TESTIMONY OF

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Drug and Device Provisions of the 'Food and Drug Administration Globalization Act' Discussion Draft Legislation

BEFORE THE
SUBCOMMITTEE ON HEALTH
COMMITTEE ON ENERGY AND COMMERCE

U.S. HOUSE OF REPRESENTATIVES
MAY 1, 2008

Good morning Chairman Pallone, Ranking Member Deal and Members of the House Energy and Commerce Committee Subcommittee on Health. Thank you for asking me to participate in this very timely and important hearing.

I am Christine Mundkur, Chief Executive Officer of Barr Laboratories, Inc., the global generic pharmaceuticals business unit of Barr Pharmaceuticals, a leading global manufacturer of generic and brand name prescription drugs, and over-the-counter medicines. Barr currently operates in more than 30 countries, with manufacturing and packaging operations of finished dosage form products in multiple sites in the United States, and manufacturing of active pharmaceutical ingredients and finished dosage form products in Croatia, Poland and the Czech Republic.

Prior to being named CEO of Barr Laboratories in March of this year, I held a variety of legal, regulatory, quality and safety management positions since joining the company in 1993. I am also a regulatory attorney. Most recently, I served as Executive Vice President Global Quality, Safety and Regulatory Affairs, and had responsibility for leading the Company's global quality, safety, regulatory affairs and pharmacokinetics/bioequivalence (PK/BE) operations. Following Barr's acquisition in 2006 of PLIVA, a leading European pharmaceutical company

based in Croatia, I had the opportunity to relocate to our European headquarters in Zagreb, Croatia. In this position, I worked to harmonize the quality, safety, regulatory and manufacturing processes across the global operation and gained valuable experience and knowledge working with the European drug regulatory system.

I have worked extensively over the past 15 years with FDA in all aspects of product review, approval and the regulation of manufacturing and quality standards, and actively managed our relationships with suppliers of active and inactive pharmaceutical ingredients in our products.

In addition, I am proud to speak on behalf of the Generic Pharmaceutical Association, which represents domestic and multinational companies that manufacture 90% of the FDA-approved generic pharmaceuticals dispensed in the United States, as well as active ingredient suppliers for this market.

Overview of Testimony

I would like to make two brief points in my testimony today, before commenting in some detail on the proposed Food and Drug Administration

Globalization Act, and in particular Title II of the Act, which addresses drug and device safety.

First, we applaud the work of this subcommittee, and the commitment of Congress to ensure the safety of America's drug supply – brand and generic. For nearly a quarter of a century America's generic drug industry has been developing, manufacturing and marketing generic versions of brand-name prescription drugs. Last year, approximately 65% of the 3.6 billion new and renewal prescriptions dispensed in the U.S. were filled with generics, saving patients and consumers literally billions of dollars. We are committed to doing everything possible to work with Congress and the FDA to ensure that adequate oversight of the nation's drug supply is in place to ensure our safety.

Second, I want to make clear that the generic pharmaceutical industry is among the most highly regulated in the world. FDA promulgates strict rules governing the development, manufacture, approval, packaging, marketing and post-marketing surveillance of prescription drugs. And to ensure the highest purity and quality, FDA has in place rigorous inspection standards for facilities that manufacture and supply prescription drugs.

These stringent regulations apply equally to all brand, generic and biological prescription drugs approved by the FDA. However, as you are aware, there are drugs being sold in the U.S. today that do not have FDA's approval. I am speaking primarily of counterfeit drugs, which are sold over the internet and on the black market. We do not want to lose sight of this untenable situation and the grave risk these unapproved and unregulated products carry for U.S. consumers. Our drug safety system is only as strong as its weakest link, and we encourage this committee to continue to place high priority on preventing counterfeit medicines from reaching consumers.

While we support your efforts to enhance foreign inspections, we encourage the subcommittee to recognize the need to carefully balance competing demands for FDA resources to prevent the increased emphasis on foreign inspections from unintentionally and negatively impacting the timely availability of U.S. generic pharmaceuticals. Generic applications already are backlogged at the FDA, with the average review and approval time for Abbreviated New Drug Applications (ANDAs) now approaching 20 months, according to the Office of Generic Drugs. This is a delay of more than a year longer than the six-month statutory approval period specified by the Hatch-Waxman Act. Action related to enhancing foreign

inspections cannot be permitted to further delay FDA's timely approval of generic drug applications.

Now, I would like to spend my remaining time outlining the generic industry's position regarding modifications to the Foreign Inspection process.

Consumer Safety is Paramount

The Government Accountability Office (GAO) reported to Congress in November that FDA's effectiveness in managing its foreign drug inspection program continues to be hindered by weaknesses, and that fundamental flaws in the program identified a decade ago continue to persist. The GAO report, coupled with the recent recall of heparin containing foreign-made active ingredients, has served to amplify the call for revamping the FDA's foreign drug inspection program to ensure the safety and quality of imported pharmaceutical products.

The generic industry applauds the diligent efforts of Chairman Dingell and Members of the Energy and Commerce Committee who, for more than a year, have been working on initiatives aimed at protecting American consumers from

substandard and unsafe medicines. Product safety and efficacy must always be paramount, and our industry has long supported measures to strengthen regulations that assure that all medicines—whether manufactured here or overseas—meet the highest standards for quality and safety.

We agree with Chairman Dingell that we cannot "inspect our way to safety." FDA must have the resources to enforce programs designed to prevent drug safety problems before they occur. And when prevention fails, the Agency must have the authority to impose appropriate penalties. That is why we are pleased to support the overall goals and fundamental provisions of the FDA Globalization Act.

Our industry has long supported measures to strengthen safety standards across the board and to deal with the problems posed by insufficient current Good Manufacturing Practices (cGMP) inspections. The key to addressing these issues is to provide FDA the resources it needs to do the job.

First, the generic industry realizes that FDA needs additional funding to defray the costs of sustaining an adequate inspection. Therefore, we support, in principle, Section 201 and the need for annual registration fees applicable to

producers of drugs. However, the draft legislation proposes that these fees be allocated to support inspections of both domestic and foreign facilities. It is the position of the generic industry that current agency appropriations already are adequate to support domestic facility inspections. Thus, our position is that annual registration fees proposed in Section 201 be allocated solely to support the inspection of foreign facilities, where there is an immediate and significant need for resources to address the larger issues that are providing the momentum for this legislation.

The generic industry advocates a "flat fee" structure that would cover both cGMP and pre-approval inspections, and would also have provisions to incorporate re-inspections. We support a fee structure that is tied to facility inspections, very similar to the system currently in place in the European Union. Under this fee model, payment of the inspection fee is due upon completion of the inspection. However, regardless of whether fees are registration-based or inspection-based, the fee structure should be tiered, with one rate for API manufacturers and another rate for finished dosage suppliers.

In conjunction with generating the funds needed to achieve a successful inspection program, the fee system should require that the FDA adhere to certain

performance metrics and adequate reporting to Congress to monitor program effectiveness and help ensure inspection goals are being met. Such performance-based metrics should help maintain a system under which manufacturers have product entry assurances that are tied to timely pre-approval inspection. In this way, the program would to a certain degree parallel the goals and assurances that are fundamental to the PDUFA user fee program for new drug applications.

It also is critical that fees collected are "locked in" for their intended purpose, namely defraying the costs of foreign inspections. We would not be inclined to support a program that permitted fees to be comingled into other accounts that do not support foreign inspections.

The inspection program must ensure a fair and level playing field between foreign and domestic manufacturers. The generic industry urges the establishment of one uniform, high quality inspection standard for all facilities, with foreign inspection as inclusive and robust as the strictly controlled processes that FDA requires of domestic manufacturers. This would include assurances that products are made in facilities that have the proper core competencies, laboratories, and operational infrastructures, and that inspections are conducted with the same frequency, whether the facility is domestic or based overseas.

We further support a "risk-based" model for the inspection program that would prioritize the allocation of inspection resources according to a company's safety and compliance track record. This system would ensure that questionable or problematic facilities receive a comprehensive review and evaluation. At the same time, companies with strong records of compliance and positive inspections could be permitted to proceed to market with their products based upon this track record, without delays resulting from waiting for FDA pre-approval or surveillance inspections on every product. By no means would a risk-based approach exempt companies with solid compliance from FDA inspections, but rather it would put them further down on the inspection schedule, allowing the Agency to focus its immediate attention on companies that have compliance needs.

We also support Section 202, which would require an initial inspection before the introduction or delivery for introduction into interstate commerce of any drug or active pharmaceutical ingredient. We particularly endorse the provision in this Section that would require both domestic and foreign drug facilities to be inspected at the same frequency. Again, we urge the drafters of this legislation to ensure that implementation of this biennial inspection does not unnecessarily

inhibit the introduction of new products from company's that have and continue to meet the highest standards of FDA cGMPs.

In talking with committee staff, we understand that there is more work needed in crafting final language relative to third-party inspections, which is covered in more depth in the Food section of the Act, but also comes into play in the Drug and Device section. We agree that additional language needs to be incorporated that ensures that third-party inspections, including other foreign regulatory authorities, are performed using consistent standards and that third parties involved in inspections meet the highest levels of conflict of interest standards.

In the matter of testing for drug purity and identity, addressed in Section 205, generic manufacturers currently test their finished products and the active ingredients they contain, for purity. However, prior to providing full support for this section, we would like to work with the Committee to ensure the appropriate testing practices are in place.

Section 206 of the Act addresses country of origin labeling. While our product labels currently specify the country in which the finish dose is made, there

would be significant practical problems associated with indicating countries of origin for every component of a finished product. Therefore, we request clarification of the Committee's intent in this Section -- whether the country of origin labeling applies only to finish dose, the active ingredient, or all components of a product.

It should be noted that country of origin information for the components of the finished dosage are already contained within ANDAs, and such information is updated annually and submitted to FDA. Because of the complexity of this issue and the myriad of technicalities involved in adding to labels the country of origin information for every component of a finished dose product – which could include all inactive ingredients, color agents, capsules or tablet coating materials, etc. – we believe that this section of the Act needs to be further examined in light of the practical issues related to its implementation if all inclusive.

There has been some talk about drug tracking, so-called pedigree, as part of the drug safety initiative. The generic industry believes this bill could be an appropriate vehicle to implement a federal pedigree program that would ensure a uniform and strong national safety regime. We advocate adoption of a federal

pedigree system, with uniform standards across all states, as opposed to a patchwork of more state-enforced regulations. The challenge will be to ensure that the technology is reasonable and feasible in light of numerous economic, technical and logistical factors.

To address potential quality concerns with inactive ingredients, we recommend that the GMP requirements as currently provided in the pharmacopeias, USP, EP and JP, be further clarified and revised as deemed appropriate.

Lastly, we support those sections of the discussion draft dealing with the destruction of adulterated, misbranded or counterfeit drugs offered for import; providing civil money penalties for violations; and granting the Secretary the same authority for detention of drugs as is currently available for devices.

Summary

Our Foreign Inspection Process is only as strong as its weakest link. Failure to infuse adequate resources and implement reform measures will perpetuate a

system where there is one standard for domestic FDA-approved prescription drug manufacturers and a lesser standard for foreign manufacturers.

In conclusion, Mr. Chairman, while we strongly believe the U.S. enjoys the world's safest pharmaceutical supply chain, we know from recent and unfortunate events that there still is room for improvement through enforcement of more rigorous standards. As an industry, we stand ready to support Congress and the FDA in strengthening the foreign inspection program to ensure we continue to lead the world in safety.

Thank you. I would be happy to address any questions of the Committee.