Comments of the Generic Pharmaceutical Association on FDA's Proposed Amendments to Regulations Governing Drug Establishment Registration and Drug Listing

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The Generic Pharmaceutical Association (GPhA) is a non-profit trade association representing the manufacturers and distributors of finished generic pharmaceutical products, manufacturers and distributors of bulk active pharmaceutical chemicals, and suppliers of other goods and services to the generic pharmaceutical industry. Our members manufacture more than 90% of all generic pharmaceuticals dispensed in the United States and their products are used in more than one billion prescriptions every year. According to IMS Health, 56% of all prescriptions dispensed in the United States are filled with generic pharmaceuticals, yet they account for only 13% of the cost of all prescriptions dispensed. GPhA is the sole association representing this sector of the pharmaceutical industry.

GPhA supports FDA's proposal of August 29th, 2006 to improve public health by using the "latest technology" to increase efficiency of establishment registration and drug listing systems. Full implementation of electronic registration and submission of listing information will yield significant benefits for public health, and ultimately conserve agency and industry resources.

However, as major stakeholders in the U.S. pharmaceutical sector, the generic pharmaceutical industry is concerned with aspects of the proposed changes that would create unnecessary burdens on the industry and ultimately fail to yield commensurate benefits to public health. For instance, several of the proposed changes would result in inefficiency rather than enhancement of the system; the proposed change to broaden data requirements for biannual reports, including distribution data for each product, would increase the administrative burden on industry and increase demands on the agency's administrative resources as well, yet the requirement would result in vastly duplicative efforts and produce little or no useful information beyond that already provided in annual reports for NDAs and ANDAs.

With respect to FDA's proposal to modify rules governing National Drug Code (NDC) numbers, GPhA has serious concerns regarding its impact on managing the production of medicine and its distribution within the U.S., and through import and export channels. As noted in our previous comments, the generic industry is particularly concerned about FDA's proposal "to designate the responsibility of assigning the NDC number to FDA." The pharmaceutical industry relies on well

established conventions for assigning NDC numbers which enable individual members of the industry to communicate internally, between different business units and among business partners, insurers and CMS regarding details of each product. Current business practices, from research and development to supply management and distribution methods have evolved based a firm's ability to assign NDC numbers. A major disruption in these practices would confound many of the refined business practices that support the infrastructure of the entire pharmaceutical supply chain. The changes proposed by FDA would have a dramatic affect on even day-to-day operations of drug development, labeling and distribution. GPhA strongly urges FDA to reconsider this proposal.

In order to address FDA's concerns that "[p]roduct and package codes are not always assigned appropriately, and industry practices for assigning codes are inconsistent" and that "manufacturers, repackers and relabelers may never list a product or may omit information or submit incorrect information to [the agency]," GPhA strongly supports an initiative to increase training and education, develop clear guidance for industry and strengthen enforcement under the current regulatory scheme. While we recognize that some additional data requirements could benefit public health, the data requirements under the proposed rule are excessive, and would be unlikely to yield significant benefits to public health. The majority of firms comply with drug listing requirements, and the current rules provide effective regulatory oversight of such conduct. In conjunction with training and education efforts, and development of clear guidance, stricter enforcement of current regulations would likely minimize or eliminate the erroneous practices and oversights of noncompliant firms. In addition, the shift to standardized electronic submissions is likely to have a positive influence on industry's aptitude for compliance with listing requirements and the agency's ability to monitor compliance. The proposed changes would fundamentally alter the pharmaceutical industry's well-established business practices that have served the interests of public health for decades. We believe that efforts should first be dedicated to increasing compliance through education, training, guidances, and greater enforcement under current regulations, before investing considerable time and energy in overhauling the entire NDC and drug listing system to enhance compliance.

In addition to the proposed changes for NDC numbers and reporting requirements, FDA's proposed rule raises numerous other issues for the generic industry including the security of information in an electronic system, the uncertainty regarding the agency's intended uses for electronically submitted drug listing information (such as the potential impact to CMS price submissions for Medicaid), the impact of the extended range of establishment registration requirements for international companies involved in drug manufacturing, repacking, relabeling, and drug product salvaging, and the revocation of registration and listing exemptions for companies engaged in any U.S. Foreign Trade Zone or Import for Export operations. GPhA respectfully submits the

following questions and comments addressing our specific concerns with FDA's proposed rule.

NDC Numbers

The generic pharmaceutical industry is very concerned about the potential impact that the proposed rulemaking may have on managing the production and distribution of medicines in the complex trade channels within the U.S. The proposals raise an array of logistics issues. Among numerous other matters, the generic industry is particularly concerned by the proposal "to designate the responsibility of assigning the NDC number to FDA." In light of the considerable impact the change would have on the fundamental day-to-day operations of drug development and labeling GPhA strongly urges FDA to reconsider this proposal.

Members of the generic industry share FDA's concerns that "[p]roduct and package codes are not always assigned appropriately, and industry practices for assigning codes are inconsistent" and that "manufacturers, repackers and relabelers may never list a product or may omit information or submit incorrect information to [the agency]." We proffer that current regulations establish sufficient authority to correct such inappropriate practices and oversights. Measures to improve compliance with listing requirements could include stricter enforcement of current rules, publishing of guidances, and educational workshops. Rather than committing the considerable administrative resources necessary to totally revamp the NDC system and dramatically altering the well established practices of drug listing, the agency could increase its supervision of the system already in place—a system for which the industry bears most of the cost and burden.

The pharmaceutical industry relies on conventions for assigning NDC codes that are fundamentally ingrained in the system and which enable individual members of the industry to communicate internally, between different business units among business partners, insurers and CMS regarding details of each product. While even slight alterations to the system create ripples in the entire pharmaceutical supply chain, a change of the magnitude proposed by FDA would result in an enormous upheaval to the business practices of the pharmaceutical industry. NDC numbers are important to supply chain control, not only for manufacturers and distributors, but also for health care facilities; they are integrated into the systems used by hospitals and pharmacies to identify products, locate inventory, control dispensing and communicate patient information. Patient safety could be compromised by confusion about NDC numbering—especially during a transition period as NDC numbers convey key information on strength and dose.

GPhA believes that the current NDC system, when properly maintained, serves the purpose of the primary stakeholders, and respectfully requests that the proposed changes to the NDC system not be implemented.

I. Assignment of NDC Numbers/Duplication

The Proposed Rule represents a major new burden to the pharmaceutical industry. This proposal appears to indicate that essentially any change to a drug product necessitates a new NDC number. GPhA wants to ensure that FDA has a full understanding of the proposal's impact to the supply chain. For example, requiring new NDC numbers for changes to active ingredients, a change in supplier of the active ingredient, a change in inactive ingredients, as well as changes in manufacturers or packagers, would exponentially increase the demand for resources from the industry.

With respect to FDA's proposed revisions in the NDC system, GPhA understands FDA's goals to be: greater compliance in the creation of NDCs, and establishment of a product and inventory tracking system. These are laudable goals. But the benefit to public health FDA may derive will not compare to the burden the proposal would place upon many levels of industry operations, tracking, reimbursement, and distribution. Because industry has built many of their daily operations and transactions around the framework of the NDC system, GPhA urges FDA to avoid significantly changing the existing system unless it is absolutely critical to public health.

Given the impact of this proposal, GPhA urges FDA to work with industry to develop compliance and education programs that foster greater consistency in the issuance and design of NDC numbers. Any changes in the current NDC system that create confusion, require revision of existing NDC numbers, or result in duplication of NDC numbers should be abandoned unless FDA can articulate a significant, existing risk to public health.

GPhA includes the following questions to give FDA a clearer and more precise understanding of how industry uses NDC numbers for internal record keeping, reporting, and communications within member organizations, across member business units, among business partners, and along supply chains. The following questions also highlight the uncertainty this proposal has created for an industry that requires predictability to accomplish its business and public health goals. GPhA believes FDA should, at a minimum, answer these questions in a revised proposed rule and preamble so that industry may have notice of and provide comments on a more defined proposal from the agency.

A. Pre-existing or Multiple Codes

- How will the FDA prevent the issuance of an NDC number which exists prior to finalization of this Proposed Rule? For instance, will FDA's proposed database be accurate enough to determine that NDC 58458-001-01 has already been issued so that a duplicate number will not be assigned to a different drug?

- It is unclear how firms should measure whether or not their existing NDC numbers are compliant with the Proposed Rule. Please clarify the criteria needed to assess compliance.

- With many product codes already assigned to development projects that are several years away from marketing – how will FDA avoid assigning those codes to another product? What if the number was requested by and assigned to a 3rd party manufacturer?

- If companies have multiple labeler codes (a DBA or "Other Firms doing Business at this Site"), will FDA mandate that all products manufactured or sold from a specific site, or a specific company across multiple sites, change their existing NDCs to a single labeler code?

- The NDC numbering system currently allows for either 9,999 or 999 unique product codes per company code depending on format. Companies with large numbers of products must retire and later re-use numbers, maintain multiple company codes specific to separate business entities to expand available product codes or use some other means to avoid running short of numbers. How will FDA handle retirement/re-use/expansion of product codes under a limited field length for product codes? What is the process for retiring numbers? This may necessitate expansion of number length.

- The proposal raises questions regarding the format and integration into related systems. Is a modification to the number of digits being considered to expand capacity as part of the new system? If so, how will this change be implemented and how will it impact other data systems such as computer programs with limited field lengths or bar code based systems? If a new number structure is deemed necessary to expand capacity, how will a new format be implemented?

B. Requesting an NDC

- GPhA has concerns regarding the confidentiality of the information submitted in order to obtain a NDC number. There is substantial proprietary information provided in order to obtain the NDC number. Please clarify when this information could be disclosed under section 510(f).

- It is unclear from the proposed rule whether final commercial package presentations need to be provided at the time of the initial NDC number request. It would be impractical to assume that firms would have this information finalized at the time of the initial NDC number request.

- Will the FDA's system allow a company to "request" a specific product code at the time of the NDC request?

- How far in advance can a firm request an NDC number from FDA?

C. Business Practice

- Industry typically assigns package codes based on established numbers for specific packaging configurations which is used consistently across a product line. What logic will be used when FDA assigns product codes and package codes?

- A firm may have assigned NDC numbers for products under review by the Agency; however, they cannot drug list without an approval letter and final printed labeling. According to the proposed rule, the NDC numbers currently assigned to a drug prior to the effective date of the rule would remain unchanged provided those NDC numbers comply with the new regulations as finalized. Does this refer to only those drugs that have been listed with the Agency prior to the effective date, or does this also include those NDC numbers assigned internally by the firm?

- For manufacturers with extensive product portfolios, labeler codes may often be a critical component to organizing and managing several business units. The proposal to use only one labeler code for any new NDC numbers assigned by FDA unnecessarily eliminates the distinction of business units within a corporation.

D. Source Materials and Active and Inactive Ingredients

- GPhA recommends that inactive ingredients not be a requirement for obtaining an NDC number; however if inactive ingredient information is mandatory, the following comments should be considered.

- Will new NDC numbers need to be assigned if an inactive ingredient is deleted from the formulation?

- The proposed rule requests that the DMF for active pharmaceutical ingredients be listed when submitting information for a new NDC number. Will a new NDC number need to be assigned if the corporation changes vendor of the active pharmaceutical ingredient and/or when multiple suppliers are approved for the active pharmaceutical ingredient at the time of ANDA approval or at a later date?

- Some ANDAs are filed with alternate sources of raw materials. Will the products need separate NDC numbers for each combination of approved alternate sources?

E. Packaging and Labeling

- Please clarify how FDA will assign package codes for bulk active pharmaceutical ingredient containers?

- There are a number of “kits” that are marketed and may contain multiple drug product components from different approved manufacturers. How will NDC numbers for "kits" with multiple manufacturers (of the components) be determined?

- Currently, tablet/capsule imprint markings are assigned which are based on the “product code” portion of the NDC number. At an early stage in the product development, the determination of the ultimate manufacturing site for the commercial product may not yet be made. Yet, firms still need the product code number to finalize the trade dress. For this reason, the requirement in the proposed rule that NDC numbers be assigned to manufacturers instead of private label distributors is objectionable.

- FDA proposes the need for only 2 digits for package size and type. Will two digits be sufficient if each bottle type (glass, HDPE, PET, etc.) and each blister type (packing foil, paper foil, aluminum foil, etc.) is specified along with bottle size (30 cc, 50 cc, 100 cc, etc.) and/or blister count (single, 28 day, 30 day etc.); will this be adequate?

- If the individual container, blister, vial, etc., is too small for a human readable NDC number, will the “correct” drug listing submission to FDA and the product’s bar code be sufficient to waive the readable NDC requirement?

F. Repackagers, Relabelers and Private Label Distributors

- If the manufacturers are to be responsible for drug listing products for private labeler distributors, which labeler code is to be used: private distributor’s labeler code, U.S. distributor’s labeler code for the foreign establishment or the manufacturer’s labeler code?

- When a manufacturer requests and receives an NDC assignment for a private label distributor, is the manufacturer also responsible for updating the DEA’s ARCOS dictionary with that NDC number, if applicable?

- FDA has proposed that the NDC number on a drug product be that of "the last manufacturer, repackager, relabeler or private label distributor responsible for the drug immediately before it is received by the wholesaler or retailer." Does this mean that the NDC number of both the manufacturer and the repackager or relabeler needs to be on the label material?

- A contract repackager or relabeler may be used on a temporary or infrequent basis. Will new labeling material with the repackager or relabeler NDC number need to be added if under normal circumstances no relabeler or repackager number would be used and only the manufacturer's NDC number would be on the label material (i.e., would the product be considered misbranded)?

G. Miscellaneous

- Will the FDA assign an NDC number to a prescription product which does not have an application number (such as a DESI drug or grandfathered drugs that still remain in the marketplace)?

- Could a finished dosage product manufactured under the same ANDA with the exact same physical appearance be drug listed by two different manufacturing sites at the same time under the same NDC number? What if the sites are in two different countries, but under the same ownership and control?

II. <u>Timing</u>

The generic industry is also concerned with the length of time it will take for FDA to assign NDC numbers. Please comment on the Agency's timeline for issuance of newly requested NDC numbers.

GPhA is concerned about potential delays in marketing of drug products upon approval. Clearly, such delays would have an adverse impact on the efficiency of the drug distribution system, availability of medicines, and public health. How will FDA address these concerns?

- Would a firm update the database and still have 3 years to update the labeling in accordance with the database? For example, if a firm changes an NDC number in the database (to correct assignment process), would the firm have 3 years to change that NDC number on the labeling?

- It is unclear whether the 3 year time frame, given to the phase-in process for NDC numbers on labeling, is only for placement of NDC numbers on

labeling or also for updating NDC numbers to be compliant with the proposed rule. Please advise.

- Would being compliant with the proposed rule within 9 months of the effective date include creating NDC numbers for the packaging levels? If so, this would tremendously increase the burden on industry by requiring 2 or 3 times the number of NDC numbers.

III. Databases/Electronic Interfacing

- How will FDA effectively communicate newly assigned NDC numbers to its various components, such as, the Import Branch and the various Ports of Entry? Will their database be updated accordingly? Will FDA monitor NDC numbers when they have changed, in terms of shipments being released at Ports of Entry?

- How will the requestor access the FDA database? With multiple companies attempting to access the same information in high volume (to meet the proposed compliance date), will the system overload, lock up, or prevent user access?

IV. Reimbursement

- With regard to CMS price submissions for Medicaid reimbursement, AMP will have calculations at the case count compared to states submitting for prescription level reimbursement. How will FDA address this issue?

- With additional NDC numbers for the case pack, shipper pack, etc., it will be necessary to ensure that pricing is designated at each level. This would include a substantial new layer of pricing reports based on the particular pack size, and to pricing services as well as the contract pricing in both the manufacturer and customer systems. This will create a major new burden for the supply chain.

- The proposals will cause a significant increase in the administrative burden of setting and maintaining accurate chargeback and rebate accrual rates.

V. Drug Listing Proposals

Private Label Distributors - GPhA requests that FDA reconsider the proposal to prohibit private label distributors from listing drugs. The Proposed Rule notes that this change is necessary due to uncertainty and confusion regarding drug listing responsibilities among private label distributors and firms that manufacture, repack, relabel or salvage drugs

for private label entities. However, the proposed approach will increase the burden for manufacturers, repackers, relabelers or salvagers when all required drug listing information should be available to the private label distributor. With electronic drug listing capabilities and enhanced efforts in training and enforcement, there is no reason to believe that private label distributors would not be fully compliant with the requirements.

Reporting Production Volume - The Proposed Rule would require firms to report production volume information every six months. One premise for this information is that it would allow the Agency to make better risk-based decisions on "quality oversight activities." Risk considerations may be based on factors such as dosage form, manufacturing process, type of product (e.g., sterile or non-sterile), and recall history, among others. Additionally, distribution data for each product is provided in the NDA or ANDA annual report. The Proposed Rule does not adequately describe how this additional reporting requirement will facilitate quality oversight activities for finished products or active pharmaceutical ingredients, especially in light of other key information regarding the drug product that is contained in the drug listing information. Listing the number and size of batches every six months appears to be of limited utility for the Agency, and would be a significant additional burden to industry. For instance, one member company currently has 7000 (and growing) active drug listings. In addition to the substantial workload for industry associated with this proposal, it also creates significant new work for FDA. In a time of diminished FDA resources and increasing responsibilities, the net value of this proposal appears uncertain.

Confidentiality - The generic industry is concerned with regard to the confidentiality of drug listings. The language in the Proposed Rule indicates that listing information would be exempt from public disclosure, but would allow the Secretary to release this information if deemed necessary. Because certain required information represents proprietary business information, its release would raise significant concern. FDA should specify under which conditions it may be necessary to release drug listing information.

Listing of Inactive Ingredients - The proposal contains a requirement to provide a listing of all inactive ingredients contained in the drug product. Yet, currently, inactive ingredients are listed on container labels and professional labeling, as well as contained in the NDA or ANDA. Thus, this information is already available from multiple sources. Additionally, under the Proposed Rule, any change in inactive ingredients will result in assignment of a new NDC number. This change would result in the same product moving through the supply channels with multiple NDC numbers. Such an instance would likely cause confusion for supply chain

stakeholders as well as for payers. Therefore, the net benefit of this requirement is unclear.

Another concern relates to importation and release of drug products at the time of a change to the NDC number. If the drug product reflects the 'old' NDC number when it arrives at a U.S. port of entry, but a new NDC number has been assigned as a result of a change to inactive ingredients, will FDA have the capability to recognize this change and release the product on a timely basis?

Information Technology – At the December 11, 2006 Public Hearing, FDA discussed the concept of sending e-mails to the company when a drug listing update is required. In most cases, company computer systems in place today are not capable of receiving hundreds or thousands of e-mails (based on the volume of NDC numbers that will be assigned to many companies under the Proposed Rule) in a short period of time. If FDA plans to notify firms by electronic messages, it must be mindful of the limitations of computer systems to manage such a volume of messages over several days or weeks.

VI. Import, Export and Foreign Establishment Considerations

The drug establishment registration and listing proposals, including the definitions of some key terms in the proposed rule, cause GPhA to question whether FDA is attempting to regulate the security of the international drug supply chain. GPhA does not believe that the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (the "Bioterrorism Act") grants this authority to FDA for drug distribution any more than it did for food distribution.

The provisions in the Bioterrorism Act upon which FDA bases its proposed revisions of registration and listing provisions say nothing about "listing." Moreover, they focus upon the identities of persons in the supply chain who actually import the drug or actually offer the drug for importation. The Act does not grant FDA the authority to require the identity, much less the contact information, of every person in the drug's supply chain or of every person who is associated with or facilitates the drug's importation. 21 U.S.C. § 360(i)(1). GPhA is of the firm conviction that the authority and congressional mandate to secure the foreign drug supply chain belongs to the Department of Homeland Security, and particularly to the Bureau of Customs and Border Protection (CBP) and not to FDA. CBP has programs, now codified by the SAFE Port Act of 2006, whereby it evaluates and validates secure supply chains. GPhA believes FDA should turn to CBP to implement its various data elements into CBP's Customs-Trade Partnership Against Terrorism rather than attempting to establish its own supply chain review process.

Under the current regulatory regime, a foreign manufacturer who is required to register and list its articles must submit information regarding the foreign facility, its owners and operators, the activities which it conducts, and the drugs involved in such activities. The proposed rule would require foreign drug manufacturers to provide in their registrations the identity and contact information of "importers" known to them and for "persons who import or offer for import" their drugs into the U.S. According to the preamble, this latter category includes agents, brokers, and other third parties, excluding carriers, who "facilitate" importation of the foreign manufacturer's drugs into the U.S. See pp. 51289-90.

Although the "importer" definition requires the person to be in the U.S., no such distinction is made for "persons who import or offer for import." The implication is that foreign agents, brokers or other entities that facilitate the importation of a foreign establishment's drugs into the U.S. must be also identified in each foreign establishment's registration and the listing of *each* drug.

GPhA objects to the agency's proposed definition of "persons who import or offer for import." GPhA notes that FDA is aware of the various interpretations that could exist for the term "facilitate" and that "persons who import or offer for import" could include "middlemen." The definition, however, is so broad that it also incorporates:

- U.S. customs brokers,
- foreign customs brokers,
- drayage companies
- foreign and domestics freight forwarders, who are not carriers and are not Non-Vessel Operating Commercial Carriers (NVOCCs),
- foreign agents;
- foreign transaction brokers;
- foreign and domestic commissioned resellers;
- foreign and domestic public warehouses;
- foreign exporters; and
- foreign shippers.

Arguably, FDA's proposed definition of "persons who import or offer to import" could encompass foreign insurance adjusters and underwriters and international banks issuing letters of credit, all of which "facilitate" the importation of or the offer for importation of foreign drugs to the U.S. The only party FDA has proposed excluding from this definition is "carriers."

When the identity or contact information for any of these "facilitators" changes, the foreign manufacturer must update its registration or listing

with the new data. Given the breadth of FDA's definitions, many manufacturers would have to submit and maintain literally hundreds, if not thousands of data elements in their registrations and listings. This would dramatically increase the information FDA would be receiving electronically and more than likely it would rapidly over burden the electronic reporting system, fully depleting any value the agency could have derived from an electronic registration and listing program. The burden placed on foreign manufacturers is self evident.

International supply chains and business relationships are not static. In the generic pharmaceutical industry, manufacturers often sell and ship drugs through various supply chains. They select their agents, brokers, shippers, exporters, and other "facilitators" based upon multiple factors, including: regulatory considerations, licensing and permitting requirements in foreign countries; and commercial, transportation, cost, and contractual reasons. At any time these "facilitators" or their contact persons may change. Under the proposed rule, foreign manufacturers would have to develop, maintain, and update a virtual telephone and address book and transmit that data to FDA to maintain their registration and listing records.

Needless to say, the burden FDA proposes with this definition far outweighs any benefit the agency could possibly derive from knowing the names and contact persons of each foreign manufacturer's "facilitator." FDA never describes why this data is necessary to protect public health or against which government data sets or watch lists the agency will compare the data to protect the security of the drug supply.

GPhA also notes that it is unclear whether an imported drug shipment accompanied by documents that either notify parties who were not previously identified in the foreign manufacturer's registration or contain the identity of foreign or domestic agents, brokers, would cause the shipment to appear to be misbranded because the registration does not match the records. GPhA envisions mass confusion on the part of industry and FDA's field personnel who must attempt to navigate the registration process and system in real time when shipments arrive.

Therefore, rather than creating a general category of persons who must be identified in a foreign facility's registration, GPhA recommends that FDA explicitly limit the persons who fall within the definition of "persons who import or offer for import" to foreign shippers and exporters.

Regarding the definition of the term "importer," GPhA notes any person in the U.S. receiving the drug, other than a consumer or patient using the drug must be disclosed (if known) by the manufacturer – even if the person is not the **initial** owner, consignee, or recipient of the drug. Under the proposed rule, therefore, foreign manufacturers must disclose in their

FDA registrations and listings the identity of third party ("down stream") purchasers who import drugs manufactured by the foreign establishment. Additionally, foreign manufacturers who sell to a small group of U.S. importers, but drop ship to significantly more regional distribution centers around the U.S., would have to disclose each down stream recipient to FDA, except for the consumer or patient using the drug. This imposes a significant reporting burden on foreign manufacturers that is not required of domestic establishments.

Alternatively, GPhA recommends that FDA limit the definition of "importer" to the definition of "importer of record," as that term is defined in 19 U.S.C. § 1484. The importer of record is required to ensure that its imported merchandise complies with FDA law and regulations at the point of entry. That party is subject to administrative, civil, and criminal sanctions for importing merchandise contrary to law. Moreover, FDA can control, through the customs importation bond, the delivery and redelivery of the imported drugs by attaching the requirement to the importer of record.

GPhA also believes that the FDA entry process will become substantially more complicated and convoluted with the rule, if finalized as it is proposed. The NDC code, registration, and listing provisions in the proposed rule contemplate the development (and required management) of significant amounts of data about hundreds of thousands of entities not currently included in any FDA record, which must be cross-linked in order for the agency to be able to use the data to establish a drug establishment and listing inventory. In addition, companies not accustomed to providing registration and listing information will be required to do so under the proposed rule. As proposed, the level and amount of detail necessary for foreign manufacturers to comply with the registration and listing requirements is extraordinary.

Historically, data amendments supplied by industry to FDA for application, registration or listing purposes are not current (or are keyed incorrectly) in FDA's own data systems. When FDA's field personnel evaluate information about imported drugs and compare that information against incorrect or out of date data in FDA's systems, the official often views the discrepancy between the data sets as the "appearance of a violation" (under 21 U.S.C. § 381(a)). In these cases, the official often detains the imported shipment, leaving the importer and the foreign manufacturer in the untenable position of attempting to justify why *FDA's* data systems are incorrect. Such shipments are often refused admission. The importer is then forced to export the drugs, even though they do not violate any provision of federal law and there is no appearance of any such violation. With the addition of the proposed NDC coding, information relating to U.S. importer or persons who import or offer for import drugs in foreign establishment registrations and listing, and the revocation of the FTZ and

IFE exemptions, it is foreseeable that FDA's data systems are not likely to be current, resulting in even greater confusion at ports of entry.

Therefore, GPhA recommends that FDA hold further discussions with industry and interested stakeholders on how to accomplish greater compliance with FDA's NDC system. Further, GPhA recommends that FDA reinvigorate its previous discussions already under way with the Office of Compliance at the Center for Drug Evaluation and Research and the Division of Import Operations and Policy in the Office of Regulatory Affairs regarding development and implementation of a secure distribution system for imported drugs. GPhA believes such a program would enable FDA to distinguish drug shipments that pose a low safety or security risk from those that represent higher risks or are of unknown risk.

GPhA believes FDA's proposal will confound industry and the agency's field personnel. Further, because of the onerous requirements in the proposed rule, GPhA believes an environment of compliance management (with respect to complying with the burdens of the regulation) will overtake a more critical risk management environment that focuses upon drug quality, safety, efficacy, and security.