PhRMA

August 7, 2009

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Comments on Food and Drug Administration Transparency Task Force; Public Meeting and Request for Comments; Docket No. FDA-2009-N-0247; 74 Fed. Reg. 26,712 (June 3, 2009)

Dear Sir or Madam:

The Pharmaceutical Research and Manufacturers of America ("PhRMA") is pleased to provide comments to the Food and Drug Administration ("FDA" or "the Agency") Transparency Task Force to assist it in providing recommendations for making useful and understandable information about FDA activities and decision-making more readily available to the public in a manner that continues to foster competitive innovation. PhRMA is a voluntary, non-profit association that represents the country's leading pharmaceutical research and biotechnology companies, which are devoted to inventing medicines that allow patients to live longer, healthier and more productive lives. In 2008, PhRMA members invested over $50 billion to develop new medicines. Accordingly, PhRMA has a substantial interest in maintaining a strong and effective FDA that facilitates the development and approval of safe and effective new medicines.

PhRMA is highly supportive of the FDA's transparency initiative, because transparency fosters accountability. It is for this reason that the pharmaceutical industry itself is firmly committed to the transparency of clinical research and safety information, as evidenced by its longstanding and proactive support of clinical trial registries and results databanks and its recent commitment to disclose information about drug products for which research programs have been discontinued. In short, the research-based pharmaceutical industry is working to increase the availability of information about one of the most significant stages of research and development – clinical trials in patients.

As an initial matter, it is important to recognize that FDA already is one of the most transparent public health agencies in the world, providing detailed information about approval decisions, enforcement actions and agency policies, among other things, on its website. However, PhRMA recognizes that additional improvements can and should be made and applauds FDA for establishing a Transparency Task Force to study the issue. PhRMA believes there are at least three actions the Agency can take to improve transparency. First, FDA should enhance its web site to ensure that the wealth of information already available is accessible to the general public. Second, FDA should do even more to explain its approval decisions and other important regulatory actions to healthcare professionals and to patients. The Agency may accomplish this by making action packages more accessible on the FDA web site. The Agency

should also consider providing summaries of its regulatory benefit-risk analyses written in consumer-friendly language in a reasonable period of time after such regulatory actions are taken. The FDA should disclose the system and processes used to support its operations and decision making. Put simply, the FDA should make it obvious, to those who are interested, how scientific data leads to its approval and other significant regulatory decisions. Third, FDA should consider a prominent link from its homepage that explains the drug approval process in detail and in consumer friendly language. PhRMA provides additional detail on these and other recommendations in Section III of these comments.

Just as PhRMA strongly supports FDA's initiative to improve openness and communication, we also believe it will be critical for the Agency to balance increased transparency with the need to encourage manufacturers to develop important medical advances in a competitive manner. Although transparency is an important goal, it must be pursued in a balanced manner that accommodates other important public health goals, such as patient privacy and incentives for innovative research. Increased disclosure requirements that fail to protect trade secrets and confidential commercial information associated with innovative research and development not only will violate existing legal requirements, but also will harm, rather than improve, the public health. PhRMA's detailed comments are set forth below.

I. The Pharmaceutical Industry's Commitment to Transparency of Clinical Trial Information

Consistent with the FDA's goal of enhancing accessibility to information, the biopharmaceutical industry has demonstrated a commitment to help assure that patients and physicians have access to all relevant information about marketed drug products and investigational drug products. In 2002, for example – well before the passage of the Food and Drug Administration Amendments of Act of 2007 ("FDAAA") – PhRMA issued its Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results ("Clinical Trial Principles"). Earlier this year, consistent with its support for the clinical trial disclosure provisions in FDAAA, PhRMA's Board of Directors voted unanimously to update and enhance the Clinical Trial Principles. As a result of these revisions, PhRMA members following the Clinical Trial Principles will enhance communications about clinical trials by, among other things:

- Registering all clinical trials in patients, including early (Phase 1) clinical trials;[1] and
- Providing results summaries for all clinical trials involving patients for medicines whose research programs are discontinued.[2]

[1] For purposes of the PhRMA Clinical Trial Principles, a "clinical trial" means an interventional trial involving human subjects from Phase 1 and beyond. For example, the term does not include the use of a drug in the normal course of medical practice or non-clinical laboratory studies. The term "patients" means those in need of medical care – not healthy volunteers.

By providing results summaries for clinical trials shortly after discontinuation of a drug's development, PhRMA members will be significantly expanding the universe of publicly available data about clinical trials in patients. In addition, if information from any clinical trial is felt to be of significant medical importance, then PhRMA members will work with investigators to publish the data. Of course, under FDAAA, PhRMA members already provide results information after a drug's approval.

II. The FDA Already Is Extremely Transparent

Before discussing ways in which FDA can improve its openness in communications, it is important to acknowledge that the FDA already is one of the most transparent federal agencies in the United States and one of the most accessible public health agencies in the world. As part of its transparency initiative, the FDA would perform a valuable public service by helping to educate the public at large about – and enhancing the accessibility of – the enormous amount of information about medical products that the Agency makes available. The FDA currently provides a wealth of information on its web site about the safety and effectiveness of particular drug products, the grounds for its approval and other regulatory decisions and the Agency's internal policies and procedures. For example, FDA's web site provides links to, among other things, the Agency's approval letters, action packages, advisory committee briefing materials, approved labeling, medication guides, risk evaluation and mitigation strategies ("REMS"), post-market study requirements, adverse event information, "early communications" on drug safety, public health advisories, warning and untitled letters, recalls, internal standard operating procedures, guidance documents, regulations, and citizen petitions.

FDA's existing transparency is a result of both statutory requirements and Agency policy. The Federal Food, Drug, and Cosmetic Act ("FDCA") requires FDA to publicly disclose a vast amount of very specific information about the drug products that are subject to FDA review and regulation. For example, the FDCA, as amended by FDAAA, now requires FDA to post on its web site the "action package for approval" of a drug product within thirty days of approval of a new chemical entity or, for any other drug, within thirty days of the third request for the action package pursuant to the Freedom of Information Act ("FOIA").[3] The action package contains detailed information regarding the basis for FDA's approval decision and must include summaries from all reviewing disciplines (e.g., chemical, pharmacological, statistical, medical) that disclose "any critical issues and disagreements with the applicant and within the review team and how they were resolved . . . ."[4]

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[2] Under PhRMA's newly revised Clinical Trial Principles, a development program is considered discontinued when the company is no longer studying the applicable molecule, does not expect to resume development, and has no plans for the molecule on its own or through collaboration or out-licensing. PhRMA believes that such a standard will greatly enhance transparency but would not disadvantage research and development for sponsors that are required to post results under FDAAA compared to those who engage in research and development outside of the jurisdiction of NIH and FDA.

[3] 21 U.S.C. §355(l)(2).

[4] *Id.* §355(l)(2)(C).

The FDCA also requires FDA to create a consolidated Internet web site that provides patients and health care providers "better access to information about drugs," particularly drug safety information.[5] Finally, FDA is required by statute to publicly disclose, among other things, the following specific categories of information: REMS action letters;[6] transcripts of any Drug Safety Oversight Board ("DSOB") meeting to resolve a dispute over a REMS;[7] FDA discipline reviews of pediatric studies and pediatric assessments;[8] the basis for any FDA decision not to require pediatric assessments;[9] applicant requests for a waiver from the requirement to develop a pediatric formulation of a drug (if such waiver is granted);[10] the status of postmarketing studies;[11] information on the discontinuance of a life saving drug;[12] orphan drug designations;[13] a list of authorized generic drug products;[14] and a quarterly report of any new safety information or potential signal of a serious risk identified by the Adverse Event Reporting System.[15]

In addition to the detailed information required to be disclosed under the FDCA, interested persons can utilize the FOIA procedures to obtain documents and other material that may not be accessible on FDA's web site, such as manufacturing inspection reports, clinical trial inspection information, and even employee manuals.[16] According to FDA, the FOIA "adopts a general rule that, except where specifically exempted, all documents in Government files shall be made available to the public."[17] Prior to adopting its current FOIA regulations, FDA estimated that it retained roughly 90 percent of the records in its files as confidential and disclosed only 10 percent; however, upon adoption of its FOIA regulations in 1974, FDA announced that "it has reversed this proportion and now makes available roughly 90 percent of the records in its files."[18] Public participation in the FOIA process remains high at FDA. In fiscal year 2008, FDA received 9,432 requests for information or documents under FOIA. In the same year, FDA

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[5] *Id.* §355(r). FDA's consolidated Internet Website is available at http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/default.htm

[6] *Id.* §355-1(h)(3)(C).

[7] *Id.* §355-1(h)(5)(E).

[8] *Id.* §§355a(k)(1), 355c(h)(1).

[9] *Id.* §355a(n)(2).

[10] *Id.* §355c(b)(2)(C).

[11] *Id.* §356b(c).

[12] *Id.* §356c(c).

[13] *Id.* §360bb(c).

[14] *Id.* §355(t)(1)(A).

[15] *Id.* §355(k)(5)(A).

[16] 5 U.S.C. §552.

[17] 37 Fed. Reg. 9128 (May 5, 1972) (proposed FOIA regulations).

[18] 39 Fed. Reg. 44,602 (Dec. 24, 1974) (final FOIA regulations).

processed 20,348 such requests, reducing its backlog to 6,568.[19] FDA fully granted over 11,000 FOIA requests in FY08 and only fully denied 79 such requests based upon a statutory exemption (e.g., trade secret).[20] The vast majority of denials were based on reasons other than a statutory exemption, such as voluntary withdrawal of the request (6,686), lack of any responsive records (825), or failure to pay a fee (125).[21] We understand that FDA faces resource constraints, and we recommend that the Agency continue to examine ways of improving the timeliness of FOIA responses.

The Public Health Service Act ("PHS Act"), as amended by FDAAA, also ensures public access to detailed information about ongoing clinical trials and the results of completed clinical investigations.[22] Under revisions to the PHS Act passed in 2007,[23] sponsors of most clinical research must post detailed information about ongoing clinical trials on the federal government web site www.ClinicalTrials.gov within 21 days of initial patient enrollment.[24] The information that must be submitted is comprehensive, covering approximately 25 separate data elements that closely track the information required in a protocol, such as the name of the intervention, key inclusion and exclusion criteria, primary and secondary outcome measures, and details of the study design.[25] These comprehensive data elements are intended to satisfy the dual goals of the registry: (1) to inform patients and their physicians about ongoing trials; and (2) to ensure the results information ultimately is posted and can be appropriately analyzed.

FDAAA also expanded the existing clinical trial registry to include results information for clinical trials.[26] Now, results information for applicable clinical trials must be posted to ClinicalTrials in a tabular format,[27] and the National Institutes of Health ("NIH") and FDA recently initiated a rulemaking process to determine whether results should be submitted in a summary format.[28] The rulemaking also will examine the feasibility of further expanding the databank by, for example, requiring the submission of studies for drugs that are never approved for any indication.[29] FDA has played and continues to play a key role in the implementation of the new clinical trial disclosure requirements.

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[19] FDA Freedom of Information Annual Report 2008, accessed on July 19, 2009 at http://www.fda.gov/RegulatoryInformation/FOI/FOIAAnnualReports/ucm136513.htm

[20] *Id.*

[21] *Id.*

[22] 42 U.S.C. §282(j).

[23] Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, §801 (2007).

[24] 42 U.S.C. §282(j)(2)(C).

[25] *Id.* §282(j)(2)(A)(ii).

[26] *Id.* §282(j)(3).

[27] *Id.* §282(j)(3)(C).

[28] *Id.* §282(j)(3)(D)(iii).

[29] *Id.* §282(j)(3)(D)(ii)(II).

In addition to the statutory requirements mandating transparency, FDA has implemented numerous voluntary policies designed to increase the public's access to and understanding of FDA's decision-making process. For example, in 1974, FDA began to publicly disclose summaries of the safety and effectiveness data underlying its decisions to approve specific drug products –a summary basis of approval (now known as action packages or approval packages).[30] Then, as now, FDA received numerous requests to disclose *all* safety and effectiveness data in IND and NDA files because such information was considered to be "important to scientists and physicians."[31] FDA recognized, however, that the law prohibited it from releasing the complete data package for an approved drug, since such information constitutes trade secrets and confidential commercial information. FDA described its options this way:

> The Commissioner concludes that the present law provides the Food and Drug Administration a choice between release of a summary or release of no safety and effectiveness information, since release of the complete data would constitute disclosure of a trade secret prohibited by 21 U.S.C. §331(j) and 18 U.S.C. §1905. *The release of a summary is preferable to no release of information.*[32]

According to FDA, the "summary will be complete enough to convey both the nature of the experiment and the scientific data generated."[33] FDA considered the release of summary information to be important "so that scientists and members of the public who are interested will have an opportunity to determine the basis on which Food and Drug Administration decisions are made."[34] The FDA's decision to release action packages voluntarily has done much to shine a light on the Agency's decision-making process in the new drug approval context. Equally important, FDA has increased transparency of drug approval decisions *without undermining the incentives for innovative research.* Many action packages currently are available on FDA's web site, and those that are not can be obtained through a FOIA request. As we discuss below, FDA can improve transparency of approval decisions by improving the accessibility of action packages.

A more recent policy implemented by FDA on a voluntary basis to increase transparency involves the communication of emerging drug safety issues. In May 2005, FDA announced plans to create a "Drug Watch" web site that would communicate information about the safety of approved drug products at a very early stage, sometimes even before FDA had made a decision about the relevance, or lack thereof, of the reported information.[35] In 2007, FDA finalized a guidance document detailing how it communicates drug safety information to the public.[36]

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[30] 39 Fed. Reg. 44,602.

[31] *Id*. at 44,634.

[32] *Id*. at 44,636 (emphasis added).

[33] *Id*.

[34] *Id*. at 44,635.

[35] 70 Fed. Reg. 24,606 (May 10, 2005).

[36] 72 Fed. Reg. 10,224 (March 7, 2007).

Although it dropped the name "Drug Watch," FDA retained the concept of communicating "emerging" drug safety information before it had been fully analyzed or confirmed by the Agency.[37] Since then, FDA has issued more than 20 "early communications" about ongoing safety reviews for a wide variety of drug products, thereby providing physicians and patients with real-time information about FDA's ongoing safety assessments.[38]

As is evident from the above discussion, FDA provides a wealth of information on its web site about the safety and effectiveness of particular drug products and the basis for the Agency's decisions. As a result of its longstanding commitment to openness, FDA is one of the most forward-leaning and transparent public health agencies in the world.

III. PhRMA Suggestions to Improve Transparency

Given the extraordinary amount of information already available to the public, much of it online, it may seem surprising that FDA has created a Transparency Task Force. However, PhRMA recognizes that there is always room for improvement and that, given FDA's critical public health mission, it is particularly important for the Agency to ensure that it is communicating to health care professionals and the public as effectively as possible. PhRMA thus commends FDA for its transparency initiative. At the same time, it is important to recognize that transparency without adequate process, resources, and infrastructure for explanation to healthcare professionals and the public could, perversely, jeopardize public health. For this reason, FDA should avoid providing data without appropriate context or useful direction to patients or healthcare professionals; disclosing analyses that are not reproducible; and publicizing drug risks in the absence of known benefits – or the context for patients and healthcare professionals to understand the extent of such risks.

As requested in the Federal Register notice, PhRMA provides the following suggestions to improve transparency at FDA:

Enhance Accessibility of Information on the FDA Web Site. Ironically, one of the biggest impediments to accessing data and information on FDA's web site may be the sheer volume of information that is already available there. Because of this wealth of information, it may be particularly difficult for members of the public, many of whom may not be familiar with FDA's web site in the first place, to find a particular piece of information (*e.g.*, a patient medication guide) about a particular drug of interest. Even seasoned physicians and researchers have reported problems navigating through the dense and complex information available on FDA's web site. For example, one commentator recently noted that "many of the publicly accessible FDA reviews are challenging to find, which undoubtedly interferes with dissemination

[37] FDA defines "emerging drug safety information" as "information FDA is monitoring or analyzing that may have the potential to alter the benefit/risk analysis for a drug in such a way as to affect decisions about prescribing or taking the drug (i.e., an important drug safety issue), but that has not yet been fully analyzed or confirmed." *Guidance: Drug Safety Information – FDA's Communication to the Public*, at 5 (March 2007).

[38] FDA's Early Communications are available at http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm070256.htm

of their findings."[39] To access the medical review for a single drug product, the commentator had to successfully navigate through a total of six different screens and found that many of the links were "poorly named," necessitating "trial and error" to find the relevant information.[40] The commentator further reported that "[t]he search window on the FDA home page does not work well[,]" and even when found, "reviews are difficult to navigate" because of a lack of accurate labeling, tables of contents and hyperlinks.[41]

As an initial matter, FDA may be able to increase transparency significantly simply by improving the navigability of its existing web site. FDA should educate the public about the breadth of information available on its web site and then ensure that such information is easy for the public to access. Improving the accuracy and efficiency of the search window would help, but FDA also could improve transparency by re-organizing its web site so that information is accurately labeled and accessible with a minimum of pass-through screens. In this regard, it may be worthwhile to consider creating separate web portals for different audiences, such as Patients/Consumers, Physicians, and Industry. FDA may also consider using market research to assess how best to optimize the web site for consumers, patients, and healthcare professionals. PhRMA is aware that FDA recently revised and re-organized its web site to make it easier to navigate, but it is unclear at this time whether these changes have had the desired effect. Moreover, the changes have resulted in numerous broken links, which further hamper efficient navigation of the web site. These links should be re-established as quickly as possible. The FDA should continue to promote the use of the Internet to clarify and prioritize in real-time the Agency's critical initiatives. In this regard, FDA's recent presence on Twitter is noteworthy. We urge the Agency to consider other online resources for effective communication.

Provide Better Explanations About How FDA Decisions Rely on Scientific Data. PhRMA believes that the FDA can do even more to explain its approval decisions and other significant regulatory actions to healthcare professionals and to patients. Put simply, the FDA should make it obvious, to those who are interested, how scientific data leads to its approval and other regulatory decisions. For example, when the FDA makes a regulatory decision following a public expert advisory committee, the FDA should explain how the committee's recommendation factored into its decision. This is particularly important when FDA does not follow the advisory committee's advice, since FDA's contrary decision may be confusing to healthcare professionals and the public. PhRMA believes that in these types of situations, it is important for FDA to explain the basis for its decision, including the data underlying the decision. Accordingly, FDA should make relevant action packages available as quickly as possible, and these action packages should address all significant data points – including the views of expert advisory committees. In addition, FDA should consider whether to paraphrase the action package or similar documents when issuing press releases related to new product approvals.

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[39] *The Need for Improved Access to FDA Reviews*, Alec B. O'Connor, Journal of the American Medical Association, Vol. 302, No. 2, at 192 (July 8, 2009).

[40] *Id.*

[41] *Id.* at 193.

Explain the Drug Approval and Regulatory Process. In addition, FDA should consider adding a prominent link from its homepage that explains, in consumer-friendly language, how drugs are approved by FDA and how they are regulated after approval. (FDA could include similar links for foods and devices as well.) PhRMA is concerned that the general public often is misinformed about the rigor of both the FDA approval process and FDA's oversight of drug product safety after approval. A consumer-friendly presentation or tutorial that is easily accessible from FDA's web site could provide accurate information demonstrating the enormous amount of data that FDA reviews both during the approval process and once a drug product is on the market. We acknowledge that FDA has developed a page that describes the FDA approval process.[42] We believe that the effectiveness of the page might be improved by posting it more prominently, illustrating it, and increasing the number of links available from the page. For example, the tutorial could explain how FDA regulates drug products; the drug discovery and development process (e.g., IND requirements); FDA's process for reviewing and approving drug products (*e.g.*, NDA, ANDA and 505(b)(2) requirements); and FDA's post-marketing authorities to help assure drug safety (e.g., post-market trials, adverse event reporting, labeling changes). In addition, the presentation should include links to relevant resources, such as a link to ClinicalTrials.gov, drug approval lists, and even adverse event and drug risk communications, to provide additional information and context for consumers who are interested in learning more about FDA's processes or are interested in accessing particular records.

Communication About Regulatory Policy. FDA officials frequently participate in public scientific meetings as speakers, session chairs, or panelists. Such interactions provide opportunity for the Agency to share its current thinking on specific scientific and regulatory issues. PhRMA strongly encourages the Agency to continue to engage in such activities. However, we note that sometimes such interactions are used to introduce new FDA regulatory policy positions without use of formal Agency processes. At other times, information shared at such meetings appears to be inconsistent with the experiences of sponsors. Such inconsistencies and lack of clarity could result in compliance challenges. To the extent that FDA speakers announce new policies, FDA should also utilize good guidance practices to allow the opportunity for public comment, and, in general, such new policies should not be implemented until the formal guidance process is complete

Communication About Enforcement. As noted above, FDA routinely posts warning letters on its website. The Agency could provide additional communication, dialogue, and clarity regarding inspection trends and FDA's concerns that may drive inspectional observations and other citations. In addition, PhRMA recommends that the Agency share trends in enforcement actions and discuss the rationale for such actions with relevant scientific groups during public meetings.

Sponsor Access to Safety Information. Because manufacturers have a responsibility to work with FDA to update product labeling when appropriate, we recommend that the Agency establish mechanisms to ensure that manufacturers have real-time access to direct adverse event (AE) reports (such as 15 calendar days for serious AEs). We also suggest that the Agency create a process to foster collaboration in identifying duplicate AE reports. In addition, FDA should

[42] *See* http://www.fda.gov/Drugs/DevelopmentApprovalProcess/default.htm.

establish procedures to provide reasonable notice to a manufacturer prior to disclosing concerns about the safety of one of its medicines publicly. Often manufacturers receive questions from healthcare professionals and patients about FDA announcements, and manufacturers must be able to provide responsive information regarding their medicines. In addition, sponsors can collaborate more effectively with FDA to address potential safety concerns when FDA provides timely and detailed information regarding such concerns.

Providing Current Guidance. For many years, FDA has provided useful and necessary guidance to manufacturers regarding topics relating to the research, manufacture, monitoring, and marketing of medicines. FDA should continue to assure that its guidance reflects current regulatory standards, especially guidance documents relating to product development. We hope that FDA will take this opportunity to renew its emphasis on developing timely, current regulatory guidelines. Such guidance furthers transparency and also serve the public's interest by having clear, consistent guidelines based on current science supporting the development of new therapies for patients.

FDA Press Office. FDA should evaluate the effectiveness of its press office and methods for communicating with the media to assure that benefit/risk communication and crisis management communications are appropriately calibrated for target audiences. FDA should provide information in a format and content that is useful for its intended target audience (*e.g.*, patients as well as healthcare professionals).

IV. FDA Must Continue to Ensure That Increased Transparency Does Not Undermine Incentives for Innovative Biomedical Research

As indicated above, PhRMA strongly supports FDA's initiative to improve openness and communication to the public. At the same time, it is imperative that FDA continue to balance increased transparency with the need to protect the substantial investments made to develop critical medical advances in a competitive manner. Simply put, increased disclosure requirements that fail to protect innovative research and development will harm, rather than improve, the public health.

For decades, the FDA has recognized the importance of protecting proprietary pre-approval information from inappropriate disclosure. Companies large and small invest billions of dollars to investigate and develop a new medicine. If FDA were to disclose valuable confidential information about a product before it is approved for marketing, thereby allowing both domestic and foreign competitors to glean otherwise unavailable insights into the development process, the government would markedly decrease the incentive for development in the first place. This was the reasoning of the FDA 35 years ago, when the Agency drafted the final provisions of its FOIA regulations, and that rationale is just as applicable today.

Even scholars who generally push for greater transparency recognize that "[o]penness and transparency in science . . . cannot be treated as absolute goods" but rather must give way in

certain situations to other important societal goals.[43] Thus, although transparency is one important goal, it must be pursued in a balanced manner that accommodates other critical public health interests, including the development of new medical products through competitive innovation.

A. FDA Must Protect Trade Secrets and Confidential Commercial Information From Premature Public Disclosure

A new drug sponsor makes a substantial investment of time, personnel, and money in research and development, which is evidenced in its submissions to FDA through the IND and NDA process. Recent data indicate that the investment required in developing a single new prescription drug exceeds $1.2 billion over 10 – 15 years.[44] This extraordinary investment would be substantially eroded if the FDA could provide information developed by innovators prior to approval to competitors and others who could then facilitate their own drug development and/or approval of competing products. Accordingly, federal law has consistently protected the confidentiality of proprietary clinical trial information, including study reports, protocols and raw safety and effectiveness data. FOIA and the Trade Secrets Act also protect similar competitively valuable information (*e.g.*, product manufacturing procedures) from unauthorized disclosure.

Since 1938, the FDCA has included an express prohibition against the public disclosure of any information submitted to FDA in a new drug application or similar filing "concerning any method or process which as a trade secret is entitled to protection . . .."[45] FDA's longstanding interpretation of this provision is that it applies to, and prevents disclosure of, among other things, animal and human data submitted in an NDA.[46] The Trade Secrets Act provides an independent legal basis for protecting confidential information submitted to FDA in an NDA or otherwise.[47] The Trade Secrets Act imposes criminal liability against any government official who discloses, in any manner not authorized by law, any submitted information which "concerns or relates to the trade secrets, processes, operations, style of work, or apparatus, or to the identity

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[43] *See* Sheila Jasanoff, *Transparency in Public Science: Purposes, Reasons, Limits*, 69 J. Law Contemp. Prob. 21, 22 (Summer 2006) ("Openness and transparency in science, then, cannot be treated as absolute goods. Rather, the degree of openness is context-specific and needs to be traded off against other important social goals.").

[44] DiMasi, JA, and Grabowski, HG. The cost of biopharmaceutical R&D: Is biotech different? Managerial and Decision Economics; 2007 (28): 469-479.

[45] 21 U.S.C. §331(j).

[46] 39 Fed. Reg. at 44,634. Since passage of the Federal Food, Drug, and Cosmetic Act in 1938, FDA's longstanding and consistent position has been that research data submitted in an NDA "ordinarily represent valuable commercial property and trade secrets that must be retained as confidential and may not be disclosed to the public." 37 Fed. Reg. 9128, 9130; *see also* 39 Fed. Reg. 44,602, 44,637 ("The Food and Drug Administration has since 1938 pledged that all trade secret information contained in a new drug application will be held in confidence, and has stated that animal and human tests can fall within that section."). As a corollary, FDA consistently has taken the position that "no data in an NDA can be utilized to support another NDA without express permission of the original NDA holder." 46 Fed. Reg. 27,396 (May 19, 1981).

[47] 18 U.S.C. §1905.

[or] confidential statistical data . . . of any person, firm, partnership, corporation or association . . . ."[48]

While FOIA contains a general presumption in favor of disclosure,[49] it also includes specific exemptions, one of which exempts trade secrets and confidential commercial information from the otherwise applicable disclosure requirements (hereinafter referred to as "Exemption 4"). In particular, Exemption 4 of FOIA provides that "trade secrets and commercial or financial information obtained from a person and privileged or confidential" are exempt from disclosure under FOIA.[50] The federal courts have held that the Trade Secrets Act is at least coextensive with Exemption 4 of FOIA.[51] FDA likewise has taken the position that Exemption 4 is at least as broad as the confidentiality provisions contained in both the FDCA and the Trade Secrets Act.[52] Accordingly, when information is exempt from disclosure under Exemption 4, "the government is precluded from releasing it under the Trade Secrets Act."[53] As FDA has explained, "even if the Commissioner wishes as a matter of discretion to release [trade secrets or confidential commercial information], such disclosure cannot lawfully be undertaken."[54]

Both FDA and the Department of Health and Human Services ("HHS") have promulgated regulations that implement the protections against disclosure for trade secrets and confidential commercial information embodied in Exemption 4 of the FOIA.[55] FDA's regulations state that "[d]ata and information submitted or divulged to the Food and Drug Administration which fall within the definition of a trade secret or confidential commercial or financial information are not available for public disclosure."[56] The regulations define a trade secret as "any commercially valuable plan, formula, process, or device that is used for the [manufacture] of trade commodities and that can be said to be the end product of either innovation or substantial effort" and for which there is "a direct relationship between the trade secret and the productive process."[57] The regulations further define confidential commercial

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[48] *Id*.

[49] 5 U.S.C. §552(a).

[50] 5 U.S.C. §552(b)(4).

[51] McDonnell Douglas Corp. v. NASA, 180 F.3d 303, 305 (D.C. Cir. 1999); CNA Fin. Corp. v. Donovan, 830 F.2d 1132, 1151 (D.C. Cir. 1987), *cert. denied*, 485 U.S. 977 (1988).

[52] 39 Fed. Reg. at 44,612.

[53] McDonnell Douglas, 180 F.3d at 305.

[54] 39 Fed. Reg. at 44,612; *see also id.* at 44,619 ("The Commissioner advises, for the reasons set out elsewhere in this preamble, that he has no discretion to release trade secret information.").

[55] HHS has promulgated FOIA regulations that are similar to FDA's and which exempt confidential commercial information from the FOIA disclosure requirements. *See* 45 C.F.R. §5.65. Since FDA is a component of HHS, these HHS regulations also apply to FDA. *Id.* §5.3 (HHS regulations apply to "all components of the Department").

[56] 21 C.F.R. §20.61(c).

[57] *Id.* §20.61(a).

information as "valuable data or information which is used in one's business and is of a type customarily held in strict confidence . . . and not disclosed to any member of the public by the person to whom it belongs."[58] FDA's confidentiality regulations are consistent with Exemption 4 of the FOIA, the Trade Secrets Act and 21 U.S.C. §331(j), all of which require the Agency to assiduously protect trade secrets and confidential information from premature public disclosure.

Biopharmaceutical manufacturers submit a wide variety of information to FDA during the drug approval process and post-approval, and the FDA generates a substantial amount of documentation in review of manufacturer submissions. Some of the manufacturer information is submitted voluntarily to assist the Agency in its public health mission while other information, such as clinical data in an NDA, is submitted per statutory and regulatory requirements. Much of this information falls within the category of "trade secrets" under Exemption 4 and FDA's regulations, such as manufacturing plans. Other information submitted during the drug development process, such as detailed study reports, innovative protocols and raw clinical data, may constitute confidential commercial information.[59] In addition, extensive correspondence between FDA and sponsors (*e.g.*, complete response letters) during the development process constitute confidential commercial information and trade secrets. Although FDA's ability to disclose any particular piece of information must be based on an individualized assessment of its status, if FDA or a court determines that such information constitutes a trade secret or confidential commercial information, FDA is prohibited from disclosing it. As discussed further below, there are strong public policy reasons – and indeed public health reasons – supporting the protection of such information against disclosure.

B. Protection of Trade Secrets and Confidential Commercial Information Preserves Integral Incentives for Innovative Research and Is In the Public Interest

As FDA itself previously has acknowledged, the protection embodied by Exemption 4 of FOIA, the Trade Secrets Act and 21 U.S.C. §331(j) ultimately serves the public interest.[60] In particular, such confidentiality serves at least three public policy goals: (1) maintaining incentives for innovative research; (2) ensuring the "continued availability" of volunteered information; and (3) ensuring the reliability of information that is required to be submitted to the government.

1. Maintaining Incentives for Innovative Research

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[58] *Id.* §20.61(b).

[59] *See* National Parks and Conservation Ass'n v. Morton, 498 F.2d 765, 766 (D.C. Cir. 1974); Pub. Cit. Health Res. Group v. FDA, 704 F.2d 1280, 1290 (D.C. Cir. 1983) (defining safety and effectiveness data as "confidential commercial information" rather than trade secrets); Pub. Cit. Health Res. Group v. FDA, 997 F. Supp. 56 (D.D.C. 1998) (applying "confidential commercial information" test to safety and effectiveness data).

[60] 42 Fed. Reg. 3099, 3102 (Jan. 14, 1977) ("The Commissioner advises that FDA is cognizant of the congressional recognition that both public and private interests are served by protecting the confidentiality of trade secret and confidential commercial information.").

Confidentiality, especially prior to product approval, is critical to maintaining incentives for innovative biomedical research because of the extremely competitive nature of the pharmaceutical industry and the onerous requirements – and resulting investments – for obtaining FDA approval. In general, the FDA will approve a marketing application for an innovative new drug only if the sponsor submits "full reports of investigations" demonstrating that the drug is safe and effective for its intended use.[61] To satisfy this "full reports" requirement, pharmaceutical companies usually must conduct extensive preclinical (laboratory and animal) and clinical (human) testing of the new drug product over the course of several years, including large, randomized, blinded, Phase 3 clinical investigations that range in size from several hundred to several thousand subjects, depending upon the compound and disease studied.[62]

The process for obtaining FDA approval of an innovative pharmaceutical product is long, expensive, and fraught with risk. It takes on average 10 to 15 years and more than $1.2 billion to bring a single new medicine to the market.[63] Moreover, only 1 in 5,000 to 10,000 compounds identified in the laboratory makes it through the development process and obtains FDA approval.[64] Strong intellectual property protections – including vigorous protection of trade secrets and confidential commercial information – are therefore critical to maintaining incentives for companies to undertake the extraordinarily expensive and risky research necessary to discover innovative new medicines and treatment options for patients. As a public health Agency, it is axiomatic that FDA should not diminish incentives for development of life-saving new medicines. The disclosure of proprietary information submitted to FDA, particularly pre-approval safety and effectiveness data, could result in competitive disadvantages to the submitting company, thereby undercutting the incentives to generate such data. Such information -- gleaned from extraordinary investment in pre-clinical and clinical research over years -- should therefore continue to be protected by the government.

The competitive impact of pre-approval information has been recognized by both FDA and the federal courts for decades. As far back as 1974, FDA explained that

> [T]here can be no question, under present law, about the tremendous economic value of the full reports of the safety and effectiveness data contained in an IND, NDA, INAD, or NADA . . . . Release of such information would allow a competitor to obtain approval from the Food and Drug

[61] 21 U.S.C. § 355(b)(1)(A).

[62] *Id.* §355(d).

[63] DiMasi, JA, and Grabowski, HG. The cost of biopharmaceutical R&D: Is biotech different? Managerial and Decision Economics; 2007 (28): 469-479.

[64] Drug Discovery and Development: Understanding the R&D Process. www.innovation.org; Congressional Budget Office (CBO). Research and Development in the Pharmaceutical Industry, Washington, DC: CBO, October 2006.

> Administration for marketing the identical product, at a mere fraction of the cost.[65]

The federal courts likewise have recognized that "[d]isclosure could result in competitive disadvantages to the submitting entity . . .."[66] In particular, "other companies 'could make use of the information in the [disclosed application] in order to eliminate much of the time and effort that would otherwise be required to bring to market a product competitive with the product for which' the submitting company filed the [application]."[67] The D.C. Circuit, in particular, has recognized that pharmaceutical companies have a strong interest in maintaining the confidentiality of such data, stating:

> A drug manufacturer which has submitted an NDA has a competitive interest in seeing that the information contained in its NDA is not prematurely released to the public. If a manufacturer's competitor could obtain all the data in the manufacturer's NDA, it could utilize them in its own NDA without incurring the time, labor, risk, and expense involved in developing them independently.[68]

Because of the nature of the drug testing and approval process and the advantages that competitors could receive by obtaining the proprietary information contained in another company's files, premature disclosure of trade secrets and confidential commercial information could significantly undermine the incentives for innovative research. At least one scholar has suggested that "[e]xcessive or premature demands for public disclosure [of scientific information] may therefore . . . produce disincentives for high-risk research."[69] FDA itself came to this conclusion more than thirty years ago, explaining:

> The Commissioner recognizes the important public policy issues that would be raised by disclosure of such trade secret data. The public is dependent upon private pharmaceutical manufacturers for development of drugs.. . . If a manufacturer's safety and effectiveness data are to be released upon request, thus permitting "me-too" drugs to be marketed immediately, it is entirely possible that the incentive for private pharmaceutical research will be adversely affected.[70]

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[65] 39 Fed. Reg. at 44,634.

[66] Judicial Watch, Inc. v. FDA, 449 F.3d 141, 148 (D.C. Cir. 2006).

[67] *Id.* at 148-149 (quoting Pub. Citizen Health Research Group v. FDA, 185 F.3d 898, 905 (D.C. Cir. 1999)).

[68] Webb v. Department of Health and Human Services, 696 F.2d 101, 103 (D.C. Cir. 1982).

[69] Jasanoff, *supra*, at 22.

[70] 39 Fed. Reg. at 44,634.

FDA's observations more than thirty years ago, about the effect of premature disclosure of confidential commercial information on the incentives for innovative research, are equally valid today.

2. Ensuring Continued Availability of Volunteered Information

The protection embodied by Exemption 4 of the FOIA, the Trade Secrets Act, and 21 U.S.C. §331(j) also serves the important public policy goal of ensuring that the government continues to have access to relevant information that can enhance its decision-making abilities. The federal courts have explained that when information is submitted to the government voluntarily, the purpose served by the confidentiality rule is that of "encouraging cooperation with the Government by persons having information useful to officials."[71] In such situations, the government has a strong interest in ensuring the "continued availability" of volunteered information in order to enhance its ability "to make intelligent, well informed decisions."[72]

Manufacturers of medical products often submit trade secret and confidential commercial information to FDA voluntarily to foster the Agency's public health mission. If FDA were to disclose this information prematurely, sponsors could be motivated to avoid such voluntary information sharing. This, in turn, could negatively affect FDA's regulatory decision-making abilities.

3. Ensuring the Reliability of Required Information

Protection of confidential commercial information and trade secrets also serves the important public policy goal of ensuring that information submitted to the government per a statutory or regulatory requirement is reliable. As the D.C. Circuit has explained, "when information is obtained under duress, the Government's interest is in ensuring its continued reliability . . .."[73] In the new drug context, the court observed: "Applicants spend a great deal of resources to obtain data for an IND or NDA, and the FDA could not expect full and frank disclosure if it later released such proprietary information into the public domain."[74]

4. Other Interests Do Not Outweigh Those Supporting the Continued Protection of Trade Secrets and Confidential Commercial Information

Other interests do not outweigh the substantial public policy justifications supporting protection of proprietary information regarding the development, manufacture, and distribution

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[71] Critical Mass Energy Project v. NRC, 975 F.2d 871, 878 (D.C. Cir. 1992) (en banc), *cert. denied*, 507 U.S. 984 (1993) (quoting National Parks and Conservation Ass'n v. Morton, 498 F.2d 765, 768 (D.C. Cir. 1974).

[72] *Id*. at 878; *see also* McDonnell Douglas, 895 F. Supp. 316, 318.

[73] Critical Mass, *supra.*

[74] Judicial Watch, 449 F.3d 141, 149.

of life saving medicines. Significantly, both FDA and the courts have reached this conclusion repeatedly.

When FDA finalized its FOIA regulations in 1974, it received several comments asserting that "the need for the public disclosure of safety and effectiveness data is so great that no justification of trade secret or confidential commercial status [is] sufficient to withhold such information."[75] Other comments argued that "outside scientists need the raw data in order to determine whether the Agency has acted wisely in a given instance."[76] Still others contended that all information submitted in an IND should be made publicly available "for the protection of the human subjects involved in the drug experiments."[77]

FDA, however, rejected all of these comments because it recognized that other important public policy reasons weighed against disclosure of trade secrets and confidential commercial information, including the need to maintain incentives for innovative research.[78] Moreover, FDA recognized that Congress already had weighed these competing interests and "concluded that the need to withhold [trade secrets and confidential commercial information] outweighs the need to release it."[79] FDA nevertheless sought to address the legitimate concerns raised in these comments, to the extent permitted under the controlling statutes, by permitting the disclosure of a *summary* of safety and effectiveness information that would be "complete enough to convey both the nature of the experiment and the scientific data generated."[80]

The federal courts likewise have rejected similar arguments in litigation seeking access to confidential safety and effectiveness data. Addressing the argument that disclosure of IND information is necessary to "prevent the exposure of human beings to a health risk," the D.C. Circuit observed that FDA already is well-equipped to detect and prevent such health risks in clinical testing. The court stated: "[W]ere a competitor to submit an IND involving a risk known to the FDA because of its experiences with [another company's] INDs, the Agency could and presumably would refuse to permit that company to begin clinical testing."[81] The court further declared, much as FDA had in 1974, that Congress already had weighed the competing interests and had determined that trade secrets and confidential commercial information must not be publicly disclosed.[82]

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[75] 39 Fed. Reg. at 44,614.

[76] *Id.* at 44,636.

[77] *Id.* at 44,633.

[78] *Id.* at 44,634 ("If a manufacturer's safety and effectiveness data are to be released upon request . . . it is entirely possible that the incentive for private pharmaceutical research will be adversely affected.").

[79] *Id.* at 44,614. Congress since has amended this policy by requiring FDA to publicly disclose the "action package" following approval. 21 U.S.C. §355(l)(2). Congress was careful to clarify, however, that FDA is not authorized to disclose "any trade secret, confidential commercial or financial information, or other matter listed in section 552(b) of Title 5, United States Code." *Id.* §355(l)(2)(E).

[80] 39 Fed. Reg. at 44,636.

[81] Public Cit. Health Research Group v. FDA, 185 F.3d 898, 905 (D.C. Cir. 1999).

[82] *Id*. at 904.

Consequently, while some may argue in favor of FDA disclosing manufacturers' trade secrets or confidential commercial information, there are substantial public policy and public health goals served by maintaining confidentiality of such information as it has been defined for decades, including: (1) maintaining incentives for innovative research; (2) ensuring the continued availability of volunteered information; and (3) ensuring the reliability of information that is required to be submitted to the government.

V. Conclusion

As discussed above, PhRMA strongly supports FDA's transparency initiative and looks forward to working with FDA to improve the Agency's communication to the public about the life-saving and life-enhancing products the Agency regulates and the scientific bases for FDA's decisions. At the same time, as a public health agency, it is imperative for FDA to protect incentives for innovators to make the enormous investments that are necessary for the development of new medicines. FDA must therefore continue to protect – as it has done for decades – the confidentiality of information that is considered to be a trade secret or confidential commercial information.

Thank you for your consideration of our comments. If you have any questions, please do not hesitate to contact us.

Respectfully submitted,

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