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Docket Officer
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20857

RE: Requirements for Foreign and Domestic Establishment Registration and Listing for Human Drugs, Including Drugs that are Regulated Under a Biologics License Application, and Animal Drugs. RIN 0910-AA49; Docket No. 2005N-0403 [71 Fed. Reg. 51276, August 29, 2006]

Dear Docket Officer:

The Healthcare Distribution Management Association (HDMA) appreciates this opportunity to provide public comments on the Food and Drug Administration's (FDA) Proposed Rule: *Requirements for Foreign and Domestic Establishment Registration and Listing for Human Drugs, Including Drugs that are Regulated Under a Biologics License Application, and Animal Drugs* (proposed rule or proposal), 71 Fed. Reg. 51276 (Aug. 29, 2006).

HDMA represents the nation's primary, full-service healthcare distributors. Our members are large national companies and regional, family-owned businesses. Each and every day, HDMA member companies safely and efficiently deliver nine million healthcare products to more than 144,000 pharmacies, hospitals, nursing homes, physician offices, and clinics across the United States. This essential function is provided with little public recognition or visibility, and at great savings to the healthcare system. HDMA members serve as the central link in a sophisticated national supply chain. As such, we have a responsibility to work closely with our supply chain partners to safeguard patient health. We take this mission very seriously, and we support manufacturers, pharmacies, and the government in ongoing efforts to ensure the U.S. medicine supply remains secure, efficient, and highly regulated.

HDMA appreciates FDA's effort to clarify its regulations governing drug establishment registration and listing. HDMA supports much of the proposed rule and believes that, if implemented, the rule could improve the drug registration and listing process. However, some elements of the proposed rule potentially have a significant negative impact upon the distribution industry. Among other things, and as discussed further below, the

proposed rule would, if made final in its present form, have important implications for the ability of pharmaceutical distributors to comply with the Prescription Drug Marketing Act (PDMA) final rule, parts of which became effective on December 1, 2006. 64 Fed. Reg. 67720 (December 3, 1999).

HDMA offers comment below on the following parts of the proposed rule:

- HDMA believes that in proposing so broad a definition of “relabel,” FDA has inadvertently reached into many common drug distributor practices and potentially significantly hampers compliance with the bar code rule and PDMA. HDMA urges FDA to exempt certain common distributor inventory control, pedigree, track-and-trace, and stickering practices from the definition of “relabel.”
- HDMA supports an Internet-enabled registration and listing process.
- HDMA supports maintenance of the current 10-digit NDC number and configuration because any change to that configuration would be enormously disruptive to industry.
- HDMA is concerned with FDA’s proposal to undertake NDC number assignment itself.
- HDMA has concerns regarding FDA’s proposal to no longer permit private label distributors to undertake registration and drug listing on their own behalf.
- HDMA believes that FDA should consider other alternatives to requiring that retail service repackaged drugs bear their own NDC number. If final, the rule would eliminate the vital retail service repackaging industry which currently adds efficiencies to the healthcare system.
- The rule, if made final as proposed, will significantly impact many common practices in healthcare distribution. For these reasons, HDMA urges the more gradual implementation timetable proposed in the rule, and asks that FDA clarify aspects of that implementation.
- HDMA urges FDA to maintain the confidentiality of information submitted for drug registration and listing.
- HDMA asks that FDA clarify the procedures for discontinuing a drug listing during the twice a year updates proposed.

- HDMA concurs with the views of others expressed at the December 11, 2006 public meeting and suggests that FDA narrow the breadth and scope of the proposed rule and approach these profound changes to the healthcare system more incrementally.

A detailed discussion of these issues is included in the attachment to this letter.

In conclusion, HDMA appreciates this opportunity to share its views with FDA and to provide our perspectives on this proposed rule. Should you have any questions about this letter, please feel free to contact Anita Ducca at 703-885-0240 or at aducca@hdmanet.org.

Sincerely,



Anita T. Ducca
Senior Director, Regulatory Affairs
and Healthcare Policy

Attachment

Cc: Ilisa B. G. Bernstein, Pharm.D., J.D.

**Comments by the Healthcare Distribution Management Association (HDMA)
on the FDA Proposed Rule
Requirements for Foreign and Domestic Establishment
Registration and Listing for Human Drugs, Including Drugs That Are Regulated
Under a Biologics License Application and Animal Drugs
RIN 0910-AA49; Docket No. 2005N-0403 (71 FR 51275)**

The Healthcare Distribution Management Association (HDMA) appreciates this opportunity to provide public comments on the Food and Drug Administration's (FDA) Proposed Rule: *Requirements for Foreign and Domestic Establishment Registration and Listing for Human Drugs, Including Drugs that are Regulated Under a Biologics License Application, and Animal Drugs* (proposed rule or proposal), 71 Fed. Reg. 51276 (Aug. 29, 2006). Below are HDMA's detailed comments on this proposed rule.

1. Definition of "relabel".

HDMA begins with an issue of enormous significance to the entire distribution industry – the broad definition of "relabel" in the proposed rule. Many aspects of the proposed rule, including registration and listing with the establishment's unique labeler code and NDC number, are triggered if an establishment relabels a drug product. FDA proposes to define relabel very broadly as follows: "Relabel means to change the label or labels on a drug or drug package, or add to the labeling for a drug or drug package, without repacking the drug or drug package." 71 Fed. Reg. at 51290; proposed § 207.1. As defined, any action on a drug label, labeling, or package will bring the entity under the definition of "relabel" and trigger establishment registration as a relabeler, assignment of a labeler code, and listing of the drug under the relabeler's own NDC number.

HDMA has grave concerns regarding the breadth of this definition. Of greatest concern to pharmaceutical distributors is how this interpretation of "relabel" interferes with inventory control practices common in pharmaceutical distribution, conflicts with the bar code rule, 21 C.F.R. § 201.25, and could impede compliance with requirements that exist or may be developed under the federal PDMA and state drug pedigree laws.

HDMA distributors ship millions of prescription drug products **each day** to customers nationwide. To do so efficiently, it is common practice for distributors to affix stickers, barcodes, tags or other identifiers to drug packages to identify recipients, to track inventory location, to identify product origins and/or to help ensure proper returns from pharmacies.

For example:

- Stickers may convey important handling information for customers (such as "refrigerate on arrival") or direct the delivery of the drugs to a particular part of a hospital or medical facility.

- Some distributors manage inventory by applying proprietary serialized codes to drug packages that enter their facilities. These additions allow a company to identify and trace the drugs entering and leaving the distribution center.
- Some products, such as certain blood plasma products, do not have a readable bar code on the package. Some distributors affix bar code stickers to the packages upon arrival at the distribution center to facilitate accuracy in picking, checking and for utilizing bar code scanning systems. These bar code scanning systems have helped to improve efficiency in the supply chain.
- Some distributors apply bar codes to drug products in order to efficiently and effectively comply with FDA's bar code rule, requirements under the PDMA final rule and/or state drug pedigree laws. To improve compliance with the state of Florida's pedigree law, for example, some HDMA members add serialized bar codes to the drug product container.
- FDA has identified Radiofrequency Identification (RFID) as "the most promising approach to reliable product tracking and tracing... RFID will provide cost-reducing benefits in areas such as inventory control, while also providing the ability to track and trace the movement of every package of drugs from production to dispensing."¹ FDA reiterated its support for RFID in its most recent Counterfeit Drug Report: "We recommend that stakeholders continue moving forward in implementing RFID across the drug supply chain."² Currently, some distributors are participating in RFID pilot programs and as this technology develops further, distributors will need the flexibility to sticker or tag products without also triggering the listing and registration requirements of this rule.³
- Additionally, individual states, which are responsible for the regulation and licensure of wholesale drug distributors, have begun mandating their own track, trace, and pedigree requirements. HDMA anticipates more states will follow the lead of California, Florida, Nevada and numerous others in upcoming legislative sessions and rulemaking efforts. What new, additional

¹ FDA Report: *COMBATING COUNTERFEIT DRUGS: A Report of the Food and Drug Administration* (Feb. 2004) http://www.fda.gov/oc/initiatives/counterfeit/report02_04.html

² FDA Report *FDA COUNTERFEIT DRUG TASK FORCE REPORT: 2006 UPDATE* (June 2006), see <http://www.fda.gov/bbs/topics/NEWS/2006/NEW01386.html>.

³ Currently, FDA has stated that it intends to exercise its enforcement discretion with regard to registration and listing requirements (and certain other requirements) that might be triggered by placement of RFID tags for purposes of RFID pilot studies. However, drugs included in the RFID pilot programs are otherwise expected to comply with all other applicable provisions of the Food, Drug, and Cosmetic Act. See http://www.fda.gov/oc/initiatives/counterfeit/rfid_cpg.html.

requirements a state may impose is, of course, currently unknown. However, we anticipate that the simplest, most cost effective method for assuring compliance with many states' new track and trace requirements will be for the drug wholesaler to add a sticker or tag to product moving through the supply chain. HDMA members need to have the flexibility to respond to the new state requirements we all expect will be enacted, without fear of inadvertently triggering FDA listing and registration requirements.

These distributor-applied stickers and tags do not otherwise alter the drug's original label, labeling, package or outer container; do not affect the safety, purity or potency of the drug; and do not disturb its existing packaging configuration in any way. Distributors merely add additional discrete pieces of information, such as bar codes and handling instructions, to assure the safe and secure movement of drug through the supply chain.

If the definition of relabel remains as proposed, the many common security and inventory tracking best practices conducted today by distributors would unintentionally trigger the relabeling designation and the requirements of the rule. If left unchanged, FDA would have to assign tens of thousands of new NDC numbers and whatever benefits FDA had hoped to obtain in assigning a single NDC number to a single drug will, we believe, be lost. Indeed, the agency would quickly run out of 10-digit NDC numbers to assign. Given that the agency stated in the rule's preamble that most drugs would be able to retain their current NDC numbers, we believe FDA did not intend these consequences.

HDMA urges FDA to exempt these common distributor stickering and tagging activities from the definition of "relabel." We suggest including, in the rule, the following language to describe such an exemption:

The following is exempt from the definition of "relabel":
Minor labeling undertaken by wholesale drug distributors that is included in the traditional practice of lawful, wholesale drug distribution practices, such as, but not limited to, labeling affixed to product for purposes of delivery to a customer, customer identification, inventory management, special handling instructions and/or to aid in compliance with federal and state pedigree requirements.

This matter is of enormous importance to the healthcare industry's developing track and trace capabilities. The proposed definition conflicts with other critically important public health initiatives to assure that safe, secure, and potent pharmaceuticals reach their intended patients and can be traced through the supply chain. HDMA welcomes the opportunity to meet with FDA to discuss this issue further and to work to develop an acceptable definition that allows the agency to meet its registration and listing goals without also endangering other critically important drug safety initiatives and useful business practices.

2. Web-enabled registration and listing process.

Overall, HDMA and its members support moving the current, paper based drug listing and registration process into an Internet-enabled system. All HDMA members currently have Internet capabilities. While the initial entry of information into the system may be lengthy and time consuming, completing FDA drug registration and listing forms currently used is a similarly onerous task. HDMA believes entering this information directly into an FDA electronic database, coupled with the ability to edit keystrokes and update existing information already entered, will shorten the time and resources drug registration and listing currently require.

HDMA does assume that FDA has sufficient safeguards in place to assure that the registration and listing system is secure and stable, and that there is sufficient capacity to accommodate the many thousands of registrants and tens of thousands of drugs. HDMA also assumes that, prior to completion of an electronic submission requirement, the FDA will work with registrants to help ensure that data security requirements and other technical features are understood and can be implemented without disruption.

3. Maintenance of current NDC numbers and configurations.

FDA states that it would use the same 10-digit NDC configuration as is currently used – a 4 or 5-digit labeler code, a 4 or 3-digit product code, and a 1 or 2-digit package code. 71 Fed. Reg. at 51299-51300. Further, the agency estimates that it has sufficient capacity to accommodate 10-digit NDC numbers for the next 30 to 50 years. 71 Fed. Reg. at 51300.

HDMA members are very supportive of FDA stated intention to allow most drugs to retain their current 10-digit NDC number, and to maintain the current 10-digit configuration for many years. As the agency notes elsewhere in the preamble, a drug's NDC number is a very important figure. 71 Fed. Reg. at 51296. NDC numbers are significant components of: purchase and sales, inventory management, distribution, prescribing decisions, dispensing practices, claims processing, rebate agreements between manufacturers and the Centers for Medicare and Medicaid Services (CMS), and reimbursement and claims payment under government funded and private health insurance plans.

For these reasons, requiring an establishment to change its drug's NDC number is a very onerous undertaking. The healthcare system is very dependent upon NDC numbers to assure that the right drugs are distributed and dispensed to the right patients and that the right payments follow those drugs. Any change to an NDC number causes significant ripples throughout the supply chain and, indeed throughout the entire

healthcare industry. The fewer changes to NDC numbers, the less disruption there will be to the supply of safe, potent, reimbursable drugs to patients.

Moreover, while the unique number assigned to a single drug is important, its 10-digit configuration is also critical. Scanners, data entry, computer systems, and other electronic tools the healthcare distribution system, rely upon, and are compatible with, a 10-digit NDC number. Changing to a different configuration, such as an 11 or 12-digit number, would have enormous repercussions for the healthcare industry. Existing scanning technologies and computer systems would simply not accept anything but a 10-digit NDC number, necessitating significant changes to existing systems. HDMA members report such a change would be comparable to “Year 2000” burden for the healthcare industry.

HDMA concurs with the testimony offered at the public meeting on December 11, 2006 regarding the costly and burdensome impact of a change to an 11-digit NDC number. In particular, we share the concerns expressed by John Roberts of GS1 US BarCodes and eCom regarding the serious consequences of requiring inclusion of an 11-digit NDC number in a drug’s bar code. Forcing inclusion of an 11-digit NDC number in a drug’s bar code would severely affect the global universality of bar codes and be highly injurious to industry.

Moreover, if FDA were to move to an 11 or 12-digit NDC number, it would become impossible for industry to comply with both the NDC rule and the bar code rule, 21 C.F.R. § 201.25. A bar code for a pharmaceutical product only has room for 10 digits and as Mr. Roberts explained in his testimony, it is not possible to change this bar code configuration. Thus, an 11-digit NDC number could not, as the bar code rule requires, be included in a linear bar code that meets European Article Number/Uniform Code Council or Health Industry Business Communications Council standards. 21 C.F.R. § 201.25(c). At a minimum, expanding the number of digits in the NDC code will inexorably lead to reopening and reexamining the bar code rule.

FDA also states that it intends to leave a space between the segments of the number so that the separate code segments of the NDC number are distinguishable (labeler/product/package). Manufacturers, repackers, relabelers, and salvagers may add hyphens or asterisks between the human readable numbers if they wish. 71 Fed. Reg. at 51299.

Inclusion of these segments also potentially intersects with the bar code rule, 21 C.F.R. § 201.25. As mentioned above, the 10-digit NDC number can currently be embedded in the 10-digit linear bar code, § 201.25(c). That embedded bar code number does not contain spaces or other markers between the segments of a drug’s NDC number. To encode those segment dividers of the new NDC number into the machine readable bar code would be to, essentially, expand the NDC number by two digits. As discussed above, any expansion of the NDC number that would have to be included in the embedded bar code cannot be accommodated without enormous difficulty.

HDMA urges FDA to clarify in the final rule that although human readable NDCs may include spaces, machine readable bar codes should not include the spaces or other dividers between the NDC segments; inclusion of the 10-digit NDC number in the bar code without the spaces should be sufficient for compliance with § 201.25. HDMA recommends addition of the following language into 21 C.F.R. Section §201.25(c)(1) of the bar code final rule, to ensure clarification (amendment to the bar code rule is set forth at 71 Fed. Reg. at 51346).

201.25 Bar code label requirements

(c)(1) *** For purposes of this section “appropriate NDC number” is described in § 201.2(b), and is a 10-digit number described in § 207.33(a), and does not include any spaces, hyphens, or other intervening symbol between the 3 segments of the NDC number: labeler code, product code, package code.

Last, we note that since the promulgation of this proposed rule, CMS has issued a proposed rule implementing the Deficit Reduction Act of 2005. 71 Fed. Reg. 77174 (Dec. 22, 2006). The CMS rule, among other things, discusses NDC numbers and proposes a definition of the NDC number that is at odds with the FDA definition. Specifically, in 42 CFR § 447.502 of the CMS proposed rule, the NDC number is defined as:

the 11-digit numerical code maintained by the FDA that indicates the labeler, product, and package size, unless otherwise specified in this part as being without respect to package size (i.e., the nine-digit numerical code).

71 Fed. Reg. at 77196. We believe that this inconsistency is due to place holder numbers that manufacturers and CMS add to the standard FDA 10-digit number for purposes of CMS reporting and/or to the fact that unlike the FDA NDC number, the CMS rebate system does not use package codes.

HDMA believes that the 11-digit code referenced by CMS in their proposed rule is satisfactorily utilized by those entities responsible for CMS reporting. Additionally, we point out that the discrepancy between the FDA and CMS definitions suggests that any change by FDA to an 11-digit code may result in confusion as to the appropriate code to use to meet CMS reporting requirements. We suggest that the agencies consult with one another prior to finalizing their rules so that, to the extent possible, they determine how best to harmonize their use and definition of the NDC codes.

Regardless of the reasons for the discrepancies in agency definitions, HDMA wishes to be clear that any changes to the current FDA configuration of 10 digits will have enormous repercussions throughout the supply chain, including, but not limited to,

compliance with the bar code rule. The FDA, manufacturers, distributors, retailers and CMS are not the only entities who rely upon NDC numbers in their current configuration. Under the Automation of Reports and Consolidated Orders System (ARCOS) the Drug Enforcement Administration (DEA) requires reporting on controlled substances using NDC numbers.⁴ Further, third party payors use the NDC numbers for purposes of payments to beneficiaries under private prescription drug benefit plans. Presumably, the same difficulties the supply chain would have in converting to an 11 or 12-digit NDC number would reverberate to the many other agencies and private entities that rely upon the same configuration.

4. FDA assignment of NDC numbers.

Proposed 21 C.F.R. Part 207, Subpart C, sets out a new system for the assignment of NDC numbers. The proposed rule provides that FDA, rather than the manufacturer/relabeler/repacker, would assign the entire 10 digit NDC number – the labeler code and the product and package codes – for all newly listed drugs.

HDMA members are concerned with FDA's decision to take on this task. First, the rule does not provide a timeframe for how long it will take before FDA will assign the NDC number. As FDA acknowledges, and as discussed above, the NDC number is enormously important. The smooth flowing of drugs through the supply chain from manufacturer to patient depends, in part, upon NDC numbers. Currently, the manufacturer/relabeler/repacker can begin using its NDC number from the moment it self-assigns that number. As discussed at the public meeting, research, development, labeling, purchasing, contractual arrangements, rebate agreements and reimbursements, among other things, all depend upon the ability to quickly obtain and use a unique NDC number.

The proposed rule and preamble provide no hint as to how long it will take for FDA to assign an NDC number. At the public meeting, FDA suggested that it might assign the number after several days or weeks, after "validating" the drug product. The final rule should specify the length of time that will elapse and how the applicant will be notified of the assignment. HDMA agrees with those at the public meeting urging that the safe, continuous and orderly development and supply of drugs depends upon FDA making NDC numbers available quickly, upon request, and confidentially when product is still under development.

Moreover, HDMA respectfully disagrees with FDA's determination that it must take on for itself a task that industry has performed well for years. HDMA understands that FDA believes that it must undertake NDC number assignment to avoid duplicative

⁴ For further information on the ARCOS program, please see:
<http://www.deadiversion.usdoj.gov/arcos/index.html>

NDC numbers. However, safeguards within databases to prevent assignment of duplicative screen names, user identifications, and other unique identifiers are, at this point, commonplace on public and commercial websites. We believe that concerns of duplicate NDC numbers can be easily resolved through this existing technology. The system that FDA designs and implements for drug registration and listing should have an integrated database that automatically searches existing NDC numbers when the filer seeks to add a new NDC number to the system. The system should prohibit an establishment from self-assigning a number already in use.

5. Provisions regarding private label distributors.

Currently, private label distributors are able to register and list drugs. FDA is proposing to eliminate this option and require that manufacturers, repackers, relabelers, and salvagers list and register on behalf of any private label distributors. Private label distributors would not be permitted to register, obtain NDC numbers for their drugs, or list those drugs. Proposed 21 C.F.R. § 207.17(b) (registration); § 207.33(b)(3)(obtaining NDC numbers); § 207.41(c)(drug listing).

This restriction is troubling for HDMA members who are also private label distributors. Of greatest concern is that private label distributors would lose all control over an aspect of their business with enormous commercial and regulatory significance. The prompt assignment of a unique NDC number to a new drug and the listing of that drug are of urgent importance to the supply chain, including the private label distributor, prescribers, dispensers, and third party payors. Assuring that marketed drugs have NDC numbers and that they are listed are matters of legal and regulatory significance as well. Recognizing these commercial realities and regulatory obligations, contractual arrangements between private label distributors and their manufacturers typically spell out who is responsible for these duties to assure that drugs are listed and to assign liability to the party that reneges on its obligations to accomplish NDC number assignment and listing.

Under the proposed rule, private label distributors will not be able to self-assign NDC numbers – indeed, no entity other than FDA will be able to do so. Private label distributors lose entirely the ability to control what NDC number it gets and even more critically, when it obtains an NDC number. A new private label distributor will have to rely upon a manufacturer/relabeler/repacker even to obtain its labeler code.

Yet, while private label distributors will not be able to list drugs, nothing in the proposed rule addresses this profound shifting of legal responsibilities. The proposed rule does not provide private label distributors with any apparent means to assure that its manufacturers have listed drugs as the rule would obligate them to do. As is well established, the entity whose name appears on a drug label is, in the first instance, legally responsible for the drug. It will, thus, be the private label distributor who would be

responsible for a drug that is improperly listed, even though it has no control over the listing process at all.

HDMA respects FDA's concerns that private label distributors have had difficulty obtaining necessary information from manufacturers, that there is confusion about which party is responsible for drug listing, and that some private label distributors do not understand the process. 71 Fed. Reg. at 51307. HDMA members who are private label distributors report no such difficulties and confusion, however. Indeed, the reason why HDMA members have undertaken to list their own privately labeled drugs is because they are confident in their abilities to time the actions correctly and to make the proper submission. To the extent that such problems have existed, HDMA posits that the remedy lies in clarifying in the final rule that if a private label distributor undertakes obtaining the NDC number and drug listing, that the manufacturer/relabeler/repacker/salvager must cooperate and provide such information as is necessary to complete the listing process. Further, HDMA suggests that the final rule clarify that all drugs marketed by a private label distributor bear the private label distributor's labeler code.

To that end, HDMA asks that FDA delete those parts of the rule prohibiting private label distributors from registering or listing (see, e.g., § 207.17(b), § 207.33(b)(3), § 207.41(c)). Further, the final rule should incorporate language that permits private label distributors to undertake registration and listing if they so wish. For example, we suggest modifying proposed § 207.17(b) as follows:

(b) Private label distributors ~~must not~~ may register with us ~~unless they also manufacture, repack, relabel, or salvage drugs and are required to register under paragraph(a) of this section,~~ or the manufacturer, repacker, relabeler or drug product salvager who manufactures, repacks, or relabels a drug for you may register for you.

Insofar as drug listing is concerned, we suggest, for example, modifying proposed § 207.33(b)(3) as follows:

If you are a private label distributor, you may obtain an NDC number from us for each drug that is subject to the drug listing requirements in this part, or the manufacturer, repacker, relabeler or drug product salvager (described in paragraph (b)(2) of this section) who manufactures, repacks, or relabels a drug for you ~~is responsible for~~ may obtain an NDC number from us for each drug that is subject to the drug listing requirements in this part. If you elect to obtain an NDC number from us, the manufacturer, repacker, relabeler or drug product salvager who manufactures, repacks, or relabels the drug for you must provide you with the information to obtain the NDC number.

The proposed prohibition upon private label distributors from listing contained within proposed § 207.41(c) would, similarly, need to be revised, as well as other sections of the proposed rule, to assure that private label distributors may register, list, update registration and listing information and cancel registration and listing information, as the rule contemplates for manufacturers, repackers, relabelers, and salvagers.

Further, to clarify that a drug marketed by a private label distributor would be marketed under its own labeler code, HDMA suggests the following be added to final §207.33(a):

Drugs manufactured, repacked or relabeled for a private label distributor, will bear the private label distributor's labeler code.

HDMA understands that FDA may not have the authority to mandate that a private label distributor register and list. 21 U.S.C. § 360. However, HDMA posits that nothing in the Food, Drug and Cosmetic Act prohibits FDA from permitting private label distributors to voluntarily register and list drugs if they wish to do so.

6. Continuing use of manufacturer's NDC number for retail service repackaging.

HDMA notes with appreciation FDA's discussion of prior comments the association has submitted to the agency. As FDA discusses in the preamble to the proposed rule, HDMA and the National Association of Chain Drug Stores (NACDS) asked the Agency to exercise enforcement discretion concerning the bar code rule (21 C.F.R. § 201.25, 69 Fed. Reg. 9170 (Feb. 26, 2004)) so that certain retail service repackagers could continue using manufacturers' National Drug Code (NDC) numbers on retail-based repackaged drug products. We respond to the agency's request for comments on this issue.

HDMA members perform many forms of packaging. For example, a packaging company may simplify the last step in the manufacturing process for the manufacturer (contract packaging) or aid in dispensing the product to the patient for hospitals using a unit-dose system (unit-dose packaging). The proposed rule, if implemented, would impact in particular, one segment of the packaging industry, known as retail service repackaging.⁵

⁵ In the proposed rule, FDA refers to such entities as "repackers". HDMA refers to these businesses as "retail service repackagers" throughout section 6 of these comments in order to distinguish them from the other packagers and repackagers noted above which are not similarly impacted by the proposed rule's requirements.

A retail service repackaging company purchases drug products from the manufacturer and repackages them into smaller quantities. The smaller packages are sold and delivered to retail pharmacy customers bearing the manufacturer's applicable NDC for that package size. Retail service repackaging safely and effectively offers package sizes that eliminates waste and provide enormous value to our members' retail pharmacy customers by delivering greater efficiencies, adding a safety element, and helping to provide consumers with more pharmacist availability/time, often at a premium given current workforce shortages.

HDMA members who conduct retail service repackaging do so in a safe, secure packaging environment. All repackaging companies must register with FDA as a Drug Establishment and operate in strict adherence with current Good Manufacturing Practices (cGMPs). In addition, retail service repackaging companies must be licensed as distributors under applicable state laws. Further, our retail service repackaging members include their name, address and the repackaged lot number on each and every repackaged drug product, enabling the product to be tracked back to the retail service repackager and, ultimately, to the original manufacturer.

Above and beyond these regulatory requirements, HDMA has established Recommended Guidelines for Pharmaceutical Distribution System Integrity and Recommended Guidelines for Pharmaceutical Repackaging Integrity. HDMA's repackaging members also voluntarily, and independently, follow even more aggressive security policies, including those that require purchasing drug products directly from manufacturers.

The proposed rule would disrupt this safe, efficient and cost-effective business service by requiring a new retail service repackager NDC number on the product label. Under CMS requirements, responsibility for payment of the Medicaid rebate follows the NDC number on the drug package – if the manufacturer's NDC number appears on the package, it is responsible for the rebate payment; if the retail service repackager's NDC number appears on the package, the repackager becomes responsible for the rebate⁶. By requiring that retail service repackaged drugs bear the repackager's NDC number, the rule effectively shifts the burden for Medicaid rebate payments from the manufacturer of the product to the retail service repackager.

To better understand the business implications of this shift, HDMA retained The Moran Company, an independent consulting firm, to conduct an evaluation of the possible economic/financial impacts of the proposed rule on retail service repackaging. The Moran Company analysis concluded that retail service repackaging companies will not be able to absorb the rebate cost, given the industry's slim margins. If the proposed rule becomes final and retail service repackaged drugs must bear the repackager's NDC

⁶ From the Rebate Agreement Between the Secretary of Health and Human Services and the Manufacturer Identified in Section XI of this Agreement, Section I (l), "Manufacturer" will have the meaning set forth in Section 1927 (k)(5) of the Act except, for purposes of this agreement, it shall also mean the entity holding legal title to or possession of the NDC number for the Covered Outpatient Drug."

number, the consultant confirmed that distributors will no longer be able to offer this valuable service to pharmacy customers, and will most likely exit the retail service repackaging industry.

Considering the economic impact to the industry and the fact that HDMA member repackagers already maintain rigorous safety and security controls, requiring a retail service repackager to place its own NDC on the drug label is not warranted. No incremental levels of safety or security will be achieved using a repackager's NDC number. However, if FDA is convinced that an additional identifier is needed, we believe the alternatives that HDMA and NACDS have previously described to FDA are still valid, and will satisfy the rule's intent, while allowing the repackaging industry to continue to serve its pharmacy customers.

Given the significant impact of the proposed rule, we ask that the agency reconsider those alternatives:

- Option one – retail service repackaging companies would apply their unique Repack Item Code (RIC) to repackaged products. The code would be in human-readable format, and would be easily distinguishable from the NDC.
- Option two – the retail service repackaging company would apply the unique RIC and an FDA-assigned facility number, to further identify the repackager and the product. This, too, would be done in human-readable format for easy differentiation from the NDC.

Either alternative proposed by HDMA and NACDS would formalize the application of the unique RIC, a number generated by the retail service repackager to assist in product tracking, including internal inventory control, product recalls, and other matters. Either of the suggested options would allow the agency to achieve its objective of further identifying a retail service repackager without requiring a new NDC number.

At the December 11, 2006 public meeting, FDA posed several questions we will endeavor to further address. First, as raised by HDMA and others at the hearing, we do not believe that the NDC number (whether the manufacturer's or the retail service repackager's number) aids in product identification for purposes of emergencies such as recalls. Given the many ways in which a drug marketed under an approved application may come to market (from, for example, different manufacturing locations), the NDC number is of very limited utility in a recall situation. All recalls are conducted by lot number, which provides far greater detail about a particular drug than does the NDC number. A lot number, for instance, can identify the location, day, and even hour and machine line on which a drug was manufactured.

Further, there is no problem with identification of retail service repackaged product moving in the supply chain. Retail service repackaged drugs are easily

identifiable already and the addition of the repackager's NDC number will not further aid in that identification. As we explained at the public meeting, retail service repackagers include their name, address and the repackaged lot number on each and every repackaged product, enabling the product to be traced back to the repackager and, ultimately, to the original manufacturer and the original manufacturer's lot number. A retail service repackager has no difficulty identifying repackaged product in the event of a recall or other emergency.

Thus, there is no particular added benefit to product safety and tracking by mandating that the repackager's own NDC number must be included on the package. Further, there is a significant cost to the retail service repackaging industry to comply with such a mandate. For these reasons, HDMA asks that FDA adopt one of the alternatives set forth here should the agency conclude that further identification is needed.

7. A gradual implementation of the final rule.

For a traditional pharmaceutical manufacturer, it is unlikely that the NDC rule would have significant, disruptive effects. The manufacturer will be able to retain its current NDC numbers and simply must register and list those drugs once the rule is final and the system is "live".

But, for retail service repackagers and (as discussed in section 1 above) newly created "relabelers," the effects of the NDC rule will be profound. If the proposed rule becomes final without significant change, thousands of retail service repackaged and "re-labeled" drugs will either no longer be offered by the current distributor or retail service repackager or, they will need new NDC numbers, which involve significant regulatory submissions to FDA and other entities, such as CMS. The drugs will need to be relabeled. Retail service repackagers will have to change their contracts with customers and indeed, change an entire processing model.

HDMA asks on behalf of its members that the agency allow sufficient time for industry to orderly restructure, or phase out, its operations. For prescription drugs, FDA had proposed a two or three-year implementation period. HDMA retail service repackagers estimate the pharmaceutical supply chain will need three to five years to renegotiate their contracts with both customers and suppliers, change and phase out the retail service repackaging operations and terminate or reassign their workforce. Their pharmacy and hospital customers will need this amount of time to evaluate their supply options and locate alternative sources for the product they currently obtain from retail service repackagers. Some manufacturers also rely on retail service repackaging to meet pharmacy needs. Hence manufacturers may require additional time to develop an alternative packaging and distribution strategy to account for the increased number of bottles manufacturers will have to package for themselves.

As noted throughout these comments, HDMA believes that substantial revisions to the proposed rule will be necessary to help support the availability of drugs and devices to patients with minimal disruptions to the supply chain. However, should the Agency choose not to make such revisions, the Agency should include provisions for the maximum compliance time frames proposed, or more, including:

- Submission of registration and listing information (including assignment of new NDC numbers) via FDA's new Web interface within 12 months of the effective date of the final rule (the rule proposes 9 months).
- Prescription drugs entering commerce no later than 3 years after the effective date of the final rule must be labeled with the appropriate NDC number that complies with the final rule. (The rule proposes to shorten this time frame to 2 years.)
- Allowing the full 7 years after the effective date of the final rule for OTC drugs entering commerce to be labeled with the appropriate NDC number that complies with the final rule. (The rule notes that FDA is considering shortening this time frame to 5 years.)

An issue not addressed in the preamble is the interaction between the date by which a drug must be listed with its new NDC number and the date by which the drug label must bear that new NDC number. For drugs that will need new NDC numbers, the proposed rule does not state which NDC number should first be listed with the agency – the old number on current labeling, or the new number that will be on the drug label within 3 years of the effective date of the final rule. Guidance from the agency regarding how it intends to address these implementation issues would be useful for industry.

8. Public availability of information submitted to FDA.

FDA proposes making most information an establishment provides in the registration and listing process available via the Internet. The agency would exempt from disclosure the NDC number of the drug a retail service repackager or relabeler obtains from the manufacturer and then repackages or relabels. FDA recognizes that business relationships among private label distributors, manufacturers, retail service repackagers, and relabelers may be disclosed, but believes such disclosures would be a "rare event" and that exempting such information from release would be "inconsistent with protection of the public health." 71 Fed. Reg. at 51321, col.3. Further, most private label distributor information would be made available as well.

HDMA members oppose making much of this information available. Business relations among trading partners, such as those between a private label distributor, retail service repackagers, or relabeler and the manufacturer are treated as highly confidential

by the parties. FDA may not unilaterally release this confidential commercial information to the public.

Certainly, allowing for precise identification of which drug products are manufactured, repackaged, or relabeled at a specific facility is vitally important information for FDA. For the general public, such information could have security implications. Similarly, FDA, but not the general public, needs to know contact information and other information FDA will now require for registration, NDC number assignment, and drug listing.

HDMA believes that the level of specificity that currently exists at the Electronic NDC Home Page <http://www.fda.gov/cder/ndc/database/Default.htm> strikes a proper balance between public access and protection of confidential commercial and security information. At a minimum, making further proprietary information publicly available should wait until the agency and filers have developed experience with the new registration and listing system and have a better understanding of what data is to be submitted and what sensitive information might be gleaned from it.

HDMA also agrees with those at the public meeting who explained that it is necessary for FDA to keep confidential company requests for NDC numbers for drugs under development. Companies frequently obtain NDC numbers for a drug far in advance of launching the drug. It is well established that a company's drug development plans are highly confidential. FDA should take steps to assure that the NDC number remains confidential for drugs under development.

9. Clarification of discontinuance of a drug listing.

HDMA notes that the provisions for the timing of drug listing appear fluid. Among other things, any drug not previously listed must be listed during the semi-annual June or December update and drugs discontinued during that interval must be reported, along with the expiration date of the last lot manufactured, repacked, relabeled, or salvaged. Proposed 21 C.F.R. § 207.57. HDMA supports the flexibility inherent in this proposed updating requirement as it reflects the commercial reality of the importance of the NDC number.

HDMA members have, however, expressed concern regarding this provision. Currently, many establishments wait to report that a drug is discontinued until they no longer have to report the drug under applicable CMS agreements, by NDC number. If the NDC number is identified as "discontinued," this creates reimbursement and rebate problems with CMS. Moreover, as a discontinued drug is still in distribution up until its expiration, there may be problems for tracking, tracing and accountability if a search of the NDC database shows no record of a drug's NDC number, or a notation that it is "discontinued."

HDMA believes that there are several potential solutions to this problem. The final rule could instruct establishments to discontinue a drug listing at any time up to the expiration date of the last lot manufactured. Alternatively, the system could include a notation for discontinued drugs that they are still in distribution for a period of time. While HDMA recognizes that FDA wishes to have an up-to-date NDC database and to see that discontinued drugs are promptly reported, there also needs to be built into this system a recognition that safe and effective, though discontinued, drugs continue in distribution for many months after the date they are no longer manufactured.

10. Urging a reexamination of the proposed rule and a more incremental approach.

At the December 11, 2006 public meeting, all stakeholders unanimously praised FDA's plans to implement an electronic, Web-based system for drug registration and listing. Stakeholders expressed broad agreement on another issue – that the rule, as proposed, was seeking to accomplish too much, too quickly. The proposed rule has grave repercussions for many well-established business practices and important regulatory initiatives. HDMA shares this view and suggests that FDA scale back its expectations regarding the regulatory usefulness of the NDC number and the scope of the proposed rule.

The NDC number is embedded in manufacturer, distributor, and retail operations. As highlighted at the December 11 meeting, NDC numbers are of enormous commercial importance to the pharmaceutical industry and the entire supply chain. NDC numbers are critical to a pharmaceutical company's research and development, marketing, and other internal business practices. NDC numbers are used in the supply chain for purchase and sales transactions, inventory management, distribution, prescribing, dispensing practices, and payment mechanisms. Industry, federal agencies, payors, and other entities all use the NDC number for many purposes that will all have to change if the number changes.

FDA also has found usefulness in the NDC number, as it permits the agency to collect basic information about what establishments are manufacturing what drugs. Cross-referenced with other information, the NDC number has some regulatory utility. FDA however, is seeking more from the NDC number, registration, and listing processes, including validation of marketing status, recalls, DailyMed, adverse event reporting, and monitoring of labeling, promotion, and manufacturing changes. As explained at the public meeting, FDA already has well-established systems in place for accomplishing many of these goals – manufacturing and labeling changes are submitted to approved applications; lot numbers on product labeling are used to identify product in recall situations.

In HDMA's view, it may not be realistic to expect a numeric code to accomplish these many goals. It seemed to HDMA that the December 11 public meeting revealed that the impacts of the rule upon critical aspects of drug manufacturing, distribution, and

retailing were incompletely understood. Further, any change to the NDC system will have significant and costly impacts upon the entire supply chain, even beyond the drug manufacturing, distribution and dispensing system. For example, NDC numbers are currently applied to products that FDA deems to be medical devices, and on this basis CMS reimburses the items. Elimination of the NDC number on these products could compromise patient care, particularly in the absence of an alternative numbering system for medical devices that CMS could implement. This impact upon vulnerable patients is another example, HDMA believes, of the rule's profound consequences that were not anticipated when first proposed.

Before proceeding with such sweeping changes to a system that is, by and large, working well, HDMA believes the proposed rule should be revisited. HDMA supports the views of other stakeholders who suggested focusing first upon the needed (and universally agreed upon) improvements to the current paper-based system and transfer to the electronic platform. Further changes should be undertaken more incrementally, in consultation with stakeholders.

Further, we suggest that agency proceed slowly, and republish the proposed rule with the many proposed changes offered for comment before being promulgated as a final rule. For example, the issues raised by the broad definition of relabel would greatly benefit from an additional round of notice-and-comment rulemaking so that an alternative definition may be proposed and commented upon before being made final.

As FDA moves forward with this far-reaching rule, HDMA suggests that the agency take a methodical approach that sets out clear, realistic goals and a plan for meeting them. The agency contemplates far-reaching changes that affect drugs (and other regulated products) and the operations of every entity that is involved with them. Such alterations to routine business practices should be made incrementally, in consultation with stakeholders. Many of the proposed changes should probably only be undertaken after thorough analysis of costs and efficiencies, feasibility testing and pilot studies. Pilot programs would have to go beyond merely using a mock electronic registration and listing system to testing the actual implementation of the rule under real world conditions. HDMA looks forward to working with FDA on these issues.

Conclusion

In conclusion, HDMA appreciates this opportunity to share its views with FDA and to provide our perspectives on this proposed rule. Should you have any questions about this letter, please feel free to contact Anita Ducca at 703-885-0240 or at aducca@hdmanet.org.