Senator Patty Murray
Chair, Senate HELP Committee
428 Senate Dirksen Office Building
Washington, DC 20510

Senator Richard Burr
Ranking Member, Senate HELP Committee
428 Senate Dirksen Office Building
Washington, DC 20510

May 20, 2022

Dear Chair Murray and Ranking Member Burr,

Thank you for your efforts in drafting the *Food and Drug Administration Safety and Landmark Advancements Act of 2022,* which includes important provisions that bolster the agency's ability to ensure the safety of medical products. As leading experts in the field of regulatory policy and organizations representing consumers, patients, and clinicians, we write today to offer ways to ensure that FDA continues its work of protecting patients and ensuring timely access to truly safe and effective health technologies. Specifically, we urge you to include critical provisions for FDA oversight related to accelerated approval and clinical trial diversity.

Accelerated Approval Reforms. In the last two decades, the accelerated approval pathway has enabled timely access to several important innovations for patients, allowing pivotal clinical trials to be based on surrogate endpoints thought to be predictive of meaningful clinical benefit. However, due to postmarket trial delays or failure to confirm clinical benefits, too many products have lingered on the market and potentially endangered patients who continue to take these medications.[1,2,3,4] We strongly recommend that your final package include the attached language, which makes important reforms to the accelerated approval process. We'd like to highlight three key provisions:

1. Advisory committees must be convened to review all accelerated approval drug candidates and upon approval, manufacturers must complete post-approval studies that confirm the drug's predicted clinical benefit. In exchange for earlier access for patients to potentially promising treatments, accelerated approval drugs are approved by the FDA based on a surrogate endpoint (e.g. changes of a lab test value or in imaging) thought to be predictive of meaningful, clinical benefit for patients (e.g. reduction in deaths or hospitalizations). It is imperative that programs to speed access are counterbalanced by strong requirements to complete timely and rigorous evaluation of product safety and effectiveness after market approval. Given this uncertainty regarding clinical benefit for drugs approved under this expedited review pathway, FDA must convene advisory committees of independent experts to review these drug candidates ahead of approval.
2. Accelerated approval drugs that fail to show clinical benefit after five years must be automatically withdrawn from the market. Currently, the FDA does not have the authority, relying on manufacturers to voluntarily withdraw their drugs from the market, which may occur long after patients have suffered medical and financial harms. A recent investigation showed that approximately 10% of drugs granted accelerated approval as of 2020 had not proven clinical benefit and remained available for patients for

[1] Elisabeth Mahase, "FDA Allows Drugs without Proven Clinical Benefit to Languish for Years on Accelerated Pathway," *BMJ* 374 (July 30, 2021): n1898, https://doi.org/10.1136/bmj.n1898.
[2] Julia A. Beaver and Richard Pazdur, "'Dangling' Accelerated Approvals in Oncology," *New England Journal of Medicine* 384, no. 18 (May 6, 2021): e68, https://doi.org/10.1056/NEJMp2104846.
[3] Bishal Gyawali, Benjamin N. Rome, and Aaron S. Kesselheim, "Regulatory and Clinical Consequences of Negative Confirmatory Trials of Accelerated Approval Cancer Drugs: Retrospective Observational Study," *BMJ* 374 (September 9, 2021): n1959, https://doi.org/10.1136/bmj.n1959.
[4] Zachary Brennan, "UPDATED: How a Pharma Company Bought 2 Accelerated Approvals — Never Ran Confirmatory Trials — and Cashed in until FDA Said Stop," *Endpoints News* (blog), accessed May 18, 2022, https://endpts.com/how-a-pharma-company-bought-2-accelerated-approvals-never-ran-confirmatory-trials-and-cashed-in-until-fda-said-stop/.

more than five years.[5] Another study also found that the median time for completion of these required confirmatory trials was 17 months;[6] thus, granting five years before automatic withdrawal may be generous for several accelerated approval drugs. By codifying an automatic withdrawal mechanism for therapies that fail to demonstrate clinical effectiveness, the agency would prevent patients from prolonged exposure to unproven therapies.

3. Required postapproval studies to confirm clinical benefit must be underway upon accelerated approval and manufacturers must submit routine reports of their progress. Manufacturers often delay or fail to initiate postapproval studies for accelerated approval drugs, thus prolonging uncertainty among patients and prescribers of these drugs' clinical benefit.[7] Requiring postapproval studies to already have been initiated when accelerated approval is granted would help prevent any unnecessary delays. Moreover, the routine submission of reports on the status of these studies to the FDA would also enable to be aware and assist, if necessary, in advancing postapproval studies to prevent any delays in confirming clinical benefit.

Clinical Trial Diversity. Voluntary efforts to improve clinical trial diversity are simply not effective.[8] A recent study showed that Black people accounted for just one-third of the required enrollment for adequate representation, regardless of whether the trials started before, during, or after the FDA action plan for clinical trial diversity went into effect. Of 225 drug approvals for which mortality and morbidity information was listed on the FDA plan website, only 20% had data showing benefits and side effects for Black patients.[9] Further, of the over 20,000 US-based trials with reported results conducted between 2000 and 2020, representing 4·76 million participants, only 43% reported any race/ethnicity data.[10] We strongly recommend that your final package include the attached language, which includes more impactful policies related to clinical trial diversity that will go further to ensure medical product safety and efficacy for all patients. We'd like to highlight two key provisions:

1. Make diversity action plans publicly available for independent evaluation. FDA should publish the plans on their own website or be integrated with ClinicalTrials.gov, as trials are required to be registered with their statistical analysis protocol ahead of enrollment. Not only will this allow for public accountability, but also advance best practices in clinical trial diversity.
2. Include enforcement measures to ensure representation in clinical trials. If there are no penalties for sponsors not submitting diversity action plans, then it is unlikely that representation of key populations within these trials will occur. Should sponsors not meet enrollment benchmarks to ensure adequate representation across age, gender, and race/ethnicity for a disease and condition, FDA must require sponsors to conduct postapproval studies inclusive of diverse subgroup populations.

Again, thank you for your work in this area, and we appreciate your consideration of our request. Any one of us would be happy to discuss any of these issues further.

Sincerely,

Reshma Ramachandran, MD, MPP
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[5] Mahase, "FDA Allows Drugs without Proven Clinical Benefit to Languish for Years on Accelerated Pathway."
[6] Joshua D. Wallach et al., "Comparison of Duration of Postapproval vs Pivotal Trials for Therapeutic Agents Granted US Food and Drug Administration Accelerated Approval, 2009-2018," *JAMA Network Open* 4, no. 11 (November 9, 2021): e2133601, https://doi.org/10.1001/jamanetworkopen.2021.33601.
[7] Julia A. Beaver et al., "A 25-Year Experience of US Food and Drug Administration Accelerated Approval of Malignant Hematology and Oncology Drugs and Biologics: A Review," *JAMA Oncology* 4, no. 6 (June 1, 2018): 849–56, https://doi.org/10.1001/jamaoncol.2017.5618.
8 "Improving Representation in Clinical Trials and Research: Building Research Equity for Women and Underrepresented Groups" (Washington, D.C.: National Academies of Science, Engineering, and Medicine, May 17, 2022), https://doi.org/10.17226/26479.
[9] Green, A, et al. Despite The FDA's Five-Year Plan, Black Patients Remain Inadequately Represented In Clinical Trials For Drugs. Health Affairs 2022; https://doi.org/10.1377/hlthaff.2021.01432.
[10] Turner, B et al. Race/ethnicity reporting and representation in US clinical trials: A cohort study. Lancet April 2022. https://doi.org/10.1016/j.lana.2022.100252

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USA Patient Network

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AMENDMENTS FOR REFORMS TO THE ACCELERATED APPROVAL PATHWAY

POSTAPPROVAL STUDIES AND PROGRAM INTEGRITY FOR ACCELERATED APPROVAL DRUGS.

(a) IN GENERAL.—Section 506(c) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356(c)) is amended—

(1) by striking paragraph (2) and inserting the

following:

‘‘(2) LIMITATION.—

‘‘(A) IN GENERAL.—Approval of a product under this subsection shall be subject to the following requirements:

‘‘(i) that the sponsor conduct an appropriate postapproval study or studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical benefit

‘‘(ii) That the sponsor submit copies of all promotional materials related to the product during the preapproval review period and, following approval and for such period thereafter as the Secretary determines to be appropriate, at least 30 days prior to dissemination of the materials.

‘‘(iii) That the Secretary convene and consult an advisory committee on the evidentiary standards for accelerated approval as well as the design of postapproval studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical benefit.

‘‘(B) POSTAPPROVAL STUDY CONDITIONS.—Not later than the time of approval of a product under accelerated approval, the Secretary shall specify the conditions for a post-approval study or studies required to be conducted under this paragraph with respect to such product, which shall include enrollment targets, the study protocol, study endpoints, and milestones, including the target

Commented [RR1]: Modification of current statute to require postapproval studies for all accelerated approval drugs.

Should current statute remain where accelerated approval *may* be subject to postapproval study requirements, we would then urge that the FDA make transparent their rationale for not requiring such studies.

Commented [RR2]: To fulfill these study requirements, this should be clinical trials. Real-world evidence may complement these studies, but not replace them as prior research has shown that currently available real-world evidence has not been able to replicate clinical trials for such studies. Recent FDA research has also demonstrated this as well.

Sources:
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2785882 and https://endpts.com/real-world-evidence-lessons-learned-from-an-fda-pilot-show-the-limits-of-emulating-rcts/

Commented [RR3]: Recent research has found that FDA has less often convened their own advisory committees of independent experts over time. Between 2010 and 2021, FDA went from convening these committees for 55% to 6% of approved drugs annually. Particularly for accelerated approval drugs where approval is based on less evidence, FDA should convene these experts to offer their recommendations for these approvals and also discuss the design of postapproval studies.

Source:
https://www.healthaffairs.org/doi/abs/10.1377/hlthaff.2021.01927

Commented [RR4]: Ahead of accelerated approval being granted, FDA should work with the sponsor on the design of the postapproval study to ensure that meaningful clinical benefit is being ascertained. Not only should the study completion date be specified, but also the study endpoints, which should be clinical endpoints in order to confirm clinical benefit – not surrogate endpoints, especially those that were the basis of the initial accelerated approval.

date of study completion:

''(i) Study endpoints shall also be specified to be clinical endpoints that demonstrate an effect on irreversible morbidity or mortality or other clinical benefit.

''(C) STUDIES BEGUN BEFORE APPROVAL.—The Secretary shall require such study or studies to be underway prior to approval.''; and

(2) by striking paragraph (3) and inserting the following:

''(3) EXPEDITED WITHDRAWAL OF APPROVAL.—

''(A) IN GENERAL.—The Secretary shall withdraw approval of a product approved under accelerated approval using expedited procedures described in subparagraph (B), if—

''(i) the sponsor fails to conduct any required postapproval study of the product with due diligence, including with respect to conditions specified by the Secretary under paragraph (2)(C);

''(ii) a study required to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical benefit of the product fails to verify and describe such effect or benefit;

''(iii) other evidence demonstrates that the product is not shown to be safe or effective under the conditions of use; or

''(iv) the sponsor disseminates false or misleading promotional materials with respect to the product.

''(B) EXPEDITED PROCEDURES DESCRIBED.—Expedited procedures described in this subparagraph shall consist of, prior to the withdrawal of accelerated approval—

Commented [RR5]: This provision would ensure that postapproval studies are underway prior to accelerated approval, thus preventing any delays to their completion. FDA found that when postapproval studies are already underway at the time of accelerated approval, they are completed a median of 2.2 years earlier than when they are not.

Source: https://jamanetwork.com/journals/jamaoncology/fullarticle/2673837

Commented [RR6]: These provisions specify the reasons for which FDA can withdraw an accelerated approval drug from the market.

''(i) providing the sponsor with—

''(I) due notice;

''(II) an explanation for the proposed withdrawal;

''(III) an opportunity for written appeal to—

''(aa) the Commissioner of Food and Drugs; or

''(bb) a designee of the Commissioner who has not participated in the proposed withdrawal of approval (other than a meeting pursuant to subclause (III)) and is not a subordinate of an individual (other than the Commissioner) who participated in such proposed withdrawal;

'(C) AUTOMATIC EXPIRATION.—The approval of a product approved under accelerated approval after the date of enactment of shall automatically expire 1 year after any target date of study completion included in an agreement described in clause (ii) of paragraph (2)(A), and in no case later than 5 years after the date on which the product is approved, unless—

''(i) a study required to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical benefit of the product has verified that predicted effect; or

''(ii) the Secretary has determined that adequate progress has been made on completion of postapproval studies required under paragraph (2)(A).

''(4) LABELING.—

''(A) IN GENERAL.—Subject to subparagraph (B), the label for a product approved under accelerated approval shall include—

''(i) a statement indicating that the product was approved under accelerated approval;

Commented [RR7]: Current withdrawal processes are lengthy involving an informal hearing with multiple parties present including the advisory committee and frequently face delays. These provisions would streamline the process for withdrawal and allow sponsors the opportunity to engage with the FDA more efficiently and with advance notice.

Commented [RR8]: This provision provides an additional safeguard and backstop should accelerated approval drugs remain available to patients despite no proven clinical benefit, allowing a generous period of time ahead of withdrawal for the studies to be completed and also FDA discretion to determine if sufficient progress has been made in completing those studies.

Commented [RR9]: Patients and clinicians are often not aware that a drug once approved by the FDA had been approved via the accelerated approval pathway, nor are they aware of what this means. Clearer labeling is needed to indicate that the drug had been approved provisionally based on surrogate endpoint and that confirmation of clinical benefit is pending.

''(ii) a statement indicating that continued approval of the product is subject to postmarketing studies to verify clinical benefit;

''(iii) identification of the surrogate or intermediate endpoint or endpoints that supported approval and any known limitations of such surrogate or intermediate endpoint or endpoints in determining clinical benefit; and

''(iv) a succinct description of the product and any uncertainty about anticipated clinical benefit and a discussion of available evidence with respect to such clinical benefit.

''(B) APPLICABILITY.—The labeling requirements of subparagraph (A) shall apply only to products approved under accelerated approval for which the predicted effect on irreversible morbidity or mortality or other clinical benefit has not been verified.

(b) REPORTS OF POSTMARKETING STUDIES.—Section 506B(a) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356b(a)) is amended—

(1) by redesignating paragraph (2) as paragraph (3); and

(2) by inserting after paragraph (1) the following:

''(2) ACCELERATED APPROVAL.—Notwithstanding paragraph (1), a sponsor of a drug approved under accelerated approval shall submit to the Secretary a report of the progress of any study required under section 506(c), including progress toward any agreed upon enrollment targets, milestones, and other information as required by the Secretary, not later than 180 days after the approval of such drug and not less frequently than every 180 days thereafter, until the study is completed or terminated.''.

(c) GUIDANCE.—

(1) IN GENERAL.—The Secretary of Health and Human Services shall issue

Commented [RR10]: This would require sponsors to submit routine reports on progress in completing their postapproval studies to FDA making clear if any studies are delayed and also offer the opportunity for FDA to provide assistance if so.

guidance describing—

(A) how sponsor questions related to the identification of novel surrogate or intermediate clinical endpoints may be addressed in early-stage development meetings with the Food and Drug Administration;

(B) the use of novel clinical trial designs that may be used to conduct appropriate post-approval studies as may be required under section 506(c)(2)(A) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356(c)(2)(A)), as amended by subsection (a);

(C) the expedited procedures described in section 506(c)(3)(B) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356(c)(3)(B)); and

(D) how adequate progress in completion of postapproval studies will be determined.

(2) FINAL GUIDANCE.—The Secretary shall issue—

(A) draft guidance under paragraph (1) not later than 18 months after the date of enactment of this Act; and (B) final guidance not later than 1 year after the close of the public comment period on each draft guidance.

AMENDMENTS RELATED TO ENSURING DIVERSITY AND REPRESENTATION IN CLINICAL TRIALS

PREMARKET REPORTING OF DIVERSITY ACTION PLANS FOR CLINICAL TRIALS AND STUDIES.

(a) DRUGS.—Section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)) is amended by adding at the end the following:

''(5)(A) In order for a new drug to be exempt pursuant to this subsection, the sponsor of a clinical investigation of such new drug shall submit to the Secretary a diversity action plan.

Commented [RR11]: Sponsors would be required to submit to FDA "diversity action plans" clearly outlining their enrollment benchmarks for diversity and their plans to meet these benchmarks ahead of initiation of the trial.

‘‘(B) Such diversity action plan shall include—

‘‘(i) the sponsor’s goals for enrollment in such clinical investigation;

‘‘(ii) the sponsor’s rationale for such goals; and

‘‘(iii) an explanation of how the sponsor intends to meet such goals.

‘‘(C) The sponsor shall, in such form and manner as specified in the guidance required by section 524B, submit such diversity action plan as soon as practicable during drug development, but not later than—

‘‘(i) one month prior to an End-of-Phase 2 meeting, as described in section 312.47(b) of title 21, Code of Federal Regulations (or successor regulations); or

‘‘(ii) if there is no End-of-Phase 2 meeting, one month prior to commencing enrollment for a Phase 3 study.

‘‘(D) The Secretary may waive the requirement in subparagraph (A) if the Secretary determines that a waiver is necessary based on what is known about the prevalence of the disease in terms of the patient population that may use the new drug and if the Secretary determines that utilizing national subgroup demographics cannot not be applied for a disease where prevalence data are not available.’’.

“(E) Sponsors shall submit their diversity action plans as part of their clinical trial registration requirements to ClinicalTrials.gov no later than 21 calendar days after the first human subject is enrolled. The NIH Director will post publicly on ClinicalTrials.gov the diversity action plans for each applicable drug clinical trial no later than 30 days after the sponsor has submitted such information.

(F) “Sponsors shall also report whether their goals for enrollment as specified within their diversity action plan as well as enrollment numbers across demographic subgroups across demographic subgroups within their diversity action plan not later than the time of approval of a product.

''(G) The Secretary shall direct local institutional review boards to assess and report the representativeness of clinical trials as one measure of sound research design that it requires for the protection of human subjects.

(b) BIOLOGICAL PRODUCTS.—Section 351(a)(3) of the Public Health Service Act (42 U.S.C. 262(a)(3)) is amended—

(1) by striking ''(3) The Secretary'' and inserting ''(3)(A) The Secretary''; and

2) by adding at the end the following:

''(B)(i) In order for a biological product to be exempt pursuant to this paragraph, the sponsor of a clinical investigation of such biological product shall submit to the Secretary a diversity action plan.

''(ii) Such diversity action plan shall include—

''(I) the sponsor's goals for enrollment in such clinical investigation;

''(II) the sponsor's rationale for such goals; and

''(III) an explanation of how the sponsor in-tends to meet such goals.

''(iii) The sponsor shall, in such form and manner

specified in the guidance required by section 524B, submit such diversity action plan as soon as practicable during biological product development, but not later than—

''(I) one month prior to an End-of-Phase 2 meeting, as described in section 312.47(b) of title 21, Code of Federal Regulations (or successor regulations); or

''(II) if there is no End-of-Phase 2 meeting, one month prior to commencing enrollment for a Phase 3 study.

'(iv) The Secretary may waive the requirement in subparagraph (A) if the Secretary determines that a waiver is necessary based on what is known about the prevalence of the disease in terms of the patient population that may use the biological product.''.

(c) DEVICES.—Section 520(g) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j(g)) is amended

by adding at the end the following:

''(9)(A) In order for a device to be exempt under this subsection, the sponsor of a clinical investigation of such device shall submit to the Secretary a diversity action plan the

Commented [RR12]: As sponsors are required to register all applicable clinical trials on ClinicalTrials.gov ahead of enrollment and provide a statistical analysis protocol, these diversity action plans should also be submitted as well and be made publicly available. Short of this, FDA can also publish these plans individually on their website to ensure public accountability, independent expert input, and sharing of best practices among sponsors.

Commented [RR13]: This is a recommendation from the recently released National Academies of Science, Engineering, and Medicine report on improving clinical trial representation.

Source: https://nap.nationalacademies.org/download/26479

sponsor of a clinical investigation of such device shall submit to the Secretary a diversity action plan.

''(B) Such diversity action plan shall include—

''(i) the sponsor's goals for enrollment in such clinical investigation;

''(ii) the sponsor's rationale for such goals; and

''(iii) an explanation of how the sponsor intends to meet such goals.

''(C) Such diversity action plan shall be—

''(i) if submission of an application for an investigational device exemption is required, submitted in such application; and

''(ii) if submission of an application for investigational device exemption is not required, submitted as soon as practicable during device development, but no later than one month prior to commencing enrollment for a study.

''(D) The Secretary may waive the requirement in subparagraph (A) if the Secretary determines that a waiver is necessary based on what is known about the prevalence of the disease in terms of the patient population that may use the device.''.

(d) GUIDANCE.—Subchapter A of chapter V of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351 et seq.) is amended by adding at the end the following:

GUIDANCE ON DIVERSITY ACTION PLANS FOR CLINICAL TRIALS AND STUDIES.

''(a) IN GENERAL.—The Secretary shall by guidance provide recommendations relating to—

''(1) the format and content of the diversity action plans required by sections 505(i)(5) and 520(g)(9) of this Act, and section 351(a)(3) of the Public Health Service Act, pertaining to the sponsor's goals for clinical trial enrollment, disaggregated by age group, sex, race, geographic location, and ethnicity, including with respect to—

''(A) the rationale for the sponsor's enrollment goals, which may include—

''(i) the estimated prevalence in the United States of the disease or condition for which the drug or device is being developed or investigated, if such estimated prevalence is known or can be determined based on available data;

''(ii) what is known about the disease or condition for which the drug or device is being developed or investigated;

''(iii) any relevant pharmacokinetic or pharmacogenomic data;

''(iv) what is known about the patient population for such disease or condition, including, to the extent data is available—

''(I) demographic information, including age group, sex, race, geographic location and ethnicity;

''(II) co-morbidities frequently affecting the patient population; and

''(III) potential barriers to enrolling diverse participants, such as patient population size and geographic location; and ''(v) any other data or information the sponsor deems relevant to selecting appropriate enrollment goals, disaggregated by demographic subgroup, such as the inclusion of pregnant and lactating women;

''(B) an explanation for how the sponsor intends to meet such goals, including demographic-specific outreach and enrollment strategies, study-site selection, clinical trial inclusion and exclusion practices, and any diversity training for trial personnel; and

''(C) procedures for the public posting of key information from the diversity action plan that would be useful to patients and providers on the sponsor's website; and ''(2) how sponsors should include in regular reports to the Secretary—

''(A) the sponsor's progress in meeting the goals referred to in paragraph (1)(A); and

''(B) if the sponsor does not expect to meet such goals—''(i) any updates needed to be made to a diversity action plan referred to in paragraph (1) to help meet such goals; and

''(ii) the sponsor's reasons for why the sponsor does not expect to meet such goals.

''(b) ISSUANCE.—The Secretary shall—

''(1) not later than 12 months after the date of enactment of this section, issue new draft guidance or update existing draft guidance described in subsection (a); and

''(2) not later than 6 months after closing the comment period on such draft guidance, finalize such guidance.''.

(e) APPLICABILITY.—Sections 505(i)(5) and 520(g)(9) of the Federal Food, Drug, and Cosmetic Act, and section 351(a)(3)(B) of the Public Health Service Act, as added by subsections (a), (b), and (c) of this section, apply only with respect to clinical investigations with respect to which enrollment commences after the date that is 180 days after the publication of final guidance under section 524B(b)(2) of the Federal Food, Drug, and Cosmetic Act, as added by subsection (d).

FDA AUTHORITY TO MANDATE POSTAPPROVAL STUDIES OR POSTMARKET SURVEILLANCE DUE TO INSUFFICIENT DEMOGRAPHIC SUBGROUP DATA.

(a) DRUGS.—

Commented [RR14]: This section would introduce an enforcement measure in that if sponsors are unable to meet their enrollment benchmarks as outlined in their diversity action plans, FDA shall mandate that postapproval studies are conducted inclusive of diverse subgroup populations.

Ideally, we would like to see FDA also having discretion to not accept applications with nonrepresentative enrollment within their clinical trials.

(1) IN GENERAL.—Section 505(o)(3)(B) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(o)(3)(B)) is amended by adding at the end the following:

"(iv) To provide safety and effectiveness data for the drug involved for a demographic subgroup or subgroups, if—

"(I) the clinical trials conducted in support of the approval of the drug did not meet the applicable targets of enrollment, as described in section 2; and

"(II) in the judgment of the Secretary, additional data should inform drug labeling.".

(2) WAIVER.—Section 505(o)(3)(D) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(o)(3)(D)) is amended by adding at the end the following:

"(iii) CLINICAL TRIAL DIVERSITY ENROLLMENT.—The Secretary may not require postapproval studies or postapproval clinical trials for the purpose specified under subparagraph (B)(iv) if the sponsor provides to the Secretary a sufficient justification for not meeting the enrollment targets referred to in such subparagraph, which may include—

"(I) factors outside of the sponsor's control, such as a lack of retention of participants;

"(II) differences in the enrollment targets, disaggregated by demographic subgroup, and actual enrollment that are determined by the Secretary to be insignificant in nature;

"(III) information not available to the sponsor at the time such enrollment targets were chosen, but that impacted enrollment of diverse participants;

"(IV) potential for selection bias; and

"(V) any other reason that the Secretary determines is sufficient justification.".

(3) USE OF REAL WORLD EVIDENCE.—Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(o)(3)) is amended by adding at the end the following:

"(G) USE OF REAL WORLD EVIDENCE.—Real world evidence (as defined in section 505F(b)) may be used to support under this paragraph.".

(b) DEVICES.—Section 522(a)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360l(a)(1)(A)) is amended—

(1) in subparagraph (A)—

(A) in clause (ii), by striking "or" at the end;

(B) in clause (iii)(II), by striking "facility." and inserting "facility; or"; and

(C) by adding at the end the following:

"(iv) with respect to which—

"(I) clinical studies submitted to support that approval or clearance did not meet the applicable targets of enrollment, as described in section 2 of the DEPICT Act; and

"(II) with respect to which a justification described in subparagraph (D) is not provided."; and

(2) by adding at the end the following:

"(C) USE OF REAL WORLD EVIDENCE.—Real world evidence (as defined in section 505F(b)) may be used to support the requirements under this paragraph.

"(D) CLINICAL TRIAL DIVERSITY ENROLLMENT.—The Secretary may not require a manufacturer to conduct postmarket surveillance under subparagraph (A) with respect to a device for the purpose specified in clause (iv) of such subparagraph if the manufacturer provides to the Secretary a sufficient justification for not meeting the enrollment targets referred to in such subparagraph, which may include—

"(i) factors outside of the manufacturer's control, such as a lack of retention of participants;

"(ii) differences in the enrollment targets, disaggregated by demographic subgroup, and actual enrollment that are determined by the Secretary to be insignificant in nature;

"(iii) information not available to the manufacturer at the time such enrollment targets were chosen, but that impacted enrollment of diverse participants;

"(iv) potential for selection bias; and

"(v) any other reason that the Secretary determines is sufficient justification.".

(c) REPORTS FOR CERTAIN DEVICES.—The Commissioner of Food and Drugs shall issue regulations revising section 814.84 of title 21, Code of Federal Regulations, to require holders of an application approved under section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360e) to include in the reports submitted under such section 814.84, to the extent possible, any data not previously submitted under such section 814.84 that may inform the safety and effectiveness of the device involved in underrepresented demographic subgroups.

(d) REGISTRY AND RESULTS DATA BANK INCLUSION.—Section 402(j)(1)(A) of the Public Health Service Act (282(j)(1)(A)) is amended—

(1) in clause (ii)—

(A) in subclause (I), by striking "and" at the end;

(B) in subclause (II), by striking the period at the end and inserting "; and"; and

(C) by adding at the end the following:

"(III) postmarket surveillance for any device as required under clause (iv) of section 522(a)(1)(A) of the Federal Food, Drug, and Cosmetic Act."; and

(2) in clause (iii)(I), by striking the period at the end and inserting the following: ", including any postapproval study or postapproval clinical trial for a drug as required under section 505(o)(3)(B)(iv) of the Federal Food, Drug, and Cosmetic Act.".

(e) PUBLIC MEETING.—

(1) IN GENERAL.—Not later than 270 days after the date of enactment of this Act, the Secretary, acting through the Commissioner of Food and Drugs, and in consultation with drug sponsors, medical device manufacturers, patients, and other stakeholders, shall convene a public meeting to consider the ways by which—

(A) drug sponsors and medical device manufacturers may disseminate information to the public on clinical trial enrollment demographic data in a timely and accessible manner;

(B) drug and device sponsors, in consultation with the Commissioner of Food and Drugs, may publicly disseminate information on subgroup analyses conducted by the sponsors in cases where—

(i) such data is not sufficient for the purpose of updating drug and device labels; or

(ii) such analyses do not show significant differences between demographic subgroups; and

(C) drug and device sponsors, in consultation with the Commissioner of Food and Drugs, may collect and publicly disseminate real world evidence that may provide information on the safety and effectiveness of drugs or devices for a demographic subgroup or subgroups.

(2) REPORT.—Not later than 180 days after the date on which the public meeting is convened under paragraph (1), the Secretary shall make available on the website of the Food and Drug Administration a report on the topics discussed at such meeting. The report shall include a summary of, and response to, recommendations raised in such meeting.

(3) ENFORCEMENT – The Secretary shall enforce existing measures to ensure representation in clinical trials and shall provide a report to Congress that will also be made available on the website of the Food and Drug Administration of progress of such enforcement no later than 1 year of passage of this bill.

PUBLIC WORKSHOPS TO ENHANCE CLINICAL TRIAL DIVERSITY.

Commented [RR15]: This is also a recommendation within the recently released report on improving clinical trial representation from the National Academies of Science, Engineering, and Medicine and is immediately actionable.

(a) IN GENERAL.—Not later than September 30, 2023, the Secretary of Health and Human Services, in consultation with drug sponsors, medical device manufacturers, patients, and other stakeholders, including but not limited to the Centers for Disease Control and Prevention and the National Institutes of Health, shall convene one or more public workshops to solicit input from stakeholders on increasing the enrollment of historically underrepresented populations in clinical trials and encouraging clinical trial participation that reflects the prevalence of the disease or condition among demographic subgroups, and other topics, including—

(1) how and when to collect and present demographic subgroup and disease or condition prevalence data from clinical trials, including with respect to—

(A) such data intended to support post-approval study requirements; and

(B) the utilization of real world evidence (as defined in section 505F(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 22355g(b)));

(2) methodologies for assessing the diversity of a patient population;

(3) methodologies for the dissemination of information to the public on clinical trial enrollment demographic data;

(4) the establishment of goals for enrollment in clinical trials with respect to the estimated prevalence in the United States of the disease or condition for which the drug is being developed or investigated, disaggregated by demographic subgroup (including by age group, race, ethnicity, and sex); and

(5) approaches to support inclusion of underrepresented populations and to encourage clinical trial participation that reflects the prevalence of the disease or condition in certain demographic sub-groups, including with respect to—

(A) the establishment of inclusion and exclusion criteria for certain demographic sub-

groups, such as pregnant and lactating women and individuals with disabilities, including intellectual or developmental disabilities;

(B) considerations regarding informed consent with respect to individuals with intellectual or developmental disabilities;

(C) clinical trial designs, including utilization of decentralized trials or digital health

tools;

(D) clinical endpoints;

(E) biomarker selection; and

(F) studying analysis.

(b) PUBLIC DOCKET.—The Secretary of Health and Human Services shall establish a public comment period to receive written comments related to the topics addressed during each public workshop convened under this section. The public comment period shall remain open for 60 days following the date on which each public workshop is convened.

(c) REPORT.—Not later than 180 days after the date of each public workshop convened under this section, the Secretary of Health and Human Services shall make available on the public website of the Food and Drug Administration a report on the topics discussed at such workshop. The report shall include a summary of, and response to, recommendations raised in such workshop; as well as those included within the National Academy of Science, Engineering, and Medicine report issued on May 17, 2022 entitled "Improving Clinical Trials and Research: Building Research Equity for Women and Underrepresented Groups."

ANNUAL REPORT ON PROGRESS TO INCREASE DIVERSITY IN CLINICAL TRIALS AND STUDIES.

(a) IN GENERAL.—Beginning not later than 2 years after the date of enactment of this Act, and each year thereafter, the Secretary of Health and Human Services shall submit to the Congress, and publish on the public website of the Food and Drug Administration, a report that summarizes, in aggregate, the diversity action plans received pursuant to section 505(i)(5) or 520(g)(9) of the Federal Food, Drug, and Cosmetic Act, or section 351(a)(3)(B) of the Public Health Service Act, as added by subsection (a), (b), or (c) of section 501 of this Act; and

(2) contains information on—

(A) whether the clinical trials conducted with respect to such applications met the demographic subgroup enrollment goals from the diversity action plan submitted for such applications;

(B) the reasons provided for why enrollment goals from submitted diversity action plans were not met;

(C) any postmarket studies of a drug or device in a demographic subgroup or subgroups required or recommended by the Secretary based on inadequate premarket clinical trial diversity, including the status and completion date of any such study; and

(D) additional authorities, if any, the Secretary plans to use or considers necessary to ensure compliance with the requirements of the amendments made by section 501.

(b) CONFIDENTIALITY.—Nothing in this section shall be construed as authorizing the Secretary of Health and Human Services to disclose any information that is a trade secret or confidential information subject to section 552(b)(4) of title 5, United States Code, or section 1905 of title 18, United States Code.

PUBLIC MEETING ON CLINICAL TRIAL FLEXIBILITIES INITIATED IN RESPONSE TO COVID–19 PANDEMIC.

(a) IN GENERAL.—Not later than 180 days after the date on which the COVID–19 emergency period ends, the Secretary of Health and Human Services shall convene a public meeting to discuss the recommendations provided by the Food and Drug Administration during the COVID–19 emergency period to mitigate disruption of clinical trials, including recommendations detailed in the March 2020 guidance entitled ‘‘Conduct of Clinical Trials of Medical Products During the COVID–19 Public Health Emergency, Guidance for Industry, Investigators, and Institutional Review Boards’’, and any subsequent updates to such guidance. The Secretary of Health and Human Services shall invite to such meeting representatives from the pharmaceutical and medical device

industries who sponsored clinical trials during the COVID–19 emergency period and organizations representing patients and independent experts.

(b) TOPICS.—Not later than 90 days after the date on which the public meeting under subsection (a) is convened, the Secretary of Health and Human Services shall make available on the public website of the Food and Drug Administration a report on the topics discussed at such meeting. Such topics shall include discussion of—

(1) the actions drug sponsors took to utilize such recommendations and the frequency at which such recommendations were employed;

(2) the characteristics of the sponsors, trials, and patient populations impacted by such recommendations;

(3) a consideration of how recommendations intended to mitigate disruption of clinical trials during the COVID–19 emergency period, including any recommendations to consider decentralized clinical trials when appropriate, may have affected access to clinical trials for certain patient populations, especially unrepresented racial and ethnic minorities; and

(4) recommendations for incorporating certain clinical trial disruption mitigation recommendations into current or additional guidance to improve clinical trial access and enrollment of diverse patient populations.

(c) COVID–19 EMERGENCY PERIOD DEFINED.—In this section, the term ''COVID–19 emergency period'' has the meaning given the term ''emergency period'' in section 1135(g)(1)(B) of the Social Security Act (42 U.S.C. 5 1320b–5(g)(1)(B)).

DECENTRALIZED CLINICAL TRIALS.

(a) GUIDANCE.—The Secretary of Health and Human Services shall—

(1) not later than 12 months after the date of enactment of this Act, issue draft guidance for public comment that addresses considerations for decentralized clinical trials, including considerations regarding the engagement, enrollment, and retention of a meaningfully diverse clinical population, with respect to race, ethnicity, age, gender, and geographic location, when appropriate; and

(2) not later than 6 months after closing the comment period on such draft guidance, finalize such guidance.

(b) CONTENT OF GUIDANCE.—The guidance under subsection (a) shall address the following:

(1) Recommendations for how digital health technology or other remote assessment options, such as telehealth, could support decentralized clinical trials, including guidance on considerations for selecting technological platforms and mediums, data collection and use, data integrity and security, and communication to study participants through digital technology.

(2) Recommendations for subject recruitment and retention, including considerations for sponsors to minimize or reduce burdens for clinical trial participants through the use of digital heath technology, telehealth, local health care providers and laboratories, or other means.

(3) Recommendations with respect to the evaluation of data collected within a decentralized clinical trial setting.

(c) DEFINITION.—In this section, the term ‘‘decentralized clinical trial’’ means a clinical trial in which some or all of the trial-related activities occur at a location separate from the investigator’s location.