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?

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- 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/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

"Biotech Tools Are Slowing Down Drug Development Process, Study Finds"

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

- Best Practices For Licensing Genomic Inventions - Federal Register (April 11, 2005) p. 18413.
- Working Group Report - nih.gov/news/researchtools/index.htm
- Research Tool Guidelines - ott.od.nih.gov/NewPages/pubs.html
- NIH Office of Technology Transfer - ott.od.nih.gov & NIHOTT@od.nih.gov