# Resolutions and Revolutions – Some Perspectives

*Jesse L. Goodman, MD, MPH*

*January 22, 2008*

*Boston, MASS BIO*

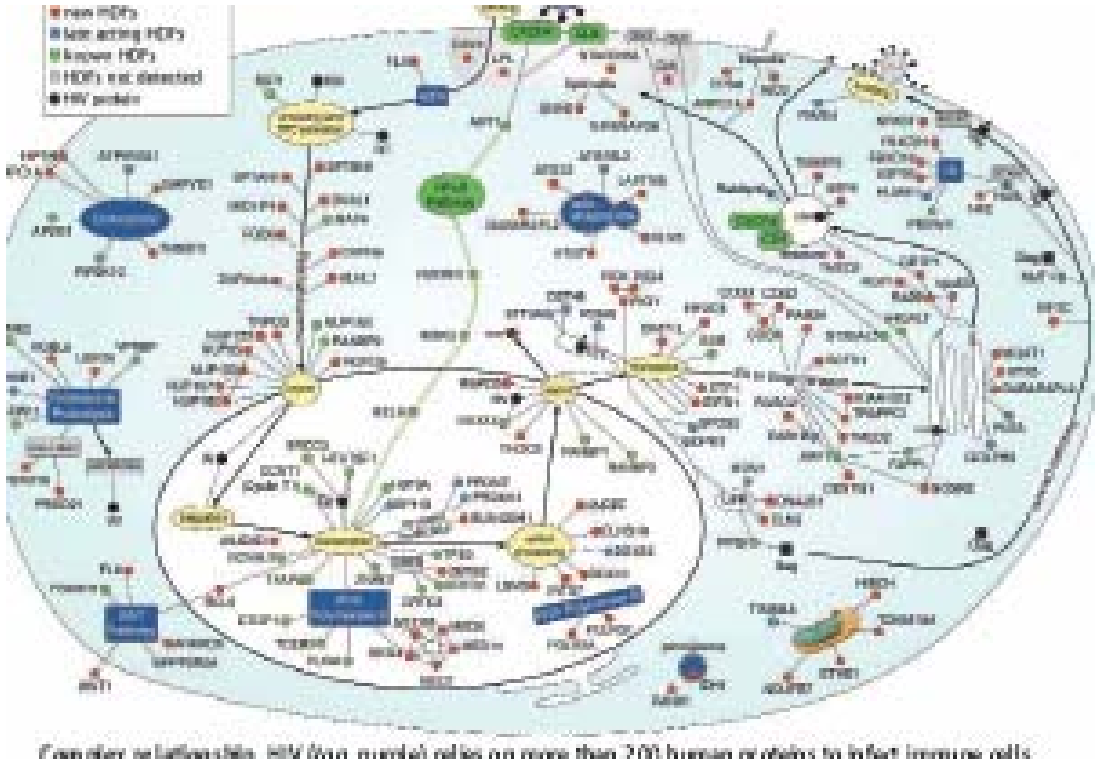
- ***Change and excitement already here***
- ***Some major directions/thoughts***
- ***The winners will envision and seek opportunities – not fight them***
- ***Though much is possible, nothing is simple…yet***
- ***Enabling - we need to do it together – early and throughout development***
- ***Common goals – improve health***

# Change and Excitement – Just a Few Examples

- Targeted and Personalized Medicine
- Repair or replace, not just treat - stem cells, gene therapy, tissue engineering
- Prevention, primary and secondary, including cancer
- Global and Public Health – increased needs and valuation
- Large Databases for Safety and Utility

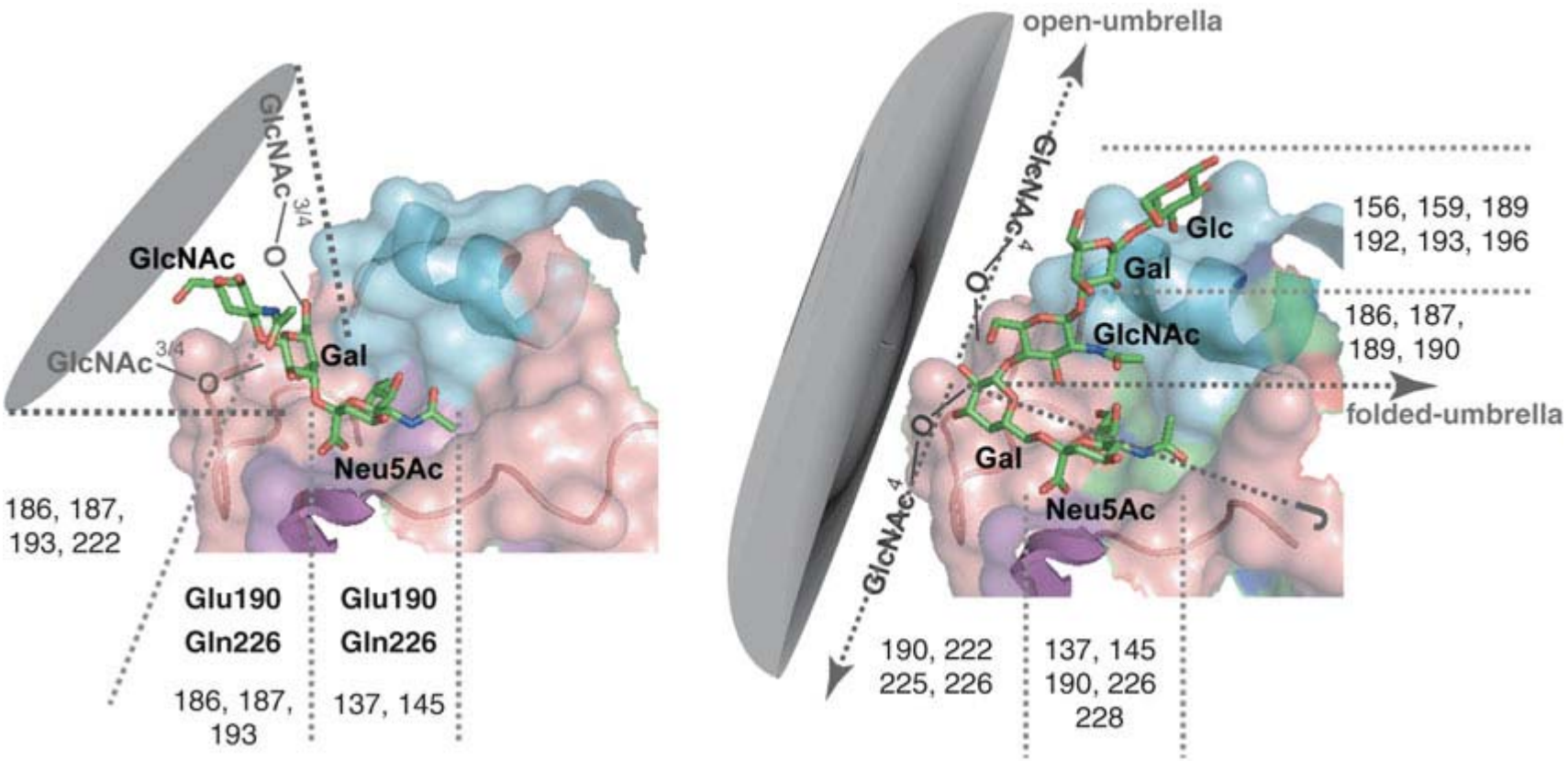
# 1 – HIT THE TARGET or…

# New Approaches to Targets – HIV – siRNA Host Genome Disruption



Brass AL et al, Identification of Proteins Required for HIV Infection Through a functional Genomic Screen, *Science*, 1/10/2008

# HA Receptor Glycan Topology Associated with Human Tropism




Glycan topology determines human adaptation of avian H5N1 virus hemagglutinin

Aarthi Chandrasekaran, Aravind Srinivasan, Rahul Raman, Karthik Viswanathan, S Raguram, Terrence M Tumpey, V Sasisekharan & Ram Sasisekharan, ***Nature Biotechnology* 26**, 107 (2008)

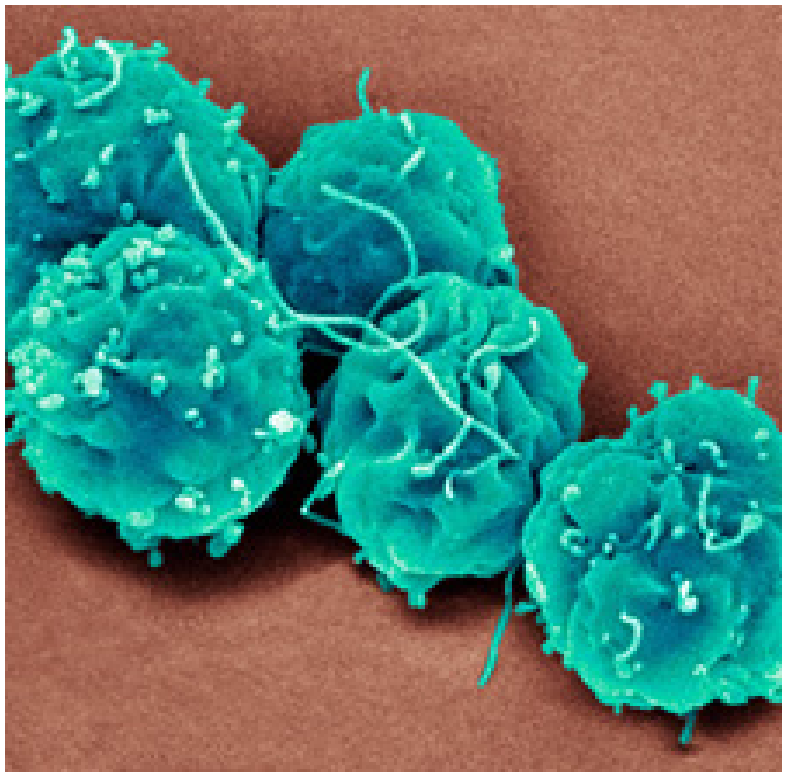
# Right Target in Right Person – Biomarkers – Critical Path

- Biomarkers can help identify promising (or risky) pathways, leads, responses, dosing etc.
- Goal – more effective/safer therapy, more efficient and less costly development
- What's not simple
  - Most biomarkers not surrogates – but still can be useful – right patient/right drug
  - Business models, costs
  - Pathway targets/actions may also be good
    - There is probably some reason that you name it (gene, protein, polymorphism) is there, and it is possible that even the most targeted therapy will mess something up
      - Examples – TNF and infection, cox-2

# Resolutions

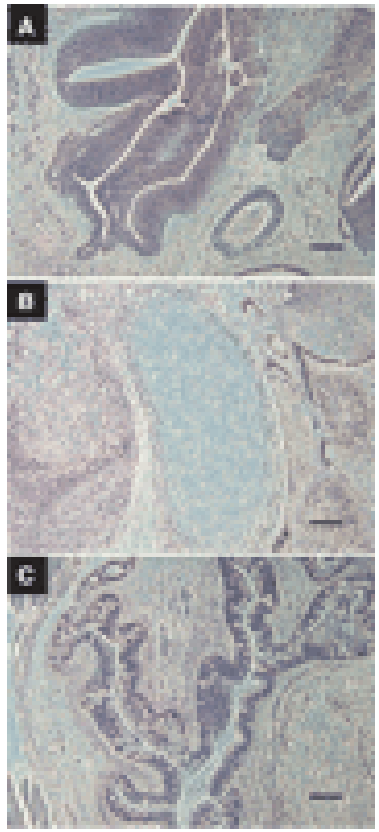
- FDA promoting biomarker research, validation
- Established VGDS. Biomarker Consortium
- FDA/NIH/NCI efforts, investments
- Projects in diabetes, imaging, Alzheimer’s
- Pharmacogenomic safety e.g. warfarin, Spx
- Pandemic, anthrax correlates
- Critical Path Research (CBER – biomarkers on stem cells, cell substrate quality, vaccine and blood product efficacy and toxicity)

# 2 - Repair/replace! - New Sources of Stem Cells



*Development of Human cloned Blastocysts Following Somatic Cell Nuclear Transfer (SCNT) with Adult Fibroblasts – French et al, Stem Cells, 2008*

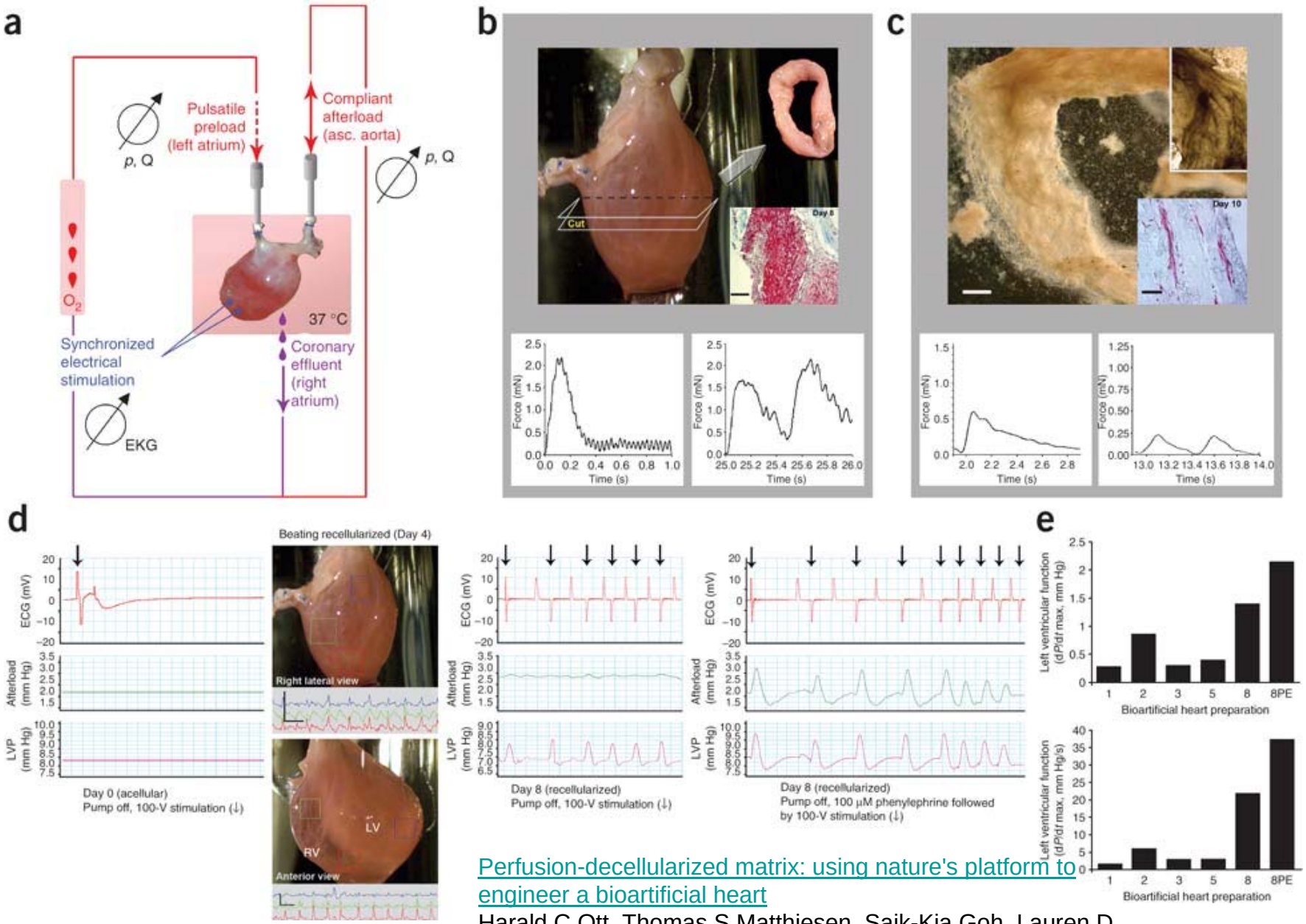
# Or…Reprogram




**Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells** Junying Yu, Maxim A. Vodyanik, Kim Smuga-Otto, Jessica Antosiewicz-Bourget, Jennifer L. Frane, Shulan Tian, Jeff Nie, Gudrun A. Jonsdottir, Victor Ruotti, Ron Stewart, Igor I. Slukvin, and James A. Thomson *Science* December 2007

# or…Remake the Target – Bioengineered Heart Valve

*OR A NEW HEART???*




[Perfusion-decellularized matrix: using nature's platform to engineer a bioartificial heart]

Harald C Ott, Thomas S Matthiesen, Saik-Kia Goh, Lauren D Black, Stefan M Kren, Theoden I Netoff & Doris A Taylor

***Nature Medicine*** 13 January 2008

# What's Not Simple?

- Fate/oncogenesis of genes/cells/tissues
- Differentiation/functionality/regulation
- Host environmental effects on new cells/tissues, functionality, survival
- Boundaries, ethics, unforeseen risks?
- Resolutions:
  - proactive workshops, AC's to define issues/pathways, study designs etc.
    - examples – cell scaffolding, islet, cartilage, cardiac cell Rx, MATES, discussion of ESC science issues
  - Collaborative CP science – e.g. NTP study

# 3 - Prevent or Intervene Early

- Classic vaccine strategy
  - Revolutions – prevention of cervical, hepatocellular cancers
- Increased interest in earlier use of therapeutics
- What's not simple?
  - Scientific challenges (e.g. malaria, TB, cancer immunology)
  - Duration and cost of large, prolonged clinical trials
  - Potential risks to healthy
  - Nontraditional outcomes
- Resolutions: cancer vaccine workshops, new biomarkers and initiatives for prevention

# 4 - Globalization and Public Health -Needs and Opportunities

- Humanitarian needs and value
- Disease threats global, no boundaries
  - Pandemic flu, HIV, malaria, TB (including drug resistance) – I'd get a safe TB vaccine
  - And don't forget - diseases of 'progress' – emerging threats as nations develop
- Manufacturing, knowledge and regulation are global
- *Needs, markets and opportunities are global*

# What's Not Simple

- Markets – uncertain or 'insufficient'
- Examples in US and globally
  - Uncertainty – emerging diseases, bioterrorism
  - Insufficient – segmented - blood diagnostics, antibiotics especially for resistant organisms
  - Value to public health and preparedness not directly economically linked – incentives/push/pull
  - But recent successes with vaccine industry
- Delivery systems and sustainability
- Resolutions: Intense FDA/CBER input and support for BioShield/BARDA and influenza projects, other priority public health projects (e.g. WNV) – global leadership, information sharing, quality, collaboration, convergence

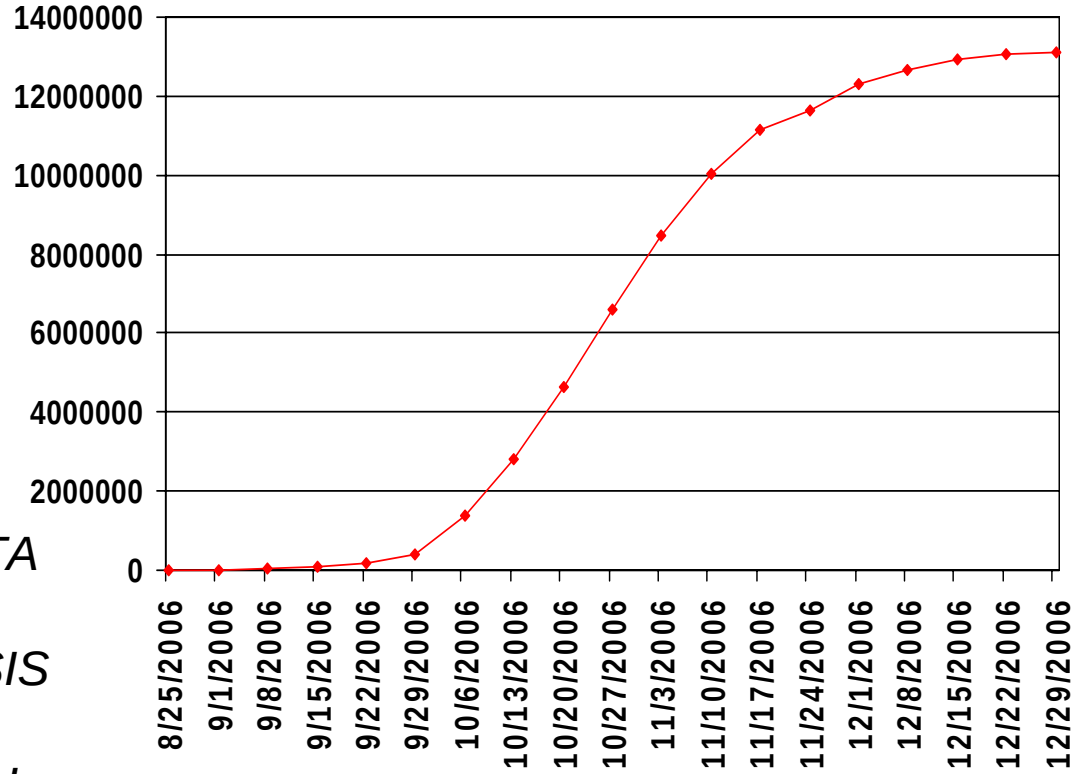
# Resolutions - Global Harmonization Collaboration: Examples

- Emerging Threat Preparedness - Leadership FDA/WHO/Health Canada Pandemic Regulators
- WHO and WHO Collaborating Center, PAHO
  - Expert Committee on Biologic Standards, SAGE, GCVS
  - Influenza, xeno and gene therapy
  - Regulatory capacity building/assistance
- Blood: GCBS leadership, WHO “Circle of Regulators” – safety screening standards
- ICH (including GT) , PIC-S, ICDRA
- Information sharing + support global product development plans/coordinated regulation
- CBER Global Vaccine Initiative
  - Consultation, standards, CP science, reg. capacity
  - MVI, Gates, TB, PATH, meningitis, etc.

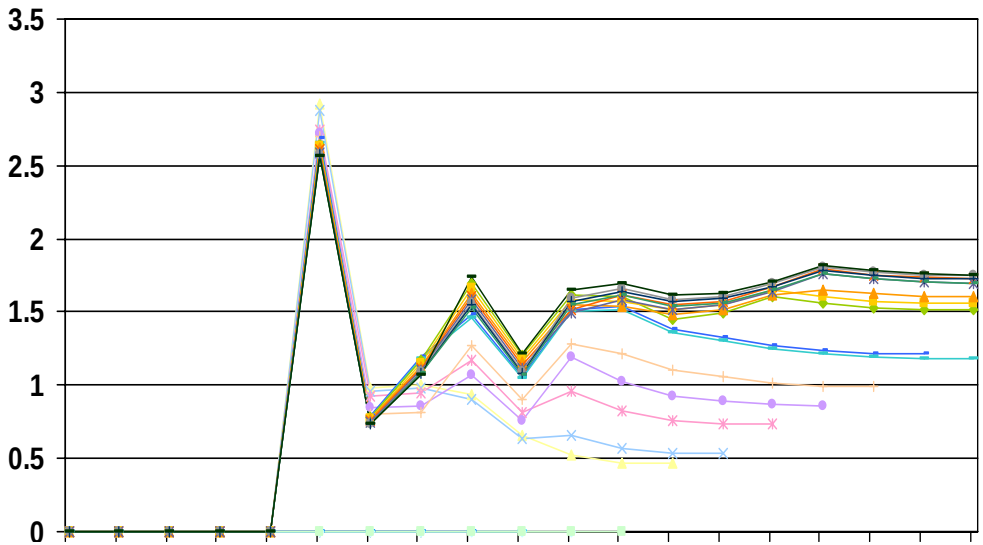
# Safety and Value: New Approaches

- *Safety* is not absolute: need for transparency and better, early communication, “risk literacy”
- Benefits & risks both considered
- CBER multidisciplinary safety teams
  - Increased use of large datasets
  - Consistent with IOM, FDAAA
- *Value* will be rewarded - lack thereof punished
  - Prevention, improved therapies, not marginal gains
  - Challenges in measurement:
    - Should consider not just value to health systems but also
    - To individual and
    - To public welfare, society and health
    - Large datasets can help with some of this, as well

*FDA/CBER DATA USING CMS – RAPID ANALYSIS OF GBS AND SEASONAL FLU VACCINE - 2006*




DOSES




GBS rates

# What's Not Simple

- Quality and format of data from health systems – variable at best
- Analytic tools and approaches not yet up to data quantity and variability
  - Clusters – false positives
  - Lack of background rates
  - Confounding is abounding
- Communication of risk and of uncertainty
- Resolutions – partnerships e.g. FDA/RUF
  - CBER: Data Analytic Unit, CDC VSD, CMS, VA, DMSS, enhanced early communication

# “Risk Literacy”

- Risk literacy – difficult and non-intuitive to understand risk and causal association statistically vs. individually
- There are risks in conveying uncertainties, including potential decreased use of safe product, public health consequence if vaccine
- Major behavioral science, educational system and risk communication science needs (FDA AC)

# Thank you!

- ***We are poised for and should embrace many revolutions and changes***
- ***Value will be rewarded – and includes, but is not limited to, safety and effectiveness***
- ***Collaboration and best science essential***
- ***Challenge us and yourselves!***
- ***We will work with you to go from "good to great"***
- ***Individual, global and public health can and must benefit***

Contact me: 301-827-0372 jesse.goodman@fda.hhs.gov

***CBER: INNOVATIVE TECHNOLOGY ADVANCING PUBLIC HEALTH***