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U.S. Senate Committee on Health Education Labor & Pensions
and
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On the Food and Drug Administration Reauthorization Act of 2022 (FDARA)

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The Association for Clinical Oncology (ASCO) is pleased to have the opportunity to offer comments on the *Food and Drug Administration Reauthorization Act of 2022* (FDARA), the legislation to reauthorize the Food and Drug Administration's (FDA) industry user fee authorizations (UFA). We appreciate the significance of the FDARA and have compiled the list below of ASCO policies that we hope you consider in addition to the reauthorization of the UFAs as the debate of the FDARA continues.

ASCO is the world's leading professional society representing physicians who care for people with cancer. With nearly 45,000 members, our core mission is to ensure that cancer patients have meaningful access to high quality cancer care.

We applaud your commitment to moving FDARA in a timely manner to continue this progress and prevent any disruption in the approval of safe and effective therapies for patients by the FDA.

Increasing Diversity in and Access to Clinical Trials

As cancer care becomes more complex and personalized, the research through which new advances are developed must include diverse representation of participants. ASCO believes that all populations should have an equal opportunity to participate in, be recognized for, and benefit from research across the spectrum, including clinical trials. However, due to a variety of barriers, many patient populations continue to be underrepresented in clinical trials and health care-related research.

ASCO has long supported policies that would increase access to clinical trials to historically underrepresented populations. The *21st Century Cures 2.0* (H.R. 6000) legislation introduced last year contains several provisions that would foster inclusion in biomedical research trials. ASCO responded to the legislation, supporting specific provisions that would require: an update from the FDA on efforts to improve diversity in trials, a GAO study on barriers to clinical trial participation, a public awareness campaign by the Department of Health and Human Services (HHS) to increase awareness and understanding, particularly in minority communities, of clinical trials and a task force on making clinicaltrials.gov more user- and patient-friendly.

In addition to the provisions in *Cures 2.0*, ASCO strongly supports passage of the *Diversifying Investigations Via Equitable Research Studies for Everyone (DIVERSE) Trials Act* (H.R. 5030/S. 2706) and urge you to prioritize this bill for enactment into law this year. The *DIVERSE Trials Act* would make it easier for all patients to participate in clinical trials while removing barriers that are known to keep certain racial and ethnic groups, older adults, rural residents, and those with limited incomes from being appropriately represented.

The three provisions of the *DIVERSE Trials Act* will result in more efficient, inclusive, and accessible research, which will benefit the health of all Americans. First, the legislation would permit individuals to receive financial support for the non-medical costs associated with their participation in clinical trials, by creating a statutory safe harbor for clinical trial sponsors to use in reimbursing such costs. Second, the bill would allow trial sponsors to provide individuals with the technology necessary for them to participate remotely in clinical trials. This commonsense approach addresses the issue that clinical trial participants almost always need to report their condition, symptoms, side effects, or other data on a regular basis and/or to have certain health indicators monitored by web-enabled technology. Finally, the legislation would require the Department of HHS to issue guidance on decentralized clinical trials. While the COVID-19 pandemic accelerated the need for patients to have clinical trials available to them at or close to home, researchers have long endeavored to make clinical trials more convenient in order to attract participants. The decentralized approach could open the door to clinical trials for a much broader array of participants, such as those who live hours from a trial site or do not have the ability to make repeated visits to the trial site due to work or caregiving schedules.

ASCO has also endorsed the *Diverse and Equitable Participation in Clinical Trials (DEPICT) Act,* legislation aimed at boosting diversity in clinical trials by requiring enhanced data reporting on clinical trial demographics and providing resources to improve access to clinical trials. Specifically, the bill requires Investigational New Drug (IND) and Investigational Device Exemption (IDE) applicants to report clinical trial enrollment targets by demographic subgroup, including age, race, ethnicity, and sex, and provide a rationale for those targets in addition to providing a Diversity Action Plan detailing the actions the sponsor will take, such as outreach and engagement strategies, to reach these enrollment targets. Additionally, the legislation would provide the FDA with the authority to mandate post-market studies when sponsors fail to meet diversity enrollment targets and do not provide a sufficient justification, and finally requires FDA to publish an annual report aggregating and analyzing the data provided by sponsors on their progress toward and strategies for improving diversity in clinical trials.

ASCO also appreciates the regulatory changes and flexibilities the Administration has allowed within federal agencies, particularly the FDA, the National Institutes of Health (NIH), and the National Cancer Institute (NCI) during the COVID-19 pandemic. The pandemic necessitated changes in clinical trial operations to mitigate disruptions in both care and research. Several of these changes proved successful and have now led to establishment of less cumbersome processes for patients and researchers. We believe there is an opportunity to learn from and build upon these design changes.

The agencies stepped in quickly to provide flexibilities that helped sites to safely maintain participants' access to study therapies, scans, and laboratory assessments – particularly allowing use of telehealth and remote clinics, scans, and labs. ASCO has urged extension of those flexibilities so trial participants can continue to access these patient-centered options even after the pandemic ends. As noted above, we support increasing patient access to clinical trials through models such as decentralization of trials and electronic consent to ensure required signatures and remote recruiting. COVID-19 caused trial

modifications such as remote assessments to be successfully deployed in the middle of large ongoing cancer trials. As mentioned, decentralized trials have the potential to reduce patient and sponsor burden and increase accrual and retention of a more diverse trial population, while at the same time reducing exposure to COVID-19 for vulnerable patient populations. ASCO is eager to work with Congress and the Administration to increase the use of decentralized clinical trial designs.

ASCO has also published a statement devoted to making clinical trials more representative by refining eligibility criteria. It is vitally important that patient access to clinical trials be broadened with the use of science-based, clinically relevant eligibility criteria. ASCO continues to work with the FDA and other stakeholders to implement these recommendations.

Expanding Access to and the Use of Real-World Evidence

Advances in health information technologies and a dramatic increase in the adoption of electronic health records (EHRs) have created new opportunities for streamlining clinical evidence through collection of real-world data (RWD). Data collection that captures demographic characteristics including race/ethnicity, sexual orientation, gender identity, socioeconomic status, age, stage of disease, comorbidities, etc. helps reduce health disparities by ensuring all patient populations are included in the development in treatments. Sources of RWD include electronic health records, insurance claims, patient registries, and digital health solutions outside of conventional clinical trials. Additionally, RWD has a largely untapped potential to supplement clinical trial data and improve external validity—and establish real-world effectiveness and toxicity, especially in oncology.

The *21st Century Cures Act* in 2016 tasked the FDA with implementing several provisions, including the Real-World Evidence (RWE) Program and Draft Guidance. This provision requires the FDA to publish draft guidance on how RWE can contribute to the assessment of safety and effectiveness in regulatory submissions and requires the FDA to explore the use of RWE for additional indications of approved drugs and post-approved study requirements. Additionally, the FDA is working with the NCI on data sharing and data aggregation. These provisions will have implications for ASCO's clinical trial, the Targeted Agent and Profiling Utilization Registry (TAPUR), and data registry, CancerLinQ.

We appreciate this guidance beginning with acknowledging the important challenges involved in standardizing data derived from RWD sources. The lack of data standards presents a problem even beyond the contemplation of their use in the RWE regulatory framework. This is especially true in specialty fields such as oncology.

Several provisions within the *21st Century Cures 2.0* legislation would increase the ability to collect and utilize RWE. The bill would require drug manufacturers/sponsors to collect and report on patient experience data as part of the clinical trial; require the FDA to fully consider all patient experience data collected during the clinical trial; and require reporting of patient experience data in a transparent manner that is uniform, meaningful and informative to patients and providers. The bill would build on FDA's efforts by requiring HHS to outline approaches to maximize and expand the use of RWE; and establishing a task force to develop recommendations on ways to encourage patients to engage in real-world data generation. Additionally, *Cures 2.0* would require the HHS to submit a report to Congress on the efforts to ensure collaboration and alignment across the centers and offices of the FDA with respect to the regulation of digital health technologies

ASCO has also endorsed the *Meaningful Access to Federal Health Plan Claims Data Act* (H.R. 5394). This policy provides clinician-led clinical data registries with access to Medicare claims data for purposes of research to improve quality and cost efficiency by linking the data with clinical data in registries, a necessary step towards ensuring providers have access to the full spectrum of relevant data.

ASCO urges the Committees to prioritize these provisions to allow our healthcare continuum to continue building on the use of RWE and RWD as a way to reduce healthcare disparities.

Ensuring Patients Access to Life-Saving Therapies

ASCO has long supported the accelerated approval and complementary expedited review programs, which provide patients with the earliest possible access to potentially life-saving therapies, instead of requiring them to wait for confirmation of long-term endpoints, such as survival. Specifically, the Accelerated Approval Program allows for earlier approval of drugs that treat serious conditions, and that fill an unmet medical need based on a surrogate endpoint that demonstrates drug value and an improvement in patient outcomes. The benefit of the program is that life-saving drugs reach patients faster, however many worry that the earlier a treatment is available to patients, the less safety information exists about a particular drug and the harder it may be to complete the confirmatory trials when a patient can receive the drug by prescription.

To mitigate the risks, the FDA uses the same standards to approve treatments via accelerated approval as they would via a traditional pathway; drugs must demonstrate substantial evidence of safety and that the "drug is safe for use under conditions prescribed, recommended or suggested in the proposed labeling" and must meet the standard for effectiveness, which requires substantial evidence based on "adequate and well controlled clinical investigations." Sponsors must also agree to conduct a post-marketing confirmatory study or studies to verify and describe the relationship between the endpoint and the expected clinical benefit following a drugs approval via the accelerated approval pathway. Additionally, as part of its review, the FDA considers the overall risk and benefit of approving, rejecting, or waiting to approve the drug. This evaluation considers the risk for patients who lack access to effective treatments.

The Accelerated Approval Program has been vital for cancer treatment development. Between 2010 to 2020, 85% of accelerated approvals were for oncology indications. While survival is always the end-goal, there are many ways to evaluate benefit of a drug to the patient and their quality of life, including reduction of the size of the tumor, delay in the progression of the disease, and the establishment of complete response rates in hematological diseases. Our understanding of cancer and its treatment is changing every day. Our regulatory systems must adapt in ways that meet a rapidly evolving science, deliver cutting edge treatments to patients, and balance safety with risk.

Despite the relative success of the program, the FDA could benefit from additional tools and flexibilities to advance this pathway with the growing need to ensure the completion of confirmatory trials. Currently, there are two bills that would assist the FDA in improving its ability to utilize the accelerated approval pathway. The *Accelerated Approval Integrity Act* (H.R. 6963) and the *Accelerating Access for Patients Act* (H.R. 6996) would both provide FDA with additional authority to ensure products that receive accelerated approval are providing a clinical benefit to patients in a timely manner.

Reforming Federal Oversight of Laboratory Developed Tests

In August 2020, the Trump Administration issued an order barring FDA from requiring premarket review for any laboratory developed tests (LDTs) unless the agency goes through formal rulemaking procedures. This action has created considerable uncertainty for clinical laboratories creating diagnostic tests and the Biden Administration has not yet rescinded the order.

ASCO calls on Congress to work with stakeholders and the FDA to provide clear guidelines for the review and approval process of LDTs. Specifically, ASCO is supportive of the bipartisan *Verifying Accurate Leading-edge IVCT Development (VALID) Act* (H.R. 4128/S. 2209), which would create a distinct regulatory framework for in vitro diagnostics and LDTs, known collectively in the draft legislation as in vitro clinical tests (IVCTs).

The framework features a tiered, risk-based system for the regulation of IVCTs. As already happens with medical devices, FDA would typically subject high-risk IVCTs to a preapproval review but low-risk diagnostics would be able to come to market after listing with the agency. The framework features a middle tier of IVCTs that would need to obtain approval but without meeting the same requirements as high-risk diagnostics. Other provisions include the creation of a breakthrough designation.

We believe that reforming the regulatory framework for clinical laboratory diagnostics is essential to protect patients and ensure access to innovative and high-quality testing. The ongoing COVID-19 pandemic has only underscored the importance of reliable testing and reinforced the need for a uniform regulatory framework that consistently holds all clinical tests to the same risk-based standards.

However, the current system of oversight is inadequate, having failed to keep pace with changes in the testing industry and to match regulatory requirements with the risk that certain tests pose to public health. ASCO encourages these Committees to prioritize diagnostics reform, taking into consideration the significant work that has been done thus far in the development of the *VALID Act.* Though more must be done to ensure regulators have access to the information and tools needed to ensure that flawed tests do not reach vulnerable patients, the *VALID Act* represents the most comprehensive reform effort to date and reflects years of negotiation and compromise among industry and stakeholder groups.

Addressing Critical Manufacturing and Supply Chain Inadequacies

Over the last several years, natural disasters, quality problems, manufacturer consolidation, disruptions to raw ingredient supplies, and other emergencies that take place in countries which house critical drug manufacturing facilities have left the U.S. healthcare system on the brink of a significant public health crisis multiple times. The COVID-19 public health emergency further underscored the vulnerability of our nation's healthcare supply chain. During the pandemic, healthcare providers struggled to obtain medications and supplies essential to patient care, including the sedatives necessary to mechanically ventilate patients, personal protective equipment (PPE) such as gloves and masks, and ancillary devices and supplies, such as syringes and swabs. The pandemic stress-tested our supply chains, highlighting their fragilities and deficiencies, throwing the need for immediate corrective action into sharp relief.

The FDA is instrumental in helping to mitigate the effect of drug shortages. To help prevent and overcome drug shortages, the FDA uses tools such as expedited facility inspection, expedited new and/or generic drug applications, and the exercise of discretion with respect to the temporary importation of products from foreign manufacturing sources. The agency may also urge manufacturers

to increase production in specific situations to meet anticipated increases in demand. In response to the COVID-19 pandemic, Congress increased FDA authority to identify, prevent, and mitigate possible drug shortages by, among other things, enhancing FDA's visibility into drug supply chains. These authorities were included in the *Coronavirus Aid, Relief, and Economic Security (CARES) Act.* ASCO supported these measures, but as noted, more permanent authority is necessary to combat future shortages and disruptions to our supply chain.

We encourage Congress to take the following actions:

- Require manufacturers to be more transparent with the FDA about potential drug shortages
- Require manufacturer transparency around their sources of raw material (active pharmaceutical ingredients, API) including which state and country the API come from
- Require manufacturers of critical medications and supplies to develop a reasonable contingency plan in the event of a production interruption or shut down
- Create requirements for supply chain resiliency, including multiple manufacturing sites for important drugs and multiple suppliers of API for the same drug
- Create incentives for manufacturers to increase production when drug shortages occur

Specifically, ASCO has endorsed the *Pharmaceutical Accountability, Responsibility, and Transparency (PART) Act* and the *Help Onshore Manufacturing Efficiencies for Drugs and Devices (HOME) Act* – yet to be reintroduced in the 117th Congress. The *PART Act* would expand reporting requirements for manufacturers and require quarterly disclosures to the FDA on critical manufacturing data such as which medications and what in amount – including active pharmaceutical ingredients – are produced domestically and abroad. The *HOME Act* would help reduce U.S. reliance on foreign sources for critical drugs and medical supplies and ramp up American manufacturing capacity.

Both the *PART Act* and the *HOME Act* take important steps in solving the complex issues that create drug shortages in the United States and put safeguards in place to ensure that future shortages are limited. It is ASCO's hope that with the safety and transparency requirements offered in these bills, we will be one step closer to creating a strong, stable pharmaceutical manufacturing pipeline to ensure U.S. health care security and pharmaceutical access for all patients with cancer.

ASCO has also provided comments on the draft legislative package, the *Prepare for and Respond to Existing Viruses, Emerging New Threats, and Pandemics Act (PREVENT Pandemics Act*), supporting the important provisions included to strengthen the medical products supply chain and mitigate future drug shortages.

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Thank you for the opportunity to provide these additional ideas as you work to renew the FDA industry user fee authorizations. We look forward to working further with you and your staff as this process moves forward. Please contact Kristin Stuart at Kristin.Stuart@asco.org with any questions.