FDA Regulatory and Compliance Monthly Recap
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FDA issues guidance granting exemptions, exclusions for certain DSCSA requirements for COVID-19 products

The guidance delineates exclusions and exemptions to certain requirements under the Drug Supply Chain Security Act (DSCSA) to ensure adequate distribution of prescription drugs during the COVID-19 outbreak. It excludes drugs distributed for emergency medical reasons from the statutory definition of "transaction" and "wholesale distribution."

The FDA published draft guidance to clarify the scope of the public health emergency exemption and exclusion under the DSCSA and to describe its enforcement discretion policy in relation to authorized trading partner requirements under the Federal Food, Drug, and Cosmetic Act (FDCA) policy throughout the COVID-19 pandemic. The policy will remain in effect for the duration of the COVID-19 public health emergency, as declared by the Secretary of Health and Human Services (HHS).

The DSCSA excludes the distribution of a product for emergency medical reasons, including a public health emergency declaration under Section 319(a)(2) of the Public Health Service Act (PHS Act), from the definition of "transaction" or "wholesale distribution." In addition, specific activities are automatically excluded from certain DSCSA requirements upon declaration of a public health emergency. Per the guidance, the DSCSA exemptions and exclusions apply to certain distribution activities that are related to covered COVID-19 products or that are directly impacted by the public health emergency and meet emergency medical needs. Covered COVID-19 products include prescription drugs under an emergency use authorization or approved by the FDA to diagnose, cure, mitigate, treat or prevent COVID-19. In the context of COVID-19, examples of situations in which the public health emergency could directly impact distribution include 1) distribution of a product to an area in which availability is limited; 2) distribution of a product by an authorized trading partner that needs to establish a new, temporary distribution facility due to the impact of COVID-19 on operating capabilities of the original facility; and 3) transfers between dispensers of products needed

as a result of COVID-19, irrespective of whether there is a specific patient need.

The exemption applies to product tracing and identification requirements triggered by a "transaction." The guidance cautions, however, that a trading partner distributing products during the public health emergency for purposes other than emergency medical reasons must continue to comply with all DSCSA requirements. The exemption does not extend to other DSCSA requirements not triggered by a "transaction," such as requirements for applicable valid registration with the FDA, licensure for authorized trading partners or the investigation of suspect products. The exclusion applies to DSCSA requirements related to wholesale distribution, including licensure provisions and reporting requirements and wholesale distributor requirements under the FDCA. Per the FDA, the exclusion does not impact states' ability to require licensure of wholesale distributors under state law. The guidance cautions that activities that meet the definition of wholesale distribution that are not for emergency medical reasons still need to comply with FDCA requirements for the distribution of the products. The FDA directs companies to maintain the security of the supply chain and to continue complying with DSCSA requirements when doing so would not create a barrier to the timely distribution of covered COVID-19 products.

The guidance also describes the FDA's intent not to take enforcement action for 1) COVID-19-related distribution involving entities that would typically meet the definition of a wholesale distributor were it not for the exclusion from the definition of wholesale distribution for emergency medical reasons, and 2) distributions involving other trading partners that are not authorized only because of situations directly related to the public health emergency, but that are working with or have been permitted by state authorities to operate during the pandemic. The FDA cautions that, where possible, trading partners should engage with trusted sources and ensure trading partners are appropriately licensed or registered by checking with the FDA and state authorities.

CDER issues MAPP describing internal process for addressing newly identified safety signals

The manual of policies and procedures (MAPP) outlines the Center for Drug Evaluation and Research's (CDER) internal process for identifying, assessing and resolving newly identified safety signals (NISS) for marketed drugs. It outlines a three-phase process for assessing and managing NISS and establishes time frames for assessing NISS based on the level of risk identified.

The FDA's CDER issued a MAPP outlining its policies and procedures for collaborative identification, evaluation and resolution of a NISS. The MAPP provides an overview of how and when communication is transmitted between different offices and disciplines within the CDER related to NISS for approved drugs and biologics, marketed yet unapproved drugs, OTC monograph products, compounded drugs, and medical gases.

The MAPP describes a three-phase evaluation and management process for NISS. In the pre-evaluation phase, the CDER will assess whether a NISS requires an evaluation, based on medical and scientific judgment in accordance with established pharmacovigilance and review practices for identifying quality and safety signals. The CDER's criteria for a NISS include:

- A serious adverse event, medication error, or adverse event that is indicative of therapeutic inequivalence or product quality issues and that warrants an investigation into whether there is a causal association or a new aspect to a known association.
- A product quality issue that may negatively impact public health or the benefit-risk profile of the product and that cannot be resolved through existing routine processes such as drug recalls.

If an evaluation is needed, a team will be formed to evaluate whether the NISS is an important potential risk or a potential risk, and will comprise representatives from the relevant scientific and regulatory disciplines. The evaluations will assess 1) whether a NISS is an identified risk, an indeterminate risk or a refuted risk; 2) whether regulatory or compliance actions may be needed; and 3) whether there should be communications to the public. Identified risk exists when there is sufficient evidence

of an association with the drug, whereas indeterminate risk exists when findings are inconclusive with respect to the association with the drug. Refuted risk exists when evidence indicates an association with the drug is unlikely. Evaluations will be completed within six months for a NISS categorized as an important potential risk and within 12 months for a NISS categorized as a potential risk.

In the action phase, the CDER will coordinate the implementation of recommended compliance or regulatory action, as well as any recommended communications to the public. Compliance actions may include warning letters, untitled letters, injunctions, seizures, recalls, regulatory meetings or other corrective actions to address violative drugs. Regulatory actions may include a safety labeling change, REMS or REMS modification, requirements for studies to further assess the drug, or removal of the drug or indication from the market.

FDA guidance outlines CARES Act requirements for notification of discontinuance, interruption in device manufacturing during COVID-19 pandemic

The guidance addresses amendments to the Federal Food, Drug, and Cosmetic Act (FDCA) that require manufacturers to notify the agency of a permanent discontinuance or interruption in the manufacture of certain devices that is likely to result in a meaningful disruption in supply of that device in the U.S. It provides recommendations for timely, informative notifications to mitigate potential shortages.

The FDA issued guidance implementing Section 506J of the FDCA, which was added by the Coronavirus Aid, Relief, and Economic Security (CARES) Act to require device makers to notify the agency of a permanent discontinuance or interruption in the manufacture of certain devices that is likely to lead to a meaningful disruption in supply. The guidance will remain in effect throughout the duration of the public health emergency declared by the Secretary of Health and Human Services (HHS).

Under Section 506J, manufacturers must notify the FDA of an interruption or discontinuance in the manufacture of devices critical to public health during the public health emergency and devices for which the FDA determines information on potential meaningful supply disruption is needed. The FDA interprets "manufacturer" to mean the entity that holds the medical device marketing submission authorization or that is responsible for listing the medical device under Section 510(j) of the FDCA. The guidance explains that device manufacturers that are required to submit a premarket notification under Section 510(k) of the FDCA and obtain agency clearance before marketing the device, but that have not received such clearance and are distributing the devices in light of enforcement discretion during the public health emergency, are not subject to the notification requirements under Section 506J.

The guidance recommends that manufacturers assess the following circumstances when ascertaining whether they need to notify the FDA of a permanent discontinuance or manufacturing interruption:

- Whether the device is life-supporting, life-sustaining or intended for use in emergency medical care (such as ventilators)
- Whether the device is intended for use during surgery
- Whether the device is used to diagnose, cure, treat, mitigate or prevent COVID-19
- Whether the device would be in higher-than-typical demand during the response to the pandemic

Manufacturers must notify the agency at least six months in advance of a permanent discontinuance, which the FDA interprets to mean a decision by the manufacturer to stop manufacturing and distributing a product indefinitely for business or other reasons, or of an interruption that is likely to meaningfully disrupt supply of the device. If adhering to that time frame is not possible, the guidance directs device makers to notify the FDA "as soon as practicable," which the FDA considers to mean no later

than seven calendar days after the discontinuance or interruption in manufacturing occurs. Per the guidance, meaningful disruption means "likely to lead to a reduction in the supply of a device by a manufacturer that is more than negligible and affects the ability of the manufacturer to fill orders or meet expected demand for its product." The FDA considers interruptions in manufacturing to include those arising as a result of a decrease in manufacturing capability or increased demand.

After the initial notification, the FDA recommends that device makers provide updates every two weeks, along with expected timelines for recovery, even if the status has not changed. Notifications should include the reason for the discontinuance or interruption, along with appropriate identifying information such as the marketing submission number and FDA Establishment Identifier (FEI) number. The FDA recommends that device makers voluntarily provide extra details to ensure the agency has the information to help prevent or mitigate shortages during the pandemic.

FDA, FTC issue joint enforcement letters targeting fraudulent COVID-19 products sold through Amazon Associates program

The letters take issue with the companies making commissions through the Amazon Associates program by promoting fraudulent COVID-19 treatments. They cite violations of the Federal Food, Drug, and Cosmetic Act for promoting unapproved and misbranded new drugs, as well as violations of the FTC Act for unsubstantiated marketing claims.

As they continue to take enforcement action against companies promoting unapproved products as potential cures, treatments or preventions for COVID-19, the FDA and the FTC are targeting products marketed through the Amazon Associates program. As part of those efforts, the agencies issued several joint enforcement letters citing companies that make commissions through the program by promoting the sale of products using claims representing or implying that they can mitigate, prevent, treat, diagnose or cure COVID-19. In addition to violations of the FDCA, the letters cite violations of the FTC Act for advertising products without competent and reliable scientific evidence to substantiate the claims. Both the FDA and the FTC have been monitoring social media hashtags and scrutinizing Amazon product descriptions to identify potentially misleading marketing. Entities cited in the letters include the following:

- Life Unlearned, a Colorado-based company, was reprimanded for promoting vitamin D products as "the key to COVID-19," using claims suggesting there is a link between vitamin D status and COVID-19 outcomes. The claims cite an analysis indicating that the severity of outcomes is "directly related" to vitamin D status and suggesting that 85.5% of COVID-19 patients with normal vitamin D status have mild symptoms.
- SpiceTac, a Florida-based company, was chided for promoting vitamin C products as the "secret weapon" against COVID-19 and for suggesting it provides "cheap insurance" against the virus.
- Benjamin McEvoy was cited for claiming supplements such as NAC (N-acetylcysteine), zinc, vitamin C, vitamin D, magnesium, ashwagandha, and echinacea can boost immune systems and "could be promising additions to your supplement stack if you're worried about coronavirus." McEvoy framed the claims as "personal supplement recommendations based on years of supplementation for improved immune response."
- AgroTerra, a Colorado-based company doing business as Patriot Hemp Company, was chastised for selling products such as colloidal silver, iodine, medicinal mushrooms, vitamin C and selenium using claims they can work as preventatives or treatments for COVID-19, and linking to Amazon Associate links as "trusted sources." The claims suggest the "antivirals are the best natural therapies ... for the COVID-19 coronavirus." The company was also cited for claims on its website that CBD products offer "the best natural

defense and treatment of coronavirus" by improving the immune system.

- Tiffany Davison, of WashingtonsLastFrontier.com, was reprimanded for promoting essential oils as "natural, very potent" antibiotics to treat COVID-19 and vitamin D3 + K2 as a preventative and immune booster. Davison was also cited for suggesting licorice root can treat the virus by suggesting "that during the SARS outbreak that certain groups of people drinking concoctions of traditional Chinese medicine that contained it during the SARS outbreak did not get infected with the virus despite having been exposed to it by having relatives in the same household who were infected."

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