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August 14, 2014

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

Re: Docket No. FDA-2014-N-0833: Request for Comments on the Food and Drug Administration Fiscal Year 2014-2018 Strategic Priorities Document; 79 Fed. Reg. 126 (July 1, 2014)

Dear Sir or Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) submits the following comments in response to the Food and Drug Administration's (FDA's) draft Strategic Priorities Fiscal Year (FY) 2014 – 2018 document ("Draft Strategic Priorities"). PhRMA hopes that FDA finds these comments useful as the Agency finalizes the Draft Strategic Priorities and plans for the implementation of program-specific actions to support the FDA's core mission goals and objectives.

PhRMA is a voluntary, non-profit association that represents the country's leading innovative biopharmaceutical research and biotechnology companies, which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives. Since 2000, PhRMA member companies have invested approximately $550 billion in the search for new treatments and cures, including an estimated $51.1 billion in 2013 alone.

II. GENERAL COMMENTS

PhRMA supports the Agency's five cross-cutting strategic priorities and four core mission goals and objectives outlined in the Draft Strategic Priorities[1] as they relate to regulated medical products and advancing the public health. Specifically, PhRMA agrees with the FDA's focus on developing and enhancing the following: (1) regulatory science that serves as the foundation for a modern, data-driven regulatory framework that uses new tools, standards, and approaches to increase the efficiency of the drug development and regulatory review process; (2) speed and efficiency of FDA's review of new therapies for patients in need; (3) collaborative communication between FDA and its international counterparts to enhance appropriate sharing of information

[1] *See* Food and Drug Administration Strategic Priorities 2014-2018, Draft for Public Comment (Draft Strategic Priorities), Lines 108-118 at 4-5 (http://www.fda.gov/downloads/aboutfda/reportsmanualsforms/reports/ucm403191.pdf).

(*e.g.,* outcomes of inspections) in light of increased globalization; and (4) accountability and transparency of the FDA's use of resources, including user fees from industry, to support the Agency's activities.

PhRMA agrees that in order for the FDA to fulfill its core mission and achieve the stated strategic objectives, the Agency needs to optimize its ability to recruit and retain top-tier experts. PhRMA supports FDA's proposed use of recruitment and retention flexibilities to ensure the Agency attracts, develops, and retains the best talent and human capital across key functions.[2] In parallel, PhRMA suggests cultivating access to expertise through proactively identifying and materially supporting opportunities for public-private partnerships.

In addition, PhRMA believes that FDA's strategic priorities should recognize the important public health role of biopharmaceutical companies in providing timely, truthful and scientifically accurate medical information about their products to healthcare professionals, and thus their patients. To facilitate communication of such information by manufacturers, PhRMA hopes that FDA will add as a strategic imperative the development of a clear safe harbor setting forth guidelines for communications with healthcare professionals that will be protected from enforcement action (please see the detailed comments below under Goal 3).

Finally, PhRMA recognizes that the effective implementation of the goals outlined in the Draft Strategic Priorities requires the engagement and coordination of Agency staff across FDA functions. This includes strategic alignment between any programs developed and executed in support of the Draft Strategic Priorities and the fulfillment of current Agency commitments (*e.g.*, the regulatory science initiatives associated with the Prescription Drug User Fee Act (PDUFA) V Performance Goals Letter[3] and statutorily mandated in the FDA Safety and Innovation Act (FDASIA)).[4] PhRMA respectfully suggests that the Agency include a signatory page with the names and signatures of FDA senior leadership at the Office- and Center-level, as appropriate, in a final version of the Strategic Priorities document. PhRMA believes that the signatory page would illustrate the collaborative nature of developing the document, and reinforce recognition of the need for integrated efforts to ensure successful fulfillment of the attendant goals.

1. Goal 1: Enhance Oversight of FDA-Regulated Products

PhRMA supports FDA's focus on Globalization as one of the cross-cutting strategic priorities. PhRMA commends the Agency for its engagement with FDA "regulatory counterparts in other nations as well as with industry and regional and international organizations, to encourage the implementation of science-based standards that ensure the safety and quality of products before they reach the United States". PhRMA supports the Agency's efforts to work with its partners "to

[2] *Id,* Lines 919-921 at 34.
[3] *See* The Prescription Drug User Fee Act Reauthorization Performance Goals and Procedures Fiscal Years 2013 through 2017 (PDUFA V Goals Letter), Sec. IX. (www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm270412.pdf).
[4] *See* The Food and Drug Administration Safety and Innovation Act (FDASIA), Pub. L. 112-144, Title IX.

enhance responsibility for and oversight of safety and quality throughout the supply chain."[5] Globalization affects nearly every aspect of the pharmaceutical supply chain, presenting unique challenges at each step of bringing medicines to patients (*e.g.*, sourcing pharmaceutical ingredients and excipients, manufacturing drug products, distributing drugs, safeguarding the availability of drugs).

PhRMA stands ready to work with FDA to ensure that the innovative pharmaceutical industry can continue to meet its commitment of making high quality, safe and effective medicines available to patients. To date, PhRMA has advocated for many of the legislative and regulatory reforms that have expanded FDA's authority to address threats to the integrity and continuity of the pharmaceutical supply chain. Additionally, PhRMA strongly supports FDA's commitment to meeting the challenges of globalization through increasing cooperation with foreign counterparts; leveraging a scientific, risk based approach to its regulatory oversight, and elevating the focus on quality issues through the Office of Pharmaceutical Quality. Below, PhRMA has outlined recommendations for FDA's consideration as the Agency seeks to improve global manufacturing quality and supply chain security:

a. Manufacturing Quality

PhRMA commends the FDA for its commitment to "increase the use of regulatory science to inform standards development, analysis, and decision-making"[6] while "reduc[ing] risks in the manufacturing, production and distribution of FDA regulated products"[7]. Patients and health care professionals rely on medicines that meet appropriately high quality standards – medicines that are safe, effective, have the correct identity, deliver the intended benefits, perform consistently over their labeled shelf-life, and are available when needed.

PhRMA members are committed to ensuring that their products are safe, manufactured according to high quality standards, and secure throughout the global supply chain. To meet today's challenges of global pharmaceutical quality and security, industry and regulators must evolve from relying on traditional, retrospective assessment of sourcing, manufacturing, distribution, and supply to adopt a modern approach that is grounded in science, uses a risk-based assessment framework and is globally harmonized as appropriate.

Regulatory guidelines have emphasized a prospective science and risk-based, "enhanced" approach to development and lifecycle management that could increase the assurance of quality in the manufacture of pharmaceutical products. Collectively, these international guidelines reinforce the adoption of risk–based and science–based approaches to establish an increased level of process understanding and product knowledge that could be translated into a defined design

[5] *Id,* Lines 218-223 at 8.
[6] *Id,* Lines 441-442 at 16.
[7] *Id,* Lines 443-444 at 16.

space and governed by an appropriate control strategy within a robust pharmaceutical quality system.

The adoption, implementation and conveyance of "quality by design" (QbD) in regulatory submissions is intended to increase process understanding and product knowledge and thereby improve the assurance of product quality against variability and through the development and implementation of a robust control strategy. PhRMA believes that by characterizing risks in manufacturing operations and improving understanding of how those risks influence or impact quality attributes of the product, a biopharmaceutical company can more effectively design, develop and manage changes in variables in a manufacturing process to meet pre-defined quality attributes and reliably assure product quality.

Opportunities remain to improve the implementation and application of QbD throughout the product lifecycle (*e.g.,* clarity of regulatory expectations regarding characterization and management of manufacturing risks, clear risk-based Chemistry, Manufacturing, and Controls (CMC) review and inspection activities, post approval change management). PhRMA respectfully urges FDA to continue to work to provide clarity for industry on these issues in order to accelerate progress of QbD implementation.

b. Supply Chain Security

In Goal 1 of the Draft Strategic Priorities, "Enhance Oversight of FDA-Regulated Products," FDA indicates its intent to pursue objectives designed to "strengthen detection and surveillance of problems"[8] and "improve response to identified and emerging problems"[9] with FDA-regulated products. Two recent laws, FDASIA (specifically, Title VII), and the Drug Supply Chain Security Act (DSCSA)[10] give FDA important new authorities to enhance the safety of the drug supply chain. PhRMA and its member companies share FDA's commitment to enhancing the security of the U.S. pharmaceutical supply chain and ensuring that all prescription drugs distributed to patients in this country, regardless of where manufactured, are legitimate and of high quality. Thus, PhRMA is committed to working with FDA and other stakeholders to ensure that provisions of Title VII of FDASIA and DSCSA are successfully enacted. PhRMA has the following specific comments to share on how these laws can best be implemented to address threats to the security of the U.S. supply chain:

Illicit Importation: One of the most significant and growing threats to the legitimate supply chain is the number of counterfeit, misbranded, and adulterated drugs (hereinafter, "violative drugs") entering the U.S., especially via mail shipments from Internet sales. To address this issue, PhRMA was and continues to be supportive of Section 708 of FDASIA which provides the FDA with a

[8] *Id,* Lines 445-446 at 16.
[9] *Id,* Lines 446-447 at 16.
[10] *See* Title II of the Drug Quality and Security Act (DQSA), Pub. L. No. 113-54, 127 Stat. 587 (2013).

critical new power to combat this threat—destruction authority. As FDA repeatedly stated prior to the passage of the Act, absent this new destruction authority "FDA is often forced to return the violative products to their senders" and the products "can then find their way back to U.S. ports of entry several times, wasting critical resources that could be better spent identifying new threats."[11] In addition to finalizing the proposed rule as drafted, PhRMA recommends that FDA conduct further studies to better understand the magnitude of the illicit drug import problem. Accurate data is needed to fully understand the size and scope of the violative drug problem derived from international mail shipments so that Congress can adequately fund the efforts of FDA and other agencies to address the illegal importation of medicines via international mail.

Streamlining and Securing Importation: Beyond question, the task facing FDA in assuring the safety and quality of the millions of finished drug products, active pharmaceutical ingredients (APIs), and other drugs offered for admission to this country each year is daunting — and the volume of foreign-sourced drugs consumed by U.S. patients each year only continues to increase. In recognition of this, FDASIA contains a number of risk-based provisions designed to give the Agency the flexibility to deploy its limited resources for their greatest utility. Sections 713 and 714 of FDASIA in particular, give FDA important authorities to create risk-based requirements for the submission of information for the admission of imported drugs and the registration of importers of commercial products. PhRMA respectfully urges FDA to take full advantage of this flexibility and create a trusted importer program, which would allow FDA to focus its limited resources on those importers and types of drugs that pose the greatest risks to the drug supply chain and would at the same time significantly reduce burdens placed on importers of legitimate, quality drugs. When establishing Good Importer Practices (GIPs), PhRMA urges FDA to distinguish between current good manufacturing practices requirements (cGMPs) and GIPs. FDA should use GIPs to address concerns about physical security and supply chain controls; considerations related to supplier controls should continue to be addressed by cGMPs. Additionally, PhRMA encourages FDA to coordinate its efforts with U.S. Customs and Border Protection (CBP), which would maximize the resources of both agencies and reduce the burdens on regulators and importers alike.

Track and Trace Implementation: The DSCSA creates important "track-and-trace" measures that will help protect the supply chain by detecting and preventing the sale of diverted and counterfeit drugs through legitimate supply channels. PhRMA members are committed to doing their part to secure the legitimate pharmaceutical supply chain and are actively engaged in providing feedback to FDA on the technical aspects of the law's implementation. One of the key challenges of the DSCSA is the ambitious timelines for implementation. To that end, PhRMA urges FDA to issue its guidance regarding standards for the interoperable exchange of information associated with transactions before the statutory deadline of November 27, 2014, given the necessary time needed

[11] *See, e.g.,* Statement of Margaret A. Hamburg, M.D., Commissioner of Food and Drugs, FDA, DHHS, Before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, U.S. House of Representatives, "Import Safety: Status of FDA's Screening Efforts at the Border," (April 13, 2011).

to make adjustments to systems in order to comply with FDA guidance by January 1, 2015. In issuing this initial guidance, PhRMA urges FDA to adopt broad, flexible draft guidance for the interoperable exchange of information for prescription drugs in paper or electronic format. It is important that FDA does not constrain the supply chain with overly prescriptive requirements as to how this information will be exchanged, given the extremely limited time entities have to prepare to meet the law's January 1, 2015 requirements. With regards to draft guidance FDA recently issued, "Guidance for Industry: Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification,"[12] PhRMA strongly encourages FDA to revise this guidance to ensure that FDA's guidelines for identifying suspect and illegitimate product do not cause unintentional and unnecessary disruptions in the supply of lifesaving medicines or result in redundant, over-notification to the Agency, which can drown out or divert attention away from product that is actually problematic.

c. Drug Shortages

PhRMA appreciates FDA's efforts to address the challenge of drug shortages within the U.S. PhRMA is committed to improving patient health and recognizes the importance of avoiding unexpected disruptions in the supply of needed medicines to patients. While shortages affect less than 1 percent of all drugs on the market, and most shortages involve generic medicines, PhRMA and its member companies hope to continue working closely with FDA, supply chain partners, and providers to identify, avoid, and mitigate potential drug shortages.

PhRMA embraces the collaborative approach FDA has taken towards identifying and mitigating drug shortages, particularly the open communication and regulatory flexibility that the Agency has exhibited since the signing of the President's Executive Order 13588, "Reducing Prescription Drug Shortages," in October 2011. We are proud that so many of our members have answered FDA's call and partnered with the Agency to prevent potential drug shortages by keeping FDA apprised of inventory status, sharing commercial intelligence about market supplies, and providing prompt voluntary notifications about API sourcing issues, manufacturing challenges, and increases in demand. As FDA continues to work to address the drug shortage problem, PhRMA suggests that FDA consider the following points:

- In exploring potential ways to mitigate the problem of drug shortages the following strategies should be considered: improved management and planning by manufacturers, incentives for manufacturing compliance, and streamlined/expedited FDA regulatory processes (*e.g.,* expedited FDA review of a CMC supplement).
- With regards to regulatory incentives, FDA should consider incentives that encourage: additional manufacturing capabilities, process enhancements related to productivity, additional sourcing for raw materials and components, improvements with analytical methods for additional reliability, and a solid track record of overall regulatory

[12] 79 Fed. Reg. 33564 (June 11, 2014).

compliance. Any regulatory incentive should be designed carefully—for example, regulatory incentives should never undermine the integrity of the submission or data being reviewed.

- FDA should consider global implications as it considers potential solutions to the drug shortage problem. Manufacturers are operating in a global market, meaning that actions by a foreign regulatory authority can trigger supply chain disruptions in the U.S. In particular, lack of regulatory harmonization regarding cGMPs leads to confusion, making it more difficult for manufacturers to deal with potential compliance risks. FDA should work to harmonize regulatory requirements for good manufacturing practices, improve communication with other regulatory authorities, and increase its inspection/ authorization of more foreign sites to increase global capacity and to help minimize drug shortage issues.

2. Goal 2: Improve and Safeguard Access to FDA-Regulated Products to Benefit Health

a. Regulatory Science

The process of translating biomedical discoveries into new therapies continues to increase in complexity as the underlying science and technologies related to drug development rapidly evolve. Therefore, regulatory decision-makers must have effective tools to keep pace with innovation. PhRMA commends the Agency on its recognition of the need to "increase [FDA's] regulatory science capacity to effectively evaluate products"[13] and also strongly supports the notion that "a core responsibility of FDA is to protect patients and consumers by applying the best available science to [the Agency's] regulatory activities and promoting innovation that addresses unmet medical and public health needs."[14] PhRMA encourages the FDA to find innovative and creative ways to use available scientific methods and data sources to evaluate the benefit-risk balance of new medicines, acting with an urgency that matches the unmet medical need or seriousness of the condition to bring new medicines to patients facing serious and life-threatening conditions.

PhRMA commends the FDA for the promising work of the Medical Device Innovation Consortium (MDIC) to advance regulatory science with the goal of improving the efficiency of bringing innovative devices to patients. PhRMA encourages CDER and CBER to explore ways to learn from the efforts of CDRH and the MDIC and incorporate relevant advancements in regulatory science into the development and review of new medicines. PhRMA notes that CDRH's efforts related to patient-focused drug development and benefit-risk assessment appear to be progressing at markedly greater speed than those efforts at CDER and CBER, and PhRMA

[13] *See* Draft Strategic Priorities, Lines 649-650 at 25 (www.fda.gov/downloads/aboutfda/reportsmanualsforms/reports/ucm403191.pdf).
[14] *Id,* Lines 652-654 at 25.

encourages the Centers to collaborate on these efforts to achieve maximum benefit of the advances in regulatory science.

PhRMA encourages FDA in advancing the use of "product development tools that can help lead to life-improving and life-saving medicines and reduce the time, complexity, and cost of medical product development."[15] As such, PhRMA encourages FDA to allow the appropriate use of data derived from the use of certain medicines in clinical practice (i.e., real-world evidence) in their benefit assessment. Previously, FDA has demonstrated an ability to make important decisions related to medical products (usually safety related) based on real-world evidence. PhRMA encourages the Agency to consider how real-world evidence may contribute to decisions regarding therapeutic benefit. PhRMA encourages the Agency to work with industry, academics, patients and other relevant stakeholders to define situations and contexts where real-world evidence may appropriately supplement, or in some cases replace, randomized controlled trials to form part of the fact base provided by sponsors to the Agency in support of regulatory filings.

b. Product Development Process

PhRMA supports the Agency's focus on improving the effectiveness of the medical product development process, "with the explicit goal of robust development pathways that are efficient and predictable and result in products that are safe, effective, and available to patients."[16] PhRMA believes that improvements in clinical trial participation are critical to enhancing the development process for innovative therapies. As such, PhRMA stands ready to work with the FDA and other key stakeholders to drive transformation of the clinical trial ecosystem. As the Agency considers approaches to improve the efficiency of the drug development process, PhRMA encourages the FDA to promote the consistent acceptance of valid innovative clinical trial designs, (*e.g.,* adaptive and enriched clinical trial designs) within the Agency. PhRMA also commends the Agency for committing to pursue initiatives designed to enhance the development of regulated medical products and PhRMA supports FDA's continued engagement with the Drug Development Tools Qualification Program[17]. PhRMA believes that active Agency and industry participation in such a program is critical to the development and use of innovative drug development tools (*e.g.*, biomarkers, Patient-Reported Outcomes).

PhRMA generally supports the Agency's stated intent to "improve tools and approaches needed to catalyze the development of personalized medicine."[18] However, while recognizing that this is an area of focus for the FDA, PhRMA encourages FDA to gather input as appropriate from key stakeholders, including the broader scientific community within biopharmaceutical companies and in academia, on potential mechanisms to drive the development of personalized medicines.

[15] *Id,* Lines 673-674 at 25.
[16] *Id,* Lines 696-697 at 26.
[17] *Id,* Lines 707-708 at 26.
[18] *Id,* Line 727 at 27.

In addition, PhRMA supports the Agency's focus on advancing the development of medical products for rare diseases, including pediatric rare diseases.[19] PhRMA commends the Agency's ongoing efforts to encourage and facilitate timely pediatric medicinal product development internationally without compromising the well-being of pediatric patients participating in clinical studies. The clinical trials necessary to support pediatric product development are global in nature given the relatively smaller number of pediatric patients who are dispersed over a wider geographic area. PhRMA believes that international regulatory harmonization of drug development for pediatric use would offer many benefits, including: preventing duplication of clinical trials in pediatric patients and minimizing the use of animal testing without compromising safety and effectiveness, enhancing the regulatory assessment process for pediatric proposals and their commitments, and reducing the timeline and resources for development of safe and effective therapeutics for use in pediatrics.

PhRMA would also encourage FDA to foster cooperation with key stakeholders, including the biopharmaceutical industry, academia, professional societies, parents and patient groups, government agencies, and existing networks, to discuss creation of a global pediatric clinical trials network. Such a network could participate in industry- and non-industry-sponsored pediatric studies and would offer multiple advantages and benefits to overcome the challenges in pediatric clinical development (e.g., enrollment challenges).

c. Review Process

PhRMA commends the Agency on its ongoing efforts to "improve the predictability, consistency, transparency, and efficiency of the review process."[20] As agreed to by FDA and Industry in the PDUFA V Goals Letter, the Agency established a new review model for innovative drugs and biologics (i.e., the NME Review Program) with the goal "to improve the efficiency and effectiveness of the first cycle review process and decrease the number of review cycles necessary for approval, ensuring that patients have timely access to safe, effective, and high quality new drugs and biologics."[21] PhRMA supports the NME Review Program and believes it can promote greater regulatory transparency by improving communication between the FDA review team and companies, resulting in improved efficiency and effectiveness during the first cycle of review, and, ultimately, ensuring timely patient access to safe and effective medicines. PhRMA looks forward to the upcoming assessments[22] of the NME Review Program by an independent contractor and believes it would be important to assess the Program's impact on the efficiency and timeliness of the regulatory review process for NME and non-NME applications. In addition, PhRMA believes

[19] *Id,* Line 721 at 26.
[20] *Id,* Lines 733-734 at 28.
[21] *See* PDUFA V Goals Letter, Sec. II. (www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm270412.pdf).
[22] *Id*, Sec. II.B.

that FDA should evaluate potential impacts of the Breakthrough Therapies Program[23] on the human drug review program.

PhRMA fully supports the goal of leveraging technology and data standards to improve the quality and efficiency of the FDA's review of new medicines.[24] PhRMA firmly believes that it is important that the Agency's expectations regarding electronic submissions requirements, particularly those that are costly and time consuming to implement, be clear and predictable.

PhRMA also supports efforts to enhance the consistency and predictability of drug reviews and to improve intra- and inter-Center coordination, as a clear and consistent regulatory pathway is essential to continued innovation. For example, PhRMA recommends that FDA consider processes and timelines for cross-Center coordination of Breakthrough Therapy-designated products where there is product co-development (e.g., CDER/CBER and CDRH coordination on the topic of drug/diagnostic co-development), as well as for development of combination products. FDA should clarify the regulatory pathway and interactions between FDA Centers to facilitate a timely and efficient product review and development pathway.

In addition, PhRMA supports efforts to ensure that medicines addressing unmet medical needs of patients with serious and life-threatening diseases or conditions, including rare diseases, are able to be brought to patients in a timely manner by appropriately balancing the benefits and risks of these therapies, and ensuring timely review of these applications.

PhRMA believes that the FDA drug review process should be grounded in a systematic evaluation and balance of benefits and risks made in the broader context of disease rarity and severity, patient perspectives, and the body of available scientific evidence. PhRMA also believes that as important stakeholders in the drug development and approval process, patients provide a unique and invaluable perspective on the benefits and risks of medicines. Specifically, it is critical for patients, FDA, and sponsors to understand early on patients' views regarding meaningful benefits and the level of risk patients are willing to assume to obtain these benefits. Systematic consideration of the views of patients – especially their perception of the acceptable balance of known and possible risks and benefits – adds crucial perspective when regulators and sponsors are faced with difficult benefit-risk decisions. PhRMA looks forward to ongoing, collaborative discussions with patients and FDA to advance the science of patient-focused drug development and the incorporation of patient perspectives into benefit-risk assessments for regulatory decision-making.

Clearly articulated, consistent, and transparent means of incorporating the patient voice will aid patient-centered drug development. Therefore, it would be helpful for FDA, sponsors, and

[23] *See* FDASIA at Sec. 902.
[24] *See* Draft Strategic Priorities, Lines 770-774 at 28-29 (www.fda.gov/downloads/aboutfda/reportsmanualsforms/reports/ucm403191.pdf).

patients to agree on: 1) appropriate ways to incorporate patient views into drug development plans, 2) the methods by which regulators incorporate patient input into the application review and product labeling processes, and 3) the types and sources of patient perspective data that can best inform drug development and regulatory decision-making. Focusing on these three points of discussion will help stakeholders reach consensus on how best to engage patients and how to best use information from patients to advance drug development and bring new medicines to patients in a timely manner.

3. Goal 3: Promote Better Informed Decisions About the Use of FDA-Regulated Products

In Goal 3 of the Draft Strategic Priorities, FDA "recognizes the invaluable role [it] play[s] in providing the American public with timely, accurate, and useful information about FDA-regulated products."[25] The Draft Strategic Priorities outline three objectives through which FDA proposes that it will help patients, consumers, and professionals make informed decisions about regulated products, improve patient and provider access to benefit-risk information about FDA-regulated products, and improve safety and health information provided to the public.[26]

PhRMA recognizes the importance of FDA's regulatory processes for approving new medicines and new indications for previously approved medicines, and we appreciate the role FDA plays in disseminating information about the products it regulates. At the same time, PhRMA believes that its members also serve an important public health role and advance the interests of patients by providing educational information to healthcare professionals about their medicines. It is critical that healthcare professionals and entities have access to the best available information about the benefits and risks of all available uses of medicines, including those uses that may not be approved by the FDA. Biopharmaceutical companies necessarily collect and retain an extensive amount of clinical data about their products—both before and after approval—in order to satisfy requirements for approval, post-approval safety monitoring, and often to evaluate or develop potential new medical uses. For this reason, manufacturers often may be best source of truthful information regarding their drugs, including unapproved uses of those drugs.[27]

Accordingly, PhRMA urges that FDA's strategic priorities should recognize that healthcare professionals, and thus their patients, can and do benefit from a wide range of timely, truthful, and scientifically accurate medical information from many sources, including biopharmaceutical manufacturers. To facilitate communication of such information by manufacturers, we also hope that FDA will add as a strategic imperative the development of a clear safe harbor setting forth guidelines for communications with healthcare professionals that will be protected from enforcement action. Such a safe harbor would serve the interests of physicians and patients alike,

[25] *Id, Lines 786-787* at 30.
[26] *Id,* at 31-33.
[27] *See* Steven R. Salbu, *Off-label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy*, 51 Fla. L. Rev. 181, 198-99 (1999).

because it would enable biopharmaceutical companies to communicate meaningfully with healthcare professionals about the medicines that companies research, develop, manufacture, and bring to patients. Such safe harbor, and any other appropriate regulation by FDA in this area, should be consistent with the protection afforded such communications under the First Amendment, which serves a particularly critical function "in the fields of medicine and public health, where information can save lives."[28]

PhRMA believes that FDA's strategic priorities and its regulation of medical communications should adhere to principles intended to ensure that healthcare professionals benefit fully from scientifically accurate, data-driven information from all sources, including the companies that research and develop new medicines. Such high level principles, which we encourage FDA to adopt, include the following:

- All communication about medicines (including that of companies, payers, and the government) should be truthful and non-misleading in order to benefit patient care. Materials should be factually correct and should contain material benefit and risk information necessary for trained professionals to make informed treatment decisions.

- To enhance patient care, healthcare professionals deserve access to accurate information about the benefits and risks of all medicines available for treatment. Any limitations on healthcare communications should be grounded in evidence of patient benefits and risks and not limited solely to the approval status of the medicine. It should instead also consider the general medical acceptance of the treatment (*e.g.,* appearance in compendia and/or clinical practice guidelines) and the level of scientific/medical sophistication of the audience.

- Appropriate disclosures regarding risks and the limitations of scientific understanding are preferable to prohibiting communications. Such disclosures can help ensure that medical communications are truthful and not misleading.

- Biopharmaceutical companies respect FDA's authoritative role in determining that medicines are safe and effective. Accordingly, companies recognize the need for incentives for sponsors to continue to seek supplemental indications for approved medicines and will work with FDA to create and maintain such incentives.

- With appropriate disclosures to ensure that the healthcare professional obtains material and balanced information about the evidentiary support for a medicine, companies must be able to provide adequate directions for use of both approved and medically accepted unapproved uses of medicines.

[28] *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2664 (2011).

- The critical role of biopharmaceutical companies in developing pharmacoeconomic analyses and associated communications should be protected via clear guidance and regulations that recognize the sophisticated nature and capabilities of formularies and healthcare institutions, and their need for open dialogue with the biopharmaceutical industry regarding the various uses of pharmaceuticals in the practice of medicine.

As FDA notes in the Draft Strategic Priorities, "clear communication about [FDA's] regulatory and scientific decisions, policies, and standards . . . is vital."[29] PhRMA supports the development of concrete guidance regarding manufacturer communications regarding their medicines and urges FDA to include as an objective in its strategic priorities the drafting of a clear safe harbor to better define the protections that exist for communication of truthful information with healthcare professionals. Doing so will help promote the free flow of scientific communication that can benefit patients through the education of their healthcare professionals, healthcare institutions, and payors.

PhRMA supports FDA's efforts to strengthen social and behavioral science to help patients, consumers, and professionals make informed decisions about regulated products".[30] Specifically, PhRMA encourages the Agency to support advancement of the scientific methods of gathering patient input for use in the drug development and regulatory review processes. Development of methods and recognition of this work as a science will promote deeper and more meaningful understanding of the patient's perspective on the acceptable balance of benefits and risks. PhRMA urges the Agency to pursue these efforts in a coordinated, collaborative manner with participation from CDER, CBER and CDRH.

PhRMA agrees with the Agency that it is important "to improve patient and provider access to benefit-risk information about FDA-regulated products".[31] PhRMA believes that the value of use of a structured approach the benefit-risk assessment is multi-fold, and that improved communication of benefit-risk assessment is only one component. PhRMA firmly believes in the value of use of a structured approach to benefit-risk assessment throughout the lifecycle of a new medicine: from early development to regulatory review to post-market assessment of benefits and risks. PhRMA strongly encourages the FDA to use a structured approach to benefit-risk assessment as the substrate for key discussions between the sponsor and the review division during drug development and regulatory review.

PhRMA would like to understand better FDA's plans for communicating the benefit-risk assessments at key points pre-approval (*e.g.,* to sponsors during various stages of development

[29] *See* Draft Strategic Priorities, Lines 790-791 at 30 (www.fda.gov/downloads/aboutfda/reportsmanualsforms/reports/ucm403191.pdf).
[30] *Id*, Lines 805-806 at 31.
[31] *Id*, Lines 840-841 at 32.

and review) and post-approval (*e.g.,* to the public). In the pre-approval space, PhRMA believes that the benefit-risk framework should become a key component of communication between FDA and the sponsor during critical points in drug development (*e.g.*, End-of-Phase II, pre-NDA/BLA meetings) and in the review process (*e.g.*, late cycle review meetings). PhRMA believes that the opportunity for early and iterative discussions of benefit-risk assessment during drug development and regulatory review between the sponsor and the review division is of great importance. An earlier understanding of the key benefit-risk considerations and areas of concern are critical to improving the quality and efficiency of the process. In the post-approval space, PhRMA recommends that the FDA work with sponsors to develop benefit-risk assessments of approved medicines to aid physicians and patients in their consideration of benefit-risk balance when evaluating treatment options. Biopharmaceutical companies would welcome guidance from the FDA on how to present truthful, non-misleading benefit-risk assessments for use by patients and physicians.

Finally, PhRMA recommends that the Agency consider ways to integrate the conclusions from a structured approach for benefit-risk assessment to improve the scientific basis of REMS programs and the need for post-marketing requirements / post-marketing commitments.

4. Goal 4: Strengthen Organizational Excellence and Accountability

PhRMA commends FDA on its progress against the goals related to implementation of PDUFA and FDASIA, while operating in challenging fiscal times. PhRMA supports the Agency's focus on Stewardship as one of the cross-cutting strategic priorities and establishing "operational excellence and accountability objectives to align resource planning, allocation, and management with [FDA] strategic priorities to better ensure timely delivery of high-quality services that are critical to fulfilling FDA's mission." [32] PhRMA also commends FDA for working on "developing performance metrics that align with program requirements and cross-cutting priorities to measure progress in achieving strategic goals." [33]

Specifically, PhRMA agrees with the Agency on "the importance of being a good steward of resources – both taxpayer dollars and user fees from industry – to achieve [FDA's] mission. As [FDA] responsibilities increase and resources remain limited, it is even more vital for FDA to maintain organizational excellence and accountability to the American public."[34]

The PDUFA program has helped patients since 1992 by providing FDA with stable, consistent funding – intended to supplement Congressional appropriations – thus helping to support timely patient access to new medicines while strengthening FDA's existing high safety and efficacy standards. Accordingly, PhRMA strongly supports the PDUFA program. PDUFA V user fees

[32] *Id.* Lines 384-386 at 14.
[33] *Id*. Lines 394-395 at 14.
[34] *Id*. Lines 913-916 at 34.

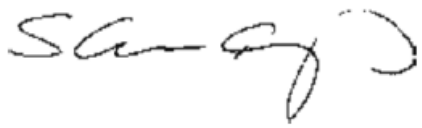
support a new system-wide approach to regulatory science that embraces the scientific tools used in 21st-century drug development for the benefit of patients. As the PDUFA program continues to grow, PhRMA believes that increasing financial transparency and accountability of FDA user fee spending under PDUFA becomes even more critical. Specifically, PhRMA believes that timely financial reporting, including comprehensive information on PDUFA collections, expenditures, and carryover balances, is essential to support the credibility of the PDUFA program and ensure transparency and accountability of FDA spending under PDUFA.

Now that sequestered FY 2013 PDUFA user fees have been restored[35] in support of activities consistent with the PDUFA V Goals Letter,[36] including activities that were negatively impacted by the sequester, such as regulatory science initiatives and the hiring of new staff, we urge FDA to provide a review of spending of the restored FY 2013 PDUFA user fees in the FY 2014 PDUFA financial report.

III. CONCLUSION

In summary, PhRMA commends the Agency for releasing the Draft Strategic Priorities 2014-2018 document for public comment. PhRMA believes that the final Strategic Priorities 2014-2018 document would allow the FDA to fulfill its core mission and address 21st-century public health challenges, while aligning with ongoing Agency programs and initiatives. We look forward to a continued dialogue and collaboration with FDA on issues related to the implementation of specific core mission goals and objectives, including those critical to the drug development and regulatory review processes.

Respectfully submitted,



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[35] The FY 2014 omnibus appropriations package restored nearly $40 million in sequestered FY 2013 PDUFA user fees with additional appropriated resources. Additionally, the Budget Act of 2013 provided sequester relief for PDUFA user fees for FY 2014 and FY 2015.

[36] *See* PDUFA V Goals Letter (www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm270412.pdf).