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Treating Clinical Trials as a Public Good: The Most Logical Reform

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Recent revelations about the suppression of adverse findings in the clinical testing of new medicines have led many to call for mandatory disclosure of all clinical trial results.[1] We agree that this proposal moves us in the right direction towards addressing the selective disclosure of pharmaceutical testing results, study design biases, and other questionable practices.[2] However, we maintain that disclosure is not the root problem but rather a symptom of a much deeper structural problem. Mandatory disclosure without addressing this deeper problem yields a less than optimal approach to rationalizing the regulatory machinery governing the supply of pharmaceutical products.

I. Public Disclosure: Only the First Step in a Broader Reform

Requiring mandatory disclosure of clinical trials will not eliminate the inherent conflict of interest underlying the commercial provision of drugs and medicine or the fundamental inefficiencies the current system promotes. So long as drug companies retain primary responsibility for conducting or funding clinical trials, they will be tempted to selectively disclose information and to avoid research programs that could reveal unfavorable outcomes. Nor would a disclosure requirement alone ensure that the stakeholding company will conduct all the tests deemed most beneficial to public safety.

For example, until the National Heart, Lung and Blood Institute funded the Women's Health Initiative, the risks and benefits of postmenopausal hormone therapy remained inadequately assessed by randomized clinical trial procedures despite its widespread use.[3] Equally troubling, drug company sponsors completed Phase IV clinical trials necessary for upgrading to regular approval in only six of twenty-three fast-track approvals of cancer drugs.[4] There are few incentives to undertake costly testing if the results might only serve to narrow use of the drug to a smaller subgroup of patients or prove unfavorable to its continued use.

A better alternative to calls for mandatory disclosure is to remove the direct link between the clinical trial sponsor (the drug company) and the drug testers. One approach would be to establish an independent testing agency to conduct clinical trials under specified conditions of transparency. Unlike the current system, drug companies would no longer directly compensate the scientists evaluating their own products. Instead, the scientists would now work for the testing agency, supported by general funds collected from the pharmaceutical industry. This separation of clinical trials from sponsorship could attenuate the conflict of interest problem, and it would better ensure objective processing with full disclosure of results under the aegis of a national testing facility than the current system. [5]

Even if the competitive logistics of such an approach posed no unsolvable problems, however, we think it would insufficiently rationalize the drug supply and pricing process, and thus fail to realize the potential benefits of treating clinical trials as a public good.[6] To this end, we argue that the federal government, rather than the drug companies, should underwrite a significant portion of the costs of clinical trials. This thesis follows from a

careful examination of the economics of drug supply and of the relation between clinical trials and overall investment in research and development (R&D), as we explain below.

II. The Case for Treating Clinical Trials as a Public Good

At the outset, we stress that the information gleaned from the clinical testing of drugs and therapies is a public good in the sense that each individual citizen benefits from such information without reducing its value to others.[7] At the same time, the results of the testing process reveal information that affects the conduct of research and development (R&D) in the industry as a whole without disturbing the validity of the underlying patent rights that protect innovative firms.

Like peer-reviewed basic research results, which have always been recognized as a public good, peer-reviewed clinical trial results should promote surer decisions about the safety and therapeutic value of both single products and product groups while stimulating follow-on innovation and providing guidance for better clinical practice. Yet, despite these potential public benefits, our current system saddles private companies with the burdens of clinical testing and thus render their results artificially scarce and excludable. This approach ignores the economic reality that privately supplied public goods will inevitably be underprovided.[8] In this context, undersupply evokes cases in which a head-to-head comparison between therapeutically equivalent drugs was not studied; an adverse drug reaction was not explored; a specified clinical indication was not appropriately narrowed; or the possibility of use for a neglected disease was not pursued.[9]

Those concerned that clinical testing to meet public health needs is currently undersupplied, and that the disclosure of drug trials should be monitored for accuracy, may nonetheless question the need for public support of drug testing. Our response is that the practice of shunting the provision of such a crucial public good as clinical trials to the private pharmaceutical sector has become unsustainable over time. Year after year, the cost of conducting clinical trials appears to outstrip the medical component of the consumer price index.[10] Between 1977 and 1995, the burden of data production increased by 43 per cent in mean number of pages per new drug application (NDA), by 37 per cent in mean number of patients per NDA, and by 44 per cent in mean number of clinical trials per NDA.[11]

We believe the most rational reform is to shift some portion of the cost of clinically testing new pharmaceutical products to the public sector. We make this recommendation with a view to rationalizing the supply chain for medicines and to lowering the prices of drugs to consumers to levels more reasonably related to their actual R&D costs.

A. Drug Companies' Costs Would Decline with Government Funding of Clinical Trials

The total direct cost of drug testing should fall with public funding, oversight, and full disclosure of clinical trial results, especially unfavorable or negative results. Such a program would enable investigators to exploit economies of scale and scope in testing, would minimize unnecessary redundancies and would allow researchers to interpret and compare the results of different tests. Public disclosure of trial results should further

reduce research and development costs as drug companies learn earlier which candidate medicines are therapeutically effective or not.

We concede that some of the benefits from central clinical testing could be achieved without public sponsorship. One could require drug companies to pay for publicly supervised tests, and some cost savings would still presumably occur. However, public support of drug testing would provide additional dividends far exceeding the direct cost savings from a privately funded program of clinical testing, as we argue below.

B. Lower Drug Company Costs Would Benefit Consumers in the Short Run

Drug companies' costs of developing and marketing new medicines should fall significantly with public funding and disclosure of clinical trials. Recent studies show the growing importance of these costs in determining the aggregate expenses of bringing new drugs to market,[12] in a lottery-like environment where "most drug candidates taken into testing fail."[13]

A reduction in the costs of supply and in the attendant risks of investing in failed drugs would enable companies to reduce the prices of new successful drugs while still earning a competitive return on investment. Public funding of clinical tests would provide more transparent estimates of the total costs of drug supply allowing health insurers to more accurately assess what revenues were required for continued pharmaceutical innovation. Unlike programs for capping drug prices that require a full accounting of *all drug company costs,*[14] our proposal would only require drug companies to reduce prices in proportion to the observed cost savings generated by public funding and disclosure of clinical tests. These savings would affect the costliest component of the entire R&D network, and would further reduce investment risks by building upon the federal government's already substantial funding of basic research.

While health providers would benefit from the lower costs of procuring prescription drugs, consumers would become the real beneficiaries of our program. Many consumers are unable to afford the monopoly prices charged by patent protected drug manufacturers. A reduction in prices afforded by lowered costs of clinical testing would allow low income and uninsured patient's greater access to medicines. The well known allocative distortions that arise from patent protected medicines would be reduced to the extent that public support of clinical testing forced drug prices to decline.

C. Long Run Efficiencies in Drug Discovery and Development

Analysts note with alarm that the overall rate of innovation for new medicines and therapies appears to be slowing, while the gap between R&D investment and output has widened.[15] Moreover, existing projects do not routinely address socially important therapeutic needs, as when firms decrease or abandon R&D opportunities pertaining to antibacterial drugs despite evidence of mounting resistance to available antibiotics.[16] Although there are multiple contributing factors to this apparent slow down in pharmaceutical innovation,[17] we argue that rationalizing the clinical trial component of the drug supply chain would stimulate more productive R&D and more affordable end products.

1. Stimulating more investment in innovative R&D with lower costs and better information

Besides reducing the costs of clinical testing and greatly lessening the risks of developing drugs for clinical use, the heightened transparency resulting from a public-good approach should enable private and public health care providers to press companies to reduce their prices. A fall in prescription drug prices would reduce the variable profit the company earned on existing drug sales. As the unit profit from each additional sale declined, the marginal incentives to market medications to increase sales might also decrease, which could help to discourage wasteful expenditures on marketing and promotion.[18]

If drug companies no longer had to defray the cumulative costs of clinical trials, the threshold level of profitability for new candidate drugs—estimated by some to range between 800 million to one billion dollars—would likely fall by a considerable amount.[19] This lower threshold could significantly reduce profit requirements that discourage the introduction and development of new drugs.

The resources drug companies now expend to market and protect existing drugs from competition could be redeployed to discover new and potentially more valuable medicines if the state bore some portion of the cost of clinical trials. In any event, given lower testing costs and lowered risk premiums, firms could expect profits from a much broader range of products taken to market than at present, and incentives to discover such products would correspondingly increase in a less lottery-like environment.[20]

Moreover, with public disclosure of previous clinical trial results concerning related medicines, companies could better predict which candidate medications should be effective and safe for clinical use. For example, early disclosure of clinical trial findings that Vioxx posed greater risks than originally known might have prompted its worldwide market withdrawal, increased scrutiny of similar drugs, and accelerated R&D to find a better product in the same therapeutic class.[21] Greater private funding for drug research and development might follow as drug companies improved at predicting clinical success earlier in the drug approval process.

Finally, a competitive framework for peer-reviewed, federal grant support of clinical trials and testing could be designed to reward those lines of investigation that promised significant pharmaceutical innovation or answered important questions about clinical cost-effectiveness. Where therapeutic competition is lacking, public funding might lower the barrier to new entrants without undermining patent rights. By so doing, this public investment in clinical trials might amplify the benefits of lower drug prices through enhanced therapeutic competition that could impact existing, not just new, drugs on the market.

2. A Secondary Market for Remedial Improvers

Public funding and disclosure of clinical trial results should also stimulate a secondary collaborative market for finding remedies to investigational obstacles that thwarted development of promising medications. Various reasons account for drug company decisions to shelve promising products rather than completing the costly clinical testing process. Sometimes it is a marketing decision, while at other times, it is a

clinical setback that mandates a new investigational course. A registry of the drugs failing clinical standards and the data yielded by the tests could be made available for improvements by third parties after a suitable period of time.

A company whose drug application had been denied would have a brief period to identify remedies to the deficiencies identified at trial, in order to qualify for a new round of testing. If the originating company failed to meet this requirement, the relevant data could be relegated to a legally defined semicommons open to would-be third party improvers, who would contribute a reasonable royalty to originators in case of commercial success to cover earlier costs of R&D.[22] A version of this approach already exists for agricultural chemical registration in the United States. After a period of exclusivity, follow-on competitors may enter the marketplace by providing compensation to the originating company that invested in the line of research to help cover the costs of obtaining public safety data.[23]

III. Implementing a Public Testing Program

We believe the government should fund clinical tests to the fullest extent permitted by sound fiscal policy. The definition of products subject to this proposal should be broad enough to include drug treatments, vaccines, medical devices, and diagnostic or monitoring tests. By clinical trials, we mean Phases I through III as understood in current FDA practice, as well as post-approval Phase IV clinical trials.[24]

A. Awarding Clinical Tests to the Most Qualified Scientists

Our proposal does not require the government to physically conduct the tests under the aegis of a specialized agency, although this remains a possibility. We anticipate that an industry comprised of the qualified and experienced scientists who have previously conducted clinical tests for the drug companies would emerge initially to perform clinical testing under this program. The primary role of the government would be to oversee competitive awards to worthy testing organizations—either public or private—that could also reflect public health priorities.

This approach builds on proven strengths of the federal government to administer extramural research grants, like those that the National Institutes of Health (NIH) routinely award. As already occurs in that grant-making process, scientific review panels would root out potential biases in study design, and with inputs from the drug regulatory authority, insist on appropriate treatment comparisons by the designated clinical trial units.

B. Revenue Neutral Financing with Cost Sharing and Social Funding Criteria

Our proposal calls for a revenue neutral implementation. Public support of clinical testing could be financed directly by the reduced drug reimbursements the federal government should pay, as the country's largest employer and provider of health insurance. We recognize that market forces and health insurers' pressures could fail to secure the desired level of social returns, in the form of lowered drug prices, from the proposed public investment without resort to additional safeguards. Some combination of moral suasion, price guidelines, compulsory licensing or other legal measures available to address patent misuse and the larger public interest might then be needed for this

purpose. [25] Yet, heightened transparency could make it costly for the drug industry to frustrate the goals of government funded clinical trials, while even the safeguard measures mentioned above should appear relatively unobtrusive against the backdrop of growing demands for the price regulation schemes practiced abroad and for mounting calls for government control of the innovation process.[26] .

We note that even in the absence of fiscal constraints, the drug companies should bear some share of the costs of conducting clinical trials. This safeguard is needed to discourage the wholesale testing of marginal drugs with little therapeutic value or candidate medicines with little chance of clinical adoption. A process that reimbursed a progressively larger share of testing for those medicines that displayed the greatest potential benefits would encourage companies to select only the most promising medicines for clinical review at public expense.

Selective funding of clinical trials would afford the government some discretion in supporting the development of drugs with greatest potential social value that might otherwise be overlooked by a totally market-driven approach. An important factor in any such selection process would be the overall public health impact of the candidate drug. This factor would be measured by the relative burden of the underlying disease, by the availability of existing clinical options to treat the disease, by the need to stimulate greater competition within a given therapeutic class, and by the need to treat certain neglected diseases, including both rare or orphan diseases, by means that might otherwise not be developed absent government assistance.

C. Phased Implementation and Eventual Globalization of the Concept

Given the magnitude of the goal of treating clinical trials as a public good, prudence suggests implementing the policy by steps, through a phased in process over time. On this approach, pilot projects could assign the highest priority to drug candidates that offered innovative therapeutic benefits or significant gains over existing treatments. Or, if early returns on revenue neutrality were sought, pilot projects might target drug candidates that offered therapeutic competition where there was none. Over time, however, the more fully that the federal government absorbed the aggregate costs of the clinical testing process, the greater would be the benefits along the drug supply chain as a whole.

Aside from the obvious benefits a public clinical trials program would yield for the United States, it would surely impact favorably on a global public health system that has come under great strain. The program of publicly supported clinical testing we propose would enhance opportunities for development aid organizations and public-private partnerships to make more essential drugs accessible at home and abroad. By reducing the costs of developing drugs for the poor, state subsidies of clinical trials could also complement private initiatives to develop and deliver beneficial drugs to developing countries.

IV. Concluding Observations

Our proposal seeks to preserve the integrity of the present incentive structure by recognizing that clinical trials are in fact a public good that must be treated as such if we are to rationalize an increasingly costly system and reverse the upward spiral of drug

prices. While the trend in public affairs is to privatize many government services in a quest for greater efficiency, we think the same process of functional reevaluation demonstrates that forcing the private sector to supply certain quintessentially public goods such as clinical trials of new pharmaceutical products will inherently produce unsatisfactory results. Our proposal to reduce the costs and increase the efficiency of clinical testing by making it a public sector process offers significant benefits to both pharmaceutical companies and the public at large.

Taken together, if the government funded the bulk of clinical trials, in addition to its current high level of funding for basic research, the heightened transparency pervading the system should oblige the pharmaceutical companies to lower prices to more accurately reflect their actual costs of production, their private R&D expenditures, and their marketing costs. This outcome would reassure the public and reduce the tensions that continued reliance on our market-driven drug delivery system has recently generated.

We realize that more work would be needed to render our proposal fully operational. We nonetheless prefer to start the discussion now, because of the timely nature of the subject, and to defer a more refined elaboration of means and ends to a later article.

End Notes

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[1] *See, e.g.*, Pierre Azoulay, "The Changing Economics of Clinical Development," paper presented at the workshop on "Innovation in the Life Sciences: Intellectual Property and Public Investment for Pharmaceuticals and Agriculture," Program on Science, Technology and Global Development, The Earth Institute at Columbia University, New York, NY, May, 20, 2004; "AMA recommends that DHHS establish a registry for all US clinical trials," *AMA Press Release*, 15 June 2004,available at: http://www.ama-assn.org/ama/pub/article/1616-8651.html; "Leading Medical Groups Endorse Public Clinical Trials Registry," *American Academy of Child and Adolescent Psychiatry* and *American Psychiatric Association* News Advisory, 9 September 2004, available from: http://www.aacap.org/press_releases/2004/0909.htm. *See also* "Senators Introduce Legislation That Would Establish Clinical Trial Registry Database," *MediLexicon*, 9 October 2004, available from: http://www.pharma-lexicon.com/medicalnews.php.newsid=14711; "Medical journals to require clinical trial registration," *NewScientist.com* news service, 9 September 2004, available from: http://www.newscientist.com/news/print.jsp?id=ns99996378.

[2] *See, e.g.*, Harris, Gardner. "Spitzer Sues a Drug Maker, Saying It Hid Negative Data," *New York Times*, 3 June 2004, p. A-1; Peter Juni et al., "Risk of cardiovascular events and rotecoxib: Cumulative meta-analysis," *The Lancet.com*, 5 November, 2004, available at http://image.theLancet.com/extras/04art10237web.pdf. *See also*, Dong BJ, Gambertoglio JG, Gee L, et al., "Bioequivalence of Levothyroxine Preparations: Industry Sponsorship and Academic Freedom," *JAMA*, 16 April 1997; 277(15): 1200-1201; *see also* Blumenthal D, Campbell EG, Anderson M, et al. "Withholding Research Results in Academic Life Science: Evidence from a National Survey of Faculty," *JAMA* 16 April 1997; 277(15): 1224-1228 (noting efforts to slow dissemination of undesired results).

[3] *See, e.g.*, Writing Group for the Women's Health Initiative Investigators, "Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women: Principal Results from the Women's Health Initiative Randomized Controlled Trial," *JAMA* 2002; 288: 321-333; Brass LM, "Hormone Replacement Therapy

and Stroke: Clinical Trials Review," *Stroke* 2004; 35[suppl I].

[4] Roberts TG, Chabner BA, "Beyond Fast Track for Drug Approvals," *New England Journal of Medicine*. 29 July 2004; 351(5): 501-505.

[5] *Cf., e.g.,* Uwe E. Reinhardt, "Perspectives on the Pharmaceutical Industry," 20 *Health Affairs* (No. 5) 136, 145-47 (2001) (suggesting creation of financially independent pharmaco-economic research institutes to assess costs and benefits of new and existing drugs).

[6] *Cf., e.g.,* Uwe E. Reinhardt, "An Information Infrastructure for the Pharmaceutical Market," 23 *Health Affairs* (No. 2) 107, 109 (2004) (stressing importance of treating information about pharmaceutical effectiveness as a public good). In his 2004 article, Professor Reinhardt proposed the creation of a publicly funded research organization to evaluate the cost effectiveness of drugs and to disseminate the results. We believe the public good rationale he expounds should be expanded to cover the production and dissemination of clinical trial data as such.

[7] See. *e.g. id.,* at 109 (stressing nonexludable and nonrivalrous character of "information that facilitates the proper function of a healthcare market—such as for drugs").

[8] See. *e.g. id.*, at 109 (stating that "the private sector typically does not produce these [public information] goods in socially efficient quantities").

[9] On the orphan drugs question, see Henry Grabowski, "Increasing R&D Incentives for Neglected Diseases: Lessons from the Orphan Drug Act," in *International Public Goods and Transfer of Technology Under a Globalized Intellectual Property Regime* 457-80 (Keith E. Makus & Jerome H. Reichman eds., Cambridge U. Press 2005) [hereinafter *International Public Goods and IP*].

[10] DiMasi JA, Hansen RW, Grabowski HG., "The price of innovation: New estimates of drug development costs," *Journal of Health Economics* 2003; 22: 151-185. These authors found: "We may approximate the increases in cost per subject over time by examining the excess of medical care inflation over general price inflation. The medical care component of the CPI increased at an average annual rate of 6.73% from 1984 to 1997, while general price inflation (applying the price index used to deflate costs for this study) rose at an annual rate of 3.06% over the same period. Thus, other things being equal, these results suggest an increase of 11.4% per year in clinical trial costs. This compares to our finding of an 11.8% annual growth rate in out-of-pocket clinical period cost between DiMasi et al. (1991) and the current study." *Id*., at 177.

[11] P. Azoulay, above n. 1 (showing figures and quoting authorities).

[12] *See. e.g.,* Grabowski, above n. 9, at 460 (stressing increase of R&D costs at an annual rate of 7.4% above inflation compared to 1980s and finding size and number of clinical trials "[a] major factor accounting for this growth in costs"). *See also* DiMasi et al., above n. 10, at 161-67; Patricia M. Danzon & Adrian Towse, "Theory and Implementation of Differential Pricing for Pharmaceuticals," in *International Public Goods and IP*, above n. 9, at 428 (R&D costs account for roughly 30% of total cost of new drugs).

[13] Grabowski, above n. 9, at 460-61 (adding that, of those that survive, only a few "succeed in generating very large returns").

[14] The difficulty of reliably establishing these costs is well established in the literature.

[15]*See e.g.,* IMS Health, "Treating the poor health of the industry," 29 September 2004, available from: http://open.imshealth.com/IMSinclude/i_article_20040929.asp; National Institute for Health Care Management Research and Educational Foundation, "Changing Patterns of Pharmaceutical Innovation," May 2002, available from: http://www.nihcm.org/innovations.pdf

[16] Projan SJ. "Why is big Pharma getting out of antibacterial drug discovery?," *Current Opinion in Microbiology* 2003; 6: 427-430; Per Nordberg, Dominique L. Monnet, Otto Cars, "Antibacterial Drug Resistance: Options for Concerted Action", Priority Medicines for Europe and the World Project: A Public Health Approach to Innovation (Geneva, Switzerland: World Health Organization, February 2005), available from: http://mednet3.who.int/prioritymeds/report/index.htm.

[17] *See e.g.,* Ian Cockburn, "The Changing Structure of the Pharmaceutical Industry, *Health Affairs*,

Jan/Feb., 2004 (stressing replenished pipeline and other causal factors for past slow down).

[18] *See, e.g.*, AHRQ Newsletter [date, cite], *citing* Ma J, Stafford RS, Cockburn IM and Finkelstein SN. "A statistical analysis of the magnitude and composition of drug promotion in the United States in 1998"; *Clinical Therapeutics*, February 2003, 25: 1503-1517: "The researchers analyzed nationally representative data on expenditures for the 250 most promoted medications in the United States in 1998 and the five most commonly used modes of promotion. During that year, the pharmaceutical industry spent $12,724 million promoting its products in the United States, of which 86 percent was accounted for by the top 250 drugs and 52 percent by the top 50 drugs. Direct-to-consumer advertising was more concentrated on a small subset of medications than was promotion directed to professionals."

Direct to consumer advertising alone reportedly cost the pharmaceutical companies $2.6 billion in 2003. *See* Harper, Jennifer, "Drug ads provide a mixed blessing, but consumers do go to the doctor," *Washington Times*, April 30, 2004, p. A08. Growth in promotion reportedly outstripped growth in research spending by more than 50 percent. See David Pauly, "Drug Companies' Cost of Pushing Pills Rivals R&D," Bloomberg, August 26, 2004.

[19] *See* DiMasi et al, above n. 10.

[20] *See.* Grabowski, above n. 9, at 460-61 (stressing lottery like atmosphere where most products fail to recoup R&D costs).

[21] Herper M, "Pfizer's Vioxx Problem," *Forbes.com*, 15 October 2004, available from: http://www.forbes.com/2004/10/15/cx_mh_1015bextra_print.html

[22] *Cf.* Reichman, JH, "Of Green Tulips and Legal Kudzu: Repackaging Rights in Subpatentable Innovation," 53 Vand. L. Rev. 1743-98 (2000); *see also* Reichman JH and Uhlir PF., "A Contractually Reconstructed Research Commons for Scientific Data in a Highly Protectionist Intellectual Property Environment," *Law and Contemporary Problems*, Winter/Spring, 2003; 66: 315-440, available from: http://www.law.duke.edu/shell/cite.pl?66+Law+&+Contemp.+Probs.+315+(WinterSpring+2003). If the original, failed product were patented, the improver under such a "compensatory liability regime" would require a tailor-made dependent compulsory license ("antiblocking" license) like those generally available for improvement patents in most developed countries (but not the U.S.).

[23] *See* Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), 7 U.S.C. §§136-136y, at §§136a(c)(2)(B). *See also* Rob Weissman, "Data Protection: Options for Implementation," *in Owning Health: Intellectual Property and Access to Essential Medicines* (Geoff Tansey, ed., Elgar Press, forthcoming 2005), who states: "[Under FIFRA], [t]he [EPA] administrator, without the permission of the original data submitter, [may] consider any such item of data [cited] in support of an application by another person…if the applicant has made an offer to compensate the original data submitter…The terms and amount of compensation may be fixed by an agreement between the original data submitter and the applicant, or, failing such an agreement, binding arbitration."

[24] Each phase of the clinical trial process is designed to answer distinct research questions. In Phase I, researchers testing a new drug or treatment in small groups for the first time seek to evaluate overall safety, determine a safe dose range, and identify side effects. During Phase II, use by a larger group of subjects focuses on effectiveness, further evaluations of safety, and finding the right dose. Phase III tests on large groups of people seek to confirm estimates of effectiveness, monitor side effects, compare the new product to commonly used treatments, and to collect more information bearing on safe usage. Phase IV studies are conducted after marketing of the drug or treatment in question to gather information about its effects on different populations and any side effects associated with long-term use. *See* the NIH resource information on clinical trials at <http://www.nlm.nih.gov/services/ctphases.html>.

[25] Some observers argue that safeguards embodied in the Bayh-Dole Act of 1980 already provide the basis for federally authorized price controls of pharmaceuticals based on federally funded research results. *See, e.g.*, 35 U.S.C. §202(a)(i)-(iii) (2002) (power of NIH to restrict patenting of federally funded research results in "exceptional circumstances"); 35 U.S.C. §203(1)(a), (b) (march-in rights under Bayh-Dole Act of 1980); Peter S. Arno & Michael H. Davis, "Why Don't We Enforce Existing Drug Price Controls?" 75

Tulane Law Review 631 (2001). Others believe that, in their present form, these same provisions are unworkable without serious administrative reforms. *See generally* Arti K. Rai & Rebecca S. Eisenberg, "Bayh-Dole Reform and the Progress of Biomedicine," 66 *Law & Contemp. Probs.* 289-314 (2003). Professor Reichman finds that the Bayh-Dole provisions provide a potentially workable framework for regulating misuse of patents on federally funded research results. *See* Jerome H. Reichman "Testimony Before NIH Public Hearing on March-In Rights Under the Bayh-Dole Act," May 23, 2004. The authors agree that the question of safeguards requires further elaboration in a later article. For the range of measures available under foreign and international law, see Reichman, JH with Hasenzahl C, "Nonvoluntary Licensing of Patented Inventions: Historical Perspective, Legal Framework under TRIPS, and an Overview of the Practice in Canada and the United States of America," UNCTAD/ICTSD, Geneva, September, 2002.

[26] *See, e.g.*, Eduardo Porter, "Do New Drugs Always Have to Cost So Much?," *New York Times*, November 14, 2004, p. Bu 5; Dean Baker, , "Financing Drug Research: What Are the Issues?" Center for Economic and Policy Research, September 22, 2004. Available from: http://www.cepr.net/publications/patents_what_are_the_issues_9-20.pdf (reviewing four reform proposals).