December 31, 2024

The Honorable Brett Guthrie
Chairman, Subcommittee on Health
Committee on Energy and Commerce
U.S. House of Representatives
Washington, D.C. 20515

Dear Chair Guthrie:

Thank you for providing the Food and Drug Administration (FDA or the Agency) with the opportunity to testify at the May 22, 2024, hearing before the Subcommittee on Health, Committee on Energy and Commerce entitled "Check Up: Examining FDA Regulation of Drugs, Biologics, and Devices." This letter is a response for the record to questions posed by the committee.

Sincerely,

Aubrie L. Paulos -S

Digitally signed by Aubrie L. Paulos -S
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Questions for the Record
Subcommittee on Health, Committee on Energy and Commerce
"Check Up: Examining FDA Regulation of Drugs, Biologics, and Devices"
May 22, 2024
Questions for Dr. Jeff Shuren, Director, Center for Devices and Radiological Health
U.S. Food and Drug Administration

Contents

The Honorable Cathy McMorris Rodgers

Telework

1. **What will it take to fill the open roles for review staff and related administrative staff at FDA?**

    a. **What efforts are under way to attract talent and hire these critical roles?**

Offering incentives like workplace flexibilities in addition to modern hiring tools and competitive compensation help the Agency to keep pace with industry and tech for the most qualified staff.

FDA has prioritized recruitment and accompanying marketing strategies. We will be aligning vacant positions to a specific recruitment strategy to include monthly/quarterly distributions of opportunities to professional associations and organizations, including colleges and universities with diverse populations. We will also leverage all recruitment and outreach efforts to both educate about career opportunities at FDA and recruit and hire candidates. The immediate goal is to leverage each touch point with potential candidates in order to hire immediately or to create an interest for future hiring.

We currently announce open positions via a variety of avenues including LinkedIn, Twitter, and Title 21 web page.[1] We are expanding our outreach to other media outlets such as scientific journals that will point the candidate back to the hiring product center to become informed and educated on the center and its mission. We are also working on the capability to accept resumes for Title 21 positions via our Jobs at FDA Website page to quickly link candidates with vacant positions and hiring managers.

The Food and Drug Administration (FDA) is committed to meeting the user fee hiring goals. This includes effectively utilizing Title 5, Title 42(g), Schedule A, Veterans Recruitment Authority (VRA), Title 21 hiring authorities, and coordinating with the Office of Talent Solutions. The Agency is also committed to communicating about our progress and reporting regular updates made towards hiring goals for FY 2023-2027. See Performance Reports[2] and Quarterly Hiring Updates.[3]

For MDUFA, CDRH has made 141 MDUFA V hires – 100 percent of the Center's MDUFA V positions FY 2023. For FY 2024, as of the end of Q1 (12/31/2023), FDA made 10 MDUFA V hires, which represents 24 percent of the FY 2024 hiring goal and is on track to meet the FY24 hiring goal by

[1] https://www.fda.gov/about-fda/jobs-and-training-fda/title-21-job-opportunities
[2] https://www.fda.gov/about-fda/user-fee-performance-reports/mdufa-performance-reports
[3] https://www.fda.gov/about-fda/user-fee-financial-reports/mdufa-financial-reports

the end of FY24.

2. **The FDA along with many other federal agencies instituted virtual work policies during the COVID-19 pandemic. There have been concerns that the ongoing virtual schedule has impacted the frequency and quality of interactions between the FDA and important stakeholders. Does the FDA plan to bring staff back to in-person work and meetings with sponsors and patients?**

3. **The Committee understands that the term "telework" refers to a work flexibility arrangement that allows an employee to work from an approved alternative worksite other than the employee's official duty location for an approved number of days each pay period. Within each center, what percentage of employees telework?**

    a. **What is the range of approved numbers of days each work period?**

    b. **What is the most typical number of approved numbers of days each work period?**

    c. **How is the specified number of days enforced?**

    d. **Within each center, what percentage of employees are fully remote?**

    e. **Can FDA provide a summary of actions it is taking to increase the frequency and quality of interactions with sponsors?**

Answer for 2 and 3:

As of January 29, 2023, FDA has transitioned into our Business-Driven Hybrid Workplace model which bases eligibility for workplace flexibilities on the nature of an employee's work and the business needs of the organization. As part of this model, FDA staff maintain official telework agreements. One of the considerations for our Business-Driven Hybrid Workplace model is the ability for FDA to recruit and retain talent. However, in-office presence and in-person interactions with supervisors, peers, other offices and centers, and external stakeholders is often beneficial for advancing and facilitating the multidisciplinary and often public facing nature of our critical work. In these circumstances, the Agency continues to ensure Agency personnel are on site.

CDRH has been accepting and holding in-person meetings with stakeholders for quite some time. CDRH grants in-person meetings for sponsors who request them, including particularly in our presubmission program. For requests tied to product submissions, we follow standard scheduling timelines consistent with MDUFA V performance goals.

Thus far, FDA has received positive feedback from industry regarding the flexibility that virtual, hybrid, and in-person meetings provide. FDA will continue to work with industry to fully meet our user fee commitments and to ensure the FDA workforce operates at the highest level as we work to further our public health mission.

In addition, FDA Advisory Committees and other patient engagement sessions invite participation via an online teleconferencing and/or video conferencing platform to support face-to-face engagements.

The productivity of FDA staff is higher than it has ever been, and the pandemic has taught us that much of our work can be accomplished efficiently and effectively while continuing to leverage workplace flexibilities.

Wound Dressings and AMR

4. **The Food and Drug Administration (FDA) has proposed a new rule, Medical Devices; General and Plastic Surgery Devices; Classification of Certain Solid Wound Dressings; Wound Dressings Formulated as a Gel, Creams, or Ointment; and Liquid Wound Washes, which would require reclassification of certain wound products containing antimicrobials or other chemicals. This proposed re-classification would fundamentally change the regulatory status of both future and existing wound care products by making them subject to 510(k) requirements with special controls or premarket approval (PMA), regardless of how long they have been on the market. The FDA has cited concerns that these products are potentially increasing human antimicrobial resistance (AMR) as the reason for this reclassification. Please explain the scientific evidence that supports FDA's belief that certain relevant products are contributing to AMR.**

   For a point of clarification, please note that this proposed rule is not a "reclassification," as stated, but rather the Agency's proposal to initially classify this large group of products that are currently unclassified preamendments devices. An unclassified preamendments device is a device that was on the U.S. market prior to the Medical Device Amendments of 1976 and for which a classification regulation has not been promulgated. This effort is critical to providing the medical device industry with much needed clarity and transparency regarding the regulatory requirements to demonstrate safety and effectiveness for wound dressings and liquid wound washes containing

antimicrobials and/or other chemicals. FDA proposed to classify over 99% of these previously cleared devices as Class II, requiring premarket notification via a 510(k) submission, which is the same submission type used to currently authorize these products. Additionally, the controls outlined in the proposed rule largely mirror the Agency's review practices over the past decade and beyond.

As part of this classification action, and with the input of multiple advisory panel meetings, the Agency has identified the potential risks to health, of which antimicrobial resistance (AMR) is one, and corresponding mitigations associated with these products. Regarding your question on the impact of the antimicrobials used in wound dressings and liquid wound washes to potentially contribute to the development and dissemination of AMR, the following information and scientific evidence from the literature referenced in the proposed rule supports the identification of AMR as a risk to health that needs to be mitigated as part of this classification effort:

- There is a wide range of antimicrobials previously cleared in this group of products, including both "medically important" and "non-medically important" antimicrobials.
- While an antimicrobial is effective when applied at an appropriate concentration, effectiveness is only exhibited on a limited segment of the microbial world. Some species of bacteria are naturally resistant to a given antimicrobial, while others may eventually acquire resistance (Ref. 23 of the proposed rule[4]).
- AMR is not limited to "medically important" antimicrobials, as the scientific literature details resistance mechanisms associated with the myriad of biocidal agents not considered to be medically important.
- Many resistance genes are found on plasmids, which play an integral role in the horizontal transfer of resistance between organisms and stack multiple resistance genes together on a single mobile element (Ref. 24 of the proposed rule[5]). As a result, many hospital-acquired infections involve bacteria that are resistant to multiple classes of antimicrobials, including both "medically important" and "non-medically important" antimicrobials (Refs. 25 and 26 of the proposed rule[6,7]).
- The application of a "non-medically important" antimicrobial has the potential to contribute to the selection and dissemination of "medically important" antimicrobial resistance mechanisms via co-

[4] https://www.federalregister.gov/d/2023-26209/p-140
[5] https://www.federalregister.gov/d/2023-26209/p-141
[6] https://www.federalregister.gov/d/2023-26209/p-143
[7] https://www.federalregister.gov/d/2023-26209/p-145

selection phenomena such as co-resistance and cross-resistance.

As such, it is important to evaluate the risk of AMR in all antimicrobial-containing wound dressings and liquid wound washes to understand the potential for selecting resistant organisms at the patient-level and further limiting a clinician's therapeutic options.

5. Assuming there is evidence that certain wound care products are contributing to AMR, how will reclassifying these products prevent patients from developing antimicrobial resistance?

As stated in response four, the cited action is an initial classification rather than a reclassification. In terms of how the proposed classification of antimicrobial-containing wound dressings and liquid wound washes mitigates the risk of these products contributing to the spread of AMR, in the proposed rule, concerns with AMR are primarily focused on the impact of resistance to "medically important" antimicrobials that pose a high level of AMR concern, such as antibiotics. For those products that contain "medically important" antimicrobials, we are proposing to classify them as Class III, the highest risk category of devices, requiring a premarket approval application (PMA) to demonstrate there is a benefit to using the product that outweighs its risks, including the spread of AMR. As noted in response to 4), we anticipate that only a small minority of these products (< 1 %) would be subject to PMA.

The proposed rule takes a different approach for wound dressings and liquid wound washes that do not contain "medically important" antimicrobials, as they pose a medium or low level of AMR concern that is proposed to be mitigated with special controls as part of the evaluation of a 510(k). The Agency has proposed the following as part of a least burdensome approach to mitigate the AMR risks in these products that do not contain "medically important" antimicrobials:

1) Antimicrobial Characterization and Preservative Effectiveness Testing- This testing is routinely requested as part of the Agency's current review practices and ensures that the concentration of antimicrobial is not too high as to create safety concerns, and also not too low as to condition microorganisms in sublethal concentrations that contribute to AMR development.
2) AMR Risk Assessment - Conducting an AMR risk assessment based on a literature review to understand emerging resistance mechanisms and the presence of resistant organisms that may compromise the effectiveness of the antimicrobial and may indirectly contribute to the spread of antibiotic resistance via co-selection mechanisms. As AMR is an evolving topic with expected novel resistance

mechanisms and resistant organisms emerging in the future, it is important for the device manufacturer to be informed with AMR trends as this information will be critical to their selection of antimicrobial applications and concentrations needed to remain effective.

3) Labeling Controls - Improved labeling to better inform the end-user of the potential presence of resistant organisms and the risks of AMR associated with the product. This information is critical to aid the end user in better understanding the potential risks of selecting for resistant organisms and determining when the use of an antimicrobial-containing wound dressing is prudent.

Taken together, we believe the combination of this proposed split classification approach, which would classify a limited number of products containing medically important antimicrobials into class III (less than one percent), along with the majority of these products being proposed for classification as class II (more than 99 percent), with the identified special controls, will provide a balanced approach to mitigate the risks to health of these products contributing to the spread of AMR, while maintaining patient access to these important products.

AMR Reclassification

6. How does the FDA intend to take patient access into consideration when it comes to reclassification?

As stated in the response to Question Four, the cited action is an initial classification rather than a reclassification. FDA is carefully reviewing and responding to public comments submitted in response to the proposed rule, including those related to patient access. The Agency takes a least burdensome approach for addressing risk to patients and the approach in the proposed rule is based on feedback from multiple FDA advisory committee meetings. Moreover, the testing requirements proposed in the rule are largely consistent with the typical data requests for wound dressings cleared in the last decade. Out of the several hundred products impacted by this proposed rule, if finalized as currently proposed, the majority would remain as 510(k)s and only a small minority (less than one percent) would be subject to PMA. Because less than one percent of currently cleared dressings that are within the scope of this proposed rule, if finalized, would be subject to PMA, and testing requirements and special controls for class II are largely reflective of typical data needs for cleared wound dressings, the proposed rule does not anticipate disruption to patient access if finalized as proposed.

The Honorable Robert Latta

Inspections

1. **Due to the difficulty conducting facility inspections of medical device manufacturers in China, is examining products at ports of entry the best way to inspect and detain products with registration and quality issues?**

While examining products at ports of entry is not a replacement for on-site inspections of medical device manufacturers and their devices that may have quality issues, FDA can collect important evidence through examining products at the port of entry. FDA does this through:

- Temporary or ongoing sampling assignments
- Import Alerts
- Import Bulletins
- Domestic Import Samples
- Other similar screening tools

To help pinpoint incoming products with quality issues, the various inputs of quality data collected by FDA can potentially be utilized within Predictive Risk-based Evaluation for Dynamic Import Compliance Targeting ("PREDICT"). PREDICT is a risk-based analytics tool that uses automated data mining, pattern discovery, and queries of FDA databases to determine the potential risk of a shipment.

Based on our experience, by increasing sampling overall, we believe FDA would be able to collect more tangible evidence about the actual quality and efficacy of a medical device at the port of entry.

   a. **Please explain the manner in which the agency scrutinizes imports from China.**

In addition to inspectional activities, products regulated by FDA are subject to review when they are offered for entry into the United States. All FDA-regulated products submitted through U.S. Customs and Border Protection (CBP) receive automated electronic screening to validate entry data and assess the initial risk of the product using PREDICT.[8] Any entry that does not receive a release by FDA's system is routed for manual review. Some reasons this may happen include:

- products identified as higher risk;
- entries that do not contain all the necessary information; or
- products identified for examination or sampling, either on a surveillance basis or specifically targeted.

If a product is held for manual review, FDA staff may need to collect more evidence or conduct an examination or sample collection to determine a product's

[8] https://www.fda.gov/industry/import-systems/entry-screening-systems-and-tools

compliance with regulatory requirements. For medical devices, this includes verifying compliance with:

- establishment registration,
- product listing,
- product approval,
- labeling, and
- current Good Manufacturing Practices/Quality Systems Regulations, as applicable.

Products that appear to be in compliance are released and products that appear to be in violation of FDA laws or regulations are detained[9] and may subsequently be refused if the importer cannot demonstrate that the product complies with FDA's regulations; products refused entry into the United States must be exported or destroyed.

FDA also utilizes import alerts, which allows for Detention Without Physical Examination (DWPE) of products subject to an import alert. Products are subject to DWPE based upon past violations. These violations could be related to the product, manufacturer, shipper and/or other information indicating the product may be in violation of FDA laws. Import alerts prevent potential violative products from being distributed into the United States, free up agency resources to examine other products, provide uniform coverage across the country, and place the responsibility back on the importer. A complete list of FDA Import Alerts which contain firms/products subject to DWPE can be found at this link: http://www.accessdata.fda.gov/cms_ia/ialist.html.

b. Can the agency exert additional pressure and focus on manufacturers with past citations?

FDA does prioritize shipments offered for import using past compliance history. It does so using the PREDICT mechanism discussed above, which is a risk-based analytics tool that uses automated data mining, pattern discovery, and queries of FDA databases to determine the potential risk of a shipment. It takes into consideration the inherent risk of a product and compliance status of importers, manufacturers, and shippers – which includes past citations.

c. What additional resources are needed to improve the vigilance over Chinese medical device imports?

The United States is heavily dependent on certain countries for medical devices, their components, and raw materials. This makes the United States vulnerable to having substandard, ineffective, or unsafe products enter the supply chain. While this issue is not new, it has become more pervasive and widespread, as

[9] https://www.fda.gov/industry/actions-enforcement/detention-hearing

demonstrated during the COVID-19 pandemic and recently evidenced by the Agency's alert to the public regarding plastic syringes from China. While FDA's existing regulatory authorities are critical, empowering the Agency with additional authorities would enable FDA to take more timely action to prevent problematic imported devices from reaching patients, healthcare providers, and the American public.

Despite extensive efforts using FDA's existing authorities, the entities responsible for developing, manufacturing, importing, and distributing these products into the United States have demonstrated the ability to elude the Agency's oversight. Many foreign companies operating in the medical technology space have a web of subsidiaries operating under various corporate structures aiming to penetrate the U.S. market simultaneously. This makes it challenging to contain and prevent their problematic devices from proliferating in the U.S. healthcare system. Additionally, there have been circumstances where FDA has gone to inspect a foreign firm and found that they failed to maintain basic records as required under the Act, limiting FDA's ability to ensure situations of concern are adequately resolved. In the face of these troubling patterns, issuing import alerts for specific foreign firms and devices is not always alone an effective strategy to protect the public health. FDA is also aware of instances in which import alerts have been less than effective in preventing substandard devices from entering the U.S. market, because, for example, importers have imported problematic devices into another country (e.g., Mexico) before importing them into the United States or incorporating them as components in different kits before importing the kits into the United States without the importer taking responsibility for ensuring that the devices are appropriately FDA-authorized for marketing, compliant with U.S. good manufacturing practices, and compliant with the necessary performance specifications.

Even when the Agency can fully investigate and pursue a specific problem with a particular foreign firm, we have seen those entities respond by ceasing operations while the same troubling conduct appears in a different though seemingly related entity, and substandard products once again make their way into the U.S. supply chain. Additionally, foreign firms frequently fail to properly maintain records as required by the FD&C Act making it challenging for the Agency to fully understand the situation when inspecting foreign firms. Stronger authority over importers of devices will make it easier for FDA to ensure that imported devices meet FDA regulatory requirements for safety, effectiveness and quality by holding the importers legally responsible as well as the foreign manufacturers.

UDI

2. **This Committee has been looking into the visibility of the medical device supply chain, especially as supply chain vulnerabilities came to light during the PHE. FDA requires medical devices to be marked with a unique device identifier (UDI) to assist with tracking, tracing and recalls. Please tell us whether FDA is planning to update its regulations, so all**

medical device sizes are following UDI requirement?

The current UDI regulation accounts for assignment of UDIs for different medical devices when appropriate.

The Unique Device Identification System final rule (UDI Rule)[10] requires device labelers[11] to include a unique device identifier (UDI) on device labels and packages, except where the rule provides for an exception or alternative (see 21 CFR 801.30, 801.40(d), and 801.45(d)). For each version or model required to bear a UDI, the UDI Rule also requires device labelers to submit device information to the Global Unique Device Identification Database (GUDID).

Under 21 CFR 801.40, the UDI must include a device identifier segment, which is defined under 21 CFR 801.3 as a mandatory, fixed portion of a UDI that identifies the specific version or model of a device and the labeler of that device. Under 21 CFR 801.3, version or model means all devices that have specifications, performance, size, and composition, within limits set by the labeler. If the device labeler determines that different sizes constitute different models or versions, then each size would be expected to have a separate UDI-DI. Updates to the UDI regulation is therefore not necessary to account for assignment of UDIs for different sizes, when appropriate.

CMS NCD

3. **The Centers for Medicare and Medicaid Services (CMS) has become increasingly interested in collecting more evidence and information about certain drugs, devices, and technologies before making them widely available to Medicare beneficiaries despite the fact that these therapies already have received approval or clearance from the Food and Drug Administration (FDA). For example, CMS effectively restricted patient access to treatment only within the context of additional clinical trials approved by CMS in the Coverage with Evidence Development (CED) National Coverage Determination (NCD) for Alzheimer's Disease drugs. In other cases, CMS has declined to cover routine clinical trial costs for therapies under investigation for new indications despite the existence of the longstanding policy (NCD 310.1) requiring Medicare coverage for routine costs of clinical trials. In other words, a growing number of administrative actions suggest that CMS is seeking to expand its role and make clinical and scientific decisions historically under the strict authority of the FDA. Given this trend, is the**

[10] https://www.federalregister.gov/documents/2013/09/24/2013-23059/unique-device-identification-system

[11] 21 CFR 801.3 defines "labeler" as

(1) Any person who causes a label to be applied to a device with the intent that the device will be commercially distributed without any intended subsequent replacement or modification of the label; and

(2) Any person who causes the label of a device to be replaced or modified with the intent that the device will be commercially distributed without any subsequent replacement or modification of the label, except that the addition of the name of, and contact information for, a person who distributes the device, without making any other changes to the label, is not a modification for the purposes of determining whether a person is a labeler.

FDA concerned that CMS has exceeded its administrative authority in taking these administrative actions?

- **Link:** https://www.cms.gov/medicare-coverage- database/view/ ncd.aspx?NCDId=1&ncdver=2not

Ensuring the availability of innovative interventions for people is a shared priority for both the Centers for Medicare & Medicaid Services (CMS) and the U.S. Food and Drug Administration (FDA). FDA recognizes the important and related – but different – roles and authorities of CMS.

FDA's decision to authorize a new medical product for marketing is based on a careful evaluation of the available data and a determination that the medical product meets the applicable safety and effectiveness standard. In some instances, FDA has the authority to require additional studies after approval to provide additional information regarding the anticipated clinical benefit for the medical product. In general, CMS determines whether an item or service in a Medicare benefit category is reasonable and necessary for the diagnosis or treatment of an illness or injury and focuses on evidence concerning the Medicare population, which can entail an independent review to determine whether an item or service should be covered by Medicare.

Questions about CMS decisions to approve or disapprove coverage could only be addressed by CMS.

We recognize the impact that FDA marketing authorization and CMS coverage decisions have on people with serious and life-threatening conditions and their loved ones. FDA and CMS share a common goal of wanting to advance the development and availability of innovative medical products.

a. Does the FDA have suggestions for ensuring that Medicare beneficiaries have appropriate access to drugs, devices and technologies that have received FDA approval or clearance?

A critical part of FDA's role in protecting the public health is ensuring the safety and effectiveness of medical products. We also realize the importance of ensuring patient access to these products, and with support of Congress have launched several initiatives that can help sponsors consider evidence generation strategies and other factors that will support patient access to their products, including, when appropriate, access for Medicare beneficiaries, throughout their product development cycles.

CDRH is committed to helping advance Medicare beneficiaries' access to novel medical devices. While the coverage decisions are made independently by CMS, FDA encourages conversations between device manufacturers and CMS during the early phases of device development to streamline the collection of the

evidence to support both FDA premarket review and CMS coverage decisions. CDRH developed the Early Payor Feedback Program (EPFP) to support better communication between the device developer and payors. The EPFP provides a voluntary opportunity for medical device manufacturers to obtain payor input (including CMS) on clinical trial design or other plans for gathering clinical evidence needed to support coverage decisions. FDA and CMS also have a parallel review program which established a mechanism for FDA and CMS to simultaneously review the pivotal clinical data to help decrease the time between FDA's approval of a premarket approval application or granting of a De Novo classification request and the subsequent CMS proposed national coverage determination (NCD). Additional information about these programs can be found at https://www.fda.gov/about-fda/cdrh-innovation/medical-device-coverage-initiatives-connecting-payors-payor-communication-task-force.

FDA has also launched and then expanded the Total Product Life Cycle Advisory Program (TAP) Pilot, which is a key component of the latest reauthorization of the Medical Device User Fee Amendments (MDUFA). TAP is intended to foster innovation in the medical device industry by promoting early, frequent, and strategic communications between FDA and medical device sponsors, while maintaining the Agency's rigorous standards for device safety and effectiveness. The long-term vision for TAP is to help spur more rapid development and increased access to safe, effective, high-quality medical devices. One integral part of this program is facilitating regular, solutions-focused engagement between FDA's review teams, TAP participants, and non-FDA stakeholders, such as patients, providers, and payors, beginning early in device development.

TAP is intended to foster innovation across the medical device industry by improving the predictability and reducing the time and cost of the "valley of death" from concept to commercialization.

b. How does the FDA view its work with CMS moving forward?

FDA will continue to share knowledge and information with CMS as needed, consistent with applicable laws, to help ensure that safe, effective medical products are available to people across the country.

c. Does the FDA expect to collaborate more broadly CMS on making clinical and scientific determinations that historically the FDA has made on its own? If yes, please describe how the FDA envisions enhanced collaboration with CMS and how such collaboration will ensure patient access to medically necessary and life- saving therapies.

As previously stated, FDA's decision to authorize a new medical product for marketing is based on a careful evaluation of the available data and a determination that the medical product meets the applicable safety and

effectiveness standard. CMS conducts its own independent review under its separate statutory authorities to determine whether an item or service should be covered nationally by Medicare, including examining whether it is reasonable and necessary for the diagnosis or treatment of an illness or injury and focuses on the evidence concerning the Medicare population. While the FDA may provide CMS with information relevant to making these determinations and has developed the aforementioned programs to facilitate engagement between some developers and payors such as CMS earlier in the development process, CMS-decision making regarding coverage is separate from the FDA's decision to authorize a product for marketing and FDA's related clinical and scientific determinations.

LDT Rule

4. **Laboratories have long filled the gap in pediatric testing because many FDA-authorized IVDs are not cleared or approved for use in pediatric patients, and modifications may be necessary to suit the pediatric population. However, I've heard concerns that the final rule will limit the availability of tests for our nation's youngest patients because such modifications would require FDA clearance or approval. Please explain how the final rule will not alter the availability of tests for pediatric patients.**

   The LDT final rule is intended to help assure the safety and effectiveness of IVDs offered as LDTs, while also accounting for other important public health considerations such as patient access and reliance. FDA recognizes the challenges faced by pediatric patients, their families, and their treating physicians. FDA also recognizes that IVDs offered as LDTs play an important role in healthcare and may address various unmet needs including for pediatric patients. We believe several of the enforcement discretion policies adopted in the LDT final rule will help to address the availability of IVDs for pediatric patients, as well as other patients with unmet needs and rare diseases. For example, FDA intends to exercise enforcement discretion and generally not enforce premarket review and quality system (QS) requirements (except for requirements under 21 CFR part 820, subpart M (Records)) for "currently marketed IVDs offered as LDTs" (i.e., those that were first marketed prior to May 6, 2024) that are not modified or that are modified in certain limited ways. In addition, FDA intends to exercise enforcement discretion and generally not enforce premarket review and QS requirements (except for requirements under 21 CFR part 820, subpart M (Records)) for LDTs manufactured and performed by a laboratory integrated within a healthcare system to meet an unmet need of patients receiving care within the same healthcare system. This policy is intended, among other things, to address situations where there is no available FDA-authorized IVD for the disease or condition, which may be the case for pediatric patients, those with rare diseases, or smaller patient populations. Note that this policy is not limited to a specific number of patients subject to diagnosis by the LDT. Moreover, the LDT final rule includes an enforcement discretion policy for premarket review

requirements for certain IVDs that are laboratory modified versions of another manufacturer's 510(k)-cleared or De Novo-authorized test.

FDA recognizes it can be challenging to validate tests for patient populations where it is difficult to obtain clinical samples, including for tests for diagnosing and managing rare diseases (approximately half of the 30 million Americans living with rare disease are pediatric patients). FDA is considering issuing guidance regarding validation of tests, including those for pediatric patients, that takes into consideration the challenges in obtaining a robust number of samples for validation.

The Honorable Gus Bilirakis

Reclassification

1. **In January 2024, CDRH announced its intent to reclassify (down-classify) most Class III IVDs to Class II. Additionally, CDRH's 2014-2015 Strategic Priorities included a review of device types subject to a PMA to determine if they are appropriate for a premarket or postmarket data shift or reclassification. Can you provide an update on this activity?**

    a. **Does FDA have a designated criteria for down-class?**

    b. **How are staff being trained on this process?**

    c. **What is the schedule/sequence of events? What is the immediate next step?**

FDA periodically reviews the classification of devices to ensure they are being regulated in the appropriate class (class III, II, I) with the necessary level of regulatory controls. CDRH has previously undertaken reclassification efforts as part of our systematic approach, including our 2014-2015 Strategic Priorities, and as part of our regular due diligence in considering the specific classification for a particular device type. This includes the reclassification of certain Hepatitis C Virus Antibody Tests and Nucleic Acid-Based Hepatitis C Virus Ribonucleic Acid Tests from class III to II.

The reclassification process generally includes issuing a proposed order, convening a classification panel as appropriate/required, receiving and considering public comment, and issuing a final order.

We have already started this process for certain IVDs. For example, at a September 2023 panel meeting, the panel discussed and made recommendations regarding a potential future reclassification from class III to class II with special controls of three types of infectious disease diagnostic tests.

Our goal is to complete the reclassification process for most IVDs by November 2027.

LDT Rule

2. **The FDA's final rule related to lab-developed tests (LDTs) includes enforcement discretion related to tests offered by a laboratory integrated within a healthcare system to meet an unmet need of patients receiving care within the same healthcare system. Rare disease patients often face a strenuous journey to achieve an accurate diagnosis. Studies indicate this can take seven years or more. Access to LDTs is often a key component of receiving an accurate diagnosis for rare disease patients, so it is critical stakeholders understand the "unmet need" enforcement discretion contained in the final rule. When do you anticipate the FDA issuing additional guidance related to the "unmet need" enforcement discretion contained in the LDT final rule?**

   a. **What factors will you be considering?**

   As discussed in the preamble to the final rule, the phaseout policy includes an enforcement discretion policy for certain LDTs for unmet needs, which may include LDTs for rare diseases. Specifically, FDA intends to exercise enforcement discretion and generally not enforce premarket review requirements and quality system requirements (except for requirements under 21 CFR part 820, Subpart M) for LDTs manufactured and performed by a laboratory integrated within a healthcare system to meet an unmet need of patients receiving care within that same healthcare system.

   This policy is based on, among other things, consideration of information received in comments indicating that laboratories integrated within healthcare systems, including academic medical centers (AMC), often make tests to meet the unique needs of their patients, and that patients may be referred to those systems because of their ability to meet patient needs that cannot be met elsewhere. The comments stated that this is often the case for patients with rare diseases for which the market is so small that there is no financial incentive for non-laboratory manufacturers to meet their needs and for which collecting data to validate a test is particularly challenging due to small patient populations (for example, rare immunohematology problems, Huntington disease, Prader-Willi/Angelman syndrome, and genetic tests for certain cancers).

   As discussed in the preamble to LDT final rule, FDA considers an LDT to be for an unmet need where there is no available FDA-authorized IVD that meets the patient's need. This may be because:

   1) There is no FDA-authorized IVD for the disease or condition;

Ex: An LDT that is intended for cytogenetic analysis of certain genes and chromosomes associated with rare diseases or conditions, certain metals testing, viral load monitoring for some transplant-associated viruses, or diagnosis of certain mosquito- and tick-borne-diseases, where there is no FDA-authorized IVD for the disease/condition.
Ex: An LDT for an emerging pathogen for which there is no FDA-authorized IVD and for which FDA has not identified an emergent situation.

2) There is an FDA-authorized IVD for the disease or condition but it is not indicated for use on the patient, or a unique attribute needs to be added to the LDT to meet the patient's needs; or
Ex: An LDT for an alternative specimen type that is infrequently tested when the specimen type required for the FDA-authorized IVD is not and cannot be made available.
Ex: An LDT for use on pediatric patients when FDA-authorized IVDs are for adults only.
Ex: An LDT that generates results in a significantly shorter period (e.g., hours versus days) than an FDA-authorized IVD with the same indication where, due to the circumstances of the patient, the shorter time period is critical for the clinical decision being made.

3) There is an FDA-authorized IVD but it is not available to the patient.
Ex: An LDT for the same indication as an FDA-authorized IVD that is offered only in another healthcare system that is not accessible to the patient and the developing laboratory will not make the IVD available outside its system.

In contrast, FDA does not consider an LDT to be for an unmet need when there is an available FDA-authorized IVD that would sufficiently meet the needs of the patient. For example, potential improvements in performance or lower cost in comparison to an FDA-authorized IVD that meets the patient's needs does not fall within this policy.

FDA is considering issuing additional guidance with examples of scenarios that may fall within and outside of this enforcement discretion policy. FDA is also considering issuing guidance on validation of tests, including those for rare diseases that takes into consideration the challenges in obtaining a robust number of samples for validation.

The Honorable Earl "Buddy" Carter

LDT Rule

1. **How is the FDA planning on enforcing the rule regarding Laboratory Developed Tests in rural communities where these hospitals and labs won't be able to afford to meet the regulatory requirements put forth by the FDA?**

The LDT final rule is intended to help assure the safety and effectiveness of IVDs offered as LDTs, while also accounting for other important public health considerations such as patient access and reliance. The final phaseout policy includes several enforcement discretion policies that the Agency anticipates will reduce costs for laboratories, including those in rural communities. For example, FDA intends to exercise enforcement discretion and generally not enforce premarket review and quality system requirements (except for requirements under 21 CFR part 820, subpart M (Records)) for "currently marketed IVDs offered as LDTs" that are not modified or that are modified as described in section V.B.3 of the preamble to the final rule and for LDTs manufactured and performed by a laboratory integrated within a healthcare system to meet an unmet need of patients receiving care within the same healthcare system.

   a. **What are the estimated annual costs required to implement this rule, both in terms of costs to U.S. taxpayers and also higher patient health care costs for lab tests?**

As detailed in the Final Regulatory Impact Analysis accompanying the final rule, FDA estimates the total cost to implement the rule is $1,287 million per year, with $1,166 million per year to Industry and $121 million to FDA. FDA also estimates the benefits of implementing the rule are $3,509 million per year based on assessment of 3 disease areas alone (cancer, cardiovascular disease, and infections). Total benefits are expected to be greater because they are expected to accrue across many disease areas. Quantified health benefits arise from improved safety and effectiveness of LDTs and include a reduction in healthcare costs associated with mortality, incorrect/unnecessary treatments, treatment delays, and disease progression resulting from the reduction of problematic LDTs. FDA's analysis of the costs and benefits shows that overall implementation of this rule is a win for the healthcare system.

HCTPs

FDA Clarification*: *The Center for Biologics Evaluation and Research regulates HCT/P products, thus Dr. Marks responded to this question.

2. **FDA appears to have departed from the preamble in the final rule outlining the requirements for 361 HCT/P classification, in which FDA stated that cutting, grinding, and shaping of HCT/Ps**

constitute minimal manipulation. (See 66 Fed. Reg. 5447, 5447) How does FDA approach "minimally manipulated" standard in human bone powder versus other types of human tissue manufactured in powder form (e.g., dermis, amniotic membrane, placental disc)?'

The 1271.10(a) criteria, including the minimal manipulation criterion, were intended to serve as the dividing line between HCT/Ps that present a lower degree of clinical safety and effectiveness risk and that are appropriately regulated solely under the communicable disease provisions of section 361 of the PHS Act and part 1271, and HCT/Ps that may present a greater degree of clinical safety and effectiveness risk and that therefore should be subject to premarket review requirements to help ensure safety and effectiveness. FDA has explained that clinical safety and effectiveness concerns depend in part on the extent of manipulation of the cells or tissues.[12]

As defined in 21 CFR 1271.3(f), minimal manipulation for structural tissue means "processing that does not alter the original relevant characteristics of the tissue relating to the tissue's utility for reconstruction, repair or replacement" and is a product/tissue specific evaluation. Different tissue types possess different original relevant characteristics, which is integral to the assessment of the minimal manipulation criterion. Original relevant characteristics of bone relate to its utility to support the body and protect internal structures. These characteristics include strength and resistance to compression. Milling, grinding, and other methods for shaping and sizing bone may generally be considered minimal manipulation when they do not alter bone's original relevant characteristics relating to its utility to support the body or protect internal structures.[13] In contrast, the original relevant characteristics of tissues such as dermis and amniotic membrane) are specific to those tissue types. If you have questions about FDA's policies and views on the application of the minimal manipulation criterion to these tissue types, please see the guidance document, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*.[14]

3. **From each of your respective standpoints, what are the criteria applied by the Device Center and the Biologic Center to determine whether product powdered wound dressing derived solely from human tissue should be classified as a device versus a biologic?**

    a. **Please explain how you apply these criteria to powdered wound dressing and other types of human tissue products that fall short of 361 HCT/P classification due to more than minimal manipulation.**

[12] https://www.fda.gov/media/70704/download
[13] https://www.fda.gov/media/109176/download
[14] Ibid.

For HCT/Ps that do not qualify for regulation solely under Section 361 of the PHS Act and 21 CFR Part 1271 (for example because the HCT/P does not meet the minimal manipulation criterion in 21 CFR 1271.10(a)(1)), FDA reviews on a case-by-case basis how to appropriately classify such products. As appropriate to the specific product at issue, FDA considers whether the product meets the definition of a biological product, drug, or device. FDA's 2017 Guidance for Industry and FDA Staff entitled *Classification of Products as Drugs and Devices and Additional Product Classification Issues* addresses FDA's thinking on many classification questions.[15]

The Honorable Neal Dunn, M.D.

Cloud-Based Tools

1. **I appreciate FDA's response to a recent bipartisan letter from me and several other members on the use of cloud services by regulated industry, including drug and medical device companies. As FDA has indicated, cloud services offer benefits—including enabling product sponsors to use the most advanced analytic and AI tools to support innovation. Are entities regulated by your center able to use cloud services?**

Yes, regulated industries are able to use cloud-services.

   a. **And what steps do you plan to take to train FDA reviewers and investigators on the ability for cloud services to support product quality, facilitate innovation, and meet compliance requirements?**

FDA shares the goal of maximizing the potential of technological advances to protect the public health, including clearer communications and digital experiences via modern platforms, streamlining data storage, ensuring data security, and promoting innovation.

The current submission processes for a variety of applications allow regulated entities to submit information electronically, in a secure and efficient manner. FDA recognizes that submissions are increasingly complex and may involve multiple data sources. The Agency is continuing to explore approaches that ensure electronic data can be robustly managed for regulatory purposes. This includes, but is not limited to, exploring the use of cloud-based platforms.

Importantly, the Agency does not prescribe how regulated entities store the data used to support their applications. The decision to store data using cloud-based

[15] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/classification-products-drugs-and-devices-and-additional-product-classification-issues

applications, such as Software-as-a-Service (SaaS), or on-premises data storage is left to each regulated entity to determine which method best suits their needs. The Agency does not endorse, nor prohibit, the use of any of these data storage methods or the use of any particular service or system, as long as the chosen method meets applicable regulatory requirements. FDA agrees that there are many potential benefits for both the Agency and regulated entities to embrace IT modernization, and that there are a variety of data storage solutions that regulated entities can use to meet regulatory requirements for recordkeeping, such as those for clinical trials or manufacturing processes.

FDA investigators undergo rigorous training and are kept up to date on current industry best practices and the Agency's expectations regarding data and information that support marketing applications and other submissions from regulated entities. FDA is committed to advancing our data and IT modernization to provide cloud-based, agile, integrated platforms that streamline and improve the ability to access, utilize, and protect electronic data.

The Honorable Dan Crenshaw

LDTs

1. **Most clinical laboratories have limited or no experience working with the FDA or with FDA expectations. Laboratories will need help interpreting FDA expectations, sooner rather than later. What is the Agency's plan for rapidly publishing guidance documents to help laboratories understand the requirements?**

FDA intends to publish several guidance documents in the coming years to help laboratories understand the device requirements under the FD&C Act and implementing regulations. Specific topics to be addressed in guidance are identified on FDA's website annually for the coming year.

2. **Most clinical laboratories have limited or no experience working with the FDA or with FDA expectations. FDA has several webinars scheduled over the next few months, but what other efforts are the Agency pursuing to quickly educate clinical laboratories on these expectations, and how laboratories can comply in a manner that does not interrupt or interfere with the critical patient care they provide?**

In addition to monthly webinars and guidance documents, FDA has established a mailbox (ldtfinalrule@fda.hhs.gov) for questions related to the rule and intends to publish responses, as appropriate, our web site[16] on a rolling basis for transparency to the entire community. Laboratory manufacturers may also utilize the same pathways other device manufacturers use for feedback on specific devices, including by submitting a pre-submission or 513(g) request

[16] https://www.fda.gov/medical-devices/laboratory-developed-tests/laboratory-developed-tests-faqs

for information to FDA.

The Honorable Troy Balderson

PDUFA

FDA Clarification*: *CDRH is not part of PDUFA, as such Dr. Cavazzoni has responded to the questions below.

1. **Strict security requirements result in a restricted pool of vendors who can provide FISMA approved solutions. This smaller pool of vendors means higher costs for products and services as the FDA has less negotiation power during the selection phase. This limits the overall technical innovation due to lower variety in solution selection. How does FDA plan to effectively balance the need for stringent security requirements and meeting the PDUFA VII commitments?**

   To ensure we meet our PDUFA VII commitments, FDA will effectively balance and sustain our technology and innovation excellence by partnering with industry-leading vendors while ensuring high standards of compliance with the Office of Management and Budget (OMB), Federal Information Technology Acquisition Reform Act (FITARA), Federal Information Security Management Act (FISMA), Federal Risk and Authorization Management Program (FedRAMP), and other federal government security requirements to prevent and protect against foreign nation state threats and other nefarious cyber threat actors.

   a. **Can you elaborate on FDA's plans to put out an RFP for third-party vendors?**

      FDA follows government procurement procedures for a request for proposal (RFP), as managed for the Agency's Office of Acquisition and Grants (OAGS). To meet PDUFA VII commitments, FDA has incorporated those requirements with existing procurements such as for the Information Request (IR) demonstration project as well as targeted procurements such as the Pharmaceutical Quality Knowledge Management (PQKM) demonstration project to support the requirements. Additionally, FDA has used public comment received pursuant to Federal Register notices to incorporate input from third parties, consistent with its PDUFA commitment of establishing FDA's Data and Technology Modernization Strategy.

   b. **What is the projected timing?**

      For projects in progress such as the Electronic Submissions Gateway

(ESG) modernization, Information Requests (IR) demonstration project and Pharmaceutical Quality Knowledge Management (PQKM) demonstration project, those contracts have already been awarded to vendors, and the projects are in progress. For awareness and transparency, FDA shares the timelines and milestones with PDUFA stakeholders on an ongoing basis.

2. **PDUFA VII states that, within 6 months of completion of a demonstration project, the FDA must compile a summary of outcomes and next steps and share with industry at the regularly scheduled FDA-industry meetings. What measures will FDA put in place to encourage engagement and feedback from industry?**

   FDA uses the quarterly scheduled FDA-industry meetings to provide interactive updates on the demonstration projects. These meetings include detailed solution demonstrations and interactive discussions with FDA leadership and industry representatives, such as the meeting on Oct 8, 2024, for the IR demonstration project. For the PQKM demonstration project, industry representative input has been incorporated in the project, and industry representatives actively participate in supporting deliverables for that demonstration project.

   a. **What can industry expect after the demonstration projects have concluded?**

      FDA will ensure its commitment to provide written recommendations on outcomes and next steps for all of its demonstration projects. Specifically, within six months of completion of a demonstration project, a summary of outcomes and next steps will be compiled and shared with industry at the regularly scheduled FDA-industry meeting. FDA will also post the information on its website.

3. **Are there barriers that are delaying or impacting FDA's ability to formally select additional demonstration projects for the regulatory information exchange reforms?**

   FDA plans to propose two additional demonstration projects that address regulatory information exchange reforms at its quarterly meeting on October 8, 2024. We currently do not anticipate any barriers to proceeding with these projects.

   a. **Does FDA plan to engage going forward with Industry on demonstration project selection?**

      FDA will continue to consult industry to ensure input from industry on demonstration project selection. Through progress updates and discussions at the FDA-Industry quarterly

meetings, FDA will gather feedback and provide plans that include industry's participation in those projects.

OTC Hearing Aids

4. **Nearly 5 years after Congress passed the 2017 FDA Reauthorization Act, which included a provision mandating that FDA establish rules for the sale of over-the-counter hearing aids, the rule finally became effective in October 2022. With this new category, we are seeing an increase of new market participants. With more pathways for individuals with hearing loss to access hearing aids, it is crucial that we ensure companies operating in this space are playing by the rules and that FDA is exercising its appropriate oversight and enforcement authority to ensure the safety and efficacy of these medical devices. To that end, multiple issues have been identified with the potential to create greater consumer confusion or, worse, place consumers at an increased safety risk.**

   a. **Is FDA aware of bad actors that are advertising and selling OTC hearing aids? Let me provide some examples:**

      - **Improper classification/registration/listing issues:**
        - **Individual devices are not listed at all or have been listed under different names than they are being sold as;**
        - **Companies using "self-fitting" terminology when not listed under the correct product code classification**
        - **Primary manufacturers offering private label products to a variety of companies may be registered and products listed, but many of the sellers are not registered and/or listed. This makes it difficult for consumers to find products on the FDA database and violates registration/listing requirements.**

      - **Advertising and claims issues:**
        - **Companies using the FDA logo on their website to imply endorsement or approval of devices**
        - **Companies advertising OTC devices as appropriate for "mild to severe hearing loss"**
        - **Companies claiming devices can "restore natural hearing" (which no company can claim)**
        - **Companies claiming to be the "top-seller for prominent hospitals and clinics globally"**

FDA has received complaints alleging regulatory misconduct (often called "trade complaints") consistent with the examples listed above. We

review and assess complaints submitted to us, whether from consumers, healthcare professionals, industry groups, or others, and take further action as warranted. Such action can include, among others, issuing a public safety communication, issuing a warning letter, holding a regulatory meeting, or initiating a seizure, as appropriate and according to our existing policies. FDA does not comment on pending or ongoing compliance actions or investigations.

b. Has FDA received reports or complaints of violations of OTC regulations?

In addition to the types of complaints mentioned above, FDA has received allegations of non-compliance with the OTC hearing aid labeling requirements for both outside and inside the box. For example, we have received reports that OTC hearing aids purchased through the internet in some cases do not provide the required outer package labeling to consumers prior to purchase. We investigate allegations in accordance with our existing policies.

c. Is FDA taking or has FDA taken any actions to monitor or ensure compliance with applicable regulations?

Each allegation submitted by consumers, healthcare professionals, industry groups and others is evaluated, and further action is taken as warranted, according to our existing policies. To help consumers easily find required labeling and other helpful information, we have updated our OTC hearing aid consumer webpage to include consumer information on OTC hearing aids, including the required "outside of the box" (outside package) labeling, and links to report problems with OTC hearing aids and allegations of regulatory misconduct to FDA.

d. Has FDA taken action against bad actors in the OTC hearing aid space either based on submitted complaints or on its own?

FDA has investigated allegations and, in accordance with our existing policies, would take action as appropriate to bring companies into compliance with the OTC hearing aid regulations. In general, compliance actions have included "it has come to our attention" letters and outreach to companies, as well as actions to improve awareness of the new OTC hearing aid regulations.

e. What specific actions has FDA taken on its own, or in conjunction with FTC, to address regulatory violations relating to OTC hearing aids?

Please see responses to subparts 4c and 4d above. As yet, we have not taken actions in conjunction with FTC on these issues.

f. State attorneys general have been at the forefront of issue consumer

warnings and even taking action against bad actors. Is FDA aware of these efforts and/or working with state authorities where appropriate?

FDA has an Intergovernmental Affairs Staff who serve as points of contact for State, local, territory and tribal officials and partners. State attorneys general can talk to our Intergovernmental Affairs Staff to obtain information from FDA regarding the statutory and regulatory requirements for hearing aids. FDA does not provide opinions on individual State investigations or enforcement actions through these consultations, but we do provide generally applicable information about the statutory and regulatory requirements—for example, what the term "prescription hearing aids" describes or an explanation of claims that may result in misbranding.

g. Is the FDA coordinating with any other federal agency (FTC, FCC) to enhance consumer knowledge of the OTC market?

The business practices involving hearing aids also fall within the purview of the Federal Trade Commission (FTC), and FDA and FTC collaborate on a case-by case basis, depending on the specifics of each case. For example, FDA has worked with FTC on hearing aids and Personal Sound Amplification Products (PSAPs) regarding advertising for PSAPs. FDA staff also participated in a 2017 FTC workshop on Competition, Innovation, and Consumer Protection Issues in Hearing Health Care.[17]

- Pursuant to the Memorandum of Understanding[18] between FDA and FTC, FTC exercises primary jurisdiction over all matters regulating the truth or falsity of advertising (other than labeling) of medical devices. FDA exercises primary jurisdiction over all matters regulating the labeling of medical devices, which includes preventing misbranding of devices. FDA is responsible for protecting the public health by ensuring that there is reasonable assurance of the safety and effectiveness of medical devices throughout the total product lifecycle.

- Whether an issue with an OTC hearing aid should be sent to FDA or FTC will depend on the specifics of the complaint. In general, complaints that relate to safety and effectiveness of the device, including complaints about confusion about the device, e.g., what it is, how to use it, or how it is labeled, should be provided to FDA.

In addition, while the National Institute on Deafness and Other Communication Disorders (NIDCD) does not have regulatory oversight over hearing aids, we coordinated with them for purposes of developing educational materials

[17] https://www.ftc.gov/news-events/events/2017/04/now-hear-competition-innovation-consumer-protection-issues-hearing-health-care

[18] https://www.ftc.gov/legal-library/browse/cooperation-agreements/memorandum-understanding-between-federal-trade-commission-food-drug-administration

consistent with the final rule establishing the over-the-counter category of hearing aids.

FDA and NIDCD also co-sponsored a meeting of the Working Group on Accessible and Affordable Hearing Health Care for Adults with Mild to Moderate Hearing Loss on June 20-21, 2024. The main focus of the meeting was to develop an agenda for new work that should be conducted to improve hearing healthcare access and affordability. Topics discussed within the meeting included hearing health needs, perception, and desire for care by adults with perceived mild to moderate hearing loss (i.e., the target population for OTC hearing aids). Additionally, participants discussed how patients seek and reach or utilize hearing healthcare. Some of the proposed strategies discussed during the meeting involved enhancement of consumer knowledge regarding hearing loss and options for treatment, including OTC hearing aids.

Although not through another Federal agency but still a collaboration to provide resources to consumers, FDA also participated in the OTC Hearing Aid and Hearing Self-Care Symposium on June 7, 2024, hosted by the University of Pittsburgh. The purposes of this symposium included enhancing consumer knowledge and increasing patient access to hearing healthcare in the United States. Pharmacists and audiologists discussed how these professions could work together to promote the safe and effective use of hearing healthcare solutions like OTC hearing aids that do not require a prescription or medical evaluation.

h. Are there jurisdictional gaps that need to be addressed through legislation or other pathways between FDA and FTC?

As you know, FDA's remit includes, among other responsibilities, to promote the public health and ensure reasonable assurance of the safety and effectiveness of devices intended for human use (see 21 U.S.C. § 393(b)(1) & (2)(C)). With respect to FDA's authority to regulate devices to achieve these ends, the regulation of hearing aids has been addressed through previous legislation and the resultant rulemaking.

i. Who is regulating or can regulate false or misleading information on the internet?

The relevant regulatory authority depends on the subject of the false or misleading information and the communicator. Generally, parties that offer medical products for sale and provide information about the product's safety or effectiveness (essentially, health-related claims) or information about the product's identity as a legally marketed therapeutic or diagnostic device would implicate FDA's authorities. For example, the intended use for OTC hearing aids is for adults aged 18 or older with perceived mild to moderate hearing loss; false or misleading information from a manufacturer on the internet about the intended use of an OTC hearing aid or false or misleading performance claims for hearing aids, would

likely be violative under the Federal Food, Drug, and Cosmetic Act, and therefore, within FDA's jurisdiction.

In contrast, FDA generally does not regulate false or misleading information on the internet about certain aspects of the exchange of goods or services—for example, a product's warranty, or false or misleading information in certain device advertising. The regulation of such information may fall within another agency's jurisdiction, for example, the Federal Trade Commission.

False or misleading information could also potentially violate State legal requirements as well as give rise to claims in tort or contract under State law. The appropriate State regulator (or enforcement authority) would, of course, depend on the organization of the State's government and its agencies' responsibilities under its laws.

j. False and misleading information is most robust on internet platforms, do you have a plan to address these issues?

We investigate allegations regarding false and misleading information, including information on internet platforms (often reported by other manufacturers and industry groups, professional societies, and individual reporters), and we take action as appropriate.

We have also created an FDA webpage for consumers, to provide them with accurate and useful information regarding OTC hearing aids and what consumers should know before and after purchasing them.[19]

k. What is the breakdown between domestic and foreign manufacturers in the OTC hearing aid market in the U.S.?

Although FDA maintains information about manufacturing facilities and devices through its device registration and listing database which is publicly available, Establishment Registration & Device Listing, this information is not intended to capture market-share data. As such, FDA does not have reliable market-share data.

l. Is there any type of verification that these companies and their products are being manufactured, sold, or distributed in compliance with applicable regulations?

All device manufacturers are subject to periodic inspections by the FDA Office of Regulatory Affairs (now the Office of Inspections and Investigations) to ensure compliance with all applicable requirements under the Federal Food, Drug, and Cosmetic Act. Additionally, we review allegations and whistleblower complaints regarding violations

[19] https://www.fda.gov/medical-devices/hearing-aids/otc-hearing-aids-what-you-should-know

of these requirements.

m. Are you concerned with reports of "fly by night" companies that pop up, sell products backed by returns or warranties, that close up shop suddenly, leaving consumers without recourse?

Although FDA generally does not regulate the content or reliability of product warranties (the adequacy of consumer recourse), we regulate device manufacturers and would be concerned if they, regardless of their longevity, do not meet the applicable requirements of and under the Federal Food, Drug, and Cosmetic Act. For example, device manufacturers have to register their establishments with FDA, list their devices, comply with any applicable good manufacturing practice requirements (for devices, called "quality system" or "quality management system" requirements), and be subject to inspection by FDA. FDA actively reviews, investigates, and takes appropriate action, according to our existing enforcement policies, when we become aware of such violations. Please also see our response to 4a.

The Honorable Dianna Harshbarger

Opioids/LDT rule

1. **We continue to face a devastating opioid and substance use disorder crisis in this country. Deadly new synthetics are hitting the street constantly and must be tracked so that doctors and other caregivers can best understand how to care for those struggling with substance use disorder. Laboratory developed testing (LDT) services play a critical role in testing for such substances because they can be developed and deployed to respond to the rapidly changing illicit drug market. However, I'm concerned that the LDT final rule will slow the availability of new diagnostic tests and hamper our nation's ability to respond to this public health crisis. Can you explain how the final rule will affect the availability of tests to detect new and rapidly changing illicit drugs?**

FDA shares your concern about the opioid and substance use disorder crisis and ensuring that patients, communities, health providers and first responders have the medical products that they need to address this crisis is a top priority for the Agency. FDA also believes it is critical that the tests available to patients and providers are appropriately accurate and reliable due to the risks to patients from false positive and false negative drugs of abuse test results. False positive results may delay treatment for the patient's true condition if that condition involves symptoms that overlap with drug intoxication (for example, missing a critical opportunity to treat cerebral hemorrhage or stroke). False negative results may put the patient at risk, for example, if they were to drive or were to need urgent treatment for overdose.

Compliance with quality system requirements, such as design controls, will help assure that these drugs of abuse tests perform as intended, and compliance with premarket review, where applicable, will help assure that the drugs of abuse test's performance is suitable for the test's intended use.

FDA acknowledges that illicit drugs may be modified and that tests for drugs of abuse may need to be modified in order to detect different or synthetic versions of these substances. Where a manufacturer may anticipate the types of changes it intends to make, it may consider seeking clearance or approval of a predetermined change control plan (PCCP). Section 515C of the FD&C Act provides that a PMA supplement or new 510(k) is not required for a modification to a device that would otherwise be required if the change is consistent with a PCCP approved or cleared by FDA. Modifications included in a PCCP must maintain the device within the device's intended use. To the extent a PCCP is authorized by FDA for a particular IVD, any changes within the bounds of that PCCP would not necessitate a new submission to FDA.

We note that as described in the preamble to the LDT final rule, and for the reasons discussed in that preamble, FDA intends to exercise enforcement discretion and generally not enforce premarket review and quality system requirements (except for requirements under 21 CFR part 820, subpart M (Records)) for "currently marketed IVDs offered as LDTs" (i.e., those that were first marketed prior to May 6, 2024) that are not modified or that are modified in certain limited ways. Certain drugs of abuse tests may fall within that policy, or may fall within the enforcement discretion policy for LDTs for unmet needs.

Inspections

2. **Agency data show that the FDA completed "zero" inspections of Chinese device manufacturers in 2022. Meanwhile, the FDA completed 1,706 inspections of domestic device manufacturers that same year. Substandard Chinese medical devices are flooding the U.S. market and threatening domestic producers that are held to a higher standard. We must ensure that foreign manufacturers are held to the same standard as domestic manufacturers, to avoid putting our domestic workers and factories at a disadvantage.**

    a. **How are Chinese medical products allowed to make their way into the U.S. and to patients if the FDA isn't able to inspect the foreign facilities they were manufactured in?**

    FDA has other tools at our disposal to ensure medical devices manufactured overseas are held to requirements consistent with those for products made in the United States, including new programs for medical devices that allow us to best utilize resources and increase the number of evaluations through Remote Regulatory Assessments, and the Medical Device Single Audit Program (MDSAP). The MDSAP is an international third-party audit

program managed by regulatory authorities in Australia, Brazil, Canada, Japan, and the United States under which firms undergo a single regulatory audit at least annually, conducted by an authorized third-party auditing organization to satisfy regulatory requirements of participating members (in FY2023, MDSAP auditing organizations performed 2,656 foreign medical device audits).

There were 37 inspections of Chinese device manufacturers in 2023 and 63 in 2024. In addition to inspectional activities, products regulated by FDA are subject to review when they are offered for entry into the United States. For drugs and medical devices, this includes verifying compliance with establishment registration, product listing, marketing authorization, labeling, and Quality Systems Regulations/CGMP, as applicable. Products that appear to be in violation of FDA laws or regulations are detained and may subsequently be refused if the importer is unable to overcome the appearance of the violation. In 2024, three of those inspections resulted in warning letters related to distribution of unauthorized Chinese-made plastic syringes.

FDA also utilizes import alerts, which inform FDA field staff that the Agency has enough evidence or other information to allow for Detention Without Physical Examination (DWPE) of products subject to an import alert. Import alerts help stop potentially violative products from being distributed into the United States, free up Agency resources to examine other products, and provide uniform coverage across the country.

b. And what steps is the FDA taking to increase the number of foreign inspections overall, and if inspections cannot be done over a reasonable timeframe, what additional steps will FDA take to ensure patients are not at risk?

The Agency remains committed to and continuously seeks to improve its foreign inspection efficiencies and processes. This includes maintaining a qualified team of investigators. FDA is committed to competitively recruiting to fill vacant investigator positions that have been unfilled for a variety of reasons, including difficulty recruiting for hardship eligible locations, especially in China during the COVID-19 pandemic, and rigorous requirements for experienced investigators, including eligibility, certifications, and security clearance requirements. Retention of these trained investigators poses an additional challenge, in that they must be willing to commit to extended periods of travel, and their skills are transferable to other employment opportunities at higher pay.

To help address staffing needs, the Agency has sent U.S.-based FDA investigators on multiple details to FDA's foreign offices in order to limit travel from the United States to foreign sites and allow us to accomplish more inspections. We have also worked to obtain one-year multi-entry visas

for India for many of our pharmaceutical investigators, which has saved a significant amount of time and avoided delays encountered in having to apply for a visa for each inspection in India. We are looking to implement similar types of efficiencies for inspections in China.

Additionally for all manufacturers, FDA reviews signals (recalls, allegations/ complaints, MDRs, etc.). If we determined that there is a high-risk issue (for example - a class I recall) and the devices are manufactured at a foreign manufacturer, FDA will inspect the domestic importer. These inspections have resulted in the foreign manufacturer being issued an advisory action and being placed on import alert.

The Honorable Mariannette Miller-Meeks, M.D.

CDS

1. **FDA has issued guidance which narrows a bipartisan 21st Century Cures act provision exempting clinical decision support from FDA regulation. As part of the guidance, FDA said that when decision support runs in time sensitive situations, the exemption should not apply because the physicians won't thoughtfully consider the pro's and con's of the recommendation and will just do what it says. Almost everything that happens in a hospital is time sensitive. By including this concept of automation bias, aren't you basically gutting this congressionally mandated exemption?**

    a. **Doctors are trained to make fast decisions in time sensitive situations. As someone who was a practicing physician for decades, I understand this firsthand. By not giving physicians credit for their ability to think and act quickly, isn't FDA moving into regulating the practice of medicine?**
    b. **Using existing authorities and funding levels, how does FDA intend to regulate the hundreds of thousands of advisories that run throughout the country?**
    c. **Are you concerned that FDA is overextending itself?**

    The final CDS guidance does not expand the Agency's oversight of device software, but instead contains non-binding recommendations that provide clarification regarding CDS software intended for healthcare professionals. This guidance explains that certain CDS software was explicitly excluded from the definition of a device under section 520(o) of the FD&C Act, whereas other CDS software may continue to meet the definition of a device under section 201(h) of the FD&C Act and remain the focus of FDA's regulatory oversight. This policy, taken together with our other guidances on the remaining provisions of section 520(o) of the FD&C Act, aims to clarify

which software functions meet the definition of device, and, of those that meet the definition of device, which software functions are the focus of FDA's oversight. FDA has also developed a tool to help in determining whether a software function is the focus of FDA's device oversight. The Digital Health Policy Navigator walks users through all of the guidances related to the provisions of section 520(o), including the CDS guidance, for a given software function.

Through the Cures Act, Congress added section 520(o) to the FD&C Act which excludes certain software functions from the definition of device. This includes software functions that meet all of the following:

1) are not intended to acquire, process, or analyze a medical image or a signal from an in vitro diagnostic device or a pattern or signal from a signal acquisition system;
2) are intended for the purpose of displaying, analyzing, or printing medical information about a patient or other medical information (such as peer-reviewed clinical studies and clinical practice guidelines);
3) are intended for the purpose of supporting or ***providing recommendations*** to a healthcare professional about prevention, diagnosis, or treatment of a disease or condition; and
4) are intended for the purpose of enabling such healthcare professional to ***independently review the basis*** for such recommendations that such software presents so that it is ***not the intent that such healthcare professional rely primarily*** on any of such recommendations to make a clinical diagnosis or treatment decision regarding an individual patient (section 520(o)(1)(E) of the FD&C Act, *emphasis added*).

The discussion in the final CDS guidance and mention of automation bias was part of an explanation of criteria (3) and (4) (above). In describing the possible factors that would help assess whether a software function met (3) and (4), FDA mentioned the level of automation and the time critical nature of the HCP's decision making. These factors are meant to provide guidance to industry on FDA's current thinking about the meaning of criteria (3) and (4), and are not to be taken as a basis for automatic exclusion from the device definition. Ultimately, whether a software function is not a device under section 520(o)(1)(E) of the FD&C Act involves an application of the statute to the specifics of the software function at issue and consideration of the recommendations in the final CDS guidance.

Further, the final CDS guidance is not intended to undermine the expertise or practice of skilled healthcare professionals, who we understand are well-equipped to think and act quickly. Rather, information in the guidance relates specifically to understanding whether a software function would likely meet the criteria to be excluded from the definition of device in the FD&C Act. For example, the CDS guidance mentions consideration of the time-critical

nature of a decision because it goes to whether an output is a recommendation and whether a provider can independently review the basis for the recommendation, both of which are statutory criteria. Ultimately, whether a software function is a device determines whether and how it is regulated by FDA and would not interfere with the practice of medicine any more than FDA regulation of other devices. For example, FDA is responsible for determining whether a device should be authorized to be marketed. Once a device is legally marketed, an HCP can use their expertise to determine how to use such device within the context of a particular patient.

FDA employs a risk-based framework where the level of regulation is based on the risk of the device. For software functions that meet the definition of device, FDA separately has announced in various guidance documents its intention to focus on those that pose risk to the public health. Therefore, even if a software function falls within the device definition, this does not necessarily mean that such a device will be the focus of FDA's regulatory oversight. This approach is consistent with FDA's approach to other device areas.

Further, FDA's congressionally mandated mission, among other responsibilities, is to ensure reasonable assurance of the safety and effectiveness of devices, and this includes devices with CDS functions. The final CDS guidance did not expand the Agency's oversight of device software. It simply contains non-binding recommendations that provide clarification regarding certain software functions that are now excluded from the definition of a device, which reduced existing regulatory burden.

FDA's digital health policies are risk-based and strive to strike the right balance in our oversight of these devices, consistent with least burdensome principles. Our approach allows us to focus our resources on those products that pose the greatest risk to patients.

Third Party Logistics Providers

FDA Clarification: The Center for Drug Evaluation and Research regulates over-the-counter and prescription drugs, thus Dr. Cavazzoni responded to this question.

2. **Dr. Shuren, as we are discussing how the United States can continue to lead in the development of cutting-edge biomedical innovations, we must address the supply chain that moves medications and health supplies from manufacturers to the patients in need. Third-party logistics providers (3PLs) play a key role in the reliability of medical supply chains by moving healthcare goods safely and quickly across the country, often with temperature and time restrictions. To ensure healthcare goods are moved safely, Congress passed the Drug Supply Chain Security Act (DSCSA) in 2013,**

requiring the FDA to create national standards for the licensure of 3PLs. However, to date final regulations have yet to be released. Can you share insight into when the FDA expects to finalize the pending third-party logistics providers regulations?

Following an extension to the comment period for the proposed rule 'National Standards for the Licensure of Wholesale Drug Distributors and Third-Party Logistics Providers,' comments were due to the public docket by September 6, 2022. FDA is working to finalize this rule.

AMR and ASTs

3. **Dr. Shuren, I am particularly interested in antimicrobial resistance. I would appreciate your thoughts on the importance of clinicians having accurate and readily available diagnostic tools to guide their prescribing decisions and foster antimicrobial stewardship. In 2020, FDA began allowing antimicrobial susceptibility test (AST) manufacturers to use preapproved change protocols for previously cleared ASTs to make breakpoint changes as organisms develop resistance to an antibiotic. This has allowed laboratories to update their AST systems more quickly which is critical for appropriate antimicrobial stewardship. Beyond the use of these types of protocols for existing ASTs, how can CDRH expedite access to new ASTs?**

FDA agrees that it is important for clinicians to have accurate and readily available diagnostic tools to guide their prescribing decisions and foster antimicrobial stewardship. Further, FDA recognizes the importance of using updated susceptibility test interpretive criteria (STIC), also referred to as breakpoints, when using antimicrobial susceptibility test (AST) systems. FDA has taken several initiatives to facilitate the development of new ASTs and the use of up-to-date breakpoints for antimicrobial susceptibility tests (ASTs).

Section 3044 of the 21st Century Cures Act ("Cures Act") created a system to expedite the recognition of antimicrobial susceptibility test interpretive criteria also known as "breakpoints" (abbreviated as STIC) and provide up-to-date information to the healthcare community in a more streamlined manner. The Cures Act also clarifies that sponsors of AST devices may rely upon these FDA-recognized or listed STIC to support premarket authorization of their devices so long as certain conditions are met. This provides for a more streamlined process for incorporating up-to-date information about antimicrobial resistance into such devices.

FDA's Center for Drug Evaluation and Research (CDER) maintains the FDA's Recognized Antimicrobial Susceptibility Test Interpretive Criteria (STIC)[20] website with the most up-to-date STIC information for antibacterial and antifungal drugs,

[20] https://www.fda.gov/drugs/development-resources/fda-recognized-antimicrobial-susceptibility-test-interpretive-criteria

including FDA's recognition of STIC established by standards development organizations (SDOs). FDA has established a docket for public comment[21] where interested third parties or drug sponsors may provide information that FDA could consider in determinations concerning recognition of a susceptibility test interpretive criteria standard or could use as a basis for listing new or for updating susceptibility test interpretive criteria. FDA reviews all substantive submissions to support updating of susceptibility test interpretive criteria and provides updates on the FDA website.

FDA has cleared hundreds of ASTs (addressing hundreds of individual organism/drug combinations) and has worked to ensure that the most up to date STIC are used, including having cleared more than 60 ASTs with breakpoint change protocols, allowing for the rapid adoption of updated breakpoints without further FDA review. FDA has been clearing change protocols for breakpoints since early 2019, providing the ability for an AST device manufacturer to update the breakpoint information for their test, without the need for a new premarket submission, if the update is consistent with the breakpoint change protocol. FDA formalized this option in September 2023 with the publication of the final guidance, Antimicrobial Susceptibility Test (AST) System Devices—Updating Breakpoints in Device Labeling[22] to help address the importance of adopting updated breakpoints quickly. The guidance describes the least burdensome approaches for AST system device manufacturers to update their device labeling with the updated breakpoints listed on the STIC website. Generally, updating the STIC could significantly affect the safety and effectiveness of the AST system device and would therefore require a 510(k) submission prior to updating the device labeling. However, the final guidance provides recommendations on the marketing submission content for predetermined change control plans (PCCP) for new AST system devices, describes an enforcement policy regarding applying such updates to "legacy" AST system devices (AST system devices that were reviewed and cleared by FDA and did not include a breakpoint change protocol), and clarifies the process for incorporating by reference a cleared PCCP or breakpoint change protocol into a new 510(k) submission for an AST system device. The processes and policies outlined in the guidance describe approaches for AST system device manufacturers to update breakpoints listed in their device labeling without submitting a new premarket submission.

Moreover, FDA is always interested in discussing novel approaches with test developers.

4. **Does FDA currently require developers to submit a 510(k) for each and every new drug/bug combination and, if so, are there ways to expedite review of these types of tests based on previous data and the agency's experience in reviewing the hundreds of previously cleared 510(k)'s for other drug/bug combinations?**

[21] https://www.federalregister.gov/documents/2018/03/01/2018-04175/susceptibility-test-interpretive-criteria-recognized-and-listed-on-the-susceptibility-test
[22] https://www.fda.gov/media/172463/download

No, FDA does not require developers to submit an individual 510(k) for each drug/organism group combination; however, each drug/organism group combination does need to be reviewed and cleared. This may be done in a single submission that includes many drug/organism group combinations. Generally, a 510(k) is required for each new antimicrobial susceptibility test (AST) device, which may include many drug/organism group combinations with breakpoints recognized by FDA. FDA's Recognized Antimicrobial Susceptibility Test Interpretive Criteria (STIC) website[23] includes the most up-to-date STIC information for antibacterial and antifungal drugs, including FDA's recognition of STIC established by standards development organizations (SDOs).

FDA also encourages the inclusion of predetermined change control plans (PCCPs) in 510(k) submissions for AST devices as outlined in FDA's guidance document, Antimicrobial Susceptibility Test (AST) System Devices—Updating Breakpoints in Device Labeling.[24] PCCPS provide the opportunity to update breakpoints based on updated recognition on the FDA STIC website without a new premarket submission. FDA is always interested in discussing additional uses for PCCPs as well as other novel approaches with test developers.

The Honorable Ann Kuster

E-Labeling

1. **Current law recognizes that device labeling, including directions for use, may be provided electronically for a wide range of devices—including all prescription devices for use in health care facilities or by health care professionals, as well as other in vitro diagnostic devices for use by health care professionals or in blood establishments.**
   Since Congress last addressed device electronic labeling in 2024, reliance on online information has expanded astronomically. Consumers and patients, as well as health care professionals, increasingly turn to electronic sources for information about products.
   Electronic labeling provides for rapid, even real-time, updates to labeling, such as clarifications to warnings or other notices. Patients, physicians, caregivers, and manufacturers may all benefit from the broader application of electronic labeling for medical devices. Benefits to device users may include increased availability, utility, interactivity, and accessibility to the instructions for use.

   Last year, the Energy & Commerce Health Subcommittee held a hearing on Public Health Security Threat Preparedness, during which I had the opportunity to ask Commissioner Califf a question

[23] https://www.fda.gov/drugs/development-resources/fda-recognized-antimicrobial-susceptibility-test-interpretive-criteria
[24] https://www.fda.gov/media/172463/download

about medical device labeling and the benefits of moving towards electronic labeling. His response was that he is very much in favor of moving in this direction, with caveats such as ensuring that patients who want or need paper copies can access them. I have joined with my colleagues on this Subcommittee – Representatives Obernolte, Craig, and Crenshaw – to introduce H.R. 3723, the Medical Device Electronic Labeling Act, which will help ensure that patients, physicians, and other users have rapid access to the most up-to-date device information. Dr. Shuren, do you commit to working with us to see this important modernization effort finalized?

FDA would be happy to continue working with you to ensure that patients and healthcare providers have the most current information and, as part of this, such as ensuring there are safeguards so patients who want or need to can still access physical labeling. Any approach should ensure there are not barriers for patients – such as those in rural areas, more elderly populations, and others – who may still rely on physical labeling, and to assure they can obtain it.

The Honorable Kim Schrier

LDT Rule

1. **I want to follow up on a question I asked about children's access to needed laboratory tests. As I said during the hearing, I have some concerns about the impact of the final LDT rule on children's timely access to needed pediatric tests, given the impact of rare diseases on children's long-term health and wellbeing. In particular, for some pediatric LDTs, there may be only one or two centers worldwide that have the expertise to perform and oversee those tests, given the specialized nature of pediatric health care. Therefore, it's not uncommon for one children's hospital to send a sample to another children's hospital that is not in the same hospital system because that children's hospital has an LDT that can test for a child's particular rare condition. For example, Seattle Children's has the unique challenge of serving very sick children from the surrounding four-state region. There are situations where a hospital in Alaska, which is not a part of the Seattle Children's Hospital system, will send a sample from a child who is need of a diagnostic test that only Seattle Children's can run. This helps ensure a timely diagnosis and prevents the whole family from having to travel to Seattle for the test. Under the final rule, would these situations be considered an "unmet need" even though the test is not developed or used in the same hospital system?**

    a. **If not, how does FDA plan to ensure that children with rare diseases have access to these types of tests?**

As discussed in the preamble to the final rule, the phaseout policy includes an enforcement discretion policy for certain LDTs for unmet needs, which may include LDTs for children with rare diseases. Specifically, FDA intends to exercise enforcement discretion and generally not enforce premarket review requirements and QS requirements (except for requirements under 21 CFR part 820, Subpart M) for LDTs manufactured and performed by a laboratory integrated within a healthcare system to meet an unmet need of patients receiving care within that same healthcare system.

This policy is based on, among other things, consideration of comments that recommended that FDA adopt an enforcement discretion policy specific to tests manufactured by academic medical center (AMC) laboratories given risk mitigations provided by the integration of the laboratory within the AMC that is providing care to the patient. Many comments stated that because other laboratories are similarly integrated within healthcare systems, any such enforcement discretion policy should not be limited to AMC laboratories. Many of these comments emphasized the built-in communication mechanisms between the laboratory and AMC/other healthcare system within which the laboratory is integrated.

For LDTs manufactured and performed by laboratories integrated within healthcare systems, FDA generally has greater confidence that ordering physicians will communicate any questions about LDTs or concerns regarding the safety and effectiveness of the LDT (e.g., when the patient's symptoms point to another diagnosis; when subsequent test results contradict the original test result) to a laboratory given the built-in communication mechanisms present. Moreover, FDA generally has greater confidence that laboratories will communicate any limitations of the LDT or other relevant information to the ordering physician given these mechanisms. We think this is particularly likely to happen in the context of LDTs for unmet needs, which are likely to be a focus of attention and communication between laboratorians and providers given the uncommon nature of the issues presented.

Communication from ordering physicians to laboratories may help laboratories to identify any problems with their LDT and make necessary adjustments, improvements, and other changes to the LDT. Although we acknowledge that any identification and subsequent modification of the LDT would happen postmarket, and thus would not prevent potentially problematic LDTs from ever being used, subsequent modification would benefit future patients and providers who are relying on the LDT. In addition, communication from laboratories to ordering physicians may help to underscore to the ordering physicians any limitations with the LDT and provide other relevant information to ordering physicians, for example that is specific to the unique needs of their patient, which in turn should help inform appropriate use and interpretation of the LDT.

The Honorable Diana DeGette

LDT Rule

1. **In the final Medical Devices; Laboratory-Developed Tests rule, FDA included several categories of tests for which it would continue to exercise targeted enforcement discretion. However, the scope of the enforcement discretion is unclear to many stakeholders. When will FDA provide additional guidance on the circumstances under which it will exercise enforcement discretion?**

FDA intends to hold monthly webinars, issue multiple guidance documents, and post responses to questions received from stakeholders on our website on a rolling basis during the phaseout period.

2. **Can FDA provide a specific definition for 1) "unmet need" and 2) when an available test would sufficiently meet the needs of a patient?**

As discussed in the preamble to the final rule, FDA considers an LDT to be for an unmet need where there is no available FDA-authorized IVD that meets the patient's need. This may be because:

1) There is no FDA-authorized IVD for the disease or condition;
   Ex: An LDT that is intended for cytogenetic analysis of certain genes and chromosomes associated with rare diseases or conditions, certain metals testing, viral load monitoring for some transplant-associated viruses, or diagnosis of certain mosquito- and tick-borne-diseases, where there is no FDA-authorized IVD for the disease/condition.
   Ex: An LDT for an emerging pathogen for which there is no FDA-authorized IVD and for which FDA has not identified an emergent situation.
2) There is an FDA-authorized IVD for the disease or condition but it is not indicated for use on the patient, or a unique attribute needs to be added to the LDT to meet the patient's needs; or
   Ex: An LDT for an alternative specimen type that is infrequently tested when the specimen type required for the FDA-authorized IVD is not and cannot be made available.
   Ex: An LDT for use on pediatric patients when FDA-authorized IVDs are for adults only.
   Ex: An LDT that generates results in a significantly shorter period (e.g., hours versus days) than an FDA-authorized IVD with the same indication where, due to the circumstances of the patient, the shorter time period is critical for the clinical decision being made.

3) There is an FDA-authorized IVD but it is not available to the patient.
Ex: An LDT for the same indication as an FDA-authorized IVD that is offered only in another healthcare system that is not accessible to the patient and the developing laboratory will not make the IVD available outside its system.

In contrast, FDA does not consider an LDT to be for an unmet need when there is an available FDA-authorized IVD that would sufficiently meet the needs of the patient. For example, potential improvements in performance or lower cost in comparison to an FDA-authorized IVD that meets the patient's needs does not fall within this policy.

The Honorable Jan Schakowsky

Device Recalls

1. **Dr. Shuren, I am very concerned that the FDA doesn't have enough authority to recall faulty medical devices. On May 8th, the FDA recalled an insulin pump phone application by Tandem Diabetes Care. A software glitch caused the insulin pump to shut down, injuring more than 200 diabetes patients. The FDA must protect patients from faulty devices. However, due to its limited authority, the FDA cannot always demand that companies remove a faulty product from their shelves. What can Congress do to make FDA's recall authority more effective?**

FDA appreciates your concerns and would be happy to discuss these issues further. One of the biggest challenges FDA faces is that some companies do not notify us immediately about product-related defects, which prevents FDA from notifying the public in a timely manner. The Agency believes it is important to be able to address this situation.

2. **Dr. Shuren, I am also concerned that hospitalized patients are in danger. Hospitals are supposed to be notified about recalls from manufacturers. These notices are communicated by mail, which can take weeks or months. As a result, patients are notified too late and are at risk of serious injuries or deaths. My bill, the Medical Device Recall Improvement Act, would require the FDA to create an electronic format for recall notifications so patients can receive timely information. How would an electronic format improve the recall notification process and further protect patients?**

FDA appreciates the effort being made to address effective communication of medical device recalls to patients and end users. When companies do not notify FDA immediately about product-related defects, it prevents FDA

from notifying the public in a timely manner.