Statement of

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COMMITTEE ON ENERGY & COMMERCE

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1. INTRODUCTION

Mr. Chairman and Members of the Committee, I am Benjamin L. England, founder and owner of an FDA consulting practice, FDAImports.com, Inc., and a practicing attorney representing foreign and domestic food, drug, medical device and cosmetic companies in matters involving the U.S. Food and Drug Administration (FDA). I am a 17-year veteran of the U.S. Food and Drug Administration (FDA). From 1986 to 2003 I held the positions of Regulatory Microbiologist in FDA's Baltimore Microbiology Laboratory, Consumer Safety Officer and Compliance Officer in FDA's Baltimore District Office, Special Agent with FDA's Office of Criminal Investigations in the Miami Field Office, Compliance Officer in FDA's Miami Resident Post, and Regulatory Counsel to FDA's Associate Commissioner for Regulatory Affairs (or ACRA) in Headquarters. I resigned my most recent FDA position as Regulatory Counsel to the ACRA in July 2003 -- a position I held in FDA for over three years as a Title 42 appointee. During my last three years at FDA, I was a key point person for Customs and Border Protection, I chaired the FDA's Counterfeit Drug Working Group, instituted the Joint Agency-

Industry Working Group to combat product counterfeiting and tampering, which laid the ground work for the preparation of FDA's initial Counterfeit Drug Task Force report, and co-chaired FDA's Import Strategic Plan Steering Committee.

Along with my colleague, Mr. Carl Nielsen, who is also before you today testifying on his own behalf, I established the Agency's first series of Import Enforcement Training Courses, and with a few dedicated FDA and Customs officials, trained nearly every FDA import inspector, investigator, import program manager, and compliance officer in the effective use of Customs enforcement tools against products imported in the U.S. in violation of FDA requirements.

At the outset, I am pleased the Committee has taken the initiative to press for solutions for managing safety risks associated with imported products – and to focus today specifically upon FDA's foreign drug inspection program. I do not feel it is necessary to reiterate all of the history in this testimony, as it is a part of the record from previous hearings. Some points, however, bear repeating. Further, since my last appearance before you on November 1, 2007, more evidence has appeared in the U.S. marketplace laying bare the brokenness of the regulatory and information technology (IT) systems FDA is hobbling along with and the real safety risks that attend the agency's present condition.

I highlighted in my previous testimony the counterfeit bulk drug investigations of the 1990s, which were all but abandoned by FDA. We discussed how reminiscent those cases were to press accounts identified by the Chair related to counterfeit articles, both finished and bulk, in any number for foreign markets. Today we are confronted with serious adverse events involving a widely used drug product that appears to have been made using substituted active ingredients at

a foreign facility that was never inspected by FDA – because of some human error in deciding whether an inspection had already been conducted or should be conducted. I believe that we are truly on the brink of a series of these events and that waiting for FDA to take some action that actually mitigates risk or encouraging the agency to act unilaterally will be an exercise in futility. As I said in the press and to your staff, Mr. Chairman, this recent case appears to be the close cousin of the same conduct discovered nearly two decades ago. At that time, it was through intensive and smart facility inspections and by the efforts of forward thinking forensic scientists and investigators the activity was discovered. Moreover, the successfully prosecuted counterfeit bulk drug case was made possible only through the intellectual connections between certain domestic inspections at U.S. facilities by a keen FDA investigator who had previously conducted the foreign inspection of the bulk supplier, coupled with follow up inspections at the foreign supplier, which were themselves targeted with knowledge of where evidence of illegal conduct was likely to be found.

It is no different today – except that we now have available to us significantly improved technological solutions that may prove useful to more precisely and efficiently identify, target, and intercept safety risks prior to their realization in the market place.

2. INTEGRATING THE SOLUTIONS ACROSS THE AGENCY

One of my greatest concerns as a former FDA official and a current consumer is that Congress would jump to solutions that are as "stove-piped" or "siloed" as the agency. This is particularly true with regard to FDA's information technology systems. As the General Accountability Office (GAO) has articulated several times over the last 15 years, the agency's legacy data systems are antiquated and not integrated. The FDA has been striving for decades

under a budget that is anemic with regard to IT funding. Most Americans, I presume, would find it quite astonishing that FDA personnel (humans) must make decisions about whether a foreign facility should be (or has previously been) inspected by reading the name and comparing it to names in a number of data systems.

Even more astonishing would be the realization that FDA's various registration systems – across all of its Centers and regulated commodities – are not relationally integrated to background agency data or to its operational systems. Humans are still entering data bases and checking to see if a registration, supplied during the importation process is "in" the system and whether the number "belongs to" the manufacturer declared in an entry. FDA still receives its manufacturer declarations via the Customs Manufacturer Identification (MID) process and that MID must be translated in FDA's systems to its own numbering system. Because of the variations in the MID process, FDA ends up with duplicate or triplicate numbers for the same facility -- or far worse. Portal overlays can help reduce the number of data base user names and passwords an FDA official may have to remember – but they will not integrate data. These realizations, among others, account for at least some of the discrepancies in the agency's data with respect to how many foreign facilities have been or should be inspected. This is an annoying result. But it is more than annoying when the lack of integration of data accounts for a regulatory regime which relies on a human to notice slight differences in company names to assess whether a facility has ever been inspected. In this regard, a unified registration system could quite easily have prevented the recent heparin scenario.

3. MORE THAN COUNTING COMPANIES

Although it is critical for FDA to be able to define its universe, regulatory oversight requires far more than counting. It is critical that FDA is able to obtain reliable and affirmative evidence that foreign facilities manufacturing drugs for the U.S market are operating within the scope of FDA's current good manufacturing practices (cGMP) requirements. This information can be derived from a number of sources – but one primary and historical information source has been the physical FDA inspection of the facility making the bulk active pharmaceuticals and the finished dosage drugs. As discussed in previous testimony, the drug manufacturing industry has undergone significant changes over the last 15 years in how and where its bulk actives and finished drugs are prepared, packed, and labeled. Many more drugs are manufactured in foreign jurisdictions now than ever before. FDA's inability to count those facilities is indeed troubling. But the point of being able to count them must be based upon FDA's ability to conduct adequate oversight of how they manufacture the drugs we take. I might add that without a number we can all point to, you are also unable to assess how FDA is doing in evaluating the safety and effectiveness of those drugs. Confidence in the system understandably erodes.

The post-marketing surveillance inspections of drug and medical device facilities are absolutely critical to assessing the quality, purity, safety and effectiveness of the articles they manufacture. I have never heard FDA or the domestic industry as a whole say otherwise, although I am sure there are different opinions as to the absolute frequency that should be applied. Further, the sophistication of the inspector, the sufficiency of agency inspection guidance, the amount of time the facility is available to the inspector, and the depth and scope of the inspection all play significant roles in the reliability of the inspection results. The frequency

of cGMP surveillance inspections correlates directly to the level of confidence FDA and the consumers enjoy respecting the critical elements of the articles.

The cGMP (or Quality System) requirements are intended to address the adequacy and appropriateness of the manufacturing process, the design of that process, the equipment used in the process, the control and adequacy of raw materials subjected to processing, the source of those ingredients, the qualifications of the facility's critical personnel, the packaging, labeling, and failure evaluation processes, and post-distribution monitoring, including company recall procedures. FDA's current inspection frequency for foreign prescription finished drug and active ingredient manufacturers is reportedly on a 13-year inspection cycle. FDA is required to inspect corresponding domestic drug facilities on a 2-year cycle. When you compare this foreign facility inspection cycle (for Rx Active Pharmaceutical Ingredient manufacturers alone) to the increase in the numbers of imported drug shipments over the last 10 years, one can see its impact historically and can predict that impact prospectively.

For instance, according to FDA data, from 1991 to 2000 the number of FDA-regulated import shipments increased by 272% and in 2001 alone there were more than 7 million imported commercial lines of entry.[1] In 2002, approximately 7.8 million lines of FDA-regulated commercial shipments were imported. From 1997 to 2002, the number of imports of every kind

[1] A commercial line of entry is the equivalent of a line on a commercial invoice covering the sale of a product from a foreign exporter to a U.S. importer, owner, or consignee. A line may consist of a single laser DVD reader from Taiwan, regulated by FDA as an electronic product, or it may consist of 10 x 40 foot refrigerated containers of cantaloupes from Mexico. With regard to drugs, a line may be a shipment of 10 cases of retail ready over-the-counter (OTC) tablets of acetaminophen or a container of several metric tons of relatively pure bulk active pharmaceutical ingredients. A single invoice may have one or dozens of lines. FDA counts its import transactions by commercial line of entry. Each FDA-regulated line is subject to FDA jurisdiction based upon the legal definitions of the various products in the FDCA.

of FDA-regulated product at least doubled. In 2007, FDA had jurisdiction over more than 17 million imported commercial lines of entry under its jurisdiction will be imported. This represents two doublings in the sheer number of entry transactions every five years since 1997. FDA's inspection resources directed at assessing the safety of imported products and evaluating the manufacturing systems of foreign facilities has remained static throughout that time period.[2]

Based upon my experience at FDA, which is further informed by statements from FDA in the press and in testimony before various congressional committees, roughly 60% of the total number of commercial lines of entry consists of food imports; 25% consists of imported medical devices; and 10% consists of imported drugs and biologics. Using these proportions, FDA is responsible for ensuring the quality, safety and efficacy of nearly 2 million imported drug shipments per year.

As I testified in November 1, 2007, FDA's list of "uninspected" foreign API manufacturers exporting to the U.S. ranged from 242 to 4,600, depending upon the criteria used to populate the list.[3] The reasons for such disparity include the FDA's multiple, "siloed", antiquated and non-integrated IT systems; the lack of a meaningful gatekeeper for the Agency's

[2] More regretfully, even though roughly half of all FDA-regulated products consumed in the U.S. are either manufactured in whole or in part in a foreign country, as I recall by the summer of 2003 approximately only 7 out of every 100 dollars spent by FDA regulating products under the Agency's jurisdiction was focused on FDA's import or foreign programs.

[3] *See* Statement of Jane E. Henney, M.D., FDA Commissioner, Before the Subcomm. on Oversight & Investigations, Comm. on Commerce, U.S. House of Representatives, http://www.fda.gov/ola/2000/counterfeitdrugs.html (Oct. 3, 2000).

drug establishment registration process; and the Agency's insistence to mitigate the usefulness of FDA's historical import entry (OASIS[4]) transactional data.

Today, it is apparent that all of these factors persist at FDA and the agency is still struggling to identify the scope of the universe of foreign drug firms under its jurisdiction – whether we speak in terms of all foreign firms exporting drugs for human or animal consumption or merely foreign firms that FDA believes "should be" inspected. Lacking the ability to identify the larger, total universe of foreign drug firms exporting drugs to the U.S., the attempt to reduce that total to a more manageable "high risk" universe for targeting inspections has little foundation in reality. Consequently, FDA's current range of foreign drug firms exporting drugs to the U.S. that *should* be inspected by FDA is from 3,000 to 6,700.[5]

So at present, FDA is tasked with evaluating the safety and effectiveness of nearly 2 million imported shipments of drugs from as many as 6,700 foreign facilities, any number of which have not been visited by an FDA inspector for as long as a decade (or have not been

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[4] "OASIS" is an acronym that stands for FDA's "Operational and Administrative System for Import Support." See FDA's discussion of OASIS at http://www.fda.gov/ora/import/oasis/home_page.html.

[5] These numbers are derived from two separate FDA data systems and thus the disparity. The lower number is reportedly from FDA's Drug Registration and Listing System (DRLS). The higher number is a downward departure from data stored in ORADDS, the OASIS data warehouse. Therefore, the lower number is taken from the process whereby foreign manufacturers report data to FDA in order to meet two of the most basic minimum requirements to export drugs to the U.S.: drug registration and drug listing; and the higher number is taken from the process whereby Customs brokers report to Customs and to FDA through OASIS the identity of foreign manufacturers *actually* exporting drugs to the U.S. This discrepancy alone is troubling. It is unclear over what time frame the two numbers were derived and whether they correlate. Further, it undercuts FDA's traditional argument that OASIS data is unreliable simply because it represents self reporting through the importation process. DRLS also represents self reporting to FDA, and in the import declaration environment, there is another agency, Customs and Border Protection, that strictly governs and enforces proper data reporting.

visited at all, as in the case of the Chinese supplier of heparin potentially linked to 81 deaths in the U.S.). FDA is doing this with an IT system that contains multiple duplicate or triplicate facilities with different or non-unified numerical identification systems, literally dozens of data bases that are disconnected, and a couple hundred people on a part time basis. This certainly seems to be a resource problem – but it is far more than that.

4. WHY NOT JUST SAMPLE MORE?

As stated in my previous testimony, when FDA is virtually absent in the foreign market assessing compliance with cGMPs, the Agency is left with attempting to assess risks associated with foreign sourced drugs and drug ingredients using its import operations. The FDA's current import program, however, focuses primarily on FDA approved application, facility registration, and drug listing database submissions, label reviews, and finished product testing. These approaches are incapable of assessing the cGMP compliance and therefore the quality and safety of imported drugs. Although testing can tell FDA something about the quality and even the safety of an imported product, finished product testing at the border (or anywhere along the supply chain) is not a statistically valid method for predicting the safety of later or earlier untested shipments – even other shipments from the same processor.

Where product (and patient) safety is so dependent upon an ongoing and rigorous manufacturing quality system, finished product testing is not even a valid way to determine product safety within the same shipment. Compliance with FDA's drug cGMP program is the only (current) framework within which the agency can justify relying upon the results obtained from finished product test. Finished product testing is confirmatory only. Without an assessment and understanding about the conditions of manufacture within the facility, the

finished product test results are anecdotal at best. Such an approach cannot predict, measure, assess, or assure drug safety.

Any question about this premise is laid to rest with a simple observation from a recent drug safety crisis. FDA now is maintaining that because it took some time for any number of laboratories to identify the contaminant in the heparin, which has caused such tragic loss of life recently, the FDA concludes that there are "limitations as to what inspections can tell you". This is an appalling and irresponsible position. To the contrary, the absence of a meaningful and recurrent FDA inspection presence has far more to do with the events of recent months than almost any other factor. The evidence as to product safety (and security) is found only in the facilities and companies that make and move products into the U.S. market. Lacking a robust foreign drug inspection program, which takes into consideration all elements of prescription *and* non-prescription foreign drug manufacturing in its scheduling and preparation, promotes a "catch me if you can" foreign drug compliance culture.

I would only add that if FDA's IT systems were capable of linkage using a unique numerical identification system with some level of verification of registration data, then I dare say the system could be designed to flag any submission to the Agency, linked with the unique numerical identifier, with an on screen warning that the facility submitting the data has not be inspected by the agency. This alone would have enabled FDA to assess whether the manufacturer of the heparin should be approved as a source for the finished dosage manufacturer. Instead, FDA personnel had to resort to recognizing slight variations in the names of two firms.

5. ACCOUNT-BASED OVERSIGHT PROVIDES ADDITIONAL BENEFITS

Other government agencies having regulatory oversight over hundreds of thousands of companies, transactions, and compliance procedures have begun to move to account-based regulatory processes to integrate the many steps the agencies must take to assess risks. For instance, Customs, with more than three times the number of import transactions, the responsibility for enforcing virtually every federal law in the importation arena, and the added weight of ensuring the security of imported products and our port infrastructure, has moved to account-based processing. As FDA notes in its various import safety proposals and (purported) risk-based food safety plans, Customs' development of its Automated Commercial Environment (ACE) and the International Trade Data Systems (ITDS) will assist the government in improving its interoperability. However, FDA's background data systems (managing, for instance approval submissions, registrations, listings, 510(k)s, Food Canning Establishment registrations, bioterrorism registrations, drug master file submissions, to name a few) will not be integrated with the final implementation of ACE or ITDS. Although Customs will require a unique numerical identifier from any company providing data into its systems (and for any company identified in such submitted data), FDA will still have to translate that unique identifier into its own registration system – and back into its duplicative, disconnected systems. So it is true that FDA will be able to obtain its import data from one place – as will the other border agencies – however, FDA's own systems will remain disconnected, non-integrated and stove-piped.

If FDA moved to an account-based system to regulate products in the supply chain, wherever they may be found, and if FDA only accepted data when a Customs-comparable unique numerical identifier is provided with the submission, the agency would be able to begin the process of internal data integration and meaningful data connectivity with Customs and other

border agencies. Inspectional data, import data, adverse event data, and submission data could all be connected via the unique numerical identifier. The data systems could then be connected to FDA's operational data systems (FACTS and OASIS) to permit integration with importation data transmitted by Customs and to help target domestic and foreign facility inspections and border evaluations, inspections, and sampling. The account-based system would develop over time eliminating the now ever-present duplications in firm data and would enable FDA to actually identify the scope and size of the "hay stack" as it exists in the real world.[6]

With an account based regulatory system, the assessment of user fees (or review fees) can be predicted with greater specificity, FDA can identify the size and scope of its regulated industry, modifications, mergers, and facility closings can be identified and tracked, post-market events can be connected to product source, objectionable conditions observed at manufacturing facilities can be tracked through supply chains more readily, supply chains are more transparent and interagency coordination improves dramatically. These are just a few of the benefits.

6. CONCLUSION

A. Missed Opportunities for Change

In conclusion I reiterate my previous testimony regarding steps going forward. The efforts of over 100 dedicated FDA personnel from all of FDA's product Centers, the Office of Regulatory Affairs (ORA), the field offices, the laboratories, the various information technology offices, and the office of international programs should be presented to Congress and industry in

[6] In my view, the unique numerical identifier should be site specific and should be capable of verification by government and private systems and processes. Because of the amount of consolidation that can occur in any economic market, whether developed or developing, the identifier must be able account for mergers, acquisitions, business closings etc. Consider, for instance, the ownership changes that can occur over the current FDA foreign inspection cycle of 13 years. Entire countries can disappear or newly emerge in the same geographical location over that amount of time.

an open forum to enable the agency to learn risk in the real world. FDA's foreign drug inspection program is only one means for FDA to assess and mitigate risks related to imported drugs. Foreign sourced drugs, whether finished or ingredients, active or inactive, must also pass through the bottleneck of FDA's and Customs' import assessment. Although it is true that FDA's import program is woefully inadequate today, only addressing imported drug risks in terms of increased foreign inspections leaves open risks that may arise in between foreign inspections (even if conducted every 2-3 years) or in the product supply chain (*e.g.*, product counterfeiting, commingling, or tampering). Further, as FDA will never cross enough foreign thresholds to enable the Agency to apply inspection data on all imported drug shipments – more than just additional resources for foreign inspections is needed.

Shortly after September 11, 2001, FDA's Leadership Council established an Import Strategic Plan Steering Committee. By spring 2003 the Import Strategic Plan was virtually complete. FDA developed the ISP from the contributions of more than one hundred Agency experts in all product Centers, field and headquarters components, laboratories, international programs staff, the General Counsel's Office and the Office of Policy, Planning and Legislation.

The ISP's principles were simple but far reaching: Push the current FDA import evaluation process from the extremely limited border transaction to a life-cycle process, which:

- Intentionally gleans information from all points along an article's supply chain;
- Assesses that information based upon FDA requirements and risk of harm;
- Delivers the assessment to border inspectors, compliance officers, and electronic screening systems for reliable targeting decisions; and

- Results in the facilitation of safe products and enforcement against products that are unsafe.

The significance of the ISP and its proposed action items rests in what it represents: an internal agency demand for a dramatic shift in thinking about the identification, assessment and mitigation of risks in the international supply chain. Many of the ISP proposals are indeed costly. However, many could have been implemented nearly immediately and would have begun the process of increasing FDA's import efficiency and effectiveness using existing resources. It is this shift in thinking that FDA's middle and upper management seems to continue to resist. I believe that all involved in the ISP process recognized the import problems – even in 2003—are complex and cannot be solved with FDA's traditional regulatory approaches and philosophy.

B. Some Proposed Changes Going Forward

First, any action by this Subcommittee should include a significant resource investment targeted directly for reengineering FDA's stove-piped IT systems. IT improvements recommended in the ISP are a contingency for executing any serious risk-targeting strategies for foreign inspections and import interdiction of unsafe drugs. This investment, however, cannot be targeted solely at drugs and devices, for the same operational systems must manage the other 90% of imported shipments and the inspection of other products. The IT fix must either be across all Centers and ORA or it must occur at the Department level to leave open the option of breaking food regulation out of FDA and combining it with other food regulators into a Food Safety Administration as a sister to the remaining Drug & Device Agency.

Second, I recommend the establishment within FDA of an organization reporting to the Commissioner with the mission of focusing on enhancing the safety of imported products – all products. I continue to believe fixing FDA's import and foreign inspection problem requires it be broken free from the domestic programs, which produce much of the bureaucratic inertia against change in this area. A new organization would enable proper staffing, allocation of human resources at ports of entry, management and implementation of ISP-based strategies. It should be responsible for all import and international focused work-planning activities; conducting facility inspections of foreign processors and importers; overseeing and conducting border operations; conducting foreign government and industry assessments and training; and support trade negotiations in a manner to enhance safety of imported products. To accomplish this, the new organization should be directly funded, rather than receiving its funding through the product Centers. A basic persistent infrastructure to manage risks associated with all imported commodities must be maintained regardless of year-to-year changes that may appropriately occur in program directions.

Third, section 302(b) of the Bioterrorism Act, which enables FDA to implement risk-based strategies for managing food imports, should be expanded to cover all other FDA-regulated products including drugs. This would clarify FDA's authority to facilitate the importation of drugs that are in compliance with FDA requirements and pave the way for distinguishing between and among shipments based upon verifiable risk data.

Fourth, FDA should be required to inspect foreign drug facilities (at least those that fall into categories FDA admits should be inspected on a regular basis) at the same frequency as domestic facilities.

Fifth, FDA should work with Customs to adopt a uniform numerical identification system to begin the process of regulating its industries using an account-based system. This would enable FDA to integrate its numerous and disparate background data systems and to interrelate the data it receives from Customs and other government agencies.

Sixth, FDA should publish and begin implementing the ISP in accordance with the plan's guiding principles, goals, and themes.

Seventh, FDA should begin developing programs for obtaining as much information as can be obtained from as many reliable sources as the agency can find regarding the cGMP compliance status and supply chain security programs of foreign drug facilities that are *not* inspected by FDA. This population of drug manufacturers will always exist, and simply saying it represents too many companies for oversight or too much data to digest is no answer at all. Additional risk data could come in the form of third party inspection and certification companies, accompanied by a robust auditing process on both sides of the border, by foreign inspectorates, or by other U.S. Government Agency inspections and information. All such data should be connected to the firm's unique identifier and incorporated into the account data to permit its assessment in light of other legacy and other agency data. I continue to hold to the view that obtaining and assessing all available risk data better enables FDA to (a) target its foreign and domestic inspections; (b) interdict and examine high-risk imported drug shipments (related to product safety); (c) follow up in the domestic market those shipments that proceeded through the border with inadequate inspections; and (d) facilitate imported drug shipments that are likely to have been manufactured in accordance with FDA's cGMP requirements. This would permit the

agency to focus its most earnest import inspection and examination efforts on shipments representing known and unknown risks.

Eighth, FDA requires additional resources to conduct more foreign inspections and import examinations and to develop and publish meaningful Agency guidance relating to identifying and managing risks in the full life cycle of imported products.

Ninth, FDA should rely on Customs and Border Protection and the Department of Homeland Security (DHS) to manage security risks associated with FDA regulated imports. DHS' security programs should be expanded to incorporate *product* security risks (such as product counterfeiting and tampering) rather than focusing solely upon the security of in-transit cargo or inbound containers.

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I thank the Subcommittee Chair and Members for the opportunity to discuss these important issues and I look forward to answering any questions.