availability of blood, blood products, and tissues; (3) broad public health, ethical and legal issues related to the safety of blood, blood products, and tissues; (4) the impact of various economic factors (e.g., product cost and supply) on safety and availability of blood, blood products, and tissues; (5) risk co of inf

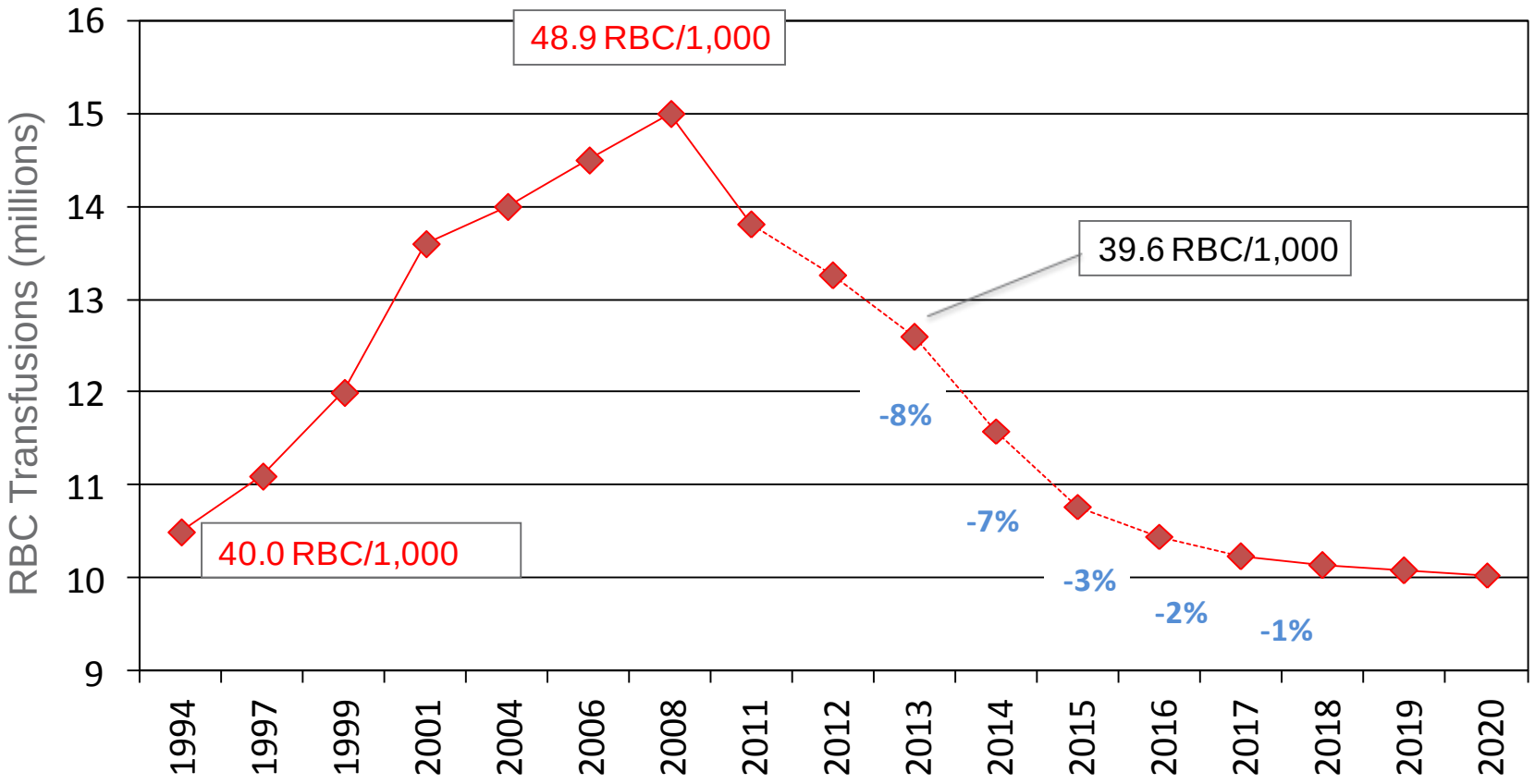
Policy is increasingly set by regulation

The Historical State

- A transfusion transmitted disease would be recognized by the community
- Companies would work with the Red Cross (and some other blood centers) to develop a screening test
- Red Cross would perform testing under IND and then continue testing until FDA approval
- Red Cross (and some independent centers) would implement universal screening on FDA approval of the test, often without immediately passing costs onto to customers
- Two to four years later FDA would recommend or mandate the test and other blood centers would be obliged to implement

RBC Transfusions in the United States

Data derived from National Blood Collection and Utilization Surveys



Blood Centers

- >20% decline in blood use in the US since 2008 has lead to intense competition between centers
- Red cell price has fallen due to oversupply in the face of diminished demand
- Blood centers are struggling financially, with >50% of the blood supply produced by centers with negative margins in 2013
- Americas Blood Centers (ABC) reports a reduction from 87 centers to 68, mostly due to mergers*
- Centers are reducing staff, closing facilities and decreasing investment in research
- In the face of intense competition, no individual center can introduce the additional costs of safety interventions without reimbursement

* New York Times, August 22, 2014

American Red Cross

- We can no longer afford to perform testing without reimbursement
- In future, we will work with test manufacturers to develop tests, but are likely to stop testing once IND work is complete unless hospitals are prepared to pay under cost recovery policies
- We are unlikely to initiate universal testing on FDA approval of a test, unless most other blood centers initiate testing at the same time and the hospitals will bear the costs
- Absent reimbursement, we are likely to wait for a FDA mandate before initiating universal screening tests

Test Manufacturers

- Uncertainty and delay around testing mandates creates untenable risk for companies investing in this area
- Testing companies no longer view developing tests for the voluntary blood supply as commercially viable
- Companies are especially unable to invest in selective testing models, e.g., dengue, chikungunya and babesia
- Companies are moving offshore or into private equity
- The US blood supply can no longer rely solely on industry innovation to support blood safety

Accrediting Agencies: AABB

Association bulletins becoming less directive:

• TRALI	AB 06-07 -	“blood centers should implement”
• Young donors	AB 08-04 -	“may find this information useful”
• Bacteria	AB12-04 -	“should develop policies”
• Dengue		No bulletin
• Chikungunya	AB 14-03 -	“facilities consider recalling…”
• Babesia	AB14-05 -	“should consider ...interventions”

Hospitals

- Reimbursement is disconnected from the price of blood and the costs of safety
- Hospitals, in general, will only pay for FDA mandated tests and often view safety recommendations as research that they are not obligated to support
- Hospitals are free to purchase blood from the lowest cost provider causing intense competition between blood collectors, inhibiting cost increases incurred by safety innovations
- Basing safety decisions on hospitals willingness or ability to pay leads to sporadic, uneven implementation
- This is not a viable strategy to protect patients or blood donors

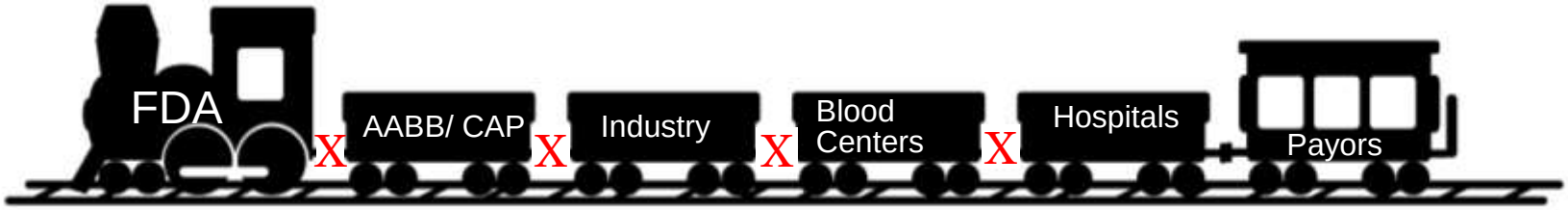
Payors

- The payors do not participate in safety decisions and make no allowance for non-mandated tests
- Funding channeled to hospitals does not necessary flow to blood collectors, as hospitals receive market basket reimbursement under DRGs and negotiate blood prices independent of reimbursement
- There is no reimbursement process to support safety innovations

FDA

- There may be many years between BPAC recommendations, approval of a new test, publication of draft guidance and then final guidance
- BPAC recommendations and *draft* guidances are non-binding (except when they cite regulations)
- With respect to emerging issues and given other changes in the industry, the guidance process may be an ineffective mechanism to ensure safety in real time

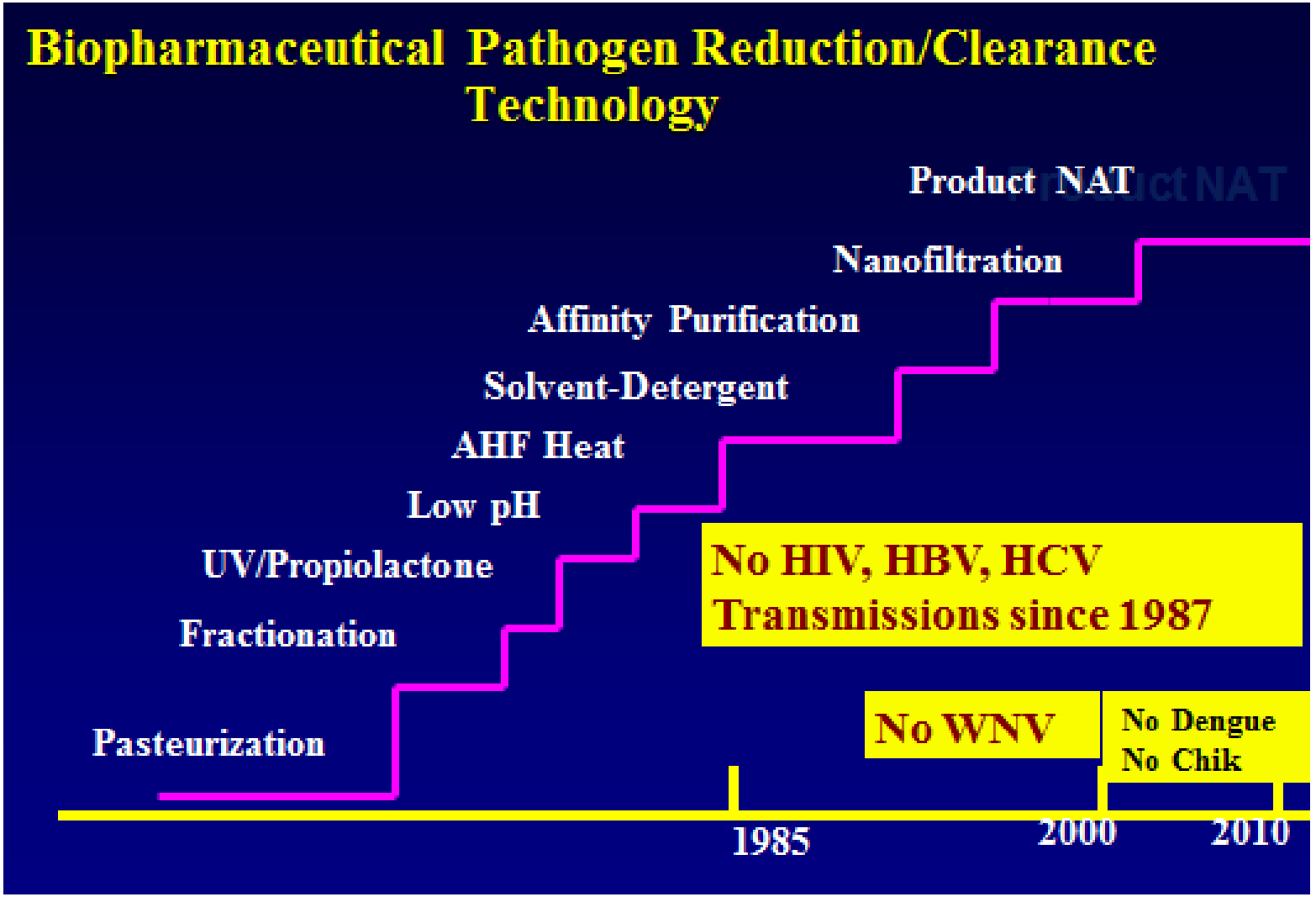
The US Safety Conundrum



The US Safety Conundrum II

- Regulation is now the only consistent method to drive implementation of safety innovations in the US
- The FDA needs to take proactive and timely steps to protect patients through direct mandates after appropriate stakeholder engagement
- Safety system that are not mandated are not safety systems
- In the absence of future investment in innovation, additional layers of safety are immediately necessary
- Pathogen inactivation provides an additional layer of safety that diminishes the need for rapid and immediate interventions

Additional Layers of Safety



Thanks to Harvey Klein MD

Pathogen Inactivation for Plasma

- Intercept^{tm} system for plasma FDA approved in Dec. 2014
- Octaplas^{tm} FDA approved in Dec. 2013
- Neither system is required nor is in widespread use
- Plasma is the highest window risk for HIV, hepatitis B & C when used with NAT testing, due to volume
- 4/6 US NAT non-reactive HIV transmissions due to plasma
- "Two FFP units and all three WB–derived PLT concentrates … were infectious, but three of nine (33%) RBC concentrates … were not infectious*"
- 12 of 18 HBV transmissions were plasma or platelets*
- With relaxation of MSM criteria, pathogen inactivation of plasma would substantially reduce current window period risks and balance theoretical additional risks

*Kleinman et al Transfusion 2009:49; 2454

Safety Systems for Platelets

FDA approved safety systems for bacterial contamination include:

- Verax PGD point of issue test
- Immunetics BacTx point of issue test
- Cerus Intercept pathogen inactivation

None of these technologies is required or widely used

Bacterial sepsis and fatality remain a major risk

The Red Cross, ABC and AABB have called for mandated use of at least one these technologies in addition to primary bacterial culture screening

Conclusions

- The US Transfusion Medicine industry has diminishing economic ability to implement new safety initiatives without direct reimbursement
- The US has come full circle, where safety decisions are now based on hospital ability or willingness to pay
- There is a need for timely and decisive action to protect patients and donors
- The FDA should mandate approved safety innovations in a timely fashion
- Pathogen inactivation systems should be mandated in the US as an additional layer of safety and financial resources made available to fund implementation