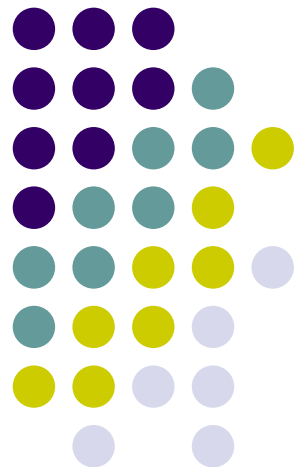
REAPING THE BENEFITS OF GENOMIC AND PROTEOMIC RESEARCH

Intellectual Property Rights, Innovation and Public Health

A Joint Project of The National Academies'
Board on Science, Technology, and Economic Policy
Committee on Science, Technology, and Law

Association of University Technology Managers
March 4, 2006



THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

Committee Membership

Shirley M. Tilghman (Co-Chair), Princeton University

Roderick R. McKelvie (Co-Chair), Covington & Burling

Ashish Arora, Carnegie Mellon University

Helen M. Berman, Rutgers University

Joyce Brinton, Harvard University (retired)

Stephen Burley, Structural GenomiX, Inc. (SGX)

Q. Todd Dickinson, General Electric Co

Rochelle Dreyfuss, New York University School of Law

Rebecca S. Eisenberg, University of Michigan

Charles M. Hartman, CW Group

Daniel J. Kevles, Yale University

David Korn, Association of American Medical Colleges

George M. Milne, Jr., Radius Ventures

Richard Scheller Genentech

Rochelle Seide Arent Fox PLLC

Robert H. Waterston, University of Washington

Nancy Wexler, College of Physicians and Surgeons of Columbia University and Hereditary Disease Foundation

Brian Wright, University of California, Berkeley

Staff

Stephen A. Merrill, Board on Science, Technology, and Economic Policy

Anne-Marie Mazza, Committee on Science, Technology, and Law

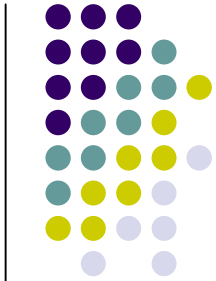
Committee Charge

Study the granting of intellectual property rights and the licensing of discoveries relating to genetics and proteomics and the effects of these practices on research and innovation.

Specifically,

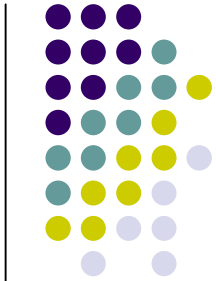
1. report on trends in the number and nature of U.S.-issued patents being granted on technologies related to genomics and proteomics;
2. report on the standards that USPTO and other patent offices (specifically in Europe and Japan) are applying in acting on these applications;
3. report on how the patenting of genomic and proteomic inventions and/or licensing practices for these inventions is affecting research and innovation; and
4. based on the committee's findings in the first three areas, recommend steps that NIH and others might take to ensure the productivity of research and innovation involving genes and proteins.

Committee Findings: Trends



- Patenting varies greatly among biotech categories
- Patenting has leveled off in most categories but pendency has increased and there is a large backlog of applications
- US inventors and assignees dominate patents in almost all categories

Committee Findings: International Differences

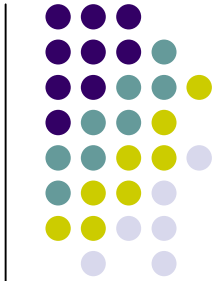


- Chief difference in approach to patenting in US, Europe, and Japan has to do with "nonobviousness" or "inventive step"
- The bar is higher in Europe and Japan
- Other differences -- most other countries have a statutory provision for compulsory licensing and shield research on patented inventions from infringement liability

Concerns Raised

- Anti-commons:
  - Demands of numerous claimants may lead to excessive licensing burden, the cessation of otherwise worthwhile projects and the loss of collective surplus, impeding development and commercialization of drugs and therapies, and possibly even basic research
- Access:
  - Limitations on subsequent discovery and improvements imposed by assertion of patents on upstream, foundational discoveries
- Erosion of the norms of open science, possibly undercutting research productivity
  - Restrictions on the sharing of research materials and publication delay

Walsh, Cho, Cohen Survey



www.uic.edu/~jwalsh/NASreport.html.

Performers: J Walsh and C Cho, UIC; W Cohen, Duke University

Sample Size: 1688 from 11 society membership rosters, 300 from publications on 3 pathways

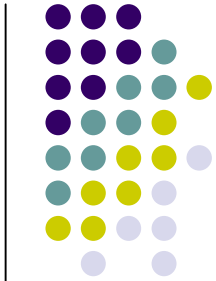
Reponses: 655 responses (148 industry) = 33 percent response rate + 90 working on pathways

-- range of fields, basic to applied research, and research team sizes

Issues/Questions:

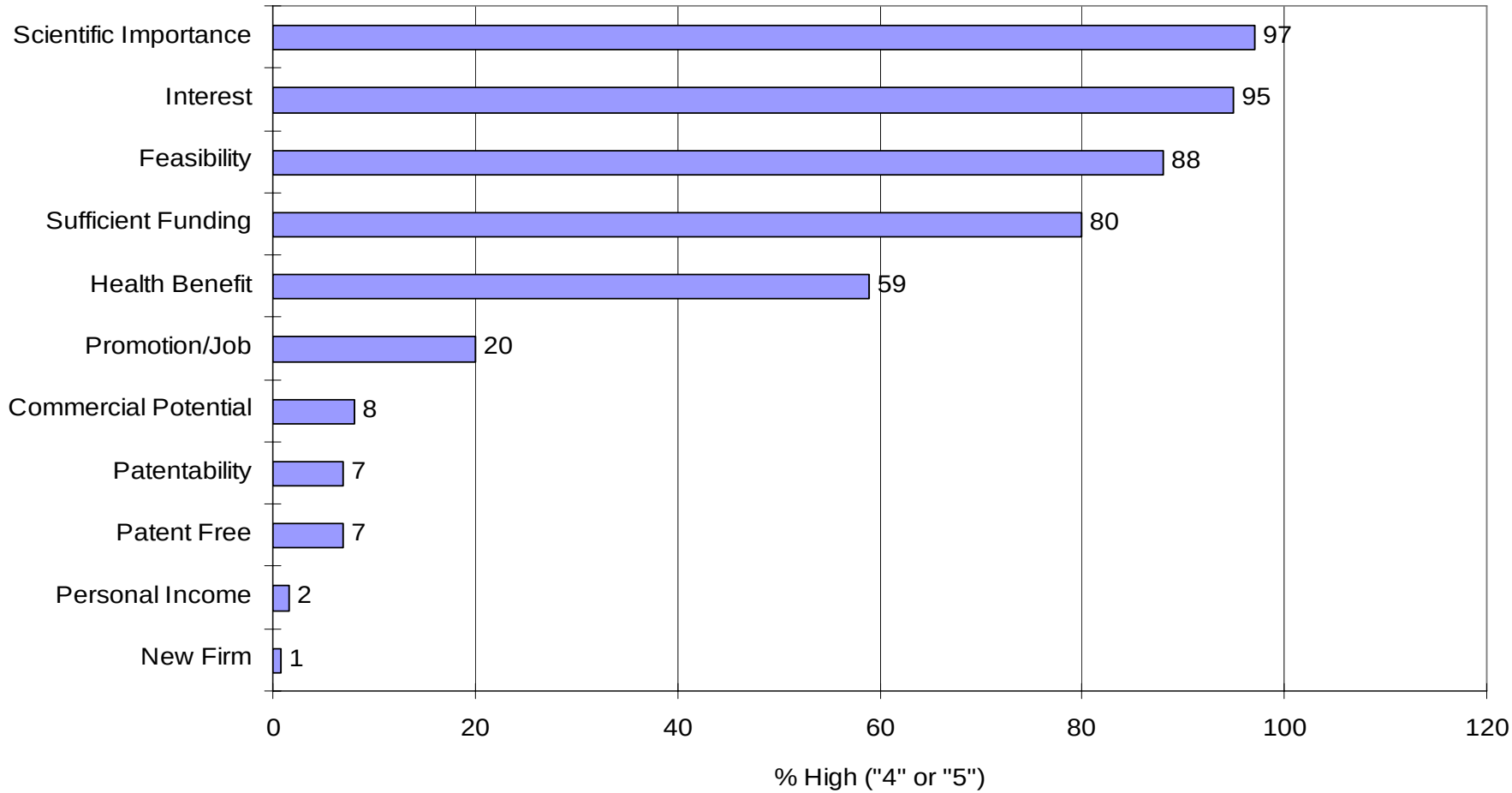
- involvement with IP acquisition, industry funding, start-ups
- motivations for research
- experience with others' IP
- experience with MTAs and data sharing

Academics' Commercial Activities

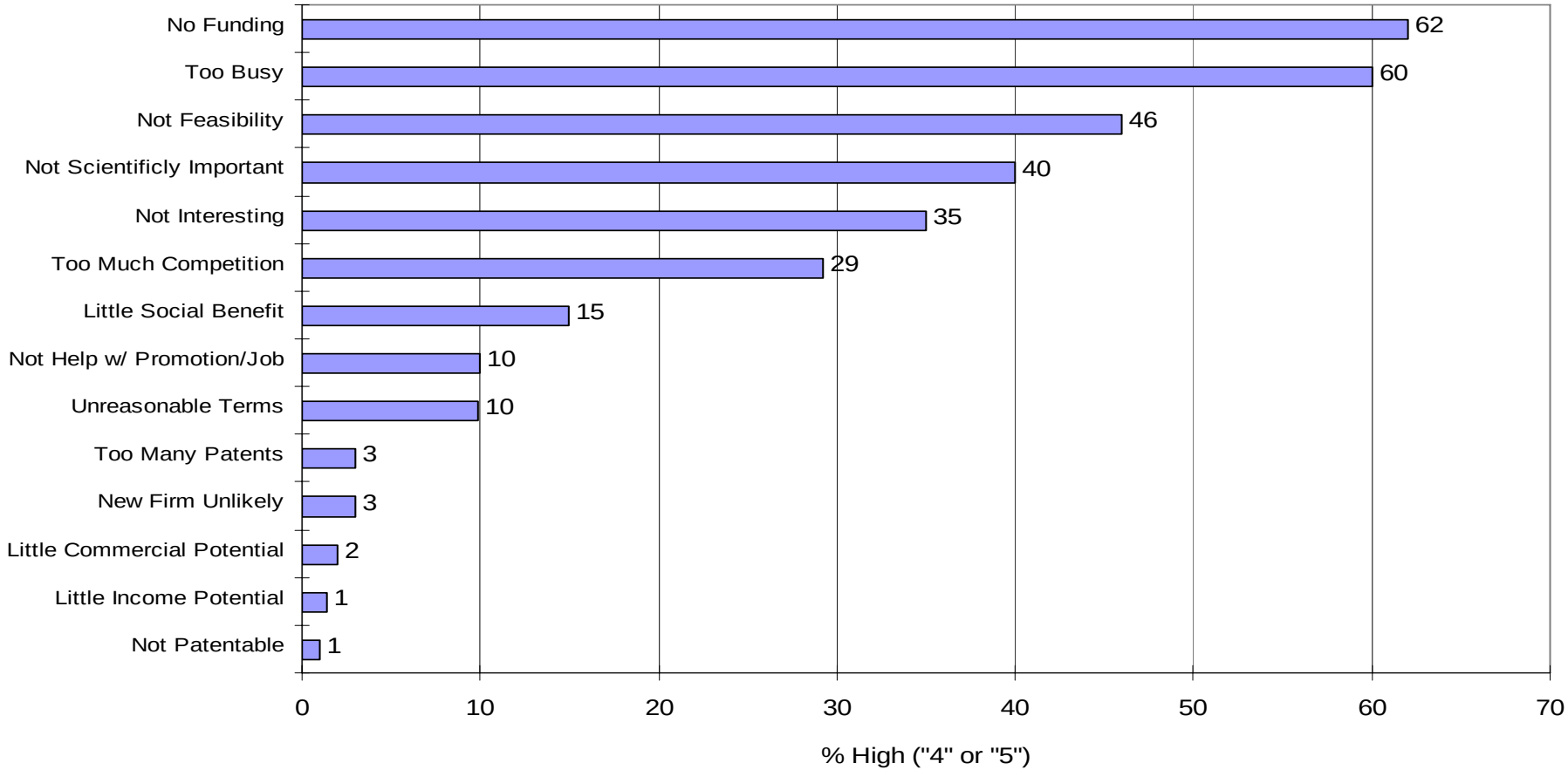


- Substantial commercial activity
  - Industry funding: 19% have some industry funding
  - Patenting (in last 2 years): 22%
  - Business activity (e.g., startup, negotiations, licensing, commercialization of discovery) : 35%
- More for those doing “drug discovery”

Reasons for Choosing Projects, Academic Respondents



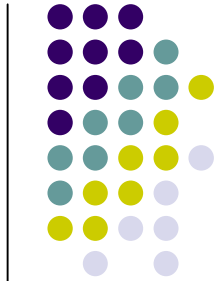
Reasons for Not Pursuing Projects



Awareness of Patents on Research Inputs

- 8%, or 32 of 381 respondents, believed they needed knowledge or information covered by patents
- Given burst in research tool patents, why so few?
  - Only 5% check regularly for patents on knowledge or material inputs (little change since *Madey*)
- 22% received instruction from institution (v. 15% 5 years ago)
  - AAAS study: 14% of universities give instructions
  - BUT, instruction does not change behavior (6% v 4%)

Sharing Material Research Inputs

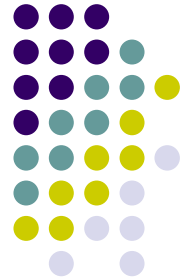


- Where others' tangible inputs necessary for research activity itself, may have different impact from pure IP
- Examples
  - Cloned gene, organism, cell line, protein, drug, unpublished information, etc.
- About 75% of our academic respondents requested materials in the prior two years
- Average # of requests (last 2 years)
  - 7 to other academics and 2 to industry

Difficulties in Accessing Tangible Research Inputs

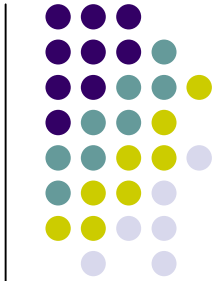
- 19% did not receive last requested research input
- Change over time?
  - For academic to academic exchanges in genomics, percent of requests not received:
    - 2003-04 (Walsh, et al): **18**% (+/-3.7%)
    - 1997-99 (Campbell, et al): **10**%
- So, appears to be some increase in recent years
- **Delay research (>1 month): 8% of requests (v. 1% for pure IP)**

MTA Terms, Negotiations



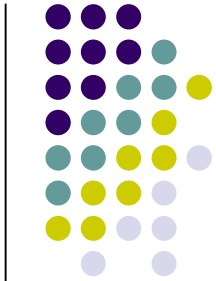
- About 40% of transfers require MTA
  - More common if request drugs (64%)
- Fees
  - 93% from academic, no charge, < 2% over $1000
  - 85% from industry, no charge, 7% over $1000
- Terms (requested)
  - Reach through-38%
  - Royalties-17%
  - Manuscript review-30%
    - Drugs to Academics: 70% of final agreements

Why Do Scientists not Provide Materials?



- Main predictors
  - **Scientific competition** (# competing labs)
  - Prior business activity
  - Burden (requests/lab dollar)
  - # Publications (Eminence or opportunity cost?)
- Insignificant
  - Industry funding (modest pos. effect)
  - Drug discovery

Committee Conclusions



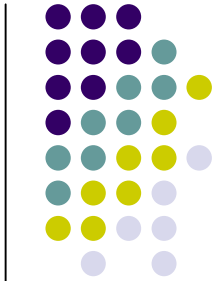
- It appears that access to patents or information inputs into biomedical research rarely imposes a significant burden for academic biomedical researchers.
- However, for a number of reasons, the committee concluded that the patent landscape, could become considerably more complex and burdensome over time.

Committee Conclusions, continued

There are reasons to be concerned about the future.

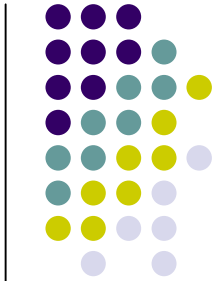
1. Lack of substantial evidence for a patent thicket or a patent blocking problem clearly is linked to a general lack of awareness/concern among academics about existing IP. This could change dramatically:
   a) Institutions, aware that they enjoy no protection from legal liability, may become more concerned about their potential patent infringement liability and take more active steps to raise researchers' awareness or even to try to regulate their behavior.
   b) Patent holders, equally aware that universities are not shielded from liability by a research exception, could take more active steps to assert their patents against them.

Committee Conclusions, continued



2. As scientists increasingly use the high-throughput tools of genomics/proteomics to study the properties of many genes/proteins simultaneously, the burden on the investigator to obtain rights to the IP covering these genes/proteins could become insupportable, depending on how broad the scope of claims is and how patent holders respond to potential infringers. The large number of issued and pending patents relating to gene-expression profiling and protein-protein interactions contributes to this concern.

Committee Conclusions, continued



3. **Survey data revealed substantial evidence of another, potentially remediable burden on private as well as public research stemming from difficulties in accessing proprietary research materials, whether patented or unpatented. Impediments to the exchange of biomedical research materials remain prevalent and may be increasing.**

Recommendations

Best Practices and Norms for the Scientific Community and Federal Research Sponsors

Recommendation 1: NIH should continue to encourage the free exchange of materials and data. NIH should monitor the actions of grantees and contractors with regard to data and material sharing and, if necessary, require grantees and contractors to comply with their approved intellectual property and data sharing plans.

Recommendation 2: NIH should adapt and extend the "Bermuda Rules" to structural biology data generated by NIH-funded centers for large-scale structural genomics efforts, making data promptly and freely available in a database via the PDB.

Recommendations

Recommendation 3: The PDB should work with USPTO, the European Patent Office (EPO), and the Japanese Patent Office (JPO) to establish mechanisms for the efficient transfer of structural biology data in published patent applications and issued patents to the PDB for the benefit of the larger scientific community. To the extent feasible within commercial constraints, all researchers, including those in the private sector, should be encouraged to submit their sequence data to GenBank, the DNA Databank of Japan, or the European Molecular Biology Laboratory and to submit their protein structure data to the PDB.

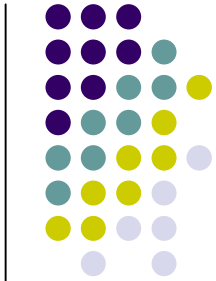
Recommendations, continued

Recommendation 4: The committee endorses NIH's ***Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources*** and ***Best Practices for the Licensing of Genomic Inventions***. Through its ***Guide for Grants and Contracts***, NIH should require that recipients of all research grant and career development award mechanisms, cooperative agreements, contracts, institutional and Individual National Research Service Awards, as well as NIH intramural research studies, adhere to and comply with these guidance documents. Other funding organizations (such as other federal agencies, nonprofit and for-profit sponsors) should adopt similar guidelines.

Recommendations, continued

Recommendation 5: Universities should adopt the emerging practice of retaining in their license agreements the authority to disseminate their research materials to other research institutions and to permit those institutions to use patented technology in their nonprofit activities.

Recommendations, continued



Recommendation 6: In cases in which agreements are needed for the exchange of research materials and/or data among nonprofit institutions, researchers and their institutions should recognize restrictions and aim to simplify and standardize the exchange process. Agreements such as the Simple Letter Agreement for the Transfer of Materials or the Uniform Biological Material Transfer Agreement (UBMTA) can facilitate streamlined exchanges. In addition, NIH should adapt the UBMTA to create a similar standardized agreement for the exchange of data. Industry is encouraged to adopt similar exchange practices.

Recommendations, continued

Recommendation 7: USPTO should create a regular, formal mechanism, such as the formation of a chartered advisory committee or a regularly scheduled forum, comprising leading scientists in relevant emerging fields, to inform examiners about new developments and research directions in their field; NIH and other relevant federal research agencies should assist USPTO in identifying experts to participate in these consultations.

Recommendations, continued

Recommendation 8: In determining nonobviousness in the context of genomic and proteomic inventions, USPTO and the courts should avoid rules of nonobviousness that base allowances on the absence of structurally similar molecules and instead should evaluate obviousness by considering whether the prior art indicates that a scientist of ordinary skill would have been motivated to make the invention with a reasonable expectation of success *at the time the invention was made*.

Recommendations, continued

Recommendation 9: Principal Investigators and their institutions contemplating intellectual property protection should be familiar with the USPTO utility guidelines and should avoid seeking patents on hypothetical proteins, random single nucleotide polymorphisms and haplotypes, and proteins that have only research, as opposed to therapeutic, diagnostic, or preventive function

Recommendations, continued

Recommendation 10: Congress should consider exempting research "on" inventions from patent infringement liability. The exemption should state that making or using a patented invention should not be considered infringement if done to discern or to discover:

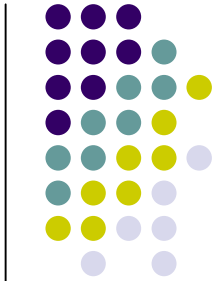
a) the validity of the patent and scope of afforded protection;

b) the features, properties, or inherent characteristics or advantages of the invention;

c) novel methods of making or using the patented invention; or

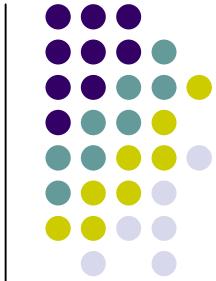
d) novel alternatives, improvements, or substitutes.

Recommendations, continued



Recommendation 11: NIH should undertake a study of potential university, government, and industry arrangements for the pooling and cross-licensing of genomic and proteomic patents, as well as research tools.

Recommendations, continued



Recommendation 12: Courts should continue to decline to enjoin patent infringement in those extraordinary situations in which the restricted availability of genomic or proteomic inventions threatens the public health or sound medical practice. Recognition that there is no absolute right to injunctive relief is consistent with U.S. law and with the Agreement in Trade-Related Aspects of Intellectual Property Rights (the TRIPS Agreement).

Recommendations, continued

Recommendation 13: Owners of patents that control access to genomic- or proteomic-based diagnostic tests should establish procedures that provide for independent verification of test results. Congress should consider whether it is in the interest of the public's health to create an exemption to patent infringement liability to deal with situations where patent owners decline to allow independent verification of their tests.

For Additional Information

The Report is available at:

www.nap.edu/catalog/11487.html