Senate HELP Committee Hearing: Nomination of Stephen M. Hahn, MD, to serve as Commissioner of Food and Drugs (November 20, 2019)
Questions for the Record from Senator Elizabeth Warren

I. Antibiotic Resistance

Antibiotic drugs are critical tools for treating serious bacterial infections, but they are becoming less and less effective as bacteria develop a resistance to the antibiotics that are currently available. Today, resistance has been seen in almost all antibiotics ever developed.[1] The World Health Organization (WHO) has described antimicrobial resistance (AMR) as "one of the biggest threats to global health, food security, and development today,"[2] and the threat is no less significant right here in the U.S. According to the Centers for Disease Control and Prevention (CDC), nearly 3 million people in the U.S. develop antibiotic-resistant infections every year, resulting in over 35,000 deaths.[3]

Unfortunately, discovery of new antibiotics is failing to keep pace with the emergence of new "superbugs." Almost every antibiotic in use today is based on a scientific discovery made more than 30 years ago. Currently, there are only 42 antibiotics in clinical development worldwide. While that number may seem sufficient, only 11 of those have the potential to address the most dangerous superbugs as identified by the WHO, and historical data indicates that only 1 in 5 infectious disease drugs entering phase 1 trials typically receive FDA approval.[4] Developing new antibiotics is essential in the effort to combat AMR, yet a number of unique scientific and economic challenges hamper drug development efforts.

Furthermore, there is strong and growing evidence that antibiotic overuse in food animals can lead to antibiotic resistance in humans. The 2014 *National Strategy for Combatting Antibiotic-Resistant Bacteria* brought together the Secretaries of Health and Human Services, Agriculture, and Defense to declare that, "the misuse and over-use of antibiotics in health care and food production continue to hasten the development of bacterial drug resistance, leading to the loss of efficacy of existing antibiotics."[5]

1. **Do you agree that supporting the development of new antibiotics is an important part of FDA efforts to combat antimicrobial resistance? If confirmed, what steps would you take to encourage the development of new antibiotics?**

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[1] P&T, "The Antibiotic Resistance Crisis," C. Lee Ventola, April 2015, https://www.ncbi.nlm.nih.gov/pmc/articles/OMC4378521/.
[2] Genetic Engineering and Biotechnology News, "As Novartis Exits, Who Will Make New Antibiotics," Julianna LaMieux, July 25, 2018, https://www.genengnews.com/insights/as-novartis-exits-who-will-make-new-antibiotics/
[3] U.S. Centers for Disease Control and Prevention, "2019 AR Threats Report," https://www.cdc.gov/DrugResistance/Biggest-Threats.html.
[4] PEW, "The Critical Need for New Antibiotics," July 14, 2016, https://www.pewtrusts.org/en/research-and-analysis/data-visualizations/2016/the-critical-need-for-new-antibiotics.
[5] "National Strategy for Combating Antibiotic-Resistant Bacteria," The White House (September 2014) (online at: https://www.whitehouse.gov/sites/default/files/docs/carb_national_strategy.pdf), p.4.

2. **If confirmed, will you commit to continue the implementation of the priorities and goals outlined in the FDA's 2019 Strategic Approach for Combatting AMR?[6]**

3. **If confirmed, what will you do to improve physician education on the safe prescribing of antibiotics?**

4. **As part of the FDA's Strategic Approach for Combatting AMR, the FDA released a five-year plan to support antimicrobial stewardship in veterinary settings.[7] A key component of the five-year plan is the establishment of defined durations of use for animal drugs. Currently, roughly 1 in 3 medically-important antibiotics can be provided to animals for "very long or undefined durations of use"—increasing the likelihood of AMR.[8] In June 2018, I introduced the Strengthening Antibiotic Oversight Act, a bill that would require the FDA to review the durations of use of medically-important antibiotics labeled for use in animals and withdraw approvals for antibiotics with unjustified duration limits.[9] In April 2019, the FDA released a funding opportunity to help jumpstart the process of defining duration limits.[10]**

    a. **If confirmed, will you commit to continue the implementation of the FDA's five-year plan to support antimicrobial stewardship in veterinary settings?**

    b. **If confirmed, will you commit to finalizing defined durations of use for medically-important antibiotics in a timely manner?**

5. **If confirmed, how will you evaluate the effectiveness of guidance designed to limit animal antibiotic overuse, including Guidance for Industry #209 and #213, and the Veterinary Feed Directive?**

6. **If confirmed, how will you direct the FDA to work with the Departments of Agriculture and Defense, among other executive agencies, to combat AMR?**

II. Blood Donation Policy

Ensuring a safe and adequate blood supply is a critical aspect of our public health system. The FDA develops blood donation policy for the nation's blood banks—a task that is even more

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[6] Washington Post, "FDA: Here Is the 2019 Strategic Approach To Combat Antimicrobial Resistance," Bruce Y. Lee, September 22, 2018, https://www.forbes.com/sites/brucelee/2018/09/22/fda-here-is-the-2019-strategic-approach-to-combat-antimicrobial-resistance/#410eb59f3210.

[7] U.S. Food and Drug Administration, "Supporting Antimicrobial Stewardship in Veterinary Settings: Goals for Fiscal Years 2019-2023," September 2018,

[8] Pew, "Highlights of FDA's 5-Year Plan to Improve Antibiotic Use in Food Animals," December 11, 2018, https://www.pewtrusts.org/en/research-and-analysis/articles/2018/12/11/highlights-of-fdas-5-year-plan-to-improve-antibiotic-use-in-food-animals.

[9] U.S. Senator Elizabeth Warren, "Senators Introduce Bill to Strengthen Oversight of Antibiotic Use in Animals" (press release), June 22, 2018, https://www.warren.senate.gov/newsroom/press-releases/senators-introduce-bill-to-strengthen-oversight-of-antibiotic-use-in-animals.

[10] U.S. Food and Drug Administration, "FDA Announces Funding Opportunity to Help Define Durations of Use for Certain Medically Important Antimicrobial Drugs for Food Animals," April 1, 2019, https://www.fda.gov/animal-veterinary/cvm-updates/fda-announces-funding-opportunity-help-define-durations-use-certain-medically-important.

important as we respond to emerging diseases that threaten the safety of our blood supply. Evidence indicates that moving to a risk-based referral policy could increase the U.S. blood supply by up to 4 percent, helping to address the nation's blood shortage.[11] In June 2016, the FDA started collecting public input on scientifically sound solutions to risk-based screening, and the information collection period closed in November 2016.[12] In 2019, the FDA solicited contractors to conduct an "HIV Risk Questionnaire (HRQ) Study" to assess the "predictive value of a panel of questions for recent infection with" HIV.[13] Building on these steps will require leadership from the next FDA Commissioner.

1. **As FDA Commissioner, how would you support the FDA's efforts to move to a risk-based referral policy for all blood donors?**

2. **Do you commit to respect the advice of the FDA's Blood Products Advisory Committee Meeting in their scientific findings and recommendations with regard to the safety and public health risks of blood donation?**

3. **Will you commit to developing a risk-based, on-site questionnaire to be used at blood donation clinics? What is the current status of the FDA's HRQ Study?**

4. **What specific steps will you take to engage with impacted groups, which may be newly eligible for blood donation, to encourage blood donation in line with new policies?**

III. Clinical Trial Data Transparency

Increased sharing of clinical trial data could strengthen academic research, improve the practice of medicine, and protect the integrity of the clinical trials system.[14] Noting the potential benefits of increased transparency, leading medical journals have begun to require authors to disclose their plans to share de-identified data from their studies as a condition for publication.[15]

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[11] Ayako Miyashita and Gary J. Gates, "Update: Effects of Lifting Blood Donation Bans on Men Who Have Sex with Men," The Williams Institute (September 2014) (online at: http://williamsinstitute.law.ucla.edu/wp-content/uploads/Blood-Ban-update-Jan-2015.pdf). *See* for example: "American Red Cross reports severe winter blood shortage," *WTHITV.com* (January 4, 2017) (online at http://wthitv.com/2017/01/04/american-red-cross-reports-severe-winter-blood-shortage/) and "San Antonio in extreme blood shortage," *KHOU.com* (January 10, 2017) (online at http://www.khou.com/news/local/texas/san-antonio-in-extreme-blood-shortage/384692455).

[12] Federal Register Notice 81 FR 49673 "Blood Donor Deferral Policy for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products; Establishment of a Public Docket; Request for Comments" (https://www.federalregister.gov/documents/2016/07/28/2016-17804/blood-donor-deferral-policy-for-reducing-the-risk-of-human-immunodeficiency-virus-transmission-by).

[13] U.S. Food and Drug Administration, Blood Products Advisory Committee Meeting, "Topic III: Blood Donation Policies Regarding Men Who Have Sex with Men," March 20-21, 2019, https://www.fda.gov/media/120953/download.

[14] U.S. Senator Elizabeth Warren, "Strengthening Research through Data Sharing," *New England Journal of Medicine* 2016; 375:401-403 (online at: http://www.nejm.org/doi/full/10.1056/NEJMp1607282).

[15] *Stat News*, "Move clinical trial data sharing from an option to an imperative," Rebecca Li, February 19, 2019, https://www.statnews.com/2019/02/19/data-sharing-imperative-clinical-trials/

Furthermore, a new scorecard tool that rates companies on their ethics and transparency practices has spurred some pharmaceutical companies to improve their reporting practices.[16]

Unfortunately, some efforts to improve data sharing have been hampered by incomplete compliance with federal requirements. The Food and Drug Administration Amendments Act (FDAAA) of 2007 required trial results to be registered and reported on ClinicalTrials.gov, with penalties up to $10,000 per day for non-compliance, but despite uneven compliance, the FDA has never levied a monetary penalty or withheld research funding for researchers who failed to meet the registration requirements.[17] In September 2016, the FDA removed a major barrier to enforcement of the FDAA penalties by issuing a final rule detailing the requirements for submitting clinical trial results to Clinicaltrials.gov,[18] and in September 2018, it published draft guidance on the circumstances and process by which the agency would seek civil money penalties against researchers who fail to submit results or submit false or misleading information.[19]

1. **What do you believe the impact of greater transparency of clinical trial data and results would be on clinical trial efficiency, the cost of drug development, drug safety, and biomedical innovation?**

2. **If confirmed, what specific steps will you take to increase sharing of clinical trial data?**

3. **Currently, the FDA allows applicants to release the complete response letters they receive in response to their applications, but does not require the letters to be made public.**

    a. **What would be the impact of making complete response letters publicly available on clinical trial efficiency, the cost of drug development, drug safety, and biomedical innovation?**

    b. **If confirmed as Commissioner, will you commit to making complete response letters publicly available?**

    c. **If confirmed, what specific steps will you take to make complete response letters publicly available?**

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[16] *BMJ*, "Sharing of clinical trial data and results reporting practices among large pharmaceutical companies: cross sectional descriptive study and pilot of a tool to improve company practices," Jennifer Miller, Joseph Ross, Marc Wilenzick, and Michelle Mello, July 10, 2019, https://www.bmj.com/content/366/bmj.l4217

[17] *Stat News, "*It's time to levy penalties for failing to report clinical trial results," Holly Fernandez Lynch, January 17, 2018, https://www.statnews.com/2018/01/17/time-levy-penalties-failing-report-clinical-trial-results/

[18] Department of Health and Human Services, "Clinical Trials Registration and Results Information Submission: Final Rule," 42 CFR Part 11, *Federal Register* 81:183 (online at: https://www.gpo.gov/fdsys/pkg/FR-2016-09-21/pdf/2016-22129.pdf).

[19] Department of Health and Human Services, "Civil Money Penalties Relating to the ClinicalTrials.gov Data Bank," September 2018, https://www.fda.gov/media/113361/download

4. **If confirmed, how will you ensure compliance with the disclosure policy implemented by FDAAA and the September 2018 guidance? Will you enforce the law using civil monetary penalties or by other means?**

IV. Drugs

Drug Pricing

Millions of Americans are struggling with the high cost of prescription drugs. Nearly one in four Americans taking prescription drugs "report difficulties affording their medications,"[20] and according to a recent poll conducted by the Kaiser Family Foundation, at least three in ten adults reported skipping drug doses, delaying filling prescriptions, or taking less of a drug than prescribed to save money.[21] As the agency responsible for evaluating the safety and efficacy of brand-name, generic, and biosimilar drugs, the FDA has a role to play in government-wide efforts to lower the costs of drugs for American families.

1. **In your view, what role should the FDA play in efforts to lower prescription drug prices?**

2. **If confirmed, what steps will you take to help lower the cost of drugs for American consumers?**

3. **If confirmed, how will you work with other agencies within HHS and the Executive Branch as a whole to coordinate and develop policies designed to reduce prescription drug costs?**

Drug Shortages

In recent months, a number of high-profile drug shortages have dominated the news, including shortages of immune globulin[22] and vincristine.[23] According to the American Society of Health-System Pharmacists, there have been more than 100 drug shortages per year since 2007. In 2018, the number of drug shortages reached 186, the second highest since the peak of 267 drug shortages in 2011.[24] In addition to harming patients, shortages cause severe financial burdens for hospitals. A recent survey of 700 hospital pharmacy managers found that all of them experienced

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[20] Kaiser Family Foundation, "Poll: Nearly 1 in 4 Americans Taking Prescription Drugs Say It's Difficult to Afford Their Medicines, Including Larger Shares Among Those with Health Issues, with Low Incomes and Nearing Medicare Age," March 1, 2019, https://www.kff.org/health-costs/press-release/poll-nearly-1-in-4-americans-taking-prescription-drugs-say-its-difficult-to-afford-medicines-including-larger-shares-with-low-incomes/.

[21] Kaiser Family Foundation, "KFF Health Tracking Poll – February 2019: Prescription Drugs," Ashley Kirzinger et al., March 1, 2019, https://www.kff.org/health-costs/poll-finding/kff-health-tracking-poll-february-2019-prescription-drugs/.

[22] U.S. Food and Drug Administration, "Information about Immune Globulin (Human) Product Shortage," August 12, 2019, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/information-about-immune-globulin-human-product-shortage.

[23] New York Times, "Faced With a Drug Shortfall, Doctors Scramble to Treat Children With Cancer," October 14, 2019, https://www.nytimes.com/2019/10/14/health/cancer-drug-shortage.html.

[24] Kristy Malacos, "Drug Shortages: Contributing Factors, Mitigating the Impact," Pharmacy Times, March 21, 2019, https://www.pharmacytimes.com/news/drug-shortages-continue-to-be-a-challenge.

a drug shortage in the previous year—forcing 81% of the pharmacy managers to hoard medications and 66% to ration medication.[25] Every year, drug shortages cost hospitals $216 million in labor costs and an additional $200 million to substitute drugs in shortages.[26]

In October 2019, the FDA released a report, "Drug Shortages: Root Causes and Potential Solutions."[27] The report identified three "root causes" of drug shortages, including (1) a "lack of incentives to produce less profitable drugs" (a problem that is particularly acute in the antibiotics market); (2) the market's failure to adequately "reward manufacturers for mature quality management systems"; and (3) "logistical and regulatory challenges" that "make it difficult for the market to recover after a disruption."[28] The report identified three potential solutions to prevent drug shortages and highlighted existing FDA efforts to combat shortages.[29]

1. **If confirmed, will you commit to making the prevention of drug shortages a top priority at the FDA?**

2. **If confirmed, what specific steps will you take to combat drug shortages in the brand-name and generic drug marketplaces, respectively? What additional steps will you take to address the unique challenges facing manufacturers of antibiotics?**

3. **If confirmed, how will you direct the FDA to work with federal agencies, Congress, manufacturers, and other stakeholders to implement the recommendations included within the 2019 report?**

4. **In July 2018, then-Commissioner Gottlieb stated that the FDA would "be looking at whether it makes sense to develop a critical drugs list, or a list of essential drugs…where it would be especially important, from a clinical perspective, to ensure an uninterrupted drug supply."[30]**

    a. **What is the current status of this "critical drugs list"?**

    b. **If confirmed, will you commit to finalizing this "critical drugs list" to help combat drug shortages?**

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[25] JAMA Internal Medicine, "Prevalence and Severity of Rationing During Drug Shortages," Andrew Hantel et. al, March 25, 2019, https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2728954.
[26] *Id*.
[27] U.S. Food and Drug Administration, "Report—Drug Shortages: Root Causes and Potential Solutions," October 29, 2019, https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions.
[28] U.S. Food and Drug Administration, "Drug Shortages: Root Causes and Potential Solutions," October 2019, https://www.fda.gov/media/132058/download.
[29] Id.
[30] U.S. Food and Drug Administration, "Statement by FDA Commissioner Scott Gottlieb, M.D., on formation of a new drug shortages task force and FDA's efforts to advance long-term solutions to prevent shortages," July 12, 2018, https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-formation-new-drug-shortages-task-force-and-fdas.

Drug Supply Chain and National Security

Last week, the U.S. China Economic and Security Review Commission released a report highlighting "China's dominance as a global [active pharmaceutical ingredient] producer and the United States' growing reliance on Chinese pharmaceutical products."[31] Active pharmaceutical ingredients (APIs) are the raw chemical components of drugs that "furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease."[32] APIs are necessary to manufacture pharmaceutical products such as generic drugs and vaccinations. Despite the critical role of APIs in drug production, the U.S. "only makes about 20 percent of the APIs used in domestic pharmaceutical production."[33] Instead, the U.S. relies heavily on China for the import of these materials.[34]

Experts warn that the nation's "growing reliance on Chinese pharmaceutical products puts U.S. consumers—including active service members and veterans—at risk."[35] However, the FDA reportedly has little formal means for quality surveillance or oversight of Chinese manufacturers and drug plants.[36]

1. **Do you agree that the United States' reliance on Chinese pharmaceutical products places American consumers at risk? If so, what role do you believe the FDA should play in mitigating this risk?**

2. **If confirmed, what steps will you take to improve the FDA's ability to monitor the quality of imported pharmaceutical products, particularly those products produced in China? What steps will you take to ensure that the United States' supply line of these pharmaceutical products is secure and safe from disruption?**

3. **If confirmed, how will you direct the FDA to work with the Department of Defense and other executive agencies to address national security and public health risks posed by the nation's reliance on Chinese pharmaceutical products?**

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[31] "U.S. Dependence on Pharmaceutical Products from China," The Council on Foreign Relations, Yanzhong Huang, August 14, 2019, https://www.cfr.org/blog/us-dependence-pharmaceutical-products-china.
[32] World Health Organization, "Definition of Active Pharmaceutical Ingredients," July 2011, https://www.who.int/medicines/areas/quality_safety/quality_assurance/DefinitionAPI-QAS11-426Rev1-08082011.pdf.
[33] Politico, "Draft report warns Congress about pharma imports from China," Doug Palmer, October 25, 2019, https://www.politico.com/newsletters/morning-trade/2019/10/25/trumka-whats-the-rush-with-usmca-781528
[34] Stat News, "China has become the pharmacy to the world – and a national security risk for the U.S.," Ed Silverman, November 5, 2019, https://www.statnews.com/pharmalot/2019/11/05/china-security-risk-gibson/.
[35] "U.S. Dependence on Pharmaceutical Products from China," The Council on Foreign Relations, Yanzhong Huang, August 14, 2019, https://www.cfr.org/blog/us-dependence-pharmaceutical-products-china.
[36] Stat News, "In generic drug plans in China and India, data falsification is still a problem," Katherine Eban and Sony Salzman, October 29, 2019, https://www.statnews.com/2019/10/29/data-falsification-still-problematic-china-india-generic-drug-plants/; U.S. Food and Drug Administration Office of Pharmaceutical Quality, "FDA Pharmaceutical Quality Oversight white paper," 2015, https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM442666.pdf.

4. **In July 2018, then-Commissioner Gottlieb stated that the FDA would "be looking at whether it makes sense to develop a critical drugs list, or a list of essential drugs…where it would be especially important, from a clinical perspective, to ensure an uninterrupted drug supply."[37] Though this statement was made in the context of reducing drug shortages, a "critical drugs list" could also be helpful as the federal government analyzes the nation's reliance on Chinese pharmaceutical products. If confirmed, what steps would you take to ensure that this list can be used to both prevent drug shortages and address national security and public health risks posed by the nation's reliance on Chinese pharmaceutical products?**

V. Ethics

With public trust in government at an all-time low,[38] it is essential for public officials to hold themselves to the highest ethical standards. This is especially true for the FDA, given that the pharmaceutical industry spent record amounts on lobbying last year: the Pharmaceutical Research & Manufacturers of America spent $27.5 million, and the industry as a whole spent more than $194 million as of October 2018.[39]

My Anti-Corruption and Public Integrity Act would require common-sense measures to avoid conflicts of interest for officials in positions of public trust to assure Americans that their government is working for them, and not for deep-pocketed lobbyists.[40] I ask that if you are confirmed, you voluntarily comply with the conflict of interest and revolving door provisions of the Act to give the public confidence that your decisions at the FDA are in the best interest of patients and consumers, rather than lobbyists and corporations.

1. **If confirmed, from what issues, if any, do you plan to recuse yourself due to your own or your family members' financial conflicts of interest?**

2. **If confirmed, will you commit to recusing yourself from all issues that could provide a financial benefit to your previous employer, M.D. Anderson Cancer Center?**

3. **If confirmed, will you commit to divesting from all individual stocks outside of widely held investment vehicles (such as mutual or index funds)?**

4. **If confirmed, will you commit to refraining from lobbying activities after your tenure ends?**

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[37] U.S. Food and Drug Administration, "Statement by FDA Commissioner Scott Gottlieb, M.D., on formation of a new drug shortages task force and FDA's efforts to advance long-term solutions to prevent shortages," July 12, 2018, https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-formation-new-drug-shortages-task-force-and-fdas.

[38] Pew Research Center, "Public Trust in Government: 1958-2019," April 11, 2019, https://www.people-press.org/2019/04/11/public-trust-in-government-1958-2019/

[39] CNN, "Big Pharma spends record millions on lobbying amid pressure to lower drug prices," Susan Scutti, January 24, 2019, https://www.cnn.com/2019/01/23/health/phrma-lobbying-costs-bn/index.html.

[40] U.S. Senator Elizabeth Warren, "Warren Anti-Corruption Bill Gains Momentum as Jayapal, Sarbanes, Others Co-Sponsor House Companion" (press release), November 26, 2018, https://www.warren.senate.gov/newsroom/press-releases/warren-anti-corruption-bill-gains-momentum-as-jayapal-sarbanes-others-co-sponsor-house-companion.

5. **If confirmed, will you commit to refraining from employment with any company that lobbied the FDA for at least one year?**

VI. FDA Workforce

FDA's work is supported by highly skilled, professional employees who uphold the agency's mission and protect public health in the United States.

1. **If confirmed, will you work cooperatively with employees and employees' representatives, including unions?**

2. **If confirmed, will you meet with national leadership of employees' union representatives soon after you begin your duties?**

VII. Over-the-Counter Hearing Aids

Approximately 48 million Americans experience age-related hearing loss, including over half of adults in their seventies.[41] However, only an estimated 14 percent of Americans with hearing loss use hearings aids, primarily because they cannot afford to buy them.[42] Medicare and most private insurance plans do not cover hearing aids, and out-of-pocket costs for a single hearing aid averaged $2,400 in 2015[43]—far out of reach for many Americans. Furthermore, in 1977, the FDA issued regulations preventing individuals from purchasing hearing aids unless they had obtained a medical evaluation (or signed a waiver of that evaluation). These regulations meant that Americans could not purchase hearing aids over-the-counter.

To expand Americans' access to hearing aid technology, I introduced the Over-the-Counter (OTC) Hearing Aid Act with Senators Grassley, Hassan, and Isakson in March 2017. In August 2017, the bill was signed into law. The OTC Hearing Aid Act makes certain types of hearing aids available over-the-counter. It requires the FDA to issue regulations establishing safety and efficacy requirements for OTC hearing aids and to update and finalize its draft guidance, "Regulatory Requirements for Hearing Aid Devices and Personal Sound Amplification Products."[44] The FDA must issue proposed regulations no later than August 2020 and must finalize its guidance when final regulations are issued.[45]

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[41] Frank R. Lin, John K. Niparko, and Luigi Ferrucci. 2011. "Hearing Loss Prevalence in the United States," *Archives of Internal Medicine* 171: 1851-1853 (online at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3564588/).
[42] National Academies of Sciences, Engineering, and Medicine. 2016. *Hearing Health Care for Adults: Priorities for Improving Access and Affordability*. Washington, DC: The National Academies Press (online at: http://www.nationalacademies.org/hmd/Reports/2016/Hearing-Health-Care-for-Adults.aspx), p. 154.
[43] President's Council of Advisors on Science and Technology, "Aging America & Hearing Loss: Imperative of Improved Hearing Technologies," October 2015, https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/PCAST/PCAST%20hearing%20letter%20report.pdf.
[44] Public Law 115-52
[45] Id.

1. **If confirmed, will you commit to issuing the proposed regulations required under the OTC Hearing Aid Act in a timely manner and in compliance with statutory deadlines?**

2. **If confirmed, will you commit to finalizing the draft guidance on personal sound amplification products in a timely manner and in compliance with statutory deadlines?**

3. **If confirmed, what additional actions will you take to expand access to affordable hearing aid technologies?**

VIII. Medical Devices

Pre-Cert for Software Pilot Program

The FDA has established a "Software Pre-Cert Pilot Program" to test the feasibility of altering the traditional device approval pathway for certain software as medical devices (SaMD).[46] Senator Murray, Senator Smith, and I have repeatedly communicated with the FDA about the Pre-Cert Pilot, and we continue to have concerns about the program's impact on public safety and its compliance with existing statute. Specifically, these concerns relate to: (1) the agency's ability to ensure public safety under a "precertification" regime, particularly through its proposed "Excellence Appraisals"; (2) the appropriateness of the De Novo pathway as a statutory basis for the pilot; and (3) the agency's use of real world performance to assess the safety and efficacy of SaMD devices approved through the pilot. Most recently, in October 2019, we sent a letter to the FDA requesting information about the program.[47]

1. **If confirmed, will you commit to re-examining the Software Pre-Cert Pilot Program to assess its compliance with existing statutory authorities?**

2. **Please provide detailed answers to the questions included in the October 2019 letter referenced above, which include:**

    a. **Since responding to us in June 2019, has the FDA gained additional clarity on the type of data or evidence that would be appropriate—and inappropriate—to demonstrate excellence during an Excellence Appraisal? If so, please describe the type of data or evidence that the agency is considering. If not, please provide a description of the steps the agency will take to identify this type of data or evidence.**

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[46] U.S. Food and Drug Administration, "Precertification (Pre-Cert) Pilot Program: Frequently Asked Questions," https://www.fda.gov/medical-devices/digital-health-software-precertification-pre-cert-program/precertification-pre-cert-pilot-program-frequently-asked-questions.

[47] U.S. Senator Elizabeth Warren, "Senators Warren, Murray, and Smith Raise Further Questions About the FDA's Oversight of Digital Health Devices" (press release), October 30, 2019, https://www.warren.senate.gov/oversight/letters/-senators-warren-murray-and-smith-raise-further-questions-about-the-fdas-oversight-of-digital-health-devices.

b. Since responding to us in June 2019, has the FDA gained additional clarity on how it will "appropriately limit" the flexibility granted to entities seeking to demonstrate excellence via an Excellence Appraisal?

c. As part of its retrospective testing, the "Pre-Cert team developed a mock Excellence Appraisal summary" for pilot participants that had previously received FDA approval for a SaMD regulatory submission. The team developed these summaries "based on the pilot participant site visits and public comments."[48]

i. Please provide a copy of each "mock Excellence Appraisal summary" developed as part of this retrospective testing, including a copy of all "public comments" used to develop these summaries.

ii. What data or evidence did the Pre-Cert team review during pilot participant site visits, and how did this data or evidence contribute to the reviewers' ability to determine whether the pilot participant complied with the Excellence Principles? Does the agency believe it has the authority to collect and review all of the data and evidence it examined during the site visits and anticipates examining in future site visits?

iii. In developing these summaries, how much flexibility—if any—did the agency grant pilot participants in demonstrating compliance with the Excellence Principles? How did granting this flexibility to participants impact the data or evidence examined during the Pre-Cert team's site visits? Was the data or evidence standardized across all sites, or did it vary from site to site?

iv. The FDA concluded that its retrospective tests demonstrated the "feasibility" of the Excellence Appraisal (along with the Streamlined Review) "to be sufficient to conduct a premarket review of SaMD."[49]

v. How did the FDA determine that the Excellence Appraisal was "sufficient"?

vi. What would "failure" of the Excellence Appraisal have looked like during this retrospective testing?

d. The FDA is currently engaged in "prospective testing" of the precertification model. This testing involves simultaneously reviewing SaMD submissions using both the traditional and Pre-Cert approval pathways.[50] In July 2019,

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[48] Id., pg. 1.
[49] Id., pg. 2.
[50] U.S. Food and Drug Administration, "Software Precertification Program 2019 Mid-Year Update," July 2019, https://www.fda.gov/medical-devices/digital-health/digital-health-software-precertification-pre-cert-program, pg. 2.

the FDA announced that, based on its tests, "the elements identified in the [Working] model can be demonstrated and provide a comprehensive view of an organization's capabilities."[51]

i. **Please provide a summary of all Excellence Appraisals performed under the FDA's prospective testing to date. For each Excellence Appraisal, please provide a list of the data and evidence used—including KPIs—to demonstrate adherence to each element and principle listed in the Working Model.**

ii. **In the Excellence Appraisals it has performed so far, what type of data or evidence has the FDA relied on to "demonstrate" the elements identified in the Working Model?**

iii. **Has this type of data or evidence been consistent across all of the Excellence Appraisals? If not, what flexibility has the FDA allowed in the type of data or evidence used to demonstrate the elements?**

e. **In July 2019, the FDA announced that it "has learned" based on testing "that some of the elements [of the Excellence Appraisal] may need to be separated or removed."[52]**

i. **Which elements of the Excellence Appraisal is the FDA considering "separating" from the appraisal? Why? How will the FDA separately assess companies' compliance with those elements?**

ii. **Which elements of the Excellence Appraisal is the FDA considering "removing" from the appraisal? Why?**

f. **In its Working Model, the FDA states that it "does not intend to make individual organizations' KPI reports or results available publicly, to the extent consistent with the Freedom of Information Act."[53] In its July 2019 update, it also described Excellence Appraisals as "confidential."[54]**

i. **On what basis would the FDA withhold Excellence Appraisals—and the KPIs used to develop them—in whole or in part from public disclosure under the Freedom of Information Act?**

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[51] Id., pg. 3.
[52] Id.
[53] U.S. Food and Drug Administration, "Developing a Software Precertification Program: A Working Model—v 1.0," January 2019, https://www.fda.gov/media/119722/download, pg. 20.
[54] U.S. Food and Drug Administration, "Software Precertification Program 2019 Mid-Year Update," July 2019, https://www.fda.gov/medical-devices/digital-health/digital-health-software-precertification-pre-cert-program, pg. 2.

ii. **What information, if any, does the FDA anticipate providing the public about Excellence Appraisals should the Pre-Cert Pilot Program extend beyond the pilot stage?**

g. **The FDA has proposed utilizing third parties to conduct precertification assessments in cases where it "can identify existing entities with the capacity and expertise to conduct a Pre-Cert appraisal"—though it will not be doing so "in the first phase of implementing the Software Pre-Cert Program." In its June 2019 response, the FDA notes that the "FD&C Act currently authorizes a third-party review program for 510(k) submissions and for accrediting third part[ies] to perform inspections of eligible device manufacturers…so the concept is not entirely new." It also states that the agency "will consider whether the future use of third parties would be consistent with our existing statutory authorities."[55] Has the FDA determined whether allowing third-party entities to conduct precertification assessments during the Pre-Cert Pilot Program would "be consistent with…existing statutory authorities"?**

h. **Given the FDA's assertion that the De Novo pathway was established "to ensure the most appropriate classification of a device consistent with the protection of the public health and the statutory scheme for device regulation,"[56] does the agency believe that Congress intended for the pathway to be used to establish pilot programs that fundamentally alter the FDA's existing method of device review and approval? If so, please explain why.**

i. **Since the De Novo pathway was established in 1997, how many times has the FDA used it as the statutory basis to establish a pilot program? Please provide a summary and the outcomes of all pilot programs identified.**

j. **The December 2018 proposed rule lists a series of content requirements for a De Novo request (proposed 21 CFR 860.234).[57] For each requirement listed in the proposed rule, please indicate whether a manufacturer participating in the Pre-Cert Pilot Program would be required to provide information fulfilling the requirement during an Excellence Appraisal or during a subsequent De Novo submission. Please also indicate whether a manufacturer participating in the Pre-Cert Pilot Program would be required to provide information not included in the content requirements for a De Novo request as outlined in the December 2018 proposed rule.**

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[55] Letter from Karas Gross, Associate Commissioner for Legislative Affairs, U.S. Food and Drug Administration, to U.S. Senator Elizabeth Warren, U.S. Senator Patty Murray, and U.S. Senator Tina Smith, June 18, 2019, pg. 8.
[56] U.S. Food and Drug Administration, "Medical Device De Novo Classification Process (proposed rule)," 83 FR 63127, December 7, 2018, https://www.federalregister.gov/documents/2018/12/07/2018-26378/medical-device-de-novo-classification-process.
[57] Id.

k. In its Working Model, the FDA has proposed two levels of precertification "based on an organization's excellence": "Level 1 Pre-Cert" would "allow organizations to develop and market certain lower risk software without review while requiring a streamlined review for other types of software," and "Level 2 Pre-Cert" would "allow organizations to develop and market certain lower and moderate risk software without review while requiring a streamlined review for other types of software."[58] Please indicate how the content requirements for De Novo requests outlined in section 513(f) of the FD&C Act and the December 2018 proposed rule would be met by Level 1 Pre-Cert and Level 2 Pre-Cert organizations that develop and market software without review.

l. The Pre-Cert Pilot Program proposes utilizing the De Novo pathway in ways that are not identified in the December 2018 proposed rule—most notably, through the receipt of required information periodically rather than all at once. How would the standards and processes described in the proposed rule, if implemented as written, affect the agency's ability to utilize the De Novo pathway for the Pre-Cert Pilot Program, given that they do not mimic the Excellence Appraisal and Streamlined Review used in the pilot?

m. The FDA proposed its De Novo Classification rule in December 2018—over one year after the agency first proposed the Pre-Cert Pilot Program in August 2017. However, the proposed rule does not mention the Pre-Cert Pilot Program, which proposes to utilize the De Novo pathway in novel ways. Why did the FDA not mention the Pre-Cert Pilot Program, and its novel use of the pathway, in its December 2018 proposed rule?

n. During the pilot, and if the Pre-Cert Program extends beyond a pilot, how does the FDA plan to ensure that the RWPA it receives from organizations are accurate, timely, and based on all available information?

o. In its 2019 response, the FDA stated that it was "still working to identify all the right information and data elements to be shared before" it addressed the "mechanisms" by which the FDA and companies would exchange data.[59] Since June 2019, has the FDA identified the right information and data elements?

p. In its Working Model, the FDA states that post-market RWPA may form the basis of a change in claims and labeling.[60] Please provide greater detail on the evidence that would be required to support such changes.

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[58] U.S. Food and Drug Administration, "Developing a Software Precertification Program: A Working Model—v 1.0," January 2019, https://www.fda.gov/media/119722/download, pg. 23.
[59] Id.
[60] U.S. Food and Drug Administration, "Developing a Software Precertification Program: A Working Model—v 1.0," January 2019, https://www.fda.gov/media/119722/download, pg. 43.

q. Why is the FDA not requiring Pre-Cert pilot participants to share data with the National Evaluation System for health Technology (NEST)?

r. Will the FDA retain the right to request and obtain all raw data collected by participants as part of the Pre-Cert Pilot Program?

Progressive Approval Pathway

Following the enactment of the Minor Use and Minor Species Animal Health Act in 2004, the FDA established a "conditional approval" pathway to accelerate the development of animal drugs in commercially limited markets. Under the conditional approval pathway, manufacturers developing drugs for certain animal species have been able to bypass traditional FDA approval processes and market qualifying drugs without fully demonstrating their effectiveness.[61] To receive conditional approval, manufacturers must only demonstrate that a drug has "a 'reasonable expectation of effectiveness'"—a lesser standard than the "substantial evidence of effectiveness"; upon receiving conditional approval, manufacturers have been able to market their drugs for up to five one-year terms as they continue to gather the data necessary to meet the "substantial evidence" standard.[62]

In August 2018, the Animal Drug User Fee Act further expanded the conditional approval pathway by creating a 10-year pilot expansion program that allows certain other animal drugs to qualify.[63] At the time, I joined Senator Murray in strongly objecting to any expansion of the conditional approval pathway to human medical products—and the HELP Committee received assurances from then-Commissioner Scott Gottlieb that the FDA would not extend the pathway to human drugs or devices. In a July 2018 letter, Commissioner Gottlieb wrote that the "FDA does not believe this pathway would be suitable for human medical products."[64]

Despite Commissioner Gottlieb's assurances, however, the FDA's Fiscal Year 2020 budget justification referenced an FDA proposal called "progressive approval for devices" which, as written, seemed hardly distinguishable from the "conditional approval" pathway.[65] In June 2019, Senator Murray and I sent a letter to the FDA requesting information about the program.[66] After

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[61] 21 U.S.C. 360ccc; 21 CFR Part 516; U.S. Food and Drug Administration, "Conditional Approval Explain: A Resource for Veterinarians," https://www.fda.gov/animal-veterinary/resources-you/conditional-approval-explained-resource-veterinarians.

[62] Sponsors seeking conditional approval are still required to meet the same safety and manufacturing standards as those set through the full approval process. Drugs undergoing conditional approval must undergo an annual review by the FDA to ensure that sponsors are making progress toward meeting the effectiveness standard.

[63] P.L. 115-234

[64]164 Cong. Rec. S5472-73 (daily ed. Jul. 31. 2018) (Letter from FDA Commissioner Scott Gottlieb and Center for Veterinary Medicine Director Steve Solomon to Senate HELP Committee Chairman Lamar Alexander and Ranking Member Patty Murray).

[65] U.S. Department of Health and Human Services, "Fiscal Year 2020 Food and Drug Administration Justification and Estimates for Appropriations Committees," pp. 39-40, https://www.fda.gov/media/121408/download.

[66] U.S. Senator Elizabeth Warren, "Senators Warren, Murray Question FDA Proposal to Weaken Approval Standards for Medical Devices" (press release), June 25, 2019, https://www.warren.senate.gov/oversight/letters/senators-warren-murray-question-fda-proposal-to-weaken-approval-standards-for-medical-devices.

receiving a response in August 2019, we sent a follow-up letter requesting additional information in November 2019.[67]

1. **Do you agree that assuring patient safety and device effectiveness must be the primary goal of any device approval system managed by the FDA?**

2. **Do you believe that developing a "progressive approval" pathway for medical devices contributes to or detracts from the FDA's goal of assuring patient safety and device effectiveness?**

3. **If confirmed, will you commit to re-examining the "progressive approval" proposal included within the FDA's FY2020 budget justification to determine whether it adequately safeguards patients?**

4. **Please provide detailed answers to the questions included in the November 2019 letter referenced above, which include:**

    a. **The FDA envisions progressive approval as a pathway that would "expedite[] access to devices…intended to treat or diagnose a life-threatening or irreversibly debilitating disease or condition and address an unmet medical need."[68]**

        i. **For the purposes of the progressive approval pathway, how would the FDA define "unmet medical need"?**

        ii. **In its August 21st response, the FDA repeatedly uses the example of children as an example of a population underserved by existing medical device pathways. Does the FDA envision limiting the progressive approval pathway to certain populations, such as children? If so, please provide an overview of the populations the FDA is considering.**

        iii. **Does the FDA envision limiting the progressive approval pathway to disease populations with a certain number of patients, similar to the Humanitarian Device Exemption pathway? If so, please provide an overview of the numbers the agency is considering.**

        iv. **What additional limits, if any, is the FDA considering on the populations and devices eligible for the progressive approval pathway?**

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[67] U.S. Senator Elizabeth Warren, "Senators Warren and Murray Raise New Questions About FDA Approval to Weaken Approval Pathway for Certain Medical Devices" (press release), November 5, 2019, https://www.warren.senate.gov/oversight/letters/senators-warren-and-murray-raise-new-questions-about-fda-proposal-to-weaken-approval-pathway-for-certain-medical-devices.

[68] U.S. Department of Health and Human Services, Food and Drug Administration, "Fiscal Year 2020: Justification of Estimates for Appropriations Committees," https://www.fda.gov/media/121408/download.

b. In its August 21st response, the FDA pointed to the limited success of the Humanitarian Device Exemption (HDE) pathway in spurring device innovation to justify the need for a progressive approval pathway. The agency notes that the HDE pathway, as "the only existing regulatory marketing pathway intended to support medical device innovation for small populations like pediatric patients," does "not adequately meet the needs of children." It continues to state that, "despite multiple actions by Congress . . . [to] optimize the potential of the HDE program to help small patient populations . . . there has been no significant change in the number of Humanitarian Use Device (HUD) or HDE applications submitted or approved." In contrast, the agency states, "progressive approval would foster safe innovation in medical devices to meet many unmet needs."[69]

i. What are the primary economic challenges facing device makers interested in producing devices for small, underserved populations, such as pediatric patients? For each economic challenge identified, please describe which aspects of the progressive approval pathway (as envisioned by the FDA) would mitigate the challenge and increase the number of devices available to these populations.

ii. What specific aspects of the HDE pathway have made it unsuccessful at increasing the number of devices available to these populations? Could modifications to the HDE pathway address the problems in product development that the FDA has identified as necessitating the conditional approval pathway? If so, what are these modifications? If not, why not?

iii. What additional policies, if any, should Congress consider in an effort to expand the types of devices available to these populations?

c. In its initial description of the progressive approval pathway, the FDA stated that devices approved via the pathway would "be eligible for provisional approval . . . and could remain on the market after an established time period only after a demonstration of reasonable assurance of safety and effectiveness."[70] In its August 21st response, the agency narrowed down the established time period to "up to three years."[71] How did the FDA decide upon the three-year provisional approval period?

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[69] Letter from Karas Gross, Associate Commissioner for Legislative Affairs, U.S. Food and Drug Administration, to U.S. Senators Elizabeth Warren and Patty Murray, August 21, 2019.
[70] U.S. Department of Health and Human Services, Food and Drug Administration, "Fiscal Year 2020: Justification of Estimates for Appropriations Committees," https://www.fda.gov/media/121408/download.
[71] Letter from Karas Gross, Associate Commissioner for Legislative Affairs, U.S. Food and Drug Administration, to U.S. Senators Elizabeth Warren and Patty Murray, August 21, 2019.

d. According to the FDA's initial description of the progressive approval pathway, in cases where a device sponsor could *not* "demonstrate reasonable assurance of safety and effectiveness," the device's "initial approval would automatically sunset and the device could no longer be legally marketed."[72]

i. What challenges, including those presented by patients, physicians, sponsors, investors, and other device industry stakeholders, does the agency anticipate could arise in cases where the agency seeks to remove provisionally approved devices from the market?

ii. How could uncertainty concerning the possible removal from the market of a device that has received provisional approval under the progressive approval pathway limit the pathway's ability to mitigate the economic forces inhibiting device development described in Question 2?

e. In its August 21st response, the FDA states that the progressive approval "proposal would provide accountability to ensure that devices demonstrate a reasonable assurance of safety and effectiveness to remain on the market."[73] The FDA also indicated that a device sponsor using the progressive approval pathway "would be required to collect additional information through a registry, electronic health records (EHRs), or another source of real-world data on more patients and for a longer duration than the time period for obtaining the initial, provisional approval, and then demonstrate a reasonable assurance of safety and effectiveness."[74]

i. Please provide a complete summary of the oversight that the FDA envisions conducting on progressive approval pathway participants to ensure that safety and effectiveness standards are met. What resources would be necessary to make this post-market surveillance effective?

ii. Independent audits of the FDA's expedited approval pathways by the HHS Office of Inspector General and the U.S. Government Accountability Office have revealed challenges associated with implementing post-marketing requirements and indicate the need for better oversight measures.[75] How would the FDA ensure that post-

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[72] U.S. Department of Health and Human Services, Food and Drug Administration, "Fiscal Year 2020: Justification of Estimates for Appropriations Committees," https://www.fda.gov/media/121408/download.
[73] Letter from Karas Gross, Associate Commissioner for Legislative Affairs, U.S. Food and Drug Administration, to U.S. Senators Elizabeth Warren and Patty Murray, August 21, 2019.
[74] Letter from Karas Gross, Associate Commissioner for Legislative Affairs, U.S. Food and Drug Administration, to U.S. Senators Elizabeth Warren and Patty Murray, August 21, 2019.
[75] U.S. Department of Health and Human Services, Office of Inspector General, "FDA is Issuing More Postmarket Requirements, but Challenges with Oversight Persist," July 20, 2016, https://oig.hhs.gov/oei/reports/oei-01-14-00390.asp; U.S. Government Accountability Office, "FDA Expedites Many Applications, But Data for Postapproval Oversight Need Improvement," December 2015, https://www.gao.gov/assets/680/674183.pdf.

market studies of provisionally approved devices are completed in a timely manner?

iii. **A recently published analysis of the Manufacturer and User Facility Device Experience (MAUDE) database has underscored the challenges of post-market data collection, including the underreporting of adverse events. The analysis also found a significant degree of miscategorization of deaths as reports of injury and malfunction.[76] If safety determinations will be made at least in part through post-market data collection and analysis, what will the FDA do to ensure that the information provided by sponsors is accurate—especially when there is a significant incentive for them to underreport and misclassify adverse events?**

iv. **Is it the agency's view that real-world evidence would be sufficient to demonstrate "a reasonable assurance of safety and effectiveness"? If so, what precedent, if any, is there for relying exclusively, or almost exclusively, on real-world evidence to support the initial approval or clearance of a device?**

v. **The FDA notes in its response that the labeling for a provisionally approved device "would have to make clear that the medical device [meets] only the safety and performance standard, rather than the reasonable assurance of safety and effectiveness standard, to allow patients and health care professionals to make informed decisions."[77] What, if any, additional patient protections does the FDA envision being necessary for devices possessing only provisional approval?**

vi. **In the agency's view, are EHRs sufficiently widespread (and interoperable) that the FDA can rely on them for data collection for the purposes of the progressive approval pathway? If not, what could Congress and HHS do to increase the reliability of EHRs as a data collection tool?**

vii. **In the agency's view, are device registries sufficiently widespread and well-developed such that the agency can rely on them for data collection for the purposes of the progressive approval pathway? If not, what could Congress and HHS do to increase the reliability of registries as a data collection tool?**

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[76] JAMA Internal Medicine, "Miscategorization of Deaths in the US Food and Drug Administration Adverse Events Database," Lily Meier, Elizabeth Wang, Madris Tomes, et al., October 7, 2019, https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/275.

[77] Letter from Karas Gross, Associate Commissioner for Legislative Affairs, U.S. Food and Drug Administration, to U.S. Senators Elizabeth Warren and Patty Murray, August 21, 2019.

f. What additional data sources are the FDA considering using to collect data for the progressive approval pathway?

g. In its August 21st response, the FDA notes that the agency "is in an ideal position to continue leveraging [real-world evidence], in part, due to its work to develop the National Evaluation System for health Technology (NEST)."[78]

i. Does the FDA plan to require sponsors seeking progressive approval to share data with NEST? If not, why not?

ii. In the agency's view, is NEST sufficiently well-developed such that the agency could rely on it for data collection for the purposes of the progressive approval pathway? If not, what could Congress and HHS do to increase the reliability of NEST as a data collection tool?

Third-Party Servicing of Medical Devices

Some medical devices, such as patient examination gloves, are disposable or designed to be used only once. Other devices, however, are used repeatedly and on multiple patients.[79] Original equipment manufacturers (OEMS) and third party entities often refurbish, repair, recondition, rebuild, remarket, or remanufacture these devices to ensure that they continue to operate safely and effectively after entering the market.[80]

Entities that perform maintenance activities face different regulatory requirements depending on the type of maintenance being performed. Activities that "significantly change" the performance, safety specifications, or intended use of a finished device are considered "remanufacturing."[81] Remanufacturers, which can include OEMs and third party entities, must comply with numerous FDA requirements to ensure the safety of remanufactured devices.[82] Activities that do *not* "significantly change" the performance, safety specifications, or intended use of a device—but instead provide "preventive or routine maintenance…for the purpose of returning [a finished device] to the safety and performance specifications established by the OEM and to meet its original intended use"—are considered "servicing." Third-party servicers are not subject to the same safety and reporting requirements as remanufacturers.[83]

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[78] Letter from Karas Gross, Associate Commissioner for Legislative Affairs, U.S. Food and Drug Administration, to U.S. Senators Elizabeth Warren and Patty Murray, August 21, 2019.
[79] U.S. Food and Drug Administration, *FDA Report on the Quality, Safety, and Effectiveness of Servicing of Medical Devices*, May 2018, https://www.fda.gov/media/113431/download, pg. 1.
[80] *Id.*, pg. 1-2.
[81] *Id.*, pg. 3.
[82] *Id.*, pg. 1-2.
[83] *Id.*, pg. 2-3.; *See also* the testimony of Dr. Jeff Shuren during a May 2, 2017, Energy and Commerce Health Subcommittee hearing, during which he stated, "So, in [the FDA's] regulation on quality systems, we had made clear that third-party servicers are manufacturers but that they have been subject to enforcement discretion. We have not enforced those requirements." House Committee on Energy and Commerce, Subcommittee on Health, "Examining Improvements to the Regulation of Medical Technologies (transcript)." May 2, 2017, https://docs.house.gov/meetings/IF/IF14/20170502/105908/HHRG-115-IF14-Transcript-20170502.pdf.

In May 2018, in response to Section 710 of the FDA Reauthorization Act of 2017 (Public Law No. 115-42), the FDA issued a report on the continued quality, safety, and effectiveness of medical devices with respect to servicing.[84] The report noted significant stakeholder confusion over the difference between "servicing" and "remanufacturing." In response, the FDA announced that it would publish guidance clarifying the difference between "servicing" and remanufacturing" to "allow more consistent interpretation and clarification."[85]

The FDA original announced that it would issue draft guidance by the end of Fiscal Year 2019;[86] however, draft guidance is now on the agency's list to release in Fiscal Year 2020.[87] In October 2019, Senator Cassidy and I sent a letter to the agency requesting information about the guidance.

1. **If confirmed, will you commit to publishing draft guidance on distinguishing between medical device servicing and remanufacturing in a timely manner and no later than the end of Fiscal Year 2020?**

2. **Please provide detailed answers to the questions included in the October 2019 letter referenced above, which are:**

    a. **In its May 2018 report, the FDA stated that "[a] majority of comments, complaints, and adverse event reports alleging that inadequate "servicing" caused or contributed to clinical adverse events and deaths actually pertain to "remanufacturing" and not "servicing."**

        i. **If so many entities believed to be involved in "servicing" are actually "remanufacturing" devices, and FDA has said "the precise number of entities that perform servicing of medical devices in the U.S. is not known,"[88] how does FDA intend to identify the universe of actors to whom its upcoming guidance will apply?**

        ii. **How does the FDA intend to educate those entities who are unknowingly involved in remanufacturing activities about their obligations when the upcoming guidance is released?**

    b. **The FDA has estimated approximately 16,000 to 20,000 entities are engaged in servicing activities. How will the FDA promote compliance with the**

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[84] U.S. Food and Drug Administration, *FDA Report on the Quality, Safety, and Effectiveness of Servicing of Medical Devices*, May 2018, https://www.fda.gov/media/113431/download.
[85] *Id.*, pg. 24.
[86] U.S. Food and Drug Administration, "CDRH Fiscal Year 2019 (FY 2019) Proposed Guidance Development," October 22, 2018, https://www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/cdrh-fiscal-year-2019-fy-2019-proposed-guidance-development.
[87] U.S. Food and Drug Administration, "CDRH Proposed Guidances for Fiscal Year 2020 (FY 2020)," https://www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/cdrh-proposed-guidances-fiscal-year-2020-fy-2020.
[88] *Id.*, pg. 19.

guidance by those entities who consider themselves as only servicers but who may in fact also be involved in remanufacturing?

c. What surveillance mechanisms are available to the FDA to detect servicers who are also performing remanufacturing?

d. What actions does the FDA currently take if it identifies unregistered entities engaged in remanufacturing? What, if any, new options for action are under consideration?

Unique Device Identification System

In 2007, Congress instructed the FDA to establish a "unique device identification system for medical devices" to better track medical device outcomes and adverse events.[89] In response, the agency developed a system requiring device labels and packages to include Unique Device Identifiers (UDIs).[90] UDIs include both a device identifier (DI), a "fixed portion of a UDI" that identifies the "specific version or model of a device," and a production identifier (PI), a "variable portion of a UDI" that identifies information about a device's expiration date, serial number, and lot or batch number.[91]

For years, Members of Congress have advocated for the inclusion of UDI information in electronic health records and insurance claims forms.[92] Insurance claims forms capture longitudinal data on patient outcomes across healthcare providers and are a critical component of the FDA's efforts to establish the National Evaluation System for health Technology (NEST).[93] However, claims forms—including the Medicare claim form—do not currently have a field to record UDIs.

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[89] Public Law 110-85

[90] U.S. Food and Drug Administration, "Unique Device Identification System," 78 CFR 58785, September 24, 2013, https://www.federalregister.gov/documents/2013/09/24/2013-23059/unique-device-identification-system.

[91] U.S. Food and Drug Administration, "UDI Basics," https://www.fda.gov/medical-devices/unique-device-identification-system-udi-system/udi-basics.

[92] Letter from Senator Elizabeth Warren and Senator Charles E. Grassley to Sylvia Matthews Burwell, Andy Slavitt, and Robert Califf, March 8, 2016, https://www.grassley.senate.gov/sites/default/files/news/upload/2016_03_09%20CEG%20to%20HHS%20regarding%20UDI.PDF; Letter from Senator Elizabeth Warren and Senator Charles E. Grassley to Gary Beatty, Accredited Standards Committee X12, August 29, 2016, https://www.warren.senate.gov/files/documents/2016-8-29_UDI_letter_to_ASC_X12.pdf; Letter from Senator Elizabeth Warren and Senator Charles E. Grassley to Gary Beatty, Accredited Standards Committee X12, June 1, 2017, https://www.warren.senate.gov/files/documents/2017-6-1_Letter_to_X12.pdf; Letter from Senator Elizabeth Warren and Senator Charles E. Grassley to CMS Administrator Seema Verma, November 8, 2017, https://www.warren.senate.gov/files/documents/2017_11_08_Letter_to_CMS_re_UDI_and_claims.pdf; Letter from Senator Elizabeth Warren and Senator Charles E. Grassley to FDA Commissioner Scott Gottlieb, June 12, 2018, https://www.warren.senate.gov/imo/media/doc/2018.06.12%20Letter%20to%20Gottlieb%20on%20UDI%20and%20claims.pdf; "Pascrell Applauds Standards Decision for Medical Devices" (press release), October 16, 2019, https://pascrell.house.gov/news/documentsingle.aspx?DocumentID=4034.

[93] U.S. Food and Drug Administration, "National Evaluation System for health Technology (NEST)," https://www.fda.gov/about-fda/cdrh-reports/national-evaluation-system-health-technology-nest.

This lack of ability to track device outcomes is costly for taxpayers. A 2017 investigation by the Office of the Inspector General at the Department of Health and Human Services found that recalls or premature failures of just seven faulty cardiac devices resulted in $1.5 billion in Medicare payments to providers and $140 million in out-of-pocket costs to beneficiaries.[94] Moreover, the report was not able to examine the total cost of all device failures because of the lack of information about specific devices in claims data. The examiners were able to assess the impact of the seven devices included in the report only through a "complex and labor-intensive" audit.[95] Ultimately, The OIG recommended that the Center for Medicare and Medicaid Services (CMS) collaborate with the Accredited Standards Committee X12 (X12), which sets standards for electronic claims, to include medical devices' unique device identifier (UDI) on health insurance claim forms.[96] Last month, X12 released draft recommendations to incorporate the device identifier portion of the UDI of high-risk implantable medical devices in claims forms.[97]

The FDA has historically supported the inclusion of UDI information on claims forms. In a July 2016 joint letter to X12, the FDA and CMS identified several benefits to collecting device identifiers on medical claims forms.[98] The agency agreed to develop a list of specific, high-risk implantable devices for which reporting on claims will be recommended[99] and in 2018 released a Medical Device Safety Action Plan highlighting the benefits of UDI information to post-market surveillance. Furthermore, in a November 2018 letter, then-Commissioner Gottlieb stated that the FDA "supports the incorporation of the full Unique Device Identifier (UDI) into claims forms and believes, at a minimum, the DI portion of the UDI should be included."[100]

1. **Do you agree that including device identifier information in medical claims could support the evaluation of medical devices after approval?**

2. **If confirmed, will you continue to support the process of adding device identifiers to claims as a critical tool to better understand the performance of these products after approval?**

3. **How will you direct FDA to work with CMS to ensure that device identifiers can be effectively used to monitor threats to Medicare program integrity and patient health?**

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[94] Department of Health and Human Services Office of Inspector General, "Shortcomings of Device Claims Data Complicate and Potentially Increase Medicare Costs for Recalled and Prematurely Failed Devices," September 2017, https://oig.hhs.gov/oas/reports/region1/11500504.pdf
[95] *Id.*
[96] *Id.*
[97] X12, "X12 Standards for Electronic Data Interchange Technical Report Type 3, Health Care Claim: Institutional (837)," October 2019, http://forums.x12.org/007030-change-logs/X324-change-log-2.pdf, pg. 84.
[98] Letter from CMS Acting Administrator Andrew M. Slavitt and FDA Commissioner Robert M. Califf to Gary Beatty, Chair, Accredited Standards Committee X12 (July 13, 2016) (online at: http://pascrell.house.gov/sites/pascrell.house.gov/files/wysiwyg_uploaded/LETTER_FDA%20CMS%20Beatty%20Letter%20on%20UDI%20in%20Claims%207.13.16.pdf).
[99] American Hospital Association, "Standards organization approves UDI changes" *AHA News Now* (September 20, 2016) (online at: http://news.aha.org/article/160920-standards-organization-approves-udi-changes).
[100] Letter from Commissioner Scott Gottlieb to Senator Elizabeth Warren, November 19, 2018.

IX. Opioids

Opioid Epidemic

For decades, the United States has found itself in the midst of the opioid epidemic—a public health crisis that takes dozens of lives and impacts countless families each day. Massachusetts has been greatly impacted by this epidemic, leading local and state officials to work closely with first responders, health care providers, and community advocates to develop a comprehensive approach to help those suffering from substance use disorder access treatment and recovery services. The Massachusetts Department of Public Health (DPH) estimates that there were 1,974 opioid overdose deaths in Massachusetts in 2019—a 4 percent reduction from 2018.[101] Despite this decrease, it is critical that we continue to provide support to states like Massachusetts through the work of relevant federal agencies, and with Congressional action to provide adequate resources to tackle this crisis.

1. **If confirmed, what FDA authorities will you use to help address the opioid crisis?**

2. **If confirmed, how will you work with other federal agencies, such as the Substance Abuse and Mental Health Services Administration (SAMHSA) and the Drug Enforcement Administration (DEA), to develop an Administration-wide approach to the opioid crisis that is evidence-based?**

3. **If confirmed, what will you do to accelerate FDA review of alternative therapies to chronic pain, while still ensuring that those who require such medications receive it?**

4. **Earlier this year, the FDA announced a public education campaign, "Remove the Risk," aimed at encouraging individuals to safely dispose of unused prescription medications in their home. This announcement noted that "in 2017, retail pharmacies dispensed more than 191 million opioid prescriptions to almost 60 million patients…as many as 90% of these patients reported not finishing what was prescribed to them."[102] If confirmed, what will you do to enhance these ongoing FDA efforts to encourage Americans to safely dispose of unused medications?**

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[101] Massachusetts Department of Public Health, "Data Brief: Opioid-Related Overdose Deaths among Massachusetts Residents," February 2019, https://www.mass.gov/doc/opioid-related-overdose-deaths-among-ma-residents-february-2019/download.

[102] U.S. Food and Drug Administration, "FDA launches public education campaign to encourage safe removal of unused opioid pain medicines from homes," April 25, 2019, https://www.fda.gov/news-events/press-announcements/fda-launches-public-education-campaign-encourage-safe-removal-unused-opioid-pain-medicines-homes.

Over-the-Counter Naloxone

Over 130 Americans die each day as a result of an opioid overdose.[103] Naloxone is an easy-to-use, life-saving drug that reverses the toxic effectives of an opioid overdose.[104] Currently, naloxone is only available via prescription, yet doctors and public health administrators across the country have called for the provision of an over-the-counter (OTC) naloxone product to help combat the rising number of opioid-related deaths.[105] In January 2019, the FDA issued a series of documents to "encourage drug companies to enter the OTC market," including two model "consumer-friendly" Drug Facts labels (DFLs), which are required—along with studies showing "that consumers can understand how to use the product without the supervision of a health care professional"—before a product can be marketed over the counter.[106]

1. **Do you agree that increased access to naloxone, including making it available over the counter, could meaningfully prevent and reduce deaths associated with the opioid crisis?**

2. **If confirmed, will you continue existing FDA efforts to expand access to OTC naloxone?**

3. **What additional steps could the FDA take to expand access to all types of naloxone, including OTC naloxone?**

4. **What efforts does the FDA have underway to encourage physicians to co-prescribe naloxone with opioid medication? What additional steps can the FDA take to safely facilitate increased rates of co-prescribing of naloxone with opioid medication?**

5. **How can the FDA encourage manufacturers to continue expanding access to all types of naloxone, including OTC naloxone and generic naloxone products?**

X. Reproductive Health

The United States is facing a maternal mortality and morbidity crisis. Women in the United States die as a result of pregnancy and childbirth at a higher rate than in any other developed country, and in the past twenty years, our nation's maternal mortality rate has doubled—making it the only industrialized nation with an increasing maternal mortality rate.[107] The causes of

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[103] U.S. Centers for Disease Control and Prevention, "America's Drug Overdose Epidemic: Data to Action," https://www.cdc.gov/injury/features/prescription-drug-overdose/index.html.
[104] Substance Abuse and Mental Health Services Administration, "Naloxone," https://www.samhsa.gov/medication-assisted-treatment/treatment/naloxone.
[105] U.S. Food and Drug Administration, "Statement on continued efforts to increase availability of all forms of naloxone to help reduce opioid overdose deaths," September 20, 2019, https://www.fda.gov/news-events/press-announcements/statement-continued-efforts-increase-availability-all-forms-naloxone-help-reduce-opioid-overdose.
[106] U.S. Food and Drug Administration, "Statement from FDA Commissioner Scott Gottlieb, M.D., on unprecedented new efforts to support development of over-the-counter naloxone to help reduce opioid overdose deaths," January 17, 2019, https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-unprecedented-new-efforts-support-development-over.
[107] Health Affairs, "The United States Maternal Mortality Rate Will Continue To Increase Without Access to Data," Rachel Mayer, Alison Dingwall, Juli Simon-Thomas, Abdul Sheikhnureldin, and Kathy Lewis, February 4, 2019,

maternal mortality are complex and include racial, ethnic, and socioeconomic disparities; comorbidities; and lack of access to the healthcare system.[108] A CDC analysis of pregnancy-related deaths found that some of the leading causes of death involve hypertensive disorders of pregnancy (i.e., preeclampsia or eclampsia), cardiovascular conditions (e.g., congenital heart disease, congestive heart failures, cardiac valvular disease, hypertensive heart disease) and noncardiovascular conditions (e.g., endocrine, hematologic, immunologic, and renal).[109]

Unfortunately, information about how to treat conditions in pregnancy is profoundly limited and very few drugs are approved for use during pregnancy. In large part, this is due to the fact that women, and especially pregnant and lactating individuals, have historically faced systemic barriers to participating in clinical trials.[110]

1. **What do you believe the impact of greater inclusion of pregnant and lactating women in clinical trial data and results would be on drug safety and biomedical innovation?**

2. **If confirmed, what efforts will you undertake to improve the inclusion of women and pregnant individuals in clinical trials?**

3. **What specific plans do you have to implement the goals, priorities, and recommendations of the Federal Task Force on Research Specific to Pregnant Women and Lactating Women?**

4. **How can FDA support the development of new therapeutic products for conditions specific to pregnant and lactating women?**

5. **Do you support efforts to strengthen the FDA's authority to require clinically relevant data on pregnant women and lactating women to inform drug dosing and safety decisions?**

6. **As FDA Commissioner, how would you strengthen the FDA's Pregnancy Exposure Registries Initiative?**

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https://www.healthaffairs.org/do/10.1377/hblog20190130.92512/full/; American College of Obstetricians and Gynecologists, "Maternal Mortality," https://www.acog.org/About-ACOG/ACOG-Departments/Government-Relations-and-Outreach/Federal-Legislative-Activities/Maternal-Mortality?IsMobileSet=false.

[108] Health Affairs, "The United States Maternal Mortality Rate Will Continue To Increase Without Access to Data," Rachel Mayer, Alison Dingwall, Juli Simon-Thomas, Abdul Sheikhnureldin, and Kathy Lewis, February 4, 2019, https://www.healthaffairs.org/do/10.1377/hblog20190130.92512/full/.

[109] Centers for Disease Control and Prevention, "Vital Signs: Pregnancy-Related Deaths, United States, 2011-2015, and Strategies for Prevention, 13 States, 2013-2017," May 10, 2019, https://www.cdc.gov/mmwr/volumes/68/wr/mm6818e1.htm?s_cid=mm6818e1_w.

[110] U.S., Department of health and Human Services, Public Health Service, National Institutes of Health, Office of Research on Women's health, "Enrolling Pregnant Women: Issues in Clinical Research," *National Institutes of Health*, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3547525/.

XI. Vaping and E-Cigarettes

Rates of youth tobacco use have skyrocketed in recent years, largely due to the popularity of e-cigarettes. According to the most recent National Youth Tobacco Survey, nearly 30 percent of high school students and over 10 percent of middle school students use e-cigarettes.[111] Of students who use e-cigarettes, seventy-two percent of high school students and 60 percent of middle school students used e-cigarettes with kid-friendly flavors like fruit and mint.[112] It is widely known that nicotine is extremely addictive and can harm brain development.[113]

Rising rates of e-cigarette use have also given rise to a series of vaping-related illnesses that have caused more than 2,000 people to fall ill and have led to at least 42 deaths.[114] Experts currently believe that these illnesses are linked to the inclusion of vitamin E acetate additives in THC vape products.[115]

1. **Do you agree that rising rates of youth e-cigarette use reflect a public health emergency that the FDA should take robust steps to combat?**

2. **Do you agree that flavored e-cigarettes, such as fruit and mint, contribute to youth use of e-cigarettes?**

3. **In September 2019, the Administration announced that it would "outline a plan…for removing flavored e-cigarettes and nicotine pods from the market," including mint and menthol.[116] Earlier this month, however, the Administration reversed course. Reportedly facing "pressure from his political advisers and lobbyists," the President "has resisted moving forward with any action on vaping."[117] This failure to act is unacceptable. If confirmed, will you push to implement the robust ban on e-cigarette flavors announced in September?**

4. **If confirmed, what additional steps will you take to combat youth e-cigarette use? What steps will you take to make it more challenging for youth to access e-cigarettes?**

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[111] JAMA, "e-Cigarette Use Among Youth in the United States, 2019," November 5, 2019, https://jamanetwork.com/journals/jama/article-abstract/2755265?resultClick=1.
[112] Id.
[113] U.S. Surgeon General, "Know the Risks: E-Cigarettes and Young People," https://e-cigarettes.surgeongeneral.gov/knowtherisks.html.
[114] Reuters, "U.S. vaping-related deaths rise to 42, cases of illness to 2,172," November 14, 2019, https://www.reuters.com/article/us-usa-vaping-cdc/u-s-vaping-related-deaths-rise-to-42-cases-of-illness-to-2172-idUSKBN1XO2LR; CBS Boston, "Massachusetts Reports 3rd Vaping-Related Death," November 6, 2019, https://boston.cbslocal.com/2019/11/06/massachusetts-vaping-related-lung-injuries-death-reports/.
[115] Vox, "Vitamin E acetate is a key culprit in the vaping illness outbreak," Julia Belluz, November 11, 2019, https://www.vox.com/science-and-health/2019/11/11/20959198/vaping-vitamin-e-acetate.
[116] New York Times, "Trump Administration Plans to Ban Flavored E-Cigarettes," September 11, 2019, https://www.nytimes.com/2019/09/11/health/trump-vaping.html.
[117] New York Times, "Trump Retreats From Flavor Ban for E-Cigarettes," Annie Karni, Maggie Haberman, and Sheila Kaplan, November 17, 2019, https://www.nytimes.com/2019/11/17/health/trump-vaping-ban.html.

5. **If confirmed, what steps will you take to address the targeting of youth by e-cigarette manufacturers through their products and advertising?**

6. **There are currently no nicotine cessation therapies approved for youth use. If confirmed, how will you direct the FDA to work with other federal agencies and Congress to expand youth access to nicotine cessation therapies?**

7. **If confirmed, what steps will you take to combat the outbreak of vaping-related illnesses? What is the status of current CDC and FDA investigations into the cause of the vaping-related illnesses?**