Developing Products For Personalized Medicine: 

NIH Research Tools Policy Applications

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Changing Healthcare – Changing Goals For Research & Development

That was then ….

• Disease symptoms
• Uniformity of disease
• Uniformity of patients
• Universal treatment
• Sickness

This is now ….

• Disease mechanism
• Heterogeneity of disease
• Variability
• Individualized Therapy
• Predictive/preventive care

Source: Burrill & Co.
Effect of Personalized Medicine on R&D

• Genetic testing becomes routine
• Disease will be understood at a molecular level
  – Proteins, pathways, mechanisms explained
• Patient populations at risk for ADR will be identified
• Targeted clinical trials – patient selection
• Healthcare moves to predictive, preventative care with pre-symptomatic Dx and Rx routine

Source: Burrill & Co.
Why Would A Tools Policy Be Important?

• Customization of diagnostic tests and therapeutics for small target populations
• Multiple / parallel R&D efforts based upon gene profiling
• Association studies for drug response/sequence variation
• Developers will need to have rapid access to current research tools & reagents.
Why Would A Tools Policy Be Important? (Continued)

• Greater interdependence between:
  – Basic & applied research
  – Interdisciplinary cooperation
  – Academic & industry: sharing of data, expertise and resources. Broad access & availability needed

• Thus, an effective public policy for research tools should be a key element for personalized medicine.
What Are Research Tools?

- “Targets” and “Tools” for scientific discovery
- Wide variety of resource types: mabs, receptors, animal models, libraries, software and databases
- Broad access & availability needed
- Readily useable & distributable as a tool
- Useful lifecycle generally short
- Patented or unpatented
What Is NIH’s Role In Research Tools?
What Is NIH’s Role In Research Tools?

- One of world’s largest users of biomedical reagents and tools (procurement)
- A leading provider of many difficult-to-find items (repositories, contractor agents)
- Supporting basic science for the public health (grants for tool users & providers)
Examples of NIH Research Tools

- D2 dopamine receptor screening
- Immortalized liver cells disease model
- ERKO mice screening
- Cytochrome P-450 toxicity studies
- MDR cell lines screening
- HIV protease screening
Tools From A Public Policy Viewpoint

• Research tools typically have value as commodity.
• Need to recognize the financial / intellectual contribution of inventors
• Good science happens in both academia and industry -- need for 2-way exchange
• Public health benefit still paramount
Where We Were ….

- Past practice of unrestricted flow of materials
- Commercial uses of molecular biology arise
- Universities & Federal labs obtain ownership & financial rights to invention
- Pharma MTA/licensing practices adopted
What Happened ....

- Problems arise due to many lengthy negotiations and undue restrictions
- Increased unavailability of research resources
- Scientific research community raised concerns
- Representatives of government, industry & academia join NIH Working Group
NIH Director’s Working Group
Recommendations

• Promote free dissemination of research tools without legal entanglements
• Further use of UBMTA
• Develop guidelines for extramural MTAs and licensing
• Review and strengthen current policies
• Establish “research tools forum”
What happened ....

• Reviewed long-standing NIH policy on the sharing of unique research resources
• Reviewed NIH’s “Developing Sponsored Research Agreements: Considerations for Recipients of NIH Research Grants & Contracts”
• Developed policy based on earlier documents & discussions
• Requested additional comments from industry, academia, and others
The Result ....

The NIH Research Tools Policy

“Sharing Biomedical Research Resources: Principles and Guidelines for Recipients of NIH Research Grants and Contracts”

December 23, 1999

[ott.od.nih.gov/NewPages/RTguide_final.html](ott.od.nih.gov/NewPages/RTguide_final.html)

[ott.od.nih.gov/NewPages/64FR2090.pdf](ott.od.nih.gov/NewPages/64FR2090.pdf)
What Is The Policy?

• **Principles:**
  – ensuring academic freedom and publication
  – minimizing administrative impediments
  – implementing Bayh-Dole Act
  – disseminating research resources

• **Guidelines:** specific information, strategies & model language for Recipient Institutions in obtaining and disseminating resources
Principle 1: Ensure Academic Freedom & Publication

- Preserve academic research freedom
- Safeguard appropriate authorship
- Timely disclosure of results
- Applies to all funding recipients
Principle 2: Ensure Appropriate Implementation of Bayh-Dole Act

- Maximize utilization by research community
- Timely transfer to industry for commercialization
- Patent protection not always needed
- License to ensure widespread distribution of final tool product to public
- Avoid unnecessarily restrictive licensing practices
Principle 3: Minimize Administrative Impediments To Research

- Streamline academic transfers using Simple Letter Agreement (or equivalent)
- Implement clear tool acquisition policies
- Avoid encumbrances such as:
  - “reach through” or product rights
  - publication / academic freedom control
  - improper valuations
Principle 4: Ensure Dissemination of NIH-Funded Tools

• Determine if you have a research tool
  – for discovery - not a FDA-approvable product
  – broad, enabling or with many uses
  – readily useable or distributable

• Widespread, timely distribution necessary
  – Simple Letter Agreement to non-profits
Principle 4: Ensure Dissemination of NIH-Funded Tools (Cont.)

• Share distribution principles with non-NIH research co-sponsors
• Simplify transfer to for-profits for internal use
• Limit exclusive licenses to appropriate fields of use
• Retain tool use & distribution rights
When Obtaining Tools For NIH-Funded Research ....

- Avoid restrictions on new tool distribution
- Publication delays (>60 days) unacceptable
- Ownership of recipient’s improvements reside with recipient (not provider)
- For-profits may obtain limited grant-backs or option rights for proprietary compounds
  - scope balances value & Bayh-Dole
  - need tool distribution, commercialization resources, enforceable development plan
Important Research Tool Issues For NIH, Universities And Companies

- Liability for overlapping agreement obligations
- Severe restrictions on use of materials
- Technology ownership versus inventorship
- Distribution limitations for new tools and derivatives
- Concern that legal encumbrances will hinder public health objectives
Usefulness of Tools Policy To Personalized Medicine R&D

• Do not discourage patenting -- encourage strategic patenting
• Do not prohibit exclusive licensing -- encourage strategic licensing
• Licensing tool companies for broad development and distribution
• Discourage holding a technology for defensive/blocking purposes
Where We Are ....

• Research Tools Policy adopted for NIH-funded research December 23, 1999
• Included in NIH Grants Policy as confirmation of longstanding policy of sharing of research tools
• Bayh-Dole amended November 1, 2000 to promote its goals “without unduly encumbering future research and discovery” in the spirit of the NIH policy
Where We Are (continued) ....

- Best Practices For Licensing of Genomic Inventions published April 11, 2005
- Ongoing NIH Projects: Human Genome Project, International HapMap Consortium, National center for Biotechnology Information (NCBI)
- Projects Outside NIH: SNP Consortium, dbEST
What We Would Really Like To Avoid

GenomeWeb (November 14, 2001)

“… technologies used in early-stage drug discovery are in for a long, cold winter …”
GenomeWeb (November 5, 2002)
NIH Research Tool Licensing
Typical Research Products License (Internal Use)

• Non-exclusive
• Materials provided / screening use permitted
• No reach through to products
• Larger firms predominant
• Paid-up term licenses or annual fees
• Products: muscarinic receptor
Typical Commercial Evaluation License

- Non-exclusive
- Materials provided / screening not permitted
- Feasibility testing only
- Short term (<18 mo.) paid-up license
- Modest paid-up cost
- Can evaluate patents or products
Typical Research Products License (Commercialization)

- Non-exclusive
- Materials provided (patented or unpatented)
- Smaller firms predominate as licensees
- High earned royalty rates
- Low upfront costs
- Products: CHAPS, antisera, mabs
Conclusions For Personalized Medicine Product Development

• Tool access & scientific cooperation key to innovation
• Additional strategic partnerships between academia & industry should be encouraged
• Bayh-Dole Act and support of open research enterprise can be complementary
• Tool technologies should be distributed/licensed to balance competitive innovation with research freedom
Sources Of Information On NIH Research Tools And Policy

- Research Tool Guidelines - ott.od.nih.gov/NewPages/pubs.html
- NIH Office of Technology Transfer - ott.od.nih.gov & NIHOTT@od.nih.gov