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Anna K. Abram,
Deputy Commissioner for Policy, Planning, Legislation, and Analysis
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

RE: Review of Existing General Regulatory and Information Collection Requirements of the Food and Drug Administration [FDA–2017–N–5093]

Dear Deputy Commissioner Abram,

The American College of Cardiology (ACC) is pleased to submit comments to the Food and Drug Administration (FDA) on its Review of Existing General Regulatory and Information Collection Requirements. The ACC is a 52,000-member medical society that is the professional home for the entire cardiovascular care team. The mission of the College is to transform cardiovascular care and improve heart health. The ACC leads in the formation of health policy, standards and guidelines. The College operates national registries to measure and improve care, provides professional medical education, promotes cardiovascular research and bestows credentials on cardiovascular specialists who meet stringent qualifications. The College appreciates the ability to provide comments to the FDA on its efforts to reduce the regulatory burden while continuing to achieve its public health mission and fulfill statutory obligations.

On a daily basis, cardiovascular professionals rely on medical therapies approved by the FDA to furnish high quality care to patients. There have been impressive strides made in cardiovascular care that could not have occurred without the assistance of medical devices, both therapeutic and diagnostic. The FDA has played a crucial role in bringing these new therapies to market. Critical to continuing the decline in deaths from cardiovascular disease are innovations in care and treatments for those conditions. At the same time, it is equally important that the FDA protect the public health. The mission of the FDA requires the government to strike a balance between protecting the public health and encouraging creativity and scientific advancement.

As the FDA assesses current regulations, it is important for the FDA to balance the reduction of regulatory burdens that inflate the cost and time associated with the development of new therapies with the need for regulatory decisions that protect patient interests and public health through rigorous scientific merit.

To help guide future regulatory reduction efforts, the ACC has developed a set of 11 overarching principles intended to serve as a guide to evaluate future regulatory efforts. As the FDA works to reduce unnecessary regulatory burdens, the FDA should:

- Ensure regulatory decisions are patient-centered and based on scientific merit
- Protect public health while fostering innovation
- Reduce the costs of new therapies and regulatory review through increased harmonization of regulations across federal agencies, as well as standardization of best practices and data collection internationally
- Encourage the use of standardized, accurate, and reusable data sources, such as the National Cardiovascular Data Registry® (NCDR®) and other clinical data registries, to improve patient outcomes, increase access to valuable clinical data, and reduce regulatory costs
- Allow for flexibility in regulatory decision-making processes to accommodate the potential for rapid therapeutic advancements
- Provide patients with access to novel therapies while maintaining the high standard for safety and effectiveness
- Take steps to ensure data used for regulatory decision making is representative of the affected patient population, as well as to communicate the availability of data on the effects of therapies on demographic subpopulations
- Encourage development of medical therapies designed for historically underrepresented patient populations
- Regularly monitor the impact of decisions to minimize adverse effects on drug supply
- Collaborate with other federal agencies to monitor the landscape affecting drug pricing and supply and address concerns
- Strengthen relationships with professional medical societies, public, private and academic partners, and other stakeholders to further the field of regulatory science through regular consultation and communication

Ensure regulatory decisions are patient-centered and based on scientific merit

As the Administration undertakes efforts to reduce regulations and control regulatory costs, it is vital that the FDA ensures that any decisions to deregulate do not adversely affect patients and are scientifically sound. According to the FDA's mission, it "is responsible for advancing the public health by helping to speed innovations that make medical products more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medical products and foods to maintain and improve their health." The College continues to support the FDA in this mission and believes it is vital to the continued well-being of patients and the public that the FDA take an active role in ensuring the

public is adequately protected as new therapies come to market. Reductions in regulatory burdens and costs should not come at the expense of patient safety or the effectiveness of the drugs and devices they rely upon for safe, effective care.

Protect public health while fostering innovation

The College cautions the FDA to avoid removing regulations that protect the public health. Instead, the FDA should take this opportunity to review and streamline existing processes to better improve public health protections while still allowing adequate flexibility to foster innovation. One example of an area the FDA could progress is the collection, monitoring and dissemination of adverse event reports. The FDA should review the adverse event tracking systems such as FDA Adverse Event Reporting System (FAERS) and MedWatch for methods of decreasing the burden for reporting an adverse event to a drug company and the FDA.

The College also cautions the FDA against inappropriate deregulation of tobacco products because of profit or business concerns; rather, any determinations to decrease regulation of tobacco products should be based on scientifically sound rationale and an interest in fulfilling the Agency's mission to protect the public. As the harmful health effects of smoking have become increasingly evident over the past 50 years, more focus has been placed on the role of the government in addressing those effects. In order to reduce the prevalence of cigarette smoking and associated health problems such as heart disease, the FDA must take appropriate measures to educate and warn consumers about the negative effects. During the recent announcement of the Agency's initiative centered around nicotine and harm reduction, Commissioner Gottlieb described the new mission to balance regulation with innovation. The College appreciates the FDA's willingness to encourage innovative developments that may render delivery mechanisms less harmful to users. However, the College believes that it is essential that the Agency implement this agenda with public health as the highest priority.

Reduce the costs of new therapies and regulatory review through increased harmonization of regulations across federal agencies, as well as standardization of best practices and data collection internationally

The College appreciates the Administration's commitment to reducing administrative burdens. At times, regulatory barriers may contribute to the increasing cost of research and development of new therapies. Because of these burdens, companies may delay initiating clinical trials in the US until well after they have been launched in Europe and elsewhere, impeding patient access to critical novel clinical therapies. The FDA should take this opportunity to consider existing regulatory requirements that unnecessarily increase the costs of conducting clinical trials and introducing new products to market in the US, particularly those that cross multiple federal agencies. Additionally, the Agency should consider international regulations and identify opportunities to better harmonize regulations, best practices, and approval processes to help reduce the burden for bringing new, innovative therapies to market. The development of reciprocity agreements or fast-track processes for therapies developed in countries whose regulatory infrastructure and approval processes mirror those in the United States may expedite the development of innovative therapies and reduce the regulatory costs and burdens. The participation of the United States in the

International Medical Device Regulators Forum, the International Pharmaceutical Regulators Forum, and other similar efforts is critical to these efforts.

Encourage the use of standardized, accurate, and reusable data sources, the National Cardiovascular Data Registry® (NCDR®) and other clinical data registries, to improve patient outcomes, increase access to valuable clinical data, and reduce regulatory costs

Recent efforts, including provisions in the 21st Century Cures Act, have promoted the use of real world data and real-world evidence to bolster regulatory decision making and the College encourages the FDA to utilize cost effective, reusable sources of data such as the ACC's National Cardiovascular Registry® (NCDR®) to supplement traditional sources of data. Additionally, utilizing data sources with standardized terminology such as registries can allow the FDA to monitor outcomes of devices and therapies, decreasing the time that it takes for new devices to get approved. By doing so, the FDA can work to improve patient outcomes, increase access to valuable clinical data, and reduce regulatory costs.

The College has extensive experience with clinical data registries and believes they have an important role to play in improving patient outcomes and reducing regulatory costs and burdens. In 1997 the ACC launched the NCDR as a result of its exploration of various strategies for collecting and utilizing clinical data to improve cardiovascular care. The outgrowth of that effort focused on improving patient care through standardized measurements for clinical practice and patient outcomes. NCDR is committed to including clinicians in its leadership and to using standardized, clinically relevant data elements and scientifically appropriate methods to collect, analyze and report outcomes.

Today, more than 2,200 hospitals and over 3,000 clinicians nationwide participate in the NCDR, resulting in the accumulation of close to 60 million patient records. As the preeminent cardiovascular data repository in the US, the NCDR provides evidence-based quality improvement solutions to cardiologists and other medical professionals who are committed to measurement, improvement and excellence in cardiovascular care. NCDR data have been studied for a variety of purposes, including consistency with guidelines,[1] appropriateness,[2] and comparative effectiveness,[3] to name a few. The FDA has long been a supporter of NCDR, providing funding for the Improving Pediatric and Adult Congenital Treatment (IMPACT) Registry and development of an atrial fibrillation registry. NCDR is also a participant in the FDA's Sentinel Initiative, looking at methods of utilizing registry data to provide information on potential safety signals to the FDA.

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[1] Chan PS, Patel MR, Klein LW, et al. Appropriateness of Percutaneous Coronary Intervention. JAMA 2011; 306(1):53-61.

[2] Al-Khatib SM, Hellcamp A, Curtis J, et al. Non-evidence-based ICD implantations in the United States. JAMA 2011; 305(1):43-49.

[3] Funded by a National Heart, Lung, and Blood Institute American Recovery and Reinvestment Act Grant, the ASCERT Study represents a unique collaboration between the ACC Foundation and the Society of Thoracic Surgeons (STS) to study the comparative effectiveness of percutaneous coronary intervention and coronary artery bypass graft surgery in patients with stable ischemic heart disease.

More recently, the College has collaborated with The Society of Thoracic Surgeons (STS) and the FDA to develop the STS/ACC Transcatheter Valve Therapy (TVT) Registry™ for use not only as a vehicle for quality improvement, but also to allow for post-approval studies of novel technologies and ongoing post-market surveillance. Various stakeholders, including the FDA, the National Heart, Lung and Blood Institute, industry and the public, advise the College on the appropriateness of ongoing activities within the TVT Registry.

Allow for flexibility in regulatory decision-making processes to accommodate the potential for rapid therapeutic advancements

Due to the rapid rate of therapeutic advancements, it is necessary for the regulatory structure of the FDA and other agencies to be able to accommodate these rapid developments. Technological innovations, such as software applications for mobile phones functioning as medical devices, require that the FDA review existing regulatory approval processes to keep up with rapid advancements without hampering innovations through a drawn-out regulatory process. The FDA should ensure decisions to reduce the regulatory burden provide the necessary flexibility in regulatory decision-making processes and allow for the potential for rapid therapeutic advancements.

Provide patients with access to novel therapies while maintaining the high standard for safety and effectiveness

While regulatory flexibility is necessary to continue to spur the development of novel therapies, it is pivotal that the FDA maintain a necessary high standard for safety and effectiveness through efficient, streamlined pre-market approval processes and continued post-market surveillance. Refining both the pre-and post-market processes will allow the FDA to review proposed therapies as they come to market, testing their effectiveness while providing important access to patients without needless delays.

However, the desire to bring these therapies to market more quickly must not sacrifice patient safety in the name of regulatory burden reduction. It is essential that the FDA strike the proper balance for an efficient approval process that provides necessary access to therapies while continuing to enforce the necessary high standard for safety and effectiveness.

Take steps to ensure data used for regulatory decision making is representative of the affected patient population, as well as to communicate the availability of data on the effects of therapies on demographic subpopulations

In January 2016, former FDA Commissioner Robert M. Califf, M.D. announced that increasing diversity in clinical trials would be a priority for FDA. Far too often, the patient populations that participate in clinical trials differ from those who rely on these therapies in the real world. Dr. Califf stated, "[H]istorically, the elderly, women (in some therapeutic areas), and racial/ethnic minorities have been underrepresented in trials. A substantial body of literature has documented this under-representation in recent years, particularly for women in some cardiovascular trials and general inclusion of black/African-American and minority

participants in clinical trials."[4] In addition to underrepresented gender/racial/ethnic minorities, data collected from patients as part of clinical trials often do not capture the complex medical conditions of patients, who often suffer from multiple comorbidities. As the FDA seeks to streamline regulations, the College encourages the FDA and other agencies to ensure doing so does not adversely affect efforts to increase diversity of clinical trial participants. In fact, a review of existing regulations may provide the FDA with an opportunity to further emphasize the importance of data collected from affected patient populations and effectively communicate the availability of data on the effects of therapies on demographic subpopulations.

Encourage development of medical therapies designed for historically underrepresented patient population

In addition to increasing the collection of data from historically underrepresented patient populations, the FDA should encourage the use of this data to lead to the development of therapies for these populations. Pediatric populations, patients suffering from multiple comorbidities, racial and ethnic minorities with diseases specific to these populations, and elderly populations all would benefit from the development of specific medical therapies designed to deal with and treat their unique circumstances. By further streamlining the regulatory process, the FDA can encourage the development of medical therapies to effectively treat these and other often complex patient populations, decreasing the cost of care while improving outcomes.

Regularly monitor the impact of decisions to minimize adverse effects on drug supply

Recent events have shown the importance of a stable drug supply in the United States. Earlier this year, cardiologists have reported increasing concerns related to ongoing shortages of epinephrine, sodium bicarbonate and dextrose. To address the shortage of sodium bicarbonate, the FDA has approved importation of the drug from an Australian supplier for as long as is necessary. While the College appreciates the flexibility shown by the FDA to ensure patients have access to an adequate supply of necessary drugs, this and other recent examples show how easily events can disrupt the drug supply, and more importantly, patient care. The College cautions the FDA against taking regulatory actions without considering the potential effects on the drug supply, working to minimize any disruptions, and ensuring patients have timely access to necessary drugs.

Collaborate with other federal agencies to monitor the landscape affecting drug pricing and supply and address concerns

The FDA should coordinate with the Centers for Medicare & Medicaid Services and other relevant federal agencies to streamline review processes and coordinate to ensure decisions take into consideration drug pricing and supply concerns. While the increasing cost of drugs is not the FDA's highest priority, it can work with other federal agencies to modernize regulatory processes for the development of innovative drugs, including bringing new generics to market,

[4] https://blogs.fda.gov/fdavoice/index.php/2016/01/2016-the-year-of-diversity-in-clinical-trials/

to help address pricing and supply concerns. The College strongly believes that cost should not prevent patients from gaining access to essential drugs, and by working with other agencies to monitor the landscape affecting drug pricing and supply, the FDA can do its part to help address drug pricing and supply concerns.

Strengthen relationships with professional medical societies as well as public, private and academic partners and other stakeholders to further the field of regulatory science through regular consultation and communication

Assistance and expertise from medical specialty societies, public/private partnerships, academic institutions, and other stakeholders represent a significant resource available to the FDA and other agencies. They can provide the government with important information to further the field of regulatory science, reduce the burdens facing practitioners and therapeutic manufacturers, and protect public health interests while continuing to foster innovation through the healthcare system. It is vital for the FDA to work closely with stakeholders, regularly consulting and communicating with experts early in the regulatory process. By doing so, both the FDA and stakeholders will benefit from an improved exchange of information, reduced miscommunication, and increased productivity.

Conclusion

The ACC thanks the FDA for allowing it to provide comments on existing general regulatory and information collection requirements and appreciates the efforts of the FDA and other agencies to help reduce administrative and regulatory burdens that affect the patients' timely access to new therapies. The College looks forward to continuing to work with the FDA as the Agency moves forward with this process. To address these comments or additional questions, please contact Joseph Cody, Associate Director, Research and Innovation Policy, at jcody@acc.org.

Thank you,

Mary Norine Walsh, MD, FACC
President