



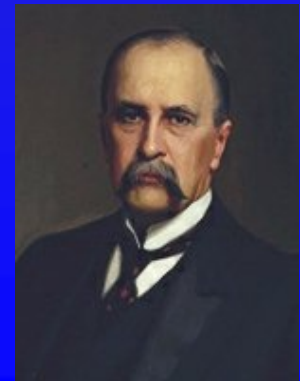
# Future of Personalized Medicine: moving from art to science

Alan McKay, PhD.  
Professor and Dean  
Bernard J. Dunn School of Pharmacy

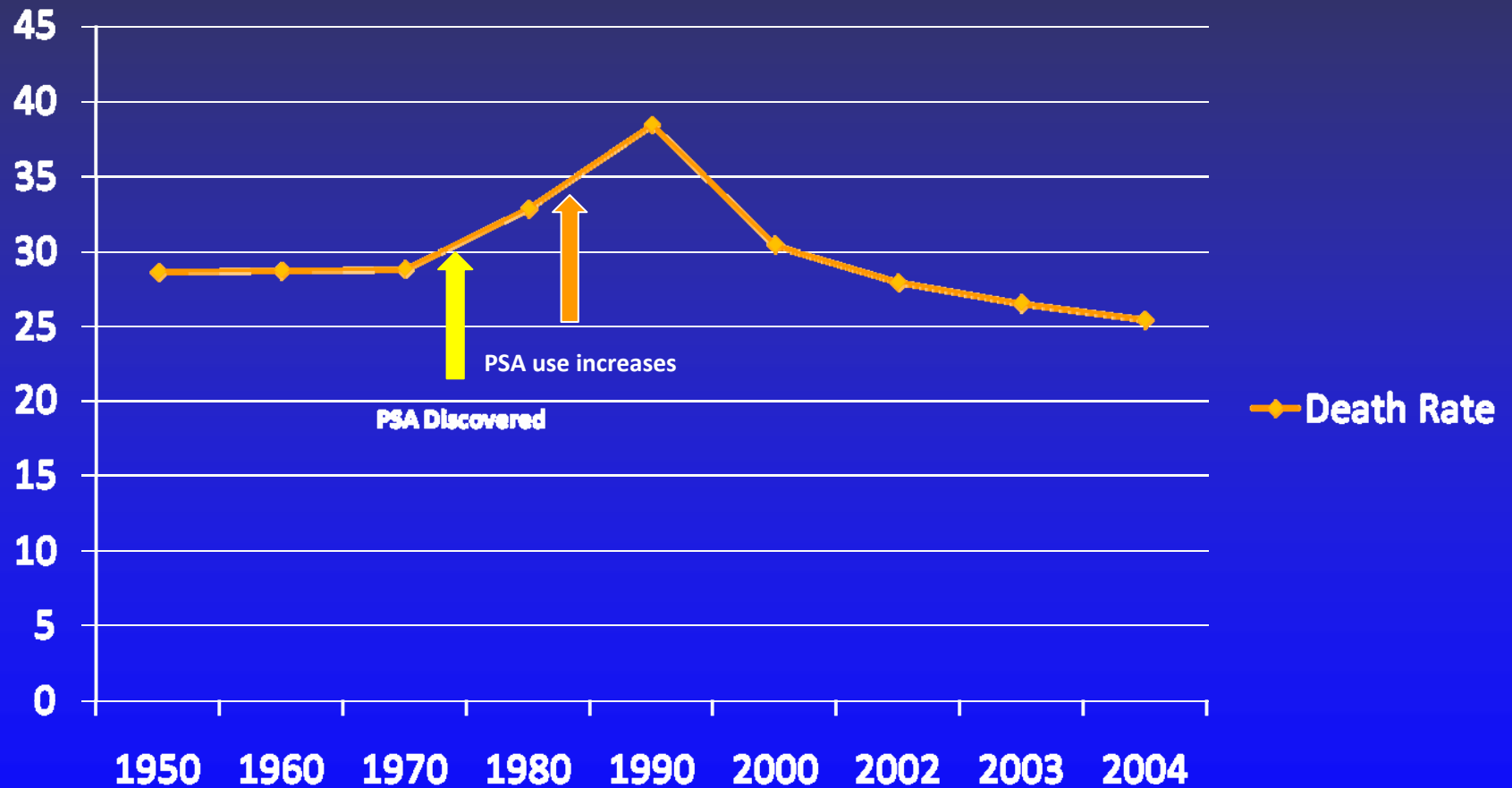


If it were not for the great variability among individuals, medicine might as well be a science and not an art.

Sir William Osler (1892)



# Age-adjusted Death Rate for Prostate Cancer (per 100,000)



Source: Chartbook on Trends in the Health of Americans (2007)

# Pharmacogenomics

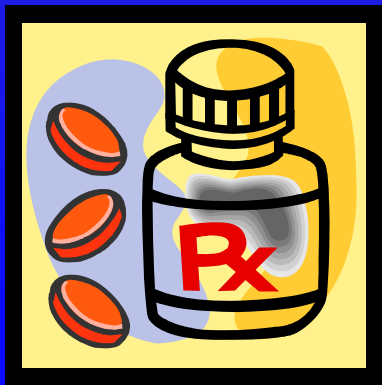
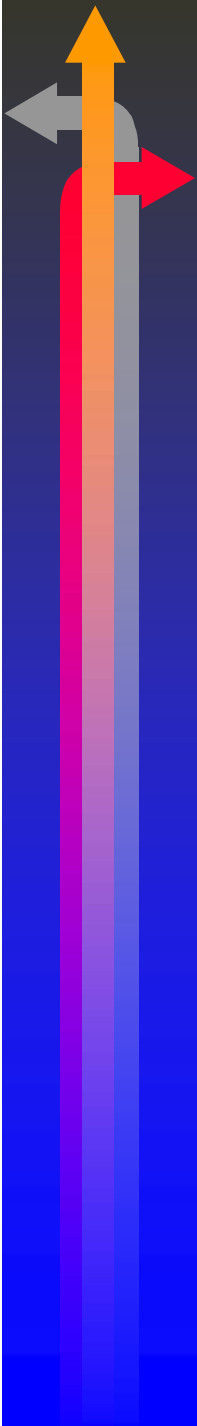
The study of how a patient's genetic makeup affects their response to drugs.



# Evolution of Pharmacogenomics

1. Sequencing of the human genome
2. Better genetic testing predicts illness, but does not, in most cases, translate into a cure
3. Genetic testing improves the use of existing drugs through better dosing and a reduction in side effects
4. Personalized medicine becomes a reality when patient's genetic sequence is matched to drugs created for that specific biomarker





Genetic Testing

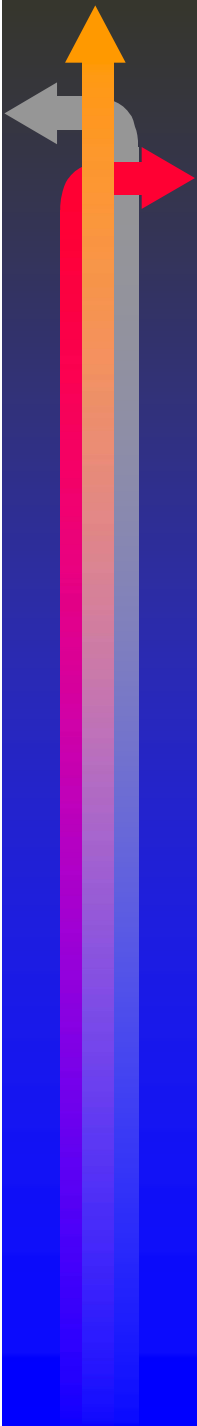
Patient databases

Niche product development

Theranostics

Personalized Medicine

Pharmacy in the 21<sup>st</sup> Century



## Genetic Testing

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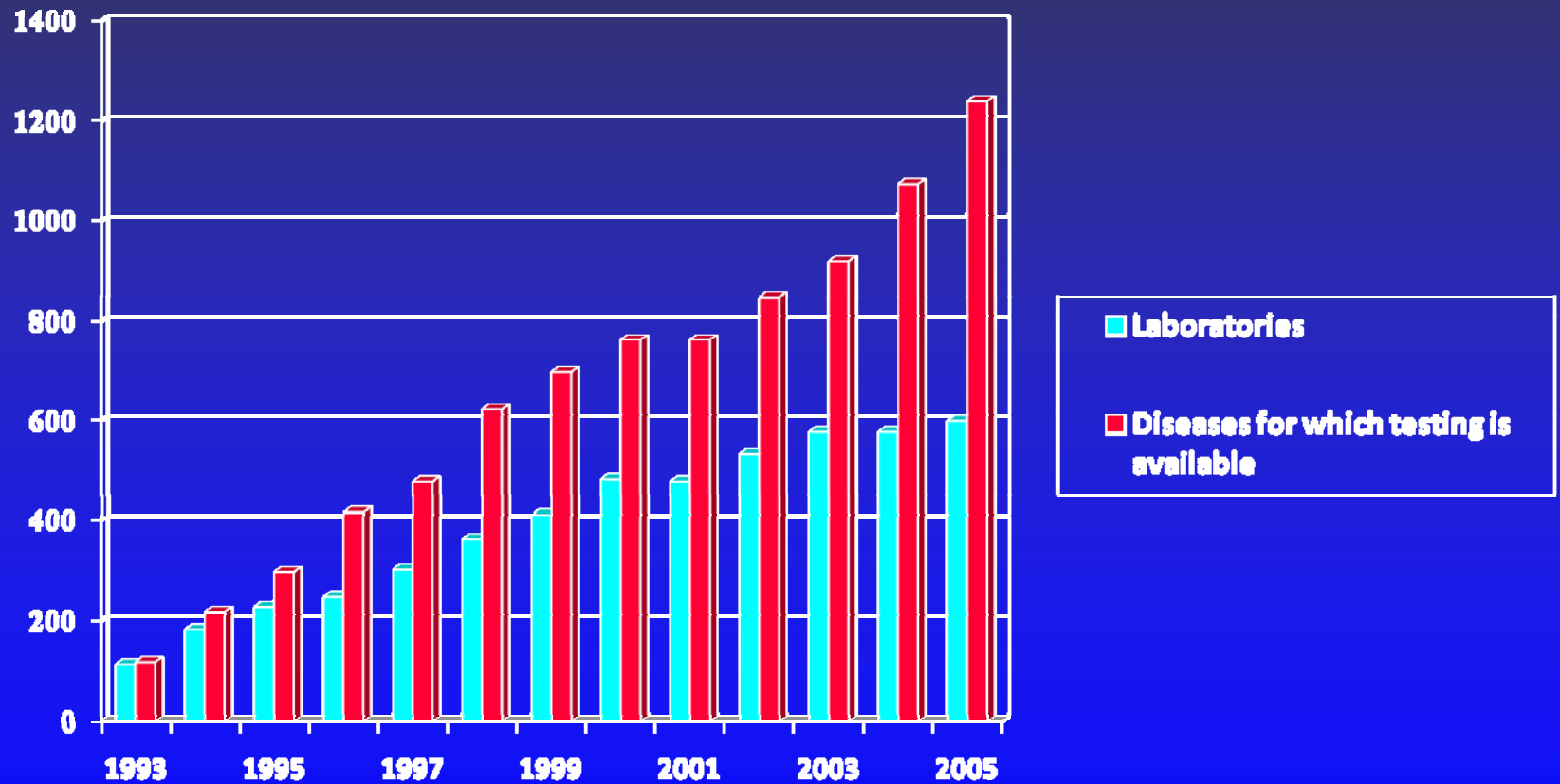
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# Growth in Genetic Testing



Source: GeneTests Database (2005)/[www.genetests.org](http://www.genetests.org)



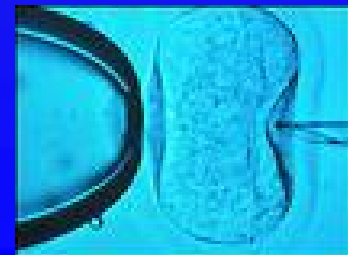
# Genetic Testing

- Ethical dilemma – Pre-implantation Genetic Diagnosis
- Genetic Profiling
- Privacy and Confidentiality
- Test variability
- Cost



# Pre-implantation Genetic Diagnosis

- Screening for genetic defects (PKU)
- Gender selection – 42%
- Creating children with disabilities – 3%



# Genetic Profiling

- Provide information but no cure
- Raise concerns over disease that may not develop
- Increase financial risk
- Limit lifestyle options (e.g. marriage)
- Rationing of testing to those with most serious diseases or who can pay



# Gene and Disease Associations

## Diseases

- Breast Cancer
- Prostate Cancer
- Diabetes
- Lupus
- Alzheimer's
- Rheumatoid Arthritis

## Other

- Behavioral disorders
- Response to medications





# Privacy and Confidentiality

Some people may choose not to use their insurance to pay for testing because the results of a genetic test can affect a person's health insurance coverage. Instead, they may opt to pay **out-of-pocket** for the test. People considering genetic testing may want to find out more about their state's privacy protection laws before they ask their insurance company to cover the costs.

Genetics Home Reference  
National Institute of Health  
(<http://ghr.nlm.nih.gov/>)



# *in vitro* diagnostic multivariate index assays

- It is estimated that 60 – 70% of medical decisions involve a diagnostic test
- September 2006, FDA proposed increased oversight of genetic testing and specifically clinical laboratories
- Sets the stage for FDA to regulate both drugs and genetic tests (devices)
- Regulation would cover the proprietary software (algorithm) that drives the analysis
- *Home Brew* (consumer diagnostics)



# Test Variability

- **Centers for Medicare and Medicaid (CMS)**

Could require proficiency testing under CLIA but has declined to do so.

- **Federal Trade Commission (FTC)**

Has the power to punish companies for making false claims has some power over the genetic testing market but has taken no enforcement actions.

- **Food and Drug Administration (FDA)**

Can regulate tests, but invoking regulatory discretion has elected not to do so for most tests.

MammaPrint<sup>®</sup> Test (2/6/07) – recurrence of breast cancer



# Cost

- Genetic tests can range from \$ 300 for relatively simple genetic screen to over \$ 20,000 for highly complex diagnostic tests. Mapping an entire human genome can cost millions
- Oncotype DX tests cost \$ 3,460/test
- X-prize in space flight won by Burt Rutan in 2004
- X-prize in genomics designed to reduce cost and improve speed of genetic testing

*This prize and the resulting technology can help bring about an era of personalized medicine.*

Steven Hawking  
Author of A brief history of time  
and a victim of ALS



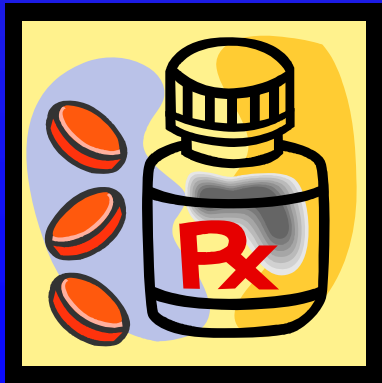
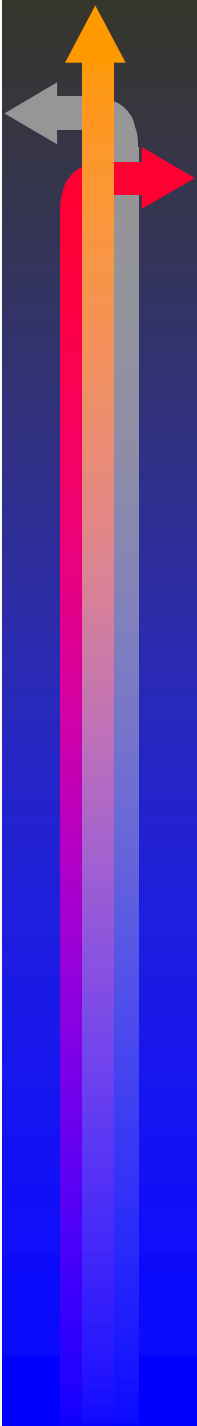




# Recent Mergers and Acquisitions

- Worldwide the In Vitro Diagnostics Market is estimated at \$25 Billion
- Growth rate in 2005 was estimated at 4%
- Characterized by increasing M & A activity
  - Thermo acquired Fisher Diagnostics (11/9/06)
  - Illumina acquired Solexa (11/13/06)
  - Siemens acquired Bayer's Diagnostic (1/1/07)
  - GE acquired Abbott's Diagnostic (1/19/07)
  - Roche Diagnostics/Protodyne Agreement (1/24/07)

**Source:** Burill, G. S., Biotech 2007 - Life Sciences: A global transformation (March 2007)



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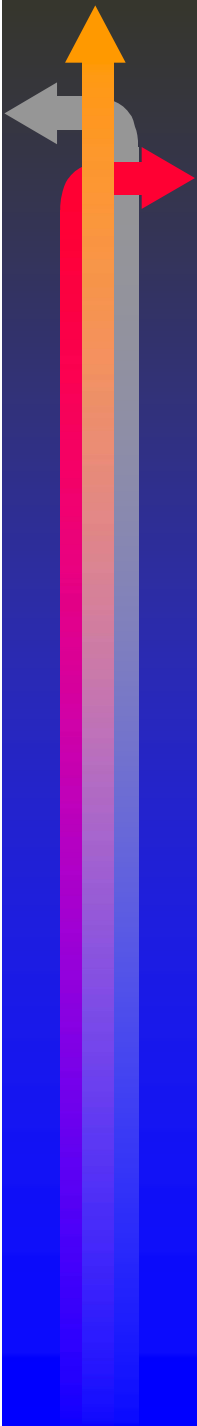
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# Patient Databases

- DNA – forensic evidence
- Military – casualty identification
- Pharmaceutical Industry
  - High-throughput screening
  - Biobanks – DNA materials from previous clinical trials and targeted subgroups
- Simulated clinical trials





Genetic Testing

Patient databases

**Niche product development**

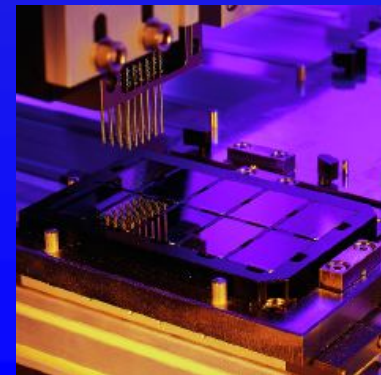
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# State of the Industry

- Research and Development (R&D) costs increased **147%** between 1993 – 2004
- Productivity – approved new drug applications increased **38%** and has been generally declining since 1999
- Innovation – only **38%** of approved drugs were for totally New Molecular Entities (NME)



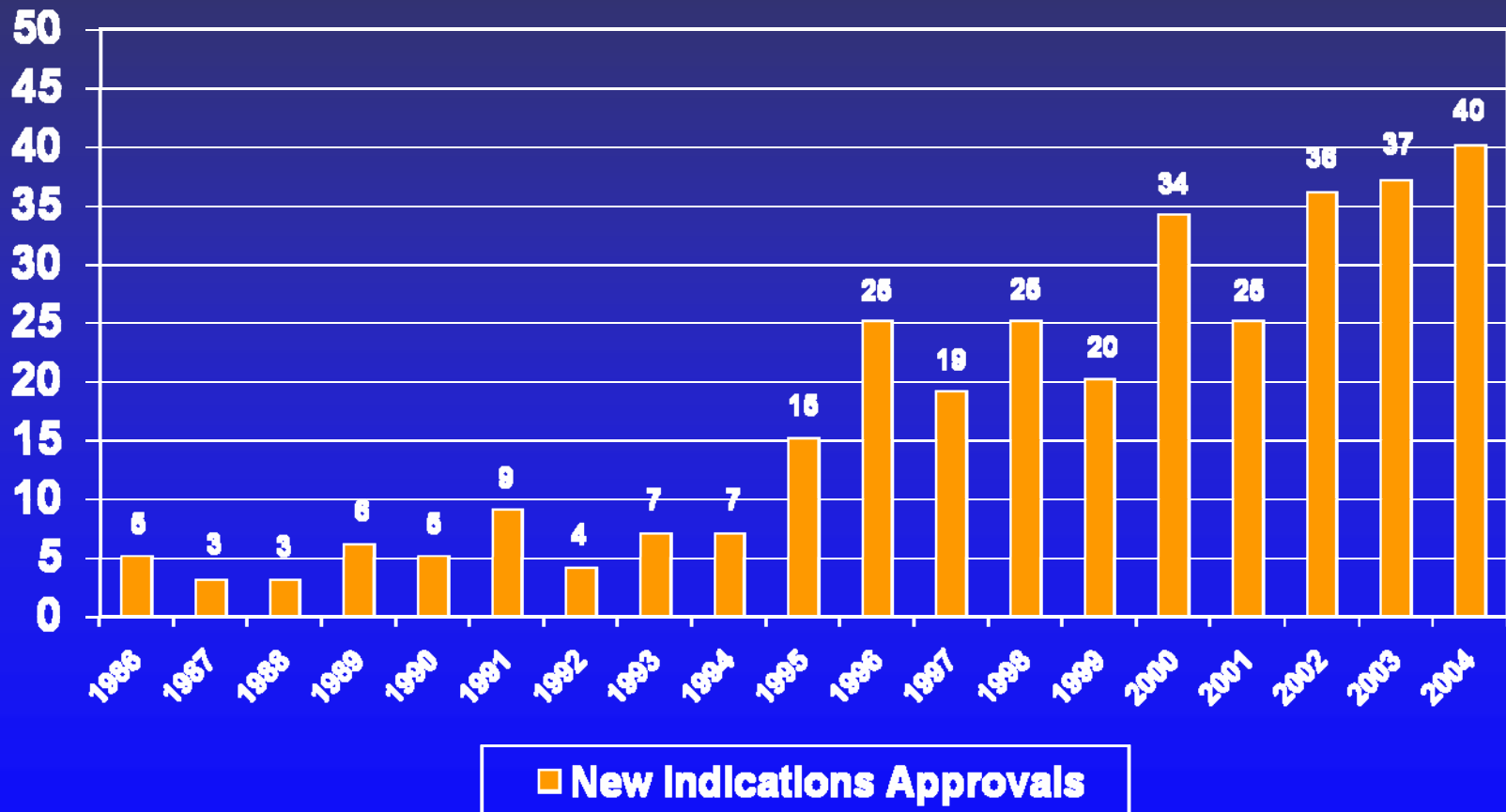
# Niche Product Development

- Vioxx<sup>©</sup> – blockbuster with problems
- Herceptin<sup>©</sup> and Gleevec<sup>©</sup> – new generation
- 25 pharmacogenomic drugs before FDA
- Cost is the determinate of niche products
- The balance may shift gradually but as validated bio-markers and genetic tests grow shift may become more pronounced

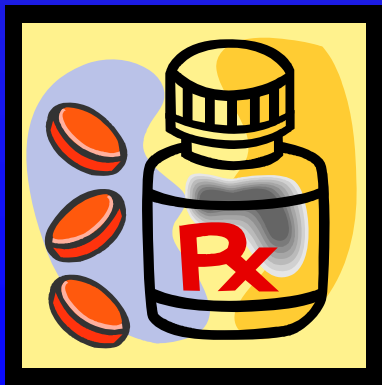
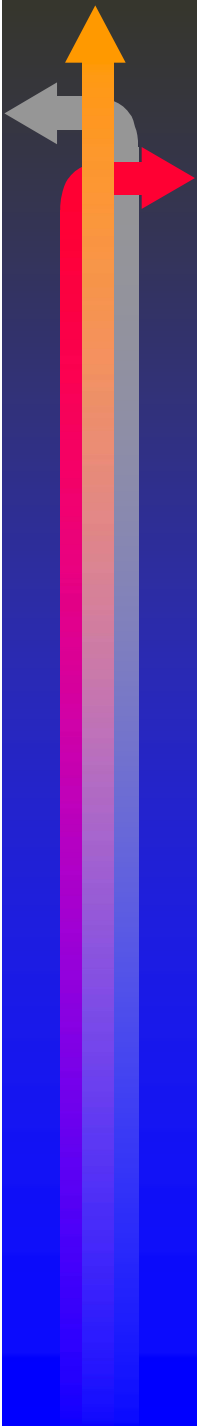
Pro	Con
Blockbusters generate revenue even if the drug doesn't work	Recalls, for known toxicity, can be very, very expensive
New genetic diagnostics can rescue discarded drugs	Company may not own diagnostic test
May lead to shift of life threatening disease to chronic	Uncertain regulatory environment



# New Biotech Drugs and Vaccines



Source: BIO 2005-2006 Guide to Biotechnology, Biotechnology Industry Organization



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# Theranostics

- Theranostics is the use of diagnostic testing to identify the disease, select the treatment regimen and monitor the outcome (using the same diagnostic)
- Ideally the diagnostic would have been developed parallel to the drug (clinical trials)
- First impact will be in existing drugs and will address adverse drug reactions and toxicity (Warfarin)

# Warfarin

- First marketed as a rat poison in 1948
- Two million patients start taking warfarin each year
- Optimal dosing critical – too much can cause bleeding, too little and you get strokes and clots
- Routine genetic testing (\$300) could correctly identify 95% of patient genotypes and 1/3 of those would be variant genotypes
- Management of variant genotypes would reduce bleeds by 85,000 and strokes by 17,000
- Reduced cost of approximately 1.1 Billion annually
- FDA modified dosing recommendation to include warning that a lower initial dose should be considered for patients with certain genetic variations.



# Herceptin

- Widely accepted as the poster child for theranostics
- Found ineffective in metastatic breast cancer, but highly effective in a sub-population (over-expressing her2/neu genes representing 30% of breast cancer)
- First FDA approved diagnostic/drug combination
- Similar diagnostic/drug strategies (25 at last count)



# Herceptin

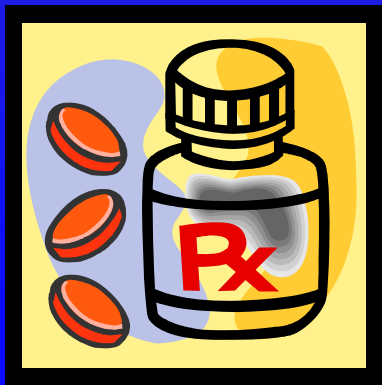
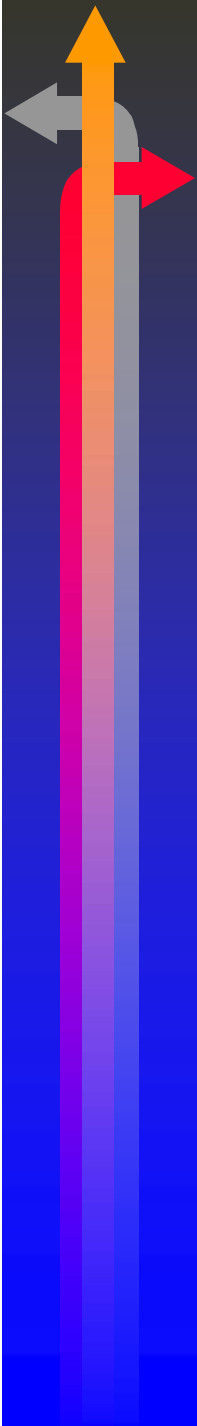
- Savings from more focused clinical trial (patient stratification) - **\$ 35 million**
- Additional income from faster (8 versus 12 year) product development - **\$ 2.5 billion**
- Patient lives saved from more rapid introduction of diagnostic/drug combination – **120,000**



# Biochip Microarrays

- Biochip microarrays are small glass slides holding up to hundreds of thousands of samples of DNA each targeting a specific gene.
- Can be used to identify
  - Diseases
  - Tumor characteristics (e.g. aggressiveness)
  - Cell mutations
- Access and cost considerations
  - \$ 999 – 2,500 per array (50 specific markers)
  - \$ 100,000 – 250,000 for scanner
  - \$ 350,000 for entire individual's DNA
- Pathway to personalized medicine





Genetic Testing

Patient databases

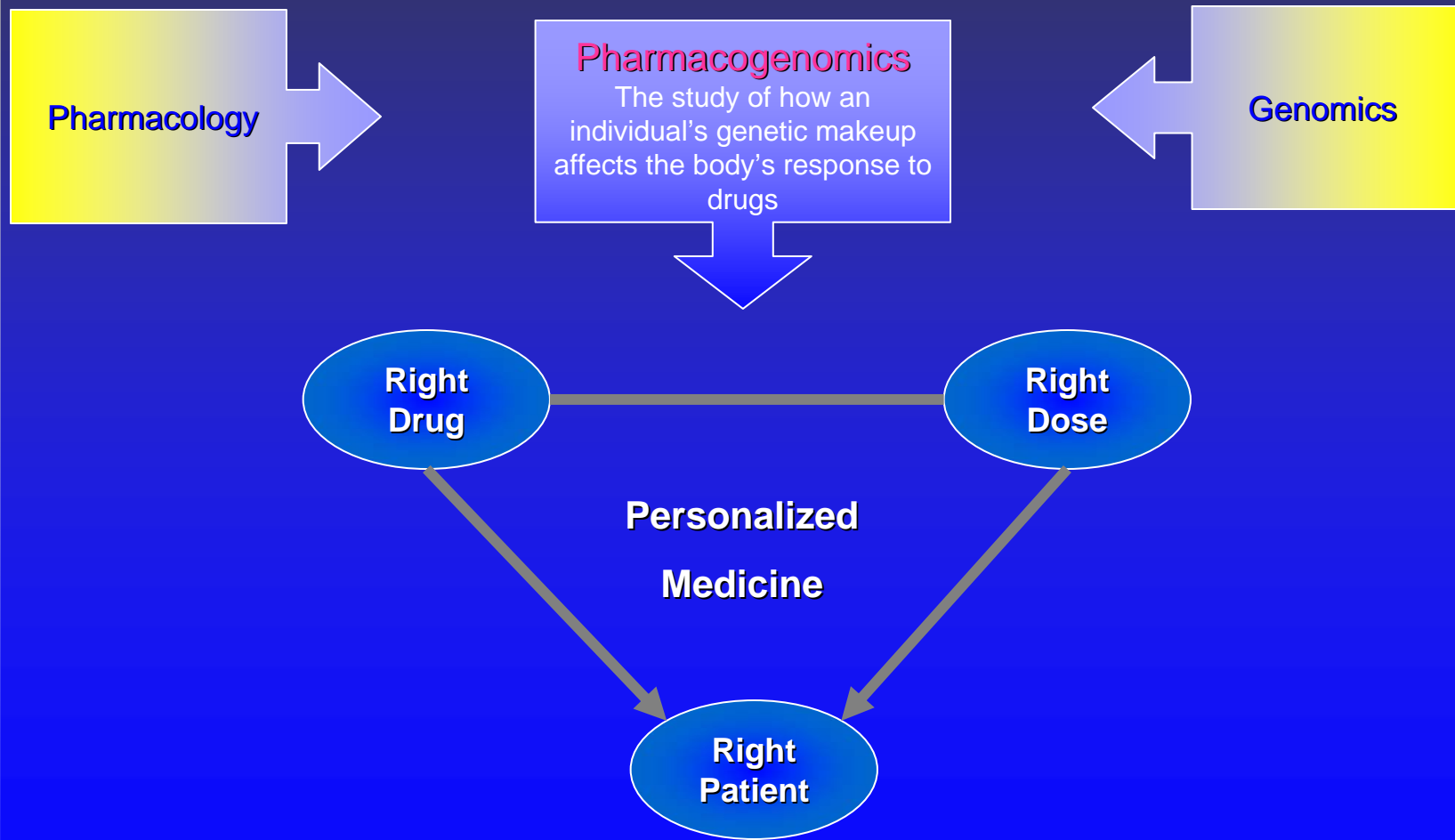
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# Personalized Medicine





# Personalized Medicine

- Personalized Medicine – Use genetic variations to develop safe and effective treatments for genetically defined sub-groups of patients
- Predict the appropriate dose of a drug
- Picking the most appropriate drug for the disease (the first time)
  - Gleevec (imatinib) – chronic myeloid leukemia
  - Tarceva (erlotinib) – lung cancer
  - Herceptin (trastuzumab) – breast cancer
- Testing for drug resistance - HIV

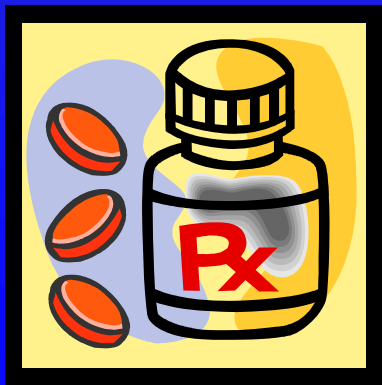
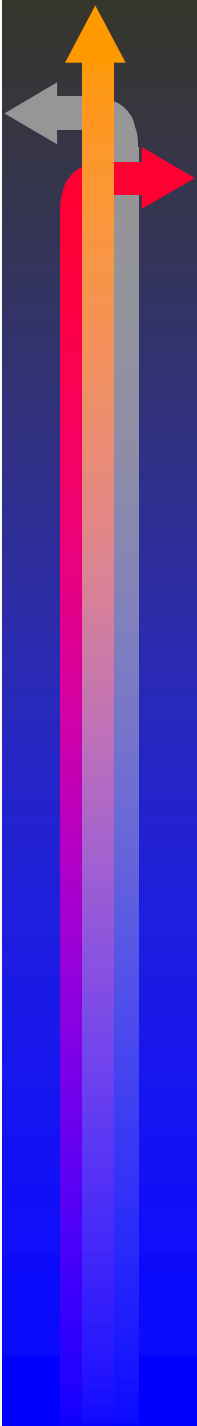




# Personalized Medicine

Personalized medicine stands poised to transform healthcare over the next several decades. New diagnostic and prognostic tools will increase our ability to predict the likely outcomes, while the expanded use of biomarkers – biological molecules that are associated with a particular disease state – could result in more focused and targeted drug development.

Burrill Report  
Personalized Medicine  
October 2005



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# Genomics and Personalized Medicine Act of 2006

*Purpose is to improve access to and appropriate utilization of valid, reliable, and accurate molecular genetics tests by all populations, thus helping to secure the promise of personalized medicine for all Americans*

- Establish interagency working group
  - Defines terminology
  - Coordinate and report progress to Congress
- Create a national Biobank to facilitate research
- Encourage health professions education in pharmacogenomics
- Tax credit to encourage co-development of diagnostic/drug therapies
- Expand consumer education of benefits of pharmacogenomics and provisions for privacy



Ready Response™  
(Home Monitoring)



Walgreens Home Care  
(Home Health Care)



Option Care™  
(Specialty Pharmaceuticals)



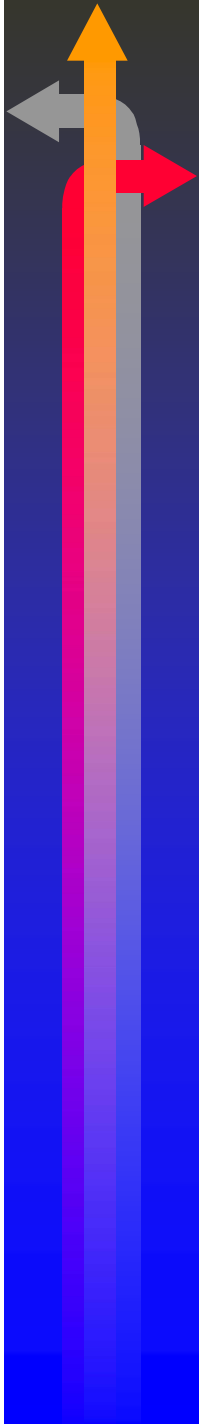
Retail and Mail Order Pharmacy



Take Care™  
(Retail Clinics)



Visiting Nurses





# References

- Genetic Engineering News (<http://www.genengnews.com/>)
- Javitt, G.H. and Hudson, K., *Public Health at Risk: Failures in Oversight of Genetic Testing Laboratories*, Genetics and Public Policy Center (<http://www.DNAPolicy.org>) September 2006.
- Draft Guidance for Industry, Clinical Laboratories, and FDA Staff - In Vitro Diagnostic Multivariate Index Assays (<http://www.fda.gov/cdrh/oivd/guidance/1610.html>)
- Hood, E., *Pharmacogenomics: The Promise of Personalized Medicine* Environmental Health Perspectives 111(11):1-9 (August 2003).
- Senator Barack Obama (D-IL), Genomics and Personalized Medicine Act of 2006 (S. 3822).
- Aspinall, M.G. and Hameermesh, R.G., *Realizing the Promise of Personalized Medicine*, Harvard Business Review (October 2007).