July 3, 2018

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RE: Comments to Waivers, Exceptions, and Exemptions; Draft Guidance for Industry; Dkt. No. FDA-2018-D-1434

Dear Doctor Jung:


HDA represents primary pharmaceutical distributors – the vital link between the nation’s pharmaceutical manufacturers and more than 200,000 pharmacies, hospitals, long-term care facilities, clinics and others nationwide. This essential function is provided with little public recognition or visibility, and at great savings to the healthcare system. HDA members serve as the central link in a sophisticated national supply chain. HDA members take this mission very seriously, and we support manufacturers, healthcare providers, and the government in ongoing efforts to ensure the U.S. medicine supply remains secure, efficient, and highly regulated.

HDA thanks FDA for issuing the Draft Guidance and the clarity that it brings to the waiver, exception and exemption (also referred to here as “WEE”) processes under the Drug Supply Chain Security Act (“DSCSA”). HDA had previously presented its thoughts and recommendations on the contents of, and processes for, WEE requests and FDA review of them under § 582(a)(3)(A) of the federal Food, Drug and Cosmetic Act (as amended by the DSCSA) in April 2015. A copy of our
previous submission is attached. HDA generally supports the Draft Guidance. Our comments in support and recommendations for changes are discussed in more detail below.

1. **Submissions for CBER-regulated Products, Lines 79-92**

   In Section III.A., FDA explains that WEE requests for products reviewed by the Center for Biologics Evaluation and Research (“CBER”) should be submitted to that Center as part of product correspondence to the appropriate “biologics license application (“BLA”), new drug application (“NDA”), abbreviated new drug application (“ANDA”), or investigational new drug application (IND).” Draft Guidance at Lines 80-82 (emphasis supplied). This instruction is also reflected in the Appendix chart.

   We believe, however, that the supply chain has long assumed that unapproved drugs (including biologics) being distributed under INDs as part of clinical development would not be covered by the DSCSA at all.\(^1\) Their use and purpose is unique and limited (i.e., they cannot be commercialized) and IND regulations restrict their distribution. Furthermore, applying a product identifier to an investigational product could allow for the identification of the product, thereby potentially undermining a clinical trial’s blinding. We also question whether IND products would meet the definitions of “prescription drugs” or “products” under §§ 581(12) and (13). For all these reasons, we do not believe a product should be subject to DSCSA requirements until it is approved and suggest that Lines 80-82 be revised so that they do not suggest that investigational products are subject to § 582.

2. **Content of WEE Request, Lines 116-128**

   Lines 116-128 specify the information a WEE request should contain. We support the framework FDA has identified and the basic information requested in Lines 118 to 126.

   Lines 127 to 128 provide that the requester should also include “A detailed statement of the reasons why FDA should grant the proposed waiver, exception, or exemption, including pertinent supporting documentation”. We believe that this point should be expanded upon in order to provide greater clarity to requesters and so that they, in turn, will provide better information to FDA. We suggest that a requester include the following information, to the extent relevant:

   - A full statement of the likely impacts of the requested WEE. The statement should address any potential impacts to drug supply chain security, patient safety and access to products. This statement should address the burdens potentially associated with granting the requested WEE, including, but not limited to, any burdens the requester anticipates and those burdens that might be borne by trading partners in the supply chain. Such burdens might include changes to systems and operations in order to implement or accommodate a WEE.

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\(^1\) See Q and A # 11 in the “Pharmaceutical Distribution Security Alliance Questions and Answers Regarding the Drugs Supply Chain Security Act” submitted to FDA on May 22, 2014.
3. Acknowledgement, Lines 130-133

We support the inclusion of the acknowledgement set out in Lines 130-133 that the requester understands that under 18 U.S.C. § 1001 it is illegal to make a materially false, fictitious or fraudulent statement or representation. We suggest additionally having the requester provide the attestation required for citizen petitions under 21 C.F.R. § 10.30(b). Specifically:

The undersigned certifies that, to the best knowledge and belief of the undersigned, this request includes all information and views upon which the request relies, and that it includes representative data and information known to the requester which are unfavorable to the request.

This would assure that requesters provide to the Agency all pertinent information, both negative and positive, and that FDA has the benefit of that information when it makes the WEE decision.

4. FDA Review of Requests, Lines 138-168

In Section III.B. of the Draft Guidance, FDA describes its process for review of WEE requests. Lines 142-147 state:

FDA may also contact a requesting trading partner or stakeholder to clarify an aspect of the request (e.g., the products covered by the request) or to ask for additional information related to the subject of the request.

During the review, FDA intends to consult with subject matter experts within the Agency as appropriate …

HDA strongly supports consultation with others when the granting of a WEE may impact others in the supply chain. We recommend further that this opportunity for consultation be formalized in the Final Guidance.

Our April 2015 submission to FDA stated our belief that the WEE process would be strengthened if members of the supply chain were able to submit comments to FDA when a proposed WEE might affect their businesses, if granted. Lines 201-205 of the Draft Guidance provide that the Agency may self-initiate exceptions and exemptions “to address an issue that affects a broad segment(s) of industry and/or multiple trading partners, impacts many activities, or involves numerous products.” In our view, these are the types of requests most likely to benefit from an opportunity for notice and public comment.

We also note that entities other than FDA may initiate these types of broadly applicable and/or impactful requests. Whether self-initiated or initiated by a member of the supply chain, we believe that FDA’s consideration of such broadly applicable WEE requests will usually be aided by public notice and an opportunity for comment. Conversely, we believe that WEE requests that are narrow,
particularly those that are specific to a single company and product, are unlikely to benefit from public comment.  

For example, there would likely be little gained by public notice and comment for WEE requests under § 582(a)(3)(A)(ii) made by manufacturers and repackagers requesting an exception from product identifier requirements because of a product container’s small size. (Though, we note that other potential requesters might benefit if they knew more of the bases on which FDA had previously granted WEEs under § 582(a)(3)(A)(ii).)

For WEE requests that would have broader applicability if granted, HDA suggests incorporating the following additions indicated in blue, bold, to the Final Guidance, perhaps directly following line 159, in order to provide an opportunity for public input:

- FDA will establish a public docket where the Agency will post WEE requests and its determinations with respect to those requests when those determinations address an issue that affects a broad segment(s) of industry and/or multiple trading partners, impacts many distribution, dispensing, or other supply chain activities, or involves numerous products.

  - FDA will announce the establishment of that docket in a Federal Register notice. FDA will also announce when it receives a request for a WEE by issuing a notice on the DSCSA listserv and publishing the non-confidential portion of any request in the docket. Interested members of the public should then be able to comment on the WEE request via a submission to www.regulations.gov.

  - To aid FDA in publishing the request, any person submitting a WEE request should identify, prominently and conspicuously, information that, in the submitter’s view, is exempt from public disclosure, such as commercial or financial information that is privileged or confidential. FDA would then assess whether any information should be redacted before public disclosure when it publishes the WEE request in accordance with 21 C.F.R. Part 20.

  - FDA should, ideally, permit 60 days to comment on a WEE request after its public posting. However, there may be urgent circumstances where notice and opportunity for comment will need to be shorter or omitted entirely, such as in a public health emergency declaration.

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2 In point 7 below, we caution that, though a particular WEE may be narrow in scope and so would be unlikely to benefit from public comment, “partial” WEEs should be avoided because of their potential to disrupt supply chain operations and 2023 readiness and compliance. As this point explains, if, for example, FDA grants an exception request that relieves a manufacturer or repackager from affixing a product identifier to a too-small package, we believe that the exception should extend to all related § 582 requirements, including the requirement to provide TI and TS, as the product moves through the supply chain.

3 HDA included this bullet because we believe that providing this information as part of the WEE request will likely help reduce the burden upon FDA and thereby speed the decision-making process.
5. **Standard of Review, Lines 149-164**

In Lines 149-161, FDA enumerates the factors and standards it will consider in reviewing and granting a WEE. Aligning with the DSCSA, the Draft Guidance provides that FDA will consider whether a request is warranted due to economic hardship or for emergency medical reasons (Lines 149-151) and if a product should be exempt from including an identifier because of the size of the container (Lines 152-155). HDA supports these provisions of the Draft Guidance.

FDA provides a third criterion for granting a WEE:

- Exempting the product(s) and/or transaction(s) identified in the request from the section 582 requirement(s) identified in the request is appropriate to maintain public health or is otherwise appropriate.

*FDA intends to also consider the potential risks that a proposed waiver, exception, or exemption poses to the security of the drug supply chain when reviewing requests.*

Draft Guidance at Lines 156-161 (emphasis supplied). The “appropriate to maintain public health or is otherwise appropriate” standard is new, and not in the DSCSA. HDA supports FDA considering public health and supply chain risk when evaluating whether to grant a WEE.

We suggest that FDA further clarify the grounds for granting an exception on this basis to expressly reflect the underlying security and patient safety principles of the DSCSA and the possible impacts of a WEE upon the supply chain as a whole. We recommend the following additions, indicated in blue, bold:

FDA intends to also consider the potential risks that a proposed waiver, exception, or exemption poses to the security of the drug supply chain when reviewing requests and whether the proposed waiver, exception, or exemption may pose a risk to patient safety or unduly burden other supply chain trading partners or stakeholders.

We note further that WEEs that might significantly burden others in the supply chain and/or implicate public health, patient access to medicine, or supply chain security are likely to have broad applicability and are the types of requests that would most benefit from the opportunity for public notice and comment as discussed above.

6. **Biennial Review of Waivers, Exceptions, and Exemptions, Lines 226-246**

The Draft Guidance states:

Once every 2 years, FDA intends to review waivers, exceptions, and exemptions that are valid until further notice from the Agency or longer than 2 years in duration (*i.e.*, the expiration date is more than 2 years after the effective date) and renew such waivers, exceptions, and exemptions, as applicable. During this review, the Agency
intends to assess whether there has been a material change in circumstances such that the waiver, exception, or exemption is no longer appropriate.

HDA supports the proposed biennial review as noted in lines 226-246 as it would allow for consideration of whether the circumstances that justified the initial grant of the WEE have changed. Should FDA deem a granted WEE to no longer be appropriate (e.g., terminated or expired), we ask that the Agency consider impacts to current processes and affected products already in the supply chain as the changeover is implemented. Impacted trading partners may need time to transition. Additionally, any product already in the supply chain that is no longer subject to a WEE, such as products in wholesale distributor and dispenser inventory, should be “grandfathered” (that is, continue to be treated as covered by the WEE) and be permitted to continue to move in transactions between trading partners as before.

7. When considering a WEE, FDA should determine how that WEE (if granted) may affect the supply chain’s ability to comply with related DSCSA requirements.

While a trading partner’s WEE request may seek relief from a particular DSCSA requirement, we urge FDA to carefully consider how that request may affect each product’s movement through the supply chain and the subsequent trading partner’s ability to comply with related DSCSA requirements for that product. WEEs involving product marking and tracing requirements are the most likely to affect trading partners’ DSCSA compliance and supply chain operations. Uniformity is critical to successful implementation of the DSCSA’s product tracing requirements and we believe “partial” WEEs could jeopardize the supply chain’s ability to meet 2023 requirements.

Three examples further illustrate this point:

- **Abbreviated Product Identifiers:** Given the millions of products moving in the supply chain every day, the 2-D data matrix bar codes need to be uniform (and consistent with GS1 standards) in order for trading partners to be able to swiftly and accurately scan them. Therefore, HDA recommends that FDA not grant a WEE that would permit deviations from these standards. For example, FDA should not grant a WEE that would allow a manufacturer or repackager to embed within a 2-D data matrix bar code a product identifier that omits part of the DSCSA-required data (e.g., lot number or expiry). If FDA were to grant such a WEE request, scans of the product identifier would show an error and result in rejection of the product and/or a delay in distribution as the error is investigated.

- **Product Identifiers and TI:** In 2023, the DSCSA requires TI to include product identifiers. For DSCSA-covered products, trading partners will be designing electronic and other systems to reject any transaction that does not include complete TI. However, if a WEE were granted whereby a product did not have to be serialized, the manufacturer or repackager would be unable to provide TI that includes the product identifier. If TI (without the product identifier) was nevertheless generated, transmitted, and received for such a product, it would be incomplete and the DSCSA systems would reject the transaction.
We therefore urge the Agency to make clear when it grants a WEE from the serialization requirement that the WEE, for that product, also applies to all DSCSA requirements that involve the product identifier (including, but not limited to, the requirement to provide TI and TS) as the product moves through the supply chain. Such FDA acknowledgement is needed to avoid potential confusion by trading partners, and to confirm to supply chain members that electronic systems are permitted to process transactions involving these WEE products by effectively treating them the same as other types of products that are not covered by the DSCSA, e.g., over-the-counter drugs.

- **Product Tracing:** If FDA were to grant a WEE relieving a party from the requirement to provide transaction data, FDA would need to consider carefully whether subsequent trading partners would be able to provide compliant transaction data as the product moves through the supply chain; in particular, TH (prior to 2023) and TS provided in a subsequent transaction might be adversely affected. We believe the Agency should make clear that if one trading partner receives a WEE relieving it from certain tracing requirements for a product transaction, subsequent trading partners also should be relieved from the same affected tracing requirements involving that product. Such clarity would be important for supply chain members and for FDA and state officials charged with enforcing the law.

In sum, as a general proposition, HDA believes that an individual product is either “all in” or “all out.” That is, a product should either be fully compliant with the DSCSA product identifier and transaction data requirements, or it should be completely excluded.

8. **Notification and Publication of a WEE Decision**

The Draft Guidance briefly addresses how FDA’s WEE decisions will be disseminated, and to whom. Section III.C., Lines 174 -176, briefly touch on this concept, and Section IV., Lines 216-219, specifically state:

If FDA establishes an exception or exemption to address a particular issue, it intends to communicate the information in writing using a method appropriate for the circumstances (e.g., a letter to the affected trading partners or - if an exception or exemption applied to a broad segment of industry - a posting on its website).

We suggest that the Final Guidance instruct that it is the responsibility of the entity granted a WEE to inform its trading partners of the decision, such as by providing trading partners with a copy of the FDA decision letter. This will be especially important when FDA has excepted a manufacturer or repackager from product identifier requirements pursuant to § 582(a)(3)(A)(ii). HDA’s wholesale distributor members have found that manufacturers and repackers have been inconsistent in their communication of WEEs. An explicit instruction in the Final Guidance that the requester is obligated to inform trading partners of an FDA-granted WEE would aid in standardizing this process.

To clarify this expectation, we encourage FDA to insert the following additional language, in blue, bold, at the end of Section III.C., and again at the end of Section IV.:
FDA strongly recommends that the requester inform its trading partners if the Agency grants a request for a waiver, exception, or exemption.

As to notification of a WEE decision beyond the immediate trading partner(s), the Draft Guidance proposes that FDA will post a decision on the Agency’s website if an exception or exemption applies to a broad segment of industry. Draft Guidance at Lines 217-219.

HDA supports this position. We believe that the supply chain is best served if FDA publishes those WEE decisions (appropriately redacted if necessary) that “affect a broad segment(s) of industry and/or multiple trading partners, impact many activities, or involve numerous products.” Draft Guidance at Lines 203-205. We urge FDA to expressly commit to posting such decisions in a WEE-related docket and on the Agency’s website when it issues the Final Guidance.

Further, we ask that FDA consider publicly posting those WEE requests – both granted and denied – that are broadly applicable because they potentially involve complex changes to additional segment(s) of the supply chain and/or multiple trading partners, impact many distribution and/or dispensing activities, or involve numerous products. We believe such decisions, appropriately redacted, would be useful and informative for industry.

We acknowledge that HDA has very little direct knowledge of the WEE requests that FDA has already received and granted or denied. Should FDA elect to make some or all WEE decisions public, we believe FDA should consider the following for the Final Guidance:

- A clear explanation of the types of WEE decisions the Agency believes are appropriate for public dissemination and the form of notice and publication that the Agency will use.

- A commitment to continuing review of the WEE decisions that are made public to determine if their publication provides value to the supply chain that is outweighed by any potential supply chain risks or burdens.

9. Lack of timeframes

We note that the Draft Guidance does not provide any timeframes, such as how long it will typically take to review a WEE request and when a WEE will become effective. To the extent that FDA has developed experience in the time for review of a completed WEE request and its effective date, further explanation of the length of time needed for a WEE review in the Final Guidance could be useful for requesters.

10. Burden Estimate

In the Federal Register notice announcing the Draft Guidance, 83 Fed. Reg. 21297, FDA indicated that it expected about 20 WEE requests per year and that each would take approximately 40 hours for a requester to prepare and submit the request. We do not have a basis for commenting on the number of submissions FDA might receive in a year as implementation of many of the
requirements that are more likely to be the subject of a WEE, such as the DSCSA requirement for affixing a product identifier, are still in a developmental stage.

However, we suspect that preparing and providing the information FDA is requesting would likely require more than 40 person-hours, particularly for a WEE that “affects a broad segment(s) of industry and/or multiple trading partners” (Draft Guidance at Lines 162-164).

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HDA thanks FDA for this opportunity to comments and suggestions on FDA’s Draft Guidance. If you have any questions, please contact me at 703-885-0240 or at aducca@hda.org.

Sincerely,

Anita T. Ducca
Senior Vice President, Regulatory Affairs

Attachment