**Key Perspectives for New Technologies in Transfusion Medicine**

*(Our System is Broke)*

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### The Thesis and Questions

- Significant investment is required for innovation, invention, and institution of technologies.
- The blood industry as currently configured risks extinction due to systemic conditions that include the inability to make adequate investment and garner return for reinvestment, a disjointed infrastructure, and high regulatory requirements (esp in the US).
- These conditions lead to us being reactive rather than proactive.
- Being reactive as an industry adversely affects advancement of the field and thus patient care. It also may mean that our future is being determined by those outside the industry and not from within.

**Who and what are the future, and how do we lead and fund it?**

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### Key Elements Affecting New Technologies

- Healthcare reform *(money)*
- Deflationary pressures on blood centers and hospitals *(money)*
- Commodity product lines without branding *(money)*
- Lack of "profit" *(money)*
- Quagmire of the NFP environment *(money)*
- Historically late adopters *(inertia/money)*
- Uncertain and high regulatory hurdles *(regulation/money)*
- Thus, lack of incentives to innovate *(money/money)*
Part I
A Look at Innovation and Invention

Fifty years later, the post-war paradigm was/is being rethought – Stokes 1997

1944 – 2000: Lack of Invention Paradigm Shift

Bush’s second canon:
"a nation which depends upon others for its new basic scientific knowledge will be slow in its industrial development and will lose its position in world trade. A new paradigm is needed as well as substantial investment"

Quest for Basic Understanding?
Consider Possibilities for Use?

Quest for Basic Understanding?
(Rigor)

Consider Possibilities for Use?
(Relevance)

A=Yes
C=Yes
B=Yes
D=No

(Relevance)

(Failure)

(Fortune)

(Fame)

(Fantasy)
Part II
Why are We Here (Financially)?

Intelligence + Industry + Rigor + Relevance + Vision = New Paradigms

1840-1920
50 cents/100 lbs

1922: $714
(Model T: $450)

Old Paradigms -Intelligence - Industry - Rigor - Relevance - Vision = EXTINCTION
Healthcare Reform and Transfusion Medicine

Healthcare reform has many unknowns including:

• Its final form; implementation timing/difficulty/scale; effect on %GDP trends, and hospital/consumer costs and quality; and where will the money go (be)?
  (Show Me the Money)

• Hospitals perceive intense pressure to provide care at the level of CMS reimbursement/Medicare(aid); which forces intense review of costs (at a time when blood inventories were in excess and future demand is unclear in a failing economy).

  (The Perfect Storm)

• These elements give leverage to hospital contracting offices, and adversely affect Center revenues, when no other hospital vendor operates as a not-for-profit, and blood pricing is below therapeutic alternatives. Thus, the hospital cost/blood center revenue (margin) value proposition is unclear.

  (Lack of Gross Profit to Fund Innovation)

• New models for blood centers to be integrated into the healthcare system are needed.

  (Lack of Innovation Paradigm Shift)

What does it mean?

Uncertainty + “Fear” = Unfocused (likely ineffective) Change

• Even before full implementation, definitions, guidance, etc…
  – Hospitals are very concerned that they will have financial declines in their top and bottom lines

• Effect on blood centers, blood banks and transfusion medicine…
  – Increased focus on product pricing and significantly decreasing utilization
  – Pressures to consolidate to cut costs
  – Creates negative “margin”

• Thus,
  – No funds to innovate, invent or institute new technologies

The Perfect Storm

(Where did the margin go?)
The Perfect Storm - I

- Traditionally a supply constrained market, the blood industry has and continues to experience a financial “perfect storm.”
- Recessionary pressures on healthcare coupled with formalized blood utilization programs have created a net reduction in demand which may be on the order of:
  - 10-30% in RBCs
  - 50-85% in Plts
  - 50-85% in plasma

The Perfect Storm - II

- First time in the history of blood banking there is an excess of supply.
  - Increased efficiencies following the mad cow disease epidemic;
  - Automated RBC collections have also increased the contribution to the RBC pool by 15%-20%; and
  - Blood donation by sixteen and seventeen year olds without strict parental permission increased the donor pool by an additional 10%.

The Perfect Storm - III

- Thus, an industry that was capacity constrained a decade ago has become an industry that now has projected excess capacity on the order of up to 25%.
- The combination of a decreasing demand with an increasing supply has had a deflationary effect and increased pressure for cost cutting measures such as consolidation.
- Blood price deflation ~30%;
- Thus, where is the money to make:
  - Significant investment is required for innovation, invention, and institution of technologies (Thesis element 1)
Part III
Lack of Gross Profit to Fund Innovation

(Can we Affect Change as not-for-profits?)

The Blood Center Predicament: A Backdrop

Community Blood Bank of Kansas City, Inc. v. FTC, 405 F. 2d 1011 (8th Cir. 1969)

- Only NFP operating as a major (commodity) vendor to hospitals
- Significantly undervalues the therapy and its method of pricing
  - Compare FVIIa
- Significantly limits R&D budgets and incentives for development failures
- Significantly limits means of M&A for system consolidation/creation

So...

The blood banking industry – vendors, blood centers, hospitals and hospital blood banks, and even universities, may not have the resources, vision, position, impetus and/or fortitude to create a disruptive paradigm/new business model.

Innovation, Invention and Adoption move to a standstill
George M. Beal, Everett M. Rogers, and Joe M. Bohlen (1957)

Rogers’ Innovation Adoption Lifecycle

Part IV
Want Examples?

• SD Plasma
  – FDA approved; upcharge ~$75 – Failed

• ISBT 128
  – issued 1994; implementation target 1998 – Almost failed

• Plastic bags w/o plasticizer:
  – FDA approved; even at a down charge no adoption – “Failed”

• Automated Component Prep
  – Compat, Orbiac, Atreus – “Failed”

• Platelet Additive Solution (PAS)
  – FDA approved; no adoption at $18 upcharge - Failing
What could the future look like? At what cost?

- Genotyping; broad antigen matching
- Prion removal
- Universal irradiation
- High Technology - Mistransfusion
- Babesia mitigation; PRTs?
- Aged RBCs; new Esol?
- VAT RBCs; a pharma-level product
- Pharm'ed Components?
  - iPSC/HPC-derived RBCs/Pts
- Cold stored platelets; PAS
- Cryopreserved organs
- Cellular Therapies and Regenerative Medicine
  - CB expansion; iPSC; MSC; Angiocrine+ Ecs; personalized graft engineering
  - MS, IDDM; heart repair; hearing loss; macular degeneration; aging?

3Ti AISD Elements

www.3TiBio.com
CRC – Sample Results
AISD (Standard = Tube)

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AISD Incompatibility Detector

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VAT-Pooled RBCs

CONCORD, Calif. & NEW YORK--(BUSINESS WIRE)–
Cerus Corporation (NASDAQ: CERS) and New York Blood Center (NYBC) announced today that they have entered into a research collaboration to explore the possibility of creating a red blood cell (RBC) biologic product with improved uniformity compared to a standard unit of red blood cells.
The Concept of VAT-Pooling

unit of red blood cells 
either from apheresis 
or whole blood collection 

10-30 RBC units 
into vat 

add storage solution for 100 day RBC 
treat RBCs to remove pathogens, WBCs and plasma; inactivate WBCs 

store uniform dose RBC at 1-C 
for up to 100 days 

RBCs as nanoparticles and a drug delivery system

PRESS RELEASE September 7th 2012

ERYTECH Pharma announces the oral presentation of very demonstrative results regarding its technology to induce specific immune tolerance by antigen-loaded erythrocytes.

Therapeutic proteins are often immunogenic, inducing anaphylactic reactions and/or specific immunoglobulins. Their administration is often stopped or inefficient due to neutralizing antibodies. ERYTECH's concept consists in encapsulating the therapeutic proteins inside erythrocytes. The membrane of the erythrocytes is modified to target the immune cells known to induce tolerance. ERYTECH's researchers demonstrated this concept with different proteins. The reduction of specific antibody TITER was strong and maintained for months.

Cellular Therapies and Regenerative Medicine

- "Twenty five years ago, biotechnology was in its infancy, but in 2010, biologics, including protein-based therapeutics and monoclonal antibodies, achieved over $100 billion in sales. We believe cell therapy is the next frontier, likely to revolutionize medicine."
Building on your idea wo numbers
astassinopoulos, 5/13/2012
A Quick Look at Cellular Therapies and Regenerative Medicine

A **Very** Expensive Proposition

- MS
- Obesity via BDNF and gene therapy
- TBI spinal cord injury
- Diabetes
- Bone repair
- Hearing loss
- Heart repair
- Liver generation
- Pharm’ed blood cells for transfusion

**Ex Vivo Generated Red Cells as Transfusion Products**

Anna Rita Migliaccio, Giuliano Grassi, and Christopher D. Hillier

*New York Blood Center, New York, NY, USA*

**In vitro generation of red blood cells for transfusion: a model for regenerative medicine**

Challenges to Large Scale Clinical Utility of cRBCs (or cPlts)

- Choice of Source: CD34+ vs iPSCs
- If iPSCs: Choice of reprogramming method (safety)
- Optimization of erythrocye differentiation
- cGMP-level industrial production
  - 1 trillion cells per pRBC unit x 100MM units/yr
Clinical-scale expansion of LT-HSCs


There Are More Questions than Answers

- What does the patient want and needs?
- What do "we" want and need?
- How do we to create capital?
- How do we achieve a balance of regulation and incentivization?
- Can we identify a common goal?
- Can we to work together to achieve that goal?
  - (see No Contest: The Case Against Competition; Kohn 1992)

- Without ongoing funding at all stages up and through commercialization, it is unlikely that we in transfusion medicine as currently configured can build our own future.... that will be left to commercial enterprises selling directly to hospitals and patients.
Got any grapes?