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S. 334: AN APPROACH TO DRUG IMPORTATION

HEARING

OF THE

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS UNITED STATES SENATE

ONE HUNDRED NINTH CONGRESS

FIRST SESSION

ON

EXAMINING S. 334, TO AMEND THE FEDERAL FOOD, DRUG, AND COSMETIC ACT WITH RESPECT TO THE IMPORTATION OF PRESCRIPTION DRUGS

APRIL 19, 2005

Printed for the use of the Committee on Health, Education, Labor, and Pensions

U.S. GOVERNMENT PRINTING OFFICE

20–814 PDF WASHINGTON : 2005

For sale by the Superintendent of Documents, U.S. Government Printing Office
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S. 334: AN APPROACH TO DRUG IMPORTATION

TUESDAY, APRIL 19, 2005

U.S. SENATE,
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS,
Washington, DC.

The committee met, pursuant to notice, at 10:03 a.m., in room SD–430, Dirksen Senate Office Building, Senator Michael B. Enzi (chairman of the committee) presiding.

Present: Senators Enzi, Hatch, Gregg, Isakson, Ensign, Burr, Kennedy, and Murray.

OPENING STATEMENT OF SENATOR ENZI

The CHAIRMAN. I call the hearing to order on "An Approach to Drug Importation." Welcome to today's hearing.

Let me begin by saying I believe it may be possible to import prescription drugs from other countries and do so safely, but we do need to answer a lot of questions before we can open our borders to imported drugs without endangering consumers or jeopardizing research and development of new, lifesaving products.

Earlier in the year, I promised that we would have a hearing within 90 days. I would like everyone to note that it is within 90 days by a few days. This is the third hearing this committee has held on drug importation this year in an effort to ask and answer the important questions.

In February, I chaired two hearings on the subject. We focused on two reports released last December by the Department of Health and Human Services Task Force on Drug Importation. We heard from the Surgeon General about safety and security issues and we heard from the Department of Commerce on the global pricing and international trade dynamics of drug importation. I want to commend the members of the task force and the scores of witnesses from whom the task force heard for identifying and wrestling with the challenges that we must address if we are serious about creating a system for safe drug importation.

Today, I am pleased to welcome Senators Dorgan and Snowe and other colleagues of ours to discuss S. 334, the Pharmaceutical Market Access and Drug Safety Act of 2005.

Senator Dorgan, when you introduced your bill this year, you made the statement that, "miracle drugs provide no miracles for those who can't afford them." I couldn't agree with you more. Most Americans who turn to imported drugs do so because of the cost.

But I am sure that you and all of the witnesses would agree that a counterfeit or tainted drug is unsafe at any price. As we consider the issue of drug importation, the safety of our citizens must be our primary concern. As chairman of the committee charged with public health, it certainly is mine.

Each of us takes a risk every time we take a drug. But Americans who buy prescription drugs in Canada and other countries or purchase drugs from Internet pharmacies that operate outside the United States are taking an even greater risk by obtaining their prescription medicines from pharmacies and Internet sites that don't always meet the high standards that we require here at home, and here is where my concern lies.

We already have a problem with counterfeit and substandard drugs here in the United States. Last year, the Washington Post published a week-long series about this problem. In addition, concern about the quickly growing counterfeit market is not just limited to the United States, as one of our witnesses today will tell us. In Europe, dangerous counterfeit drugs are already a problem, and the problem is growing as the European Union expands. In addition, we have little or no knowledge of the extent of counterfeiting in the Asian markets.

Prior to legalizing an untested drug importation program on a large scale across our Nation, we must consider any new vulnerabilities in our drug distribution system, especially since those vulnerabilities could be massive in size. S. 334 would allow drug importation from more than 20 countries worldwide. A program as envisioned by S. 334 has never been undertaken, so a cautious approach to drug importation is required.

We will also hear perspectives about other drug safety and security issues, such as the importance of limiting imported drugs only to those that have been approved by the FDA. It is important for this committee to understand how small differences between drugs can make differences in the health of patients.

In addition, we will hear a perspective about the effect that drug importation legislation might have on patent rights and international law, and possible Constitutional limitations, as well.

And last, but certainly not least, and actually first, we will hear from our colleagues who support S. 334 or another approach to drug importation. I appreciate your willingness to take the time to be here today and I look forward to hearing from all of you.

As we know, this committee has jurisdiction over any legislation that would amend the Food, Drug, and Cosmetic Act to remove the restrictions against importing prescription drugs. As chairman of the HELP Committee, I fully intend to work with my fellow committee members, any interested members, and various stakeholders to develop a bill that will allow for safe drug importation.

I know that we all share the same goals. We all want to ensure that drugs that are imported are safe, effective, and will not compromise the integrity of our Nation's prescription drug supply or our world-leading pharmaceutical research.

Like many Americans, I am concerned about the high and rising cost of prescription drugs. However, I doubt that importation of drugs from other countries will solve this problem all by itself. That is why I believe that if we are going to open our borders to

imported drugs, we had better be certain about exactly what we are doing and how we are going to do it. We should not tell companies with whom they must do business, how they must sell, and at what price, mandates what I strongly believe will ultimately limit consumer access to new drugs.

So I look forward to this spirited discussion. I think it will answer my questions about this legislation and will hopefully inform us all of the best direction for us to take from here.

I will now recognize Senator Kennedy for his opening statement. As is the tradition on this committee, only the Chairman and Ranking Member are recognized to deliver opening statements so that we can spend more time with the witnesses and the questions. I do ask unanimous consent that the opening statements of all of my colleagues on the committee be entered into the record. Without objection, so ordered.

Senator Kennedy.

OPENING STATEMENT OF SENATOR KENNEDY

Senator KENNEDY. Thank you very much, Mr. Chairman, and thank you for meeting the commitment to having this hearing. We have had additional hearings, as well. None of us are really surprised. Once you make a commitment, as we know on this committee and know otherwise, you are a person of your word and we are very grateful for your attention to the hearing that we are having today on this issue.

We live in the period of the life sciences. This is the life science century. And the breakthroughs that we are seeing across the world are breathtaking and the possibilities are unlimited. I think the Congress has recognized that with the doubling of the NIH budget. We are having challenges at the present time, and that is another issue for another time. But when we see the sequencing of the gene, the mapping of the human genome, the potential in terms of stem cell research, it is virtually unlimited.

I think the great challenge that we have is to try to make sure that those miracles which are out there are going to actually reach and benefit the families in this country, and really families around the world. To a great extent, this debate and discussion is very much a part of that public policy issue, and I thank my colleagues for their interest, Senator Stabenow, Senator Dorgan, Senator Snowe, Senator Vitter, and all those who are strongly committed to trying to meet this particular challenge.

Often, these drugs can prevent diseases from spiraling out of control and from causing enormous suffering. Yet for millions of Americans, the breakthroughs are far out of reach. Today, the respected medical journal, *Health Affairs*, published a major study showing that over a quarter of American seniors went without needed prescriptions or split pills due to the high cost of medicine. One in 20 illegally imported drugs from Canada.

This issue is as relevant as today's *Washington Post* article, "Drug Benefit Disparities Cited." The first paragraph states,

> "The Medicare prescription drug benefit available next year will cost senior citizens an average of $722 annually. But retirees with chronic conditions such as diabetes and heart disease can expect to pay about double that amount and

will face gaps in their coverage for as long as 5 months, according to projections being published today."

So we have a real crisis for real people and real families. Drug importation isn't going to mean the end of the crisis, but it does provide an enormous opportunity to make progress.

Sadly, the administration feels that it is more important to protect drug company profits than to help Americans to afford the medical miracles that their tax dollars helped to discover, and it is tragic that the only way for millions of our fellow citizens to afford the prescription that their taxes pay to develop is to attempt to purchase them from Canada or other nations where their prices are more reasonable. It is legal for drug companies to bring their products into America from overseas and should be legal for patients to do so, too, and it is the responsibility of Congress to see that it can be done safely, just as it is the responsibility of Congress to see that U.S. drug manufacturers do so safely when their products are manufactured overseas.

So Americans, as we know, Mr. Chairman, now pay almost double the price charged for identical drugs in other developed countries. Year after year, the costs of drugs in the United States continues to skyrocket in a way that is unfair and unsustainable, and year after year, the pharmaceutical industry is among the most highly profitable industries in America. And with the enormous difference in price between the drug sold in the United States and the same drug sold across the border in Canada, it is no surprise that innovative senior citizens discovered the opportunity for instant relief that was available in Canada and began organizing the bus trips to Canada that we have heard about before.

In Massachusetts, the City of Springfield began using Canadian pharmacies to provide prescription drugs for its city employees and retirees, and Springfield's example led the way for other cities, such as Boston, to do the same. Whole States are now involved, as well. And the legislation that Senators Dorgan, Snowe, Grassley, McCain, Stabenow, Jeffords, Clinton, Bingaman, many others, and I have introduced will allow the importation of safe FDA-approved drugs manufactured in plants inspected by FDA. It would allow American patients to buy safe drugs at the fair prices that Canadians and Europeans pay, not the exorbitant prices that seniors and the uninsured are forced to pay in the United States.

The place of manufacture and the name of the importer will also appear on the label of imported drugs, as will differences in inactive ingredients, if any, that may affect patients, such as a person with particular allergies.

In short, under our bill, a large number of Americans who cannot afford their medicines today will have safe access to less expensive drugs.

So I welcome our colleagues here this morning. I also welcome former FDA head David Kessler, who is an old friend of this committee, and other witnesses today, and I look forward to their testimony. I thank you again for this hearing.

The CHAIRMAN. Thank you. I would like to welcome this first panel of distinguished colleagues to the committee today. We have Senator Byron Dorgan of North Dakota and Senator Olympia Snowe of Maine, who have spent a great deal of time putting to-

gether the bill that we are having the hearing on today. We have Senator Debbie Stabenow of Michigan, who has been working on drug reimportation since before she got to the Senate. And we have Senator David Vitter of Louisiana, who has another version of drug reimportation that he has been working on diligently with a number of people.

I welcome you all, and Senator Dorgan.

STATEMENT OF SENATOR DORGAN

Senator DORGAN. Mr. Chairman, thank you very much, and indeed, you have kept your word and this hearing is on time and we deeply appreciate it.

Mr. Chairman, the reason I and my colleagues feel so strongly about this issue is probably best described by just a short story. I was on a North Dakota farmstead a while back and there was a fellow there in his 80s. His wife was with him. She was in her 80s. We were sitting around talking and he said, "Well, you know, it has been a tough several years. We have spent most of the time driving to the doctors and driving to Canada." I said, "Why is that?" He said, "Well, my wife has suffered from breast cancer and," he said, "We spend a lot of time driving to the doctors." This is in a rather remote area, so they had a long drive to the doctors. Then he said, "We had to drive to Canada in order to afford the medicine she needed, to buy the Tamoxifen, and we bought it at an 80 percent discount in Canada, and so over the years that she has been treated, we have had to continue to make that drive in order to be able to afford her treatment."

It is not surprising. We all know this story. Here is the story told in a pill bottle. This is Lipitor. We all know that Lipitor is one of the most popular drugs for controlling cholesterol. As you can see, this is an identical bottle, same coloring, same size, same cap. This is a bottle that contains tablets made by the same company, the same pill made by the same company, put in the same bottle. The difference? This one was sold in Canada. This one was sold in the United States. The difference? Price, $1.81 per tablet in the United States, $1.01 per tablet in Canada.

Now, why are the U.S. consumers charged nearly double? What is the justification for that, that they are charged nearly double for this prescription drug, incidentally, which is made in Ireland. A prescription drug made in Ireland, imported by both Canada and the United States, except the U.S. consumer is charged nearly double.

Well, the answer is in the drug price controls that exist in the United States. As you know, we do have price controls in the United States on pharmaceutical drugs. Those controls are handled by the pharmaceutical industry themselves and they have decided to charge the highest prices in the world to the U.S. consumer. I and my colleagues think that is patently unfair and we believe the U.S. consumer ought to have access to the world trade market, with proper safety precautions, and use that approach to drive down prices and force a repricing here in the United States.

I am very proud to be a part of a group of 31 Senators that have put together a broad bipartisan piece of legislation that is very carefully constructed. This legislation can hardly be called speed-

ing. The first bill that I and some others introduced in the Senate was in 1999. That is 6 years ago. Seldom has the U.S. Senate been accused of speeding, and that is not the case here. We are talking about an issue that is getting worse, not better, one that cries out for Senate action, and I think we are finally at the precipice where such action will be taken and this hearing is an important first step.

Let me just say that the Dorgan-Snowe bill that we are all talking about here today creates a closed system of commercial drug importation that ensures the safety of imported drugs from the point of manufacture to the drug stores shelf. And S. 334 includes a wide range of safety features. Mr. Chairman, you talked about safety and counterfeiting and so on. This bill is the solution to that.

First of all, only FDA-approved drugs made in FDA-inspected facilities can be imported under this bill. Moreover, commercial importation by pharmacists and wholesalers could only occur from a limited number of countries—Canada, some European countries—and they have drug regulatory systems comparable to our own. That is why these countries are eligible under this bill. Only U.S.-licensed pharmacies and drug wholesalers that register with the FDA can import these prescription drugs. Registered pharmacies and wholesalers would be required to maintain the pedigree of imported medicines all the way back to the FDA-inspected manufacturing plant. Finally, registered importers would be subject to frequent random FDA inspection and could have their registration suspended or terminated if they don't comply with the bill's requirements.

Most importantly, I think, this bipartisan bill will allow safe reimportation and enable American consumers to stay at home and use their local pharmacy, who can then access these lower-priced FDA-approved medicines, and they will still benefit from lower drug prices, but also from the involvement of their local pharmacist in their health care, which I think is so important. Pharmacists then can coordinate their patients' pharmaceutical care and help prevent adverse drug reactions.

There are so many other provisions of this bill, and I think I will have my colleague, or my colleagues, I should say, respond to some of them, as well, but I want to just make this point. You all know, because we have had testimony before the Congress—I don't know that that testimony has been before this committee, but in the Commerce Committee, it has—you know that Europe has done this routinely. If you are in Germany and want to buy a prescription drug from Spain, no problem. If you are in Italy and you want to buy a prescription drug from France, no problem.

There is something called parallel trading. It has been going on for over 2 decades and parallel trading that the Europeans do, by which the European consumers can access a lower-price drug by importing it from another country, has worked, worked very successfully. There are no safety issues. I would encourage, if there are still questions about that, I would encourage you to invite the people involved in the parallel trading system in Europe to testify.

But clearly, we can do this. There are some who say we can't do what Europe does. Nonsense. This is not a safety issue any longer. The issue is, who are we going to stand with? Are we going to

stand with the American consumers, who are the victims of unfair pricing strategies, or with the pharmaceutical industry, who hides behind this current law that prohibits reimportation by anyone except themselves and then imposes their own set of price controls in this country in our marketplace in a manner that is patently unfair in my judgment?

Mr. Chairman, there are other features of the bill. I will allow my colleague, Senator Snowe, to deal with some of those, as well. This is a broad-based bipartisan coalition of nearly one-third of the United States Senate. I hope and expect that we will be able to make progress to get a bill to the President's desk this year. America is waiting, and this Congress ought to take action.

Mr. Chairman, thank you very much for allowing us to hold this hearing.

The CHAIRMAN. Thank you.

[The prepared statement of Senator Dorgan follows:]

PREPARED STATEMENT OF SENATOR DORGAN

Chairman Enzi, Ranking Member Kennedy, and other Members of the HELP Committee, I want to thank you for having this legislative hearing on S. 334, the bipartisan prescription drug importation bill that I have sponsored along with Senators Snowe, Grassley, Kennedy, McCain, Stabenow, and many others. I especially want to express my appreciation to Majority Leader Frist and Chairman Enzi for meeting the commitment they made to Senator Snowe and me to hold this hearing specifically on our bill.

As my colleagues know, this is an issue that I have been working on for quite some time. In fact, I introduced the very first prescription drug re-importation legislation in the Senate back in 1999, and the first Senate vote on this issue was way back in 2000 on an amendment Senator Jeffords and I offered to an Agriculture Appropriations bill.

Most recently, I have introduced S. 334, the Pharmaceutical Market Access and Drug Safety Act. This bill currently has 31 cosponsors from across the political spectrum, including, I'm pleased to note, a number of members of this committee.

In short, my bipartisan bill would allow American consumers, pharmacies and drug wholesalers to import FDA-approved prescription drugs at the substantially lower prices available on the world market. Many studies have confirmed what millions of Americans already know—the same prescription drugs cost significantly less in Canada, Europe, and other developed countries than they do here in the United States. And in fact, the Congressional Budget Office has confirmed that brand-name drugs cost, on average, 35 to 55 percent less in other industrialized nations than they do in the United States.

Unfortunately, the price discrepancy for prescription drugs between the United States only continues to get worse, even despite the weakening of the American dollar. Drug prices continue to rise at a rate much higher than inflation—a study released just last week by AARP has found that brand-name prescription drug prices went up an average of 7 percent just in the last year. Clearly, Congress must act to inject some competition into the pharmaceutical marketplace in order to put downward pressure on drug prices.

CONFRONTING THE SAFETY ISSUES

I have worked very hard with Senators Snowe, Kennedy, Grassley, McCain and others to assure the safety of drugs imported under our legislation.

Unfortunately, there exists in the United States a situation today whereby American citizens are resorting to potentially unsafe measures in order to afford their medicines—including cutting pills in half, skipping doses, and ordering drugs from possibly rogue foreign and domestic Internet pharmacies. In fact, the amount of potentially unsafe drugs coming into the country has exploded because people who can't afford high U.S. prices have been buying their medications over the Internet under a system that is virtually unregulated by the Food and Drug Administration (FDA).

Mr. Chairman, not acting on drug importation legislation is a far greater safety hazard than acting on this bill would be. S. 334 will empower consumers to purchase safe, approved prescription medicines from Canadian pharmacies via mail-order or the Internet under a regulated program. Consumers who choose this option will be assured that they are dealing with a legitimate, licensed Canadian pharmacy that is registered and inspected by the FDA. The FDA will post the list of approved Canadian pharmacies on its Web site and through a toll-free number, so Americans can readily check to see if they are dealing with a legitimate pharmacy and not a rogue Web site.

The Dorgan-Snowe bill also creates a closed system of commercial drug importation that ensures the safety of imported drugs from the point of manufacture to the drugstore shelf. Again, S. 334 includes a range of safety features. First of all, only FDA-approved drugs made in FDA-inspected facilities can be imported under the Dorgan-Snowe bill. Moreover, commercial importation by pharmacists and wholesalers could only occur from a limited number of countries—Canada, some European countries, Japan, Australia, New Zealand, and Switzerland—that have drug regulatory systems comparable to our own. And only U.S.-licensed pharmacies and drug wholesalers that register with the FDA can import prescription drugs. Registered pharmacies and drug wholesalers would be required to maintain the pedigree of imported medicines all the way back to the FDA-inspected manufacturing plant. Finally, registered importers would be subject to frequent, random FDA inspection and could have their registration suspended or terminated if they don't comply with the bill's requirements.

Perhaps most importantly, the bipartisan bill enables American consumers to stay at home and use their local pharmacy, while still benefiting from lower drug prices. This would ensure that pharmacists could coordinate their patients' pharmaceutical care and help to prevent adverse drug interactions.

Let me make one final point about safety: Some have suggested that we should rely on a requirement that the Health and Human Services Secretary should certify to the safety of imported medicines before importation legislation be implemented. As I mentioned earlier, we currently have an unsafe system whereby as many as 5 million packages containing drugs come into the United States with virtually no regulation. We cannot allow this unsafe

situation to continue, and that is what a Secretarial certification requirement would cause.

CLOSING LOOPHOLES

It is also very important that drug importation legislation include provisions that would prevent drug companies from exploiting loopholes to shut down drug importation and prevent consumers from saving money. The Dorgan-Snowe bill includes a number of necessary provisions to close these loopholes.

The situation in Canada is evidence that the provisions in the bipartisan bill are vitally needed to ensure real savings for American consumers. The drug companies have already demonstrated in Canada that, if they cannot shut down importation by lobbying Congress, they will take steps to do so by backdoor methods.

More specifically, our bill:

• Prevents drug companies from taking actions, such as discriminating against a foreign pharmacy or wholesaler that exports drugs to the United States by shutting off their drug supply, that would thwart drug importation. Such an action would be an unfair and discriminatory practice, subject to treble economic damages.

• Prevents a drug manufacturer from blocking importation of drugs in more subtle ways, such as by changing the color, an inactive ingredient, or place of manufacture of the drug so that it is no longer FDA-approved. Drug manufacturers that make these kinds of changes would be required to notify the FDA, and the FDA would be given the authority to approve these changes, if approval is warranted. In other words, our bill ensures that all imported drugs will be FDA-approved, while also ensuring there will be drugs to import.

• Protects pharmacies, wholesalers, and individuals from patent damages arising from the importation of drugs.

Opponents of drug importation have alleged that some of the provisions in the Dorgan-Snowe bill may be unconstitutional. Most of these claims seem to be based on a notion that our non-discrimination provisions would somehow force a drug company to sell a drug for a price that it doesn't want to accept in a country where it doesn't want to sell it. Our bill language specifically makes clear, on page 78, that nothing "shall be construed to compel the manufacturer of a drug to distribute or sell the drug in a country." Moreover, our bill only allows importation from other major industrialized nations, and I don't think any of us believe the drug industry is actually selling its products for a loss in these countries. In other words, the drug companies have already voluntarily sold their medicines for a profit once, so importing them for the benefit of American consumers does not in any way violate the drug industry's Constitutional rights.

Regrettably, it is not terribly surprising that the drug industry would make this claim—the drug industry always argues that legislation to reduce the cost of medicines for consumers violates the Constitution. However, objective legal authorities tell me the bipartisan bill is constitutional.

CONCLUSION

Let me make one final point: Within the Europe Union, they have had a thriving trade in prescription drugs called "parallel trade" for the past 2 decades. We have heard testimony previously before other hearings that this trade occurs routinely with no safety problems whatsoever and with substantial savings to European governments and consumers. As Dr. Peter Rost, a pharmaceutical company executive who has endorsed S. 334 has pointed out: "During my time responsible for a region in northern Europe, I never once—not once—heard the drug industry, regulatory agencies, the government, or anyone else saying that this practice was unsafe. And personally, I think it is outright derogatory to claim that Americans would not be able to handle reimportation of drugs, when the rest of the educated world can do this."

In closing, the Senate must—and I hope will—act promptly to pass the bipartisan Dorgan-Snowe bill. This hearing is an important step toward Senate passage of strong, beneficial drug importation legislation, and I thank the Chairman once again for holding it. I have no doubt that we have the votes in the Senate to pass my bill, and I intend to push aggressively for a vote on it soon.

I'd be pleased to answer any questions the committee members may have.

The CHAIRMAN. Senator Snowe.

STATEMENT OF SENATOR SNOWE

Senator SNOWE. Thank you, Mr. Chairman. First, I do want to thank you for your prompt and timely response to this hearing. Hopefully, we can reach a resolution as a result of your leadership in this committee. To all members of the committee and to Senator Kennedy as Ranking Member of this committee, as well, we truly thank you.

I am very pleased to be with my colleagues. Senator Dorgan has been a longstanding champion and advocate, as he indicated, introducing the first bill back in 1999, along with Senator Stabenow, who has been a leader, and Senator Vitter. So I am very pleased to be here today. As Senator Dorgan indicated, we have a broad bipartisan coalition in support of our legislation, echoing those 7 out of 10 Americans who favor safe importation.

I don't think anybody needs to be told here in this committee that Americans are paying the highest prices in the world for prescription drugs that are available in other industrialized countries at a fraction of the price. As the Government Accountability Office recently reported to Senator Wyden and myself in a report regarding the cost, prescription drugs most commonly used by seniors are increasing two to three times the rate of inflation, as indicated here in this chart, the degree to which the prices are rising, just on those used by seniors.

The outcome of those relentless price increases make access to life-saving drugs, as we know, more and more difficult for consumers, and we all know that a drug that is not affordable is one that is neither safe nor effective.

There are two key issues that our legislation attempts to address. One, of course, is the issue, first and foremost, is it safe?

Second, will it be effective in delivering real savings to consumers, and I believe and we believe that our legislation will accomplish both of those goals.

Opponents claim importation will cause harm, but they fail to observe that the greatest threat to the security of Americans and to their health and well-being is the fact that they are not able to fill a prescription. That exacts a toll on thousands and thousands of American lives every year.

Thanks to the attentive reporting of health professionals, we are seeing more evidence of the cost of unaffordability. In my own State of Maine, for example, one physician recently reported that two of his patients had to be hospitalized for dangerous conditions, such as heart rhythm, simply because they could not afford to refill a prescription.

Our constituents, and certainly that has been true in Maine, have taken busloads and busloads of seniors to Canada repeatedly over the years to access affordable medications, and they have demonstrated that importation can be safe. In fact, the former Secretary General of the European Trade Organization indicated in 2003, 12 million prescriptions were brought in from Canada and there was no evidence of harm. In Europe, as Senator Dorgan indicated, where over 30 years of parallel trading of pharmaceuticals, no death or injury has ever been documented. They have known it to be safe.

Dr. Rost, in fact, who is the Vice President of Marketing at Pfizer, said this,

> "During my time responsible for a region in northern Europe, I never once, not once heard the drug industry, regulatory agencies, the government, or anyone else saying that this practice was unsafe."

And personally, I think it is outright derogatory to claim that Americans would not be able to handle reimportation of drugs when the rest of the educated world can do this.

Under our legislation, Mr. Chairman, Americans will receive imported drugs from over 30 countries. In most cases, Americans will purchase an imported prescription drug from their local pharmacist. Pharmacists will receive these drugs from U.S. wholesalers which import them. These wholesalers will be registered, they will be inspected, they will be monitored by the FDA. The highest level of safety is a first step in establishing the highest standards possible for handling of prescription drugs in the United States. This bill will be a model for domestic drug safety in America.

Our legislation also allows individuals to directly order medications from outside the United States when using an FDA-registered and approved Canadian pharmacy. It will be restricted to Canadian pharmacists. And again, just as with wholesalers handling prescription drugs, the FDA will examine these pharmacies, register them, inspect them on a frequent basis.

FDA will assure the highest standards for such essential functions as recording medical history, verifying the prescriptions, tracking shipments. But regardless of whether one purchases these drugs from your local pharmacies that are imported or uses a Canadian pharmacy—the bottom line in this legislation is that we assure that a legitimate prescription and a qualified pharmacist will be vital ingredients in assuring safety.

The bottom line is, we are importing drugs from countries that have comparable regulatory regimes to that of the United States. That is the bottom line.

Now, for those who say that consumers could unwittingly purchase an unapproved or suspect drug, our legislation once again assures that the drug received will always be FDA approved. If any difference exists in a foreign drug, even a trivial one, our legislation assures the FDA will evaluate the product and determine the acceptability.

For those who say that counterfeiting is a threat, our legislation requires the use of anti-counterfeiting technologies, exactly the type that is used today for the new $20 bills. In fact, our legislation requires the development of future anti-counterfeiting and track-and-trace technologies, which we hope will protect our drugs. The fact is, the serious incidents of counterfeiting that are occurring within our borders and it is a problem that needs to be addressed and our legislation does just that.

Now, for those who say that consumers won't know who has handled an imported prescription drug, our bill requires a pedigree, a chain of custody be maintained and inspected to help ensure the integrity of imported drugs. A pedigree, by the way, for prescription drugs was required in legislation that was passed in Congress back in 1988 and the FDA has yet to implement it. The fact is, today, consumers in America do not know where their drugs are coming from, Mr. Chairman, but they will under this legislation. They will not only know where they are coming from, they will know who has handled these medications.

Now, some have even attempted to alarm Americans about the countries from which we import drugs, citing Latvia, Estonia, and Slovakia, members of the European Union. So, too, is Ireland, as Senator Dorgan indicated, where Lipitor is made, what we use here in America. Now in this chart here, Mr. Chairman, it indicates the European Union and other countries from which we import appear in blue. We import drugs from there today, used here in America. These countries meet our standards. That is what our legislation would do.

In contrast, the chart shows those countries in red. Well, here again, we have many additional countries in which FDA inspects pharmaceutical plants manufacturing the medications. These include China, India, Bulgaria, Jordan, and others with lower standards, Mr. Chairman. I think what this demonstrates is that we are importing medications from all around the world for use. That is the point. So many manufacturing plants that FDA has to inspect.

Now, unfortunately, over the years, manufacturing inspections have declined by the FDA over the last 20 years. But the fact is, they are required to do it. We have seen charges made, well, you know, Canadian drugs come from foreign countries. Well, I think the point is, so do ours, and that is the point. It says, take a wild guess where your Canadian medicine is actually coming from, and demonstrating that it comes from foreign countries. Well, so do our medicines. They are manufactured from all over the world.

So I think the point is, for those who say importation is safe, we show a way to make it safe absolutely. We share that concern. We have set a standard in this legislation. We create a high level of

monitoring. Consumers can achieve significant savings and we create a comparative analysis in our legislation, because the drugs will be labeled imported drugs so they will be able to make a side-by-side comparison.

Some say that we won't have the resources. We impose a fee of 1 percent of the value of imported drugs so FDA has the resources. Because of this high-deficit climate, Mr. Chairman, we have to do something, and this is the option that we have determined in the final analysis to finance this legislation, and it is fiscally responsible, it is doable and provides the adequate resources.

Finally, one other issue. Some say importation will threaten research and development. Well, as we know, the taxpayer has been a partner. It has been a public-private partnership in research and development in America and taxpayers provided more than $30 billion to basic science and applied research at the National Institutes of Health on an annual basis. Well, it is interesting to note that Americans pay 35 to 55 percent more for their drugs than their counterparts around the globe, 35 to 55 percent. That means Americans are spending $87 billion more than people in other countries because they are paying the highest prices in the world.

And yet, what is the differential in research and development? Research and development spent in Europe by companies is $26 billion. In America, it is $32 billion. So they are only paying $5.6 billion more in research and development here than in Europe, and yet we are spending $87 billion more because of higher prices than people around the world.

So, Mr. Chairman, I appreciate this opportunity to be here today to share with you our thoughts. I hope that we can work it out. I think that there is a way. Our legislation at least demonstrates it. And obviously, we are open to suggestions on this part, but I think that we are addressing the major issues that we think are important to overcome the hurdles to achieving this ultimate goal. Thank you.

The CHAIRMAN. Thank you.

Senator Stabenow.

STATEMENT OF SENATOR STABENOW

Senator STABENOW. Thank you, Mr. Chairman. I want to thank you for convening this hearing today. I want to thank my colleagues, Senator Dorgan and Senator Snowe, for their eloquent statements. Senator Vitter, we will welcome him to this bipartisan effort that shows that there is strong support in the United States Senate, and that is also reflected in the U.S. House of Representatives, to finally do something about prices in a safe way to be able to address one of the largest concerns that not only individuals have, but businesses have.

Every business that I know in Michigan is concerned about health insurance costs, the explosion in health costs for them, and we know that prescription drug price increases are a major part of that. So this is important for business, for individuals, for seniors, for families.

I also want to, first, before talking about S. 334, though, Mr. Chairman, thank you for joining me when we offered a successful amendment to the Senate budget resolution which laid the founda-

tion for our discussion today and the groundwork for passing drug reimportation. Last year, my amendment passed 13 to 8. This year, it passed unanimously. That shows the power of your cosponsorship, so I want to thank you for your being a part of that important effort.

You are right, Mr. Chairman, I go back a long way on this issue. When I was in the U.S. House, I played a major role there in bringing this to the forefront, and also, this was the first issue that I brought to the Senate in the form of a bill as a United States Senator, so I very much appreciate everyone's involvement in this issue.

We all agree that prescription drugs need to be more affordable and accessible. I know that we all agree with that, not just for Medicare, but for everybody.

AARP reported last week that wholesale price drug costs rose an average of 7.1 percent last year. We can't sustain that. When we look at the inflation for prescription drugs, costs going up 3 times the average rate of inflation—for the top brand-name drugs it is as much as 10 times the rate of inflation—businesses can't sustain that in their costs and certainly our seniors who are without help can't sustain that.

Rising drug costs place a huge financial burden on all Americans, and there is no way that our health system, our citizens and our Nation can continue to endure these kinds of increases every year. So there is a great sense of urgency about getting this bill passed.

The rising costs have enormous health consequences for us. Prescription drugs aren't like other products. They can do wonderful and amazing things, but only if you can afford them, and we might be able to make do and not buy a new pair of shoes or a new automobile—although I would hope everyone would buy a new one every year made in Michigan—

[Laughter.]

But the reality is that we can't afford, without consequences to ourselves and our families, putting off the purchase of needed medicine.

Opponents tell us that Americans have to swallow the bitter pill of high prices if they want safety and innovation. This is a false choice for our Nation and for the world. We can achieve both. Drug makers are already bringing in drugs from other countries into the United States, as has already been stated. FDA inspectors go all over the world to inspect manufacturing lines that will produce drugs that ultimately will be brought to the United States. I think many Americans would be surprised to learn that their drugs might be from China, India, or Slovakia right now.

Drug makers have a complete monopoly on those prescription drugs. No one else—doctors, pharmacists, patients, employers—has the same opportunity to purchase those FDA-approved drugs at low prices. Again, only the drug makers.

Mr. Chairman, in my State, you can go to Detroit or Port Huron or Sault St. Marie and literally look across the river or look across a bridge, 5 minutes across a bridge or tunnel, and you can see where your prescription drug prices can be dropped as much as 50 percent, or in the case of drugs like Tamoxifen, 70 or 80 percent. My pharmacists say, why is it the drug makers can bring those

drugs back and forth safely but I can't do business? My business is prohibited from doing business with businesses, pharmacies in Canada. It makes no sense.

We can create a safe, fair system that allows our pharmacists, patients, and providers to use the global marketplace to find the lowest-price drugs. Our bill does provide the framework to allow our government to help our citizens and businesses lower their health costs and our bill will only allow reimportation from nations that have strong safety standards, as Senator Snowe spoke about so eloquently.

Again, I don't believe that Americans need to make a tradeoff between innovation and affordability. We make a commitment to research in this Nation through tax subsidies for R&D costs and funding for the National Institutes of Health. Last year, Congress appropriated nearly $29 billion to NIH, money that is used to develop the basic building blocks that lead to the next generation of medical breakthroughs.

We are also losing out on great opportunities to keep our Nation as a leader in scientific innovation. According to PhRMA trade association Web site, PhRMA companies in 2003 invested an estimated $33.2 billion on research to develop new treatments for diseases. I might add that we helped to support that through tax deductions and tax credits, as American taxpayers.

For the same period, the European Federation of Pharmaceutical Industries and Associations invested about $28 billion, not far behind. The number of biotech companies in Europe increased dramatically in recent years. In 2001, there were more companies in the E.U. than in the United States—more companies in the E.U. than in the United States. Those are jobs and opportunities we are losing here in the United States.

When drug makers spend more than two-and-a-half times as much on advertising and marketing as R&D, it makes you wonder what cures, what breakthroughs we have missed.

I think the bottom line, Mr. Chairman, is that we can work together to make a major difference, to lower prices, to do so safely, to address what I believe is one of the great moral issues of our time, the explosion in the prices of medicine in our country that are affecting businesses large and small and our families and our seniors, and I look forward to working with you on this important issue. Thank you.

The CHAIRMAN. Thank you.

Senator Vitter.

STATEMENT OF SENATOR VITTER

Senator VITTER. Mr. Chairman, Senator Kennedy, members of the committee, thank you for the opportunity to discuss this vitally important issue, and I am certainly pleased to be testifying today with my colleagues, leaders on this issue, Senators Dorgan, Snowe, and Stabenow.

It is an issue I feel very strongly about. My first legislative action as a U.S. Senator was to introduce the Pharmaceutical Market Access Act of 2005, S. 109, with Senator Salazar and others, and that bill has an identical companion in the U.S. House of Representatives by Congressman Gill Gutknecht and a bipartisan roster of co-

sponsors, 80 in total so far. A prior version of that House bill passed that chamber 2 years ago, and is the only bill on the subject to pass either body.

I want to make clear at the beginning, while I have a slightly different bill with a slightly different approach in some ways, I stand shoulder to shoulder on the broad issue with all of my colleagues here and my other colleagues in the Senate who care passionately about this issue, and certainly want to say up front if their bill was on the Senate floor for final passage right now, I would enthusiastically speak for it, vote for it, and I believe vice-versa.

Why is this so important? Well, two fundamental reasons, one of which is obvious, one of which is perhaps less obvious, maybe even counterintuitive, but very important.

The first obvious reason prescription drug prices are much higher in the United States than in all other countries, and we have talked about this, but let me make a few points about it. As I traveled Louisiana particularly last year, I heard countless seniors tell similar stories about the outrageous costs of their prescription drugs and how it burdens their lives. They noted correctly that the United States is the world's largest market for pharmaceuticals, and yet we pay the world's highest prices.

Senator Dorgan had a great example with Lipitor, a very common drug. As he noted, a 90-day supply costs about $320 in the United States, but only $180 in Canada. As noted by the Congressional Research Service, the price discrepancy for this one drug is not unique. A general CRS comparison of United States and Canadian prices revealed that, on average, brand name drug prices in the United States were 70 percent higher, and this is not limited to Canada. This is a much broader problem and a much broader issue. Citizens in virtually every other industrialized country pay significantly lower prices for patented drugs than Americans, lower by 30 percent or more, and this figure includes many countries that are not dominated by old-fashioned status price control regimes.

So why is that? In my opinion, the reason is simple. This country does not have a global free market for prescription drugs. We have a closed market, and that leads to disparate pricing, including the highest prices worldwide in this country, and we deliberately block American consumers' access to the same drugs at much cheaper costs from other sources.

Now, this price issue is very important to real seniors, real people, real families, but it also has very important and broad social and government program implications. According to the Congressional Budget Office, spending on prescription drugs grew at a real average annual rate—that is adjusted for inflation—of 14.5 percent from 1997 to 2002, reaching $162 billion in 2002. That explosive growth raised prescription drug spending's share of the total health expenditure to 10.5 percent in 2002, compared to just 5.8 percent a decade earlier.

As noted by CBO, in 1999, prescription drugs surpassed nursing homes as the third-largest category of personal health care expenditures after hospitals and physicians' services. Now, this has enormous implications for programs and challenges we worry about and try to face every day, particularly Medicaid and Medicare.

Let me now move on to the second big reason I, along with my colleagues, believe we need to take action in this area of prescription drug importation. It is because prescription drug importation is already occurring right now by American consumers without the proper safeguards. And so, in fact, I would argue strongly that safety is a huge reason we must pass legislation like this. It is not a reason we should fail to act.

Two scenarios, very simple. The first scenario is getting more and more common every day. Millions of Americans are refusing to shoulder the increasingly heavy burden of prices and they are defying law and they are purchasing their prescription drugs elsewhere. By one estimate, over 6 million Americans have purchased their medication from online Canadian pharmacies. According to CRS, in 2003 alone, Americans bought over $1 billion of prescription drugs that way, twice as much as the year before. When American consumers buy unapproved prescription drugs from other countries without equivalent regulatory safeguards, they run a real risk that those drugs could be of poor quality. So unless we act on this sort of legislation, we are allowing a major safety problem to grow and grow and grow.

The other scenario is just as concerning to me. Take the Americans who do live by the law, and they are on a limited budget, so they choose the alternative, to comply with the law, buy their prescription drugs here. What happens? We all know what happens. They may be forced to choose between medication and other necessities. We have all heard accounts where they cut pills in half or take their medication every other day instead of daily because they cannot afford the cost of their prescription drugs. To quote my friend and House colleague, Congressman Gil Gutknecht, an unaffordable drug is neither safe nor effective.

So those are the two real scenarios that I believe make action in this area imperative, specifically for safety reasons. Safety is not a reason not to act. It is the most compelling reason to act with clarity and with care.

We can, I certainly agree with my colleagues, we can address these safety concerns, and in doing so, we can make present circumstances much more secure and safer. There are a lot of provisions in both of our bills. Let me mention some of the most important specific provisions.

First, the requirement of tamper-resistant packaging. That is spelled out in a lot of detail in the Vitter-Salazar bill. It requires a new requirement that drugs be either packaged and shipped using state-of-the-art tamper-resistant anti-counterfeit technologies, or if that doesn't happen, be carefully tested for authenticity when entering the market in this country. And by the way, at least under the Vitter-Salazar bill, that requirement applies to most drugs in this country, as well, so it could, with new technology, help address the growing problem in this country that you noted in your opening remarks.

Second, limitation on participating countries. My colleagues have spoken directly to that.

Third, limitation on the types of drugs covered. At least in the Vitter-Salazar bill, we are not talking about drugs requiring refrigeration. We are not talking about drugs requiring biotechnology

processes or photoreactive drugs or intravenously injected drugs or inhaled drugs during surgery or bioequivalents.

Fourth, major safeguards against adulteration and misbranding. As my colleagues have said, we are talking about asking, or requiring these importers to meet the very same FDA safety and efficacy standards as drugs currently sold in this country.

Fifth, unannounced inspections of foreign sellers, completely unannounced and random.

Sixth, registration requirements for importers so that domestic entities that will distribute drugs directly to American consumers would have to provide information to the FDA to ensure safety.

Seventh, registration requirements for foreign sellers.

And eighth, a catch-all safety provision in the Vitter-Salazar bill to give the FDA significant very broad authority to do whatever it determines is necessary to protect all of these safety concerns.

Let me end on one final topic, and that is something I feel strongly about. Drug importation should not be limited to Canada. Canada's methods of ensuring the safety of prescription drugs are comparable to those of the United States, and so we clearly should allow that importation from Canada. Our own GAO in June 2004 found very few problems with prescription drugs obtained from Canadian Web sites. But I do feel it would be a mistake to completely limit the importation program to just one country.

Not long ago, a team of specialists appointed by the Governor of Illinois researched the question of whether Americans can safely and effectively purchase prescription drugs from industrialized countries other than Canada and their findings are described in a significant report issued last summer entitled, "Can Illinois Residents and Businesses Safely and Effectively Purchase Prescription Drugs From Europe?" The authors of this major report concluded that it is both possible and desirable to allow these purchases from approved facilities in Europe. Again, as my colleagues have pointed out, we are talking about industrialized countries with a pharmaceutical infrastructure comparable in every way to that of the United States.

In closing, Mr. Chairman and members, let me say that this issue is not a conservative or liberal issue. It is not a Democratic or Republican issue. It is a universal issue, a challenge to provide our Nation's consumers access to safe and affordable drugs. That is why I have worked to assemble a coalition of Senators and Representatives from across the political spectrum in support of this, and that is why I also strongly support the efforts of my colleagues on the Dorgan-Snowe approach.

I look forward to working with all of my new Senate colleagues to advance this very important cause, and, of course, my door is always open to those who want to join our effort or who have any other ideas of how we can do this safe and effectively and bring prices down for all American consumers.

Thank you very much, Mr. Chairman.

The CHAIRMAN. Thank you.

I want to thank all of you for your testimony. I share your concern, and I am sure everyone does, for the high cost of health care in this country. I appreciate how much work all of you have put

in on this issue and even did some research on prior work that you have done on this issue.

In one of the previous hearings, on the reports that we received, one of the concerns was that, yes, it will save money, but the cost of providing the protection will cost as much money as what will be saved. Now, it is a cost shifting because it would be the United States picking up the cost of doing the checking as opposed to the people buying the imported drugs.

But a number of States have started outlining some pilot projects where they would take the responsibility on the importation of the drugs, and in fact, I want to commend you, Senator Dorgan, for a thoughtful proposal that you made to Secretary Thompson just last year, the Prairie Prescriptions Pilot Project. Your idea was a 2-year importation project that would allow pharmacists and wholesalers in North Dakota to purchase FDA-approved prescription drugs from licensed Canadian pharmacies and wholesalers.

Now, I know some other States have also petitioned HHS to do similar projects. I think Vermont, Oregon, and Illinois have done so, though your proposal was the most detailed of any that I read. I like the idea of having States work together with the FDA on a limited basis at first. Then we can see what kind of problems there would be, kind of as a local laboratory as opposed to a national laboratory. I would ask if you would be willing to work with me to create a proposal that would permit your Prairie Prescriptions Project and others like it.

Senator DORGAN. Mr. Chairman, I proposed that only because we were unable to make any progress with the Administration on a broader approach. In fact, I believe I am still waiting for a response from Secretary Thompson down at HHS. He is, of course, long gone. But I went down and made a presentation to the Secretary and to the Surgeon General and they indicated they would be making a formal response. I have yet to receive that formal response.

My goal would be to have an action by the Congress that broadly allows, with proper safeguards, and I think those safeguards are described in our legislation, allows the American people to reimport prescription drugs.

Now, if, for example, the Congress, if there are votes in the Congress and the President would veto a bill and we are stymied and stopped dead in our tracks, would I then agree to some pilot project or pilot program? Yes. Yes, I would. But that is not the case. I believe we have the votes to pass this legislation in the House and in the Senate. I believe when presented to the President—he has not yet been presented with legislation of this type—I think he would be hard-pressed to veto it.

So my feeling is that we ought to proceed. This hearing is an important first step. Let us proceed to move these kinds of plans or some derivation of these plans to the floor of the Senate, get a vote, do the same in the House, and get a bill to the President, and I believe the consumers would be advantaged by that all across America.

The CHAIRMAN. I just wanted to comment that your Prairie Prescriptions Project is even more detailed than what you have in your bill and, I think, provides some safeguards that aren't in the bill.

But my question for the panel, when commercial importation is legalized, who would bear the legal liability if the patient was injured by imported drugs? Would it be the manufacturers or the wholesalers or the pharmacies or the pharmacists, Internet providers, or does no one bear the liability? If it is a foreign wholesaler, pharmacy, or pharmacist, how would that liability be enforced for patients in the United States?

Senator DORGAN. Well, the premise of that question, the premise of the allegations by some that there would be prescription drugs imported that were less safe and less effective than prescription drugs now taken by the American people is just a false premise, in my judgment. The drugs under the bipartisan bill that we have described will have to meet exactly the same standards of safety and effectiveness because importers will have to document the chain of custody from the point of manufacture to the drug store itself. That, in fact, is a requirement that drugs sold domestically in the United States do not even now meet. So I think the proposition that there is some liability issue that is extraordinary or above that which now exists is not accurate.

Senator STABENOW. Mr. Chairman, if I might just say, one question I would have is who is responsible now? Lipitor is made in Ireland. We send FDA inspectors there to inspect the plant. There is a closed supply chain. It comes back to this country. Who is responsible in terms of liability now for a product, as for example, made in Ireland?

From my perspective, the legislation that we have does more to protect people than current law because I am concerned about Internet pharmacies. There is a lot of attempt to confuse Internet pharmacies with what we are talking about, the pharmacy being able to do business with another pharmacy. Right now, I think it is possible for someone to go to the Internet, not to know where the drugs are coming from.

And, in fact, we need to fix that and this legislation would go a long way to address really what is happening for people right now out of desperation. I mean, I know people that are doing things that are not as safe as they should be out of desperation because we can't—we aren't acting. We aren't giving them a safe alternative, and that is what this legislation would do.

The CHAIRMAN. Of course, with the legislation we are actually opening it up considerably. I know we had the chart that showed the importation from other countries, but that is the manufacture, manufacturing it in the other country, sending it to the United States to their own entity and then having a distribution system from here in the United States, which more clearly defines the liability situation.

My time has expired.

Senator Murray.

OPENING STATEMENT OF SENATOR MURRAY

Senator MURRAY. Mr. Chairman, thank you very much. Thank you for the hearing and thank all of you for testifying today.

I think all of us recognize that the cost of drugs in this country is a real challenge and I think you are looking at one way to deal with that. I would hope at some point we look at how we lower

costs here in the United States with the drugs that are made and sold here in the United States.

I do have a couple of questions. I think that all of us are really concerned about safety. We all want prices reduced. We all want safety to be a consideration. It seems to me that part of what we have to recognize with reimportation is the new burdens on FDA to make sure that we have safety as a strong consideration. None of us want a point where we can't trust our own systems.

Is there anything within the bill that if we are unable to realize the costs for FDA, if the new user fees are not sufficient or not allocated by Congress, that there will be any suspending of the reimportation, or will it just be a cost to FDA that they will have to find from somewhere else if the real costs don't become realized?

Senator SNOWE. Based on our estimates and everything that we have gotten for information, we think that it will. I don't think that—obviously, we would want to adjust that if that was not the case with the 1 percent of the value of imported drugs wasn't sufficient to accommodate the resources. But from what we expect—even like Canadian pharmacies, I mean, the appropriate based on that alone would be $200,000 per Canadian pharmacist for inspections, monitoring, and everything else. We think that it is pretty generous in that sense in covering the cost of this legislation, but obviously, that can be adjusted based on the estimates. But we think it is pretty well covered.

Senator MURRAY. I think it is an important consideration, because as we have seen with the medical device user fee, if the funds aren't appropriated or allocated or sufficient, it does create problems, so I just want to make sure that we are aware of that and hopefully——

Senator SNOWE. Hopefully, the former Commissioner, David Kessler, will be testifying to these points, as well, and he has indicated that it is, but we would certainly welcome any additional input if someone suggested it wouldn't be the case. I mean, we would be raising $1 billion from importers and $1 billion from exporters in 2006 alone under this legislation.

Senator MURRAY. Thank you, Mr. Chairman.

The CHAIRMAN. Thank you.

Senator Gregg.

OPENING STATEMENT OF SENATOR GREGG

Senator GREGG. Thank you, Mr. Chairman. This is a complicated issue. Although it has been postured in political terms, the practical implications are whether or not people will be benefitted by it through purchasing drugs which will help them. If you buy a pill, you want it to cure you, not kill you. The essence of our system in this country has been that the FDA has protected Americans. You walk into a pharmacy. You expect to get a drug that is going to be good. And we have a system that works, and when you open it up to the world for people to purchase from, you want to make sure that people buying from wherever, whether it is Canada or Greece or Portugal or Luxembourg, that the pill they purchase will cure them and not kill them.

And thus, to step into this area requires that we make sure that we do it correctly, and that is why I have some very serious res-

ervations about the bill that is sponsored by Senator Dorgan and Senator Snowe, especially. The problem I have, I guess, with your bill is—well, there are a variety of issues. I will submit for the record about 20 pages of specific representations as to how the bill specifically changes the present FDA regime.

Senator Dorgan has represented that the safety issues will be the same standards of safe and effectiveness that presently the FDA pursues, which is not, in my opinion, accurate. In fact, under the bill, you essentially replace Section 501, which deals with adulteration, Section 502, which deals with labeling, Section 506, which deals with manufacturing standards, and Section 505, which deals with clinical examinations, with a brand new regime. You have got about 40 pages. The essence of that regime that you set up is something called manufacturing changes. It is a new term, new definitional term. It is what the FDA is to look to relative to its standards.

So I would ask you, Senator Snowe, what does manufacturing changes mean in Section 506, as it applies to Section 506?

Senator SNOWE. I think the point is I would expect, first of all, that there would be a change in regimes because obviously the current system isn't working. I mean, even with respect to——

Senator GREGG. So you don't subscribe to Senator Dorgan's view that your safety and efficacy standards are the same as the FDA presently has for American drugs?

Senator SNOWE. Well, yes, but yes, but we are also talking about creating a higher standard in this legislation.

Senator GREGG. And is that defined by manufacturing changes?

Senator SNOWE. Obviously, we wouldn't expect——

Senator GREGG. Is there any chance you are going to answer the question, Senator? What is the definition of manufacturing changes? What is its implication?

Senator SNOWE. The implication is to make sure that we have the highest standard.

Senator GREGG. What is manufacturing changes, Senator?

Senator SNOWE. What?

Senator GREGG. What are manufacturing changes? This is your new standard. This is the standard which changes Section 501, Section 505. These are critical issues for the consumers of America. You are setting up a new standard. What is manufacturing changes? What does the FDA mean?

Senator SNOWE [continuing]. Have an inspection and FDA-approved and FDA-inspected medications. Frankly, Senator Gregg, we send men and women to space every day. We cannot figure this out? I mean, seriously.

Senator GREGG. Senator——

Senator SNOWE. FDA-approved and——

Senator GREGG. Senator, I am reclaiming my time.

Senator SNOWE. Well, what——

Senator GREGG. You are obviously not going to answer the question.

Senator SNOWE. I am answering the question, but you don't like the answer.

Senator GREGG. No, you are not.

Senator SNOWE. I mean, the point——

Senator GREGG. Senator, manufacturing changes, just explain to us what the FDA is looking to under this new standard.

Senator SNOWE. Manufacturing changes is establishing a new standard, because it is a new regime. It is a new process——

Senator GREGG. And what is the standard?

Senator SNOWE [continuing]. Because we are not importing, which is to be approved and inspected, registered, and monitored. That is what it is all about. And so——

Senator GREGG. Actually, Senator, it is inspected, not approved.

Senator SNOWE. Let me just say one other point here, because I think that we need to understand what we are dealing with in terms of reality——

Senator GREGG. All I want to understand is how you are going to change the FDA rules.

Senator SNOWE. Well, I am. I am trying to explain the realities, because in explaining the rules, because they obviously do need to be changed. I mean, we are creating a new regime to begin with because it isn't allowed. We do——

Senator GREGG. I am going to reclaim my time, Senator, because——

Senator SNOWE. Well, can I just make one point?

Senator GREGG. No, Senator. Let me reclaim my time. It is my time, Senator. I only have 5 minutes. You had your 5 minutes. Let me point out the problem here. There is a manufacturing facility in India, hypothetically. That manufacturing facility under your proposal ships a product to Portugal, ships a product to Luxembourg, ships a product to Italy. That product is then transshipped to the United States.

There is no requirement in your bill—in fact, it is basically replaced that that product be subject to clinical review in one or more clinical investigations. All that is required in your bill is that that facility had been inspected in India. It doesn't even require in your bill that that facility be approved, just inspected. In fact, the FDA could go into that facility under your new standard, look at that facility and determine that the vats weren't at the right temperature, that the binding agents were different and might cause problems, that the labeling process was inaccurate, and the approval process would not be conditioned—the inspection process would not be conditioned on an approval which would be effective against that facility. In other words, the FDA would have no enforcement capability against that facility compared to present law.

In addition, if the product came to the United States and created harm, the question has been asked by the Chairman, who would be liable? That Indian facility would not necessarily be liable under your bill. Your bill has taken 100 years of law under 501, 100 years of law under 502, and a significant amount of history under 506 and 505 and essentially replaced it with 40 pages of new regulation which you won't explain because you don't have an explanation for it. "Manufacturing changes" is not a standard of health care in this country which the FDA understands or recognizes.

And the simple fact is that if you want to create a brand new regime, you say you want to create a brand new regime, you are going to put a lot of people at risk in this country. You are creating

a Russian roulette regime for the American consumer in the name of politics, and that is the difference we have on this issue.

Senator DORGAN. Mr. Chairman, would you let me respond to his questions?

The CHAIRMAN. The Senator's time has expired.

Senator DORGAN. Mr. Chairman, does he want a response to the questions that he has asked?

Senator GREGG. I will be happy to take response, and then I would like to respond to your response, but I don't suspect this panel wants to pursue that in that framework. But we are going to have plenty of time to discuss this in significant depth.

Senator DORGAN. Well, this would be a good time to have plenty of time, wouldn't it?

Senator GREGG. It certainly would be. I would be happy to pursue it right now.

Senator DORGAN. Mr. Chairman, if this is the time, then let us go ahead and discuss this.

The CHAIRMAN. I will hear your response and then the Senator's response.

Senator DORGAN. Mr. Chairman, first of all, let me commend the Senator for 20 pages of questions. That is some amount of homework for a Senator. But I appreciate——

Senator GREGG. I didn't say I had 20 pages of questions. I have 20 pages of points as to the problems——

Senator DORGAN. It is still a great deal of homework——

Senator GREGG [continuing]. As to the difference with your bill——

Senator DORGAN. It is still a great deal of homework and I admire that.

Senator GREGG. You represent that your bill is exactly the same as the standards of safety and effectiveness.

Senator DORGAN. Mr. Chairman, did you recognize me at this point?

Senator GREGG. No, he is not recognized to—he is recognized to respond to my questions.

The CHAIRMAN. It is part of his time, the Senator from North Dakota.

Senator DORGAN. Mr. Chairman, I will wait until it is appropriate for the responses to the questions that have been posed by Senator Gregg.

The CHAIRMAN. The Senator from North Dakota.

Senator DORGAN. Well, first of all, I was attempting to compliment the Senator for the amount of work that he has done here. I must say that the description of the Senator misses a couple of key points.

Number one, we are talking about a closed system and only FDA-approved drugs approved in an FDA-approved facility. So that is not any different than what now exists with respect to prescription drugs that the Senator from New Hampshire may take this evening or tomorrow morning, if he takes prescription drugs. He purchased them at a pharmacy and they may come from anyplace in the world and they will be FDA-approved drugs made in an FDA-approved facility. So this is a closed system. We don't propose to change any of that.

But with respect to the standards issues, if a manufacturer decides, for example, well, there is a way around all of this. What we will simply do is we will change the color of the prescription drug. We will make some slight difference, slight change in the drug in a way to claim that it is a different drug. If we simply give the FDA the authority to take a look at that and decide whether that difference is germane and important or whether it is an irrelevant difference and that drug still should be able to be sold to a consumer. If a difference in a drug causes a difference in the bioequivalence, the FDA would apply the exact same standards for approval as it already applies to drug manufacturers that want to make a change to a previously approved prescription drug.

That is what this is about. Look, I respect differences of opinion. I understand the Senator feels very strongly about this. But I must say, this is a circumstance where we are talking about a closed system of FDA-approved drugs produced from FDA-approved facilities, sold to an American consumer in a closed system, and that is all it is.

Senator GREGG. Mr. Chairman, let me respond to the incomplete response by the Senator, because the point I was making was that it is not the same system. You have replaced the system that the FDA presently uses for approving drugs in this country with a brand new set of standards, a brand new set of standards. You have replaced 501. You have replaced 502. And you have replaced the requirements under 505, and 506, for that matter.

And these new standards appear to be linchpinned off something called "manufacturing change," which the FDA is supposed to look at, and I don't know what that means and the FDA doesn't know what it means. I was hoping you would know what it means, because it is going to have a huge impact on the safety of drugs coming into this country.

The simple fact is that you cannot create a new set of standards for drugs coming into this country simply because they are reimported versus drugs which are traditionally sold in this country under a—through a closed system, which is what you are doing.

Why do you have 20 pages of new legislation replacing the 501 section and the 502 section? Why do we have a new standard which replaces the ability of the FDA to review these drugs before they reach the market? Under your bill, a drug could be on the market in the United States through reimportation and the FDA would still be investigating whether or not the labeling is correct, the binding is correct, and the coloring is correct.

Senator SNOWE. That is not——

Senator DORGAN. That is not accurate, Senator.

Senator GREGG. That is correct.

Senator SNOWE. Mr. Chairman.

Senator GREGG. In addition, why do you say to the facility, it has to be inspected and not approved in the foreign country?

So if we are going to continue this discussion, explain to me the definition of manufacturing change, and if I am inaccurate on this issue of whether or not a drug can be on the market here in the United States and have received a complaint about labeling, coloring, and binding agencies prior to the FDA having made the decision as to whether or not labeling, coloring, and binding is correct,

it can be sold here, and that could happen under your reimportation. And second and third, whether or not the facility in the foreign country has to be not only inspected, but actually approved by the FDA.

The CHAIRMAN. The Senator's time has expired——

Senator SNOWE. But can I just answer?

The CHAIRMAN. The purpose of a hearing is to gather as much information as possible. It doesn't all have to be said in the meeting. So all of you will be allowed to expand on your comments. Full testimony will be in the record as well as the oral comments that you made——

Senator SNOWE. Mr. Chairman——

The CHAIRMAN [continuing]. But I have other people that have been here quite a while that deserve a chance to ask their questions, so Senator Isakson.

Senator ISAKSON. Thank you, Mr. Chairman.

Senator Dorgan, in your first part of your remarks, you made a comment, and I was making notes here, so if I missed it, you can correct me, but you said in the United States, the pharmaceutical companies set the U.S. price. Forgetting about—assuming your—I don't want to get into what we just got out of, but assuming that your inspection procedure and approval procedure is identically the same as it is today, isn't all you are doing here is turning over the control of the price of U.S. pharmaceuticals to another country, in particular, Canada? And if that is the case, why don't you just set up price controls in the United States?

If you assume your inspection, safety, and security are equivalent to what they are today, and that is not an argument which I am not saying is or isn't true, I just don't want to get him stirred up again—[Laughter.]—then isn't it true—then why not just establish price controls in the United States rather than, in effect, abdicating them to Canada?

Senator DORGAN. Senator Isakson, in the global economy, when you import anything, you import all of these circumstances of that production in the country from which it is imported. If you happen to be wearing a Chinese silk tie, you may well be paying this morning for the retirement costs of Zung Zu Minh and the Communist government of China, but that is the way the global system works.

So if you are asking the question, if we import a prescription drug from Canada, are we importing price controls? No. We are importing a prescription drug from Canada.

Senator ISAKSON. That has price controls.

Senator DORGAN. Canada does have price controls, absolutely. If we import a prescription drug from Germany or Italy or Spain or England, we will import whatever the circumstances exist there. It is the case, I am sure, however, that the pharmaceutical industry sells in all of these countries because they make a profit under whatever pricing scheme they develop in those countries, at least relative to the laws that exist in that country.

Senator ISAKSON. My only point on that is this, that a necktie won't kill you unless you tie it awfully tight—[Laughter.]—but a bad pharmaceutical will, and there is a lot of difference between neckties and pharmaceuticals. And I do think the question is a valid question. But, I am not taking a side right now. I am trying

to make a point, that if you wipe out all this other stuff we were talking about, you are advocating price controls to another country versus being for price controls in the United States.

My second question is to Ms. Stabenow from Michigan. You made a statement that we are giving Americans a false choice of higher costs in return for safer and newer drugs. Don't you believe that there is some value to recovery of R&D and incentives on that to develop drugs versus being in a stagnant situation where you don't have that incentive?

Senator STABENOW. Absolutely, Senator——

Senator ISAKSON. Then why is that a false choice?

Senator STABENOW [continuing]. What I am saying is that what we hear from the other side is that somehow to lower price means that we won't have research, where, in fact, we know that the industry is spending much, much more on advertising and marketing today than they are on research and that all you have to do is turn on your television set and you see it.

And in addition to that, we as taxpayers in America are spending close to $30 billion this last year for basic research that we then give to the companies at no charge because it is so important that they continue to develop these breakthrough drugs.

So this is just already something that American taxpayers are helping to pay for, and yet we, in return for doing that and all the tax credits and incentives, which I support, the gift that we get back are the highest prices in the world. It is not a good deal.

Senator VITTER. Senator, could I respond very quickly, too, to the two questions——

Senator ISAKSON. Quickly.

Senator VITTER [continuing]. Because this goes to the heart of this issue. I only speak for myself. I am strongly for these proposals not because I want to support and import price control, but because I believe if we establish a true worldwide free market through measures like this, we will break down disparate pricing around the world and make it extremely difficult to have these different pricing regimes, including old-fashioned price control regimes. That is why I am for this proposal, to break through that disparate global pricing and to make it difficult or impossible for other countries to do what they are doing now, which is to push all of their R&D costs onto us and us alone as American consumers.

Senator ISAKSON. That is a noble goal, because my question is rooted in my serious concern that we have abdicated to our country the total responsibility for pharmaceutical development and breakthrough, and yet putting a disincentive on the entire system to turn around and import, in whole or in part, price controls, which is a double-whammy.

Now, since you all abused your time, I am going to abuse mine. I will have to tell you, now, your thing on advertising is right on. I still don't understand all those ads. I don't know if they spend more on ads than they do on R&D, but they spend more on ads than they probably ought to, in my judgment, and it ought to be going into R&D.

But we can't—I am sure your goals are noble. I hope, and Senator Vitter has said it in a very eloquent way, we have to protect what we have in this country in terms of a safe and innovative and

a breakthrough pharmaceutical climate and do so because that is as healthy for our consumers and our constituents as is anything else that we can do. So I just wanted to make that comment and I appreciate David's remark.

I yield, Mr. Chair.

Senator SNOWE. Mr. Chairman.

The CHAIRMAN. Senator Burr.

OPENING STATEMENT OF SENATOR BURR

Senator BURR. Thank you, Mr. Chairman, and I will tell the witnesses I am not going to ask questions. I am going to save them for Dr. Kessler and others later on. I just want to make a statement for the propose of my colleagues.

In 1997, we passed the Food and Drug Modernization Act. I was one of the co-authors of that legislation. I worked with Dr. Kessler on it. Details do matter. Details are important as it relates to how we instruct the FDA to proceed, all the way down to the smallest details. I can remember months in a room with FDA officials and the wrong word implies something different.

Let me just share with everybody the titles that Judd Gregg was just talking about. Section 501, Adulterated Drugs and Devices. Section 502, Misbranded Drugs and Devices. Section 505, New Drugs. Section 506, Fast–Track Products. This is an extremely delicate area that we talk about the potential of a wholesale change, all in the quest of trying to reimport drugs.

I am not here raising questions about it. I think that working with individuals at the FDA, with staff on the Hill looking at specific language, working with each other, trying to both know what the impact of any change, even just a change in words—I mean, if this were so easy, the United States of America would have harmonized our drug laws with the E.U. already.

And the fact is, we found out we couldn't do it because we couldn't accept their standards and we wouldn't accept the paper trail that existed between E.U. countries. And I won't name any of the countries in the E.U., but there are some that the standard—it is so low that I am sure that if they weren't part of a group, nobody would accept it. But we are here talking about us accepting it. And if, in fact, this body or any body accepted legislation that put us on that pathway, then we had better make sure that we have minimized the effects on the American people.

I believe to suggest to do this is, in fact, to bring a higher level of safety is misguided. But I do appreciate the time that all of the sponsors have put into it. I am sure that this will receive the debate that I believe it deserves, and I believe at the end of the process, we will not be experts, but we will certainly be smarter for having gone through it. I thank the Chairman.

Senator SNOWE. Mr. Chairman. Mr. Chairman. I will answer—Mr. Chairman.

The CHAIRMAN. Did the Senator ask the question?

Senator BURR. I yielded back.

The CHAIRMAN. He yielded back his time.

Senator SNOWE. Mr. Chairman, could I just answer a question, because I really didn't have the opportunity to respond and I think it is important before we depart that certain misrepresentations do

not occur with respect to our legislation. We may have differences on the legislative language, and that is legitimate. Agencies have been doing that for centuries. I don't think there is any question. But we have put a great deal of time and input in drafting this legislation for a very serious approach.

Now, you may have differences over the language, but first and foremost, understand that the European Union has comparatively the same regulatory standards as we do in America. What I was showing you in my earlier display were countries where we import drugs today that are used by Americans from countries that have lower standards, and I think that is important to indicate.

Now, to the question that Senator Gregg was raising, as Senator Dorgan indicated, we created a different standard for looking at drugs that have changes. It is not replacing the existing standard, but those that may have changes so that there is a system in place. Today, that isn't the case, frankly, and that is what we indicated.

And third, let me just indicate something else. FDA has reduced its factory inspections over the last 20 years. I mentioned that in my earlier statement. They have reduced them from 4,300 in 1980 to 1,600 in 2001. Fewer inspections. That map that I had up here earlier that showed all the countries from which we are importing drugs that have lower standards than the United States, I got that information from the FDA's own report showing that, Mr. Chairman. And on the blue, the European Union and the other countries from which we would import have the same standards as the United States. And we have testimony from the former Secretary General of the European Trade Organization, there has been not one problem in 30 years of parallel trading among the European countries.

So I think it is important to establish that. We may have differences over legislative language and approach. Yes, I would hope we would have a different standard because we have none now on the importation. That is a problem. And so we need change, and hopefully it would be to supercede the status quo and examine any changes in medications coming across the border so that we have a process in place by FDA.

If there is a better suggestion, we welcome it. I think we all would work to welcome change. After 6 years since Senator Dorgan first introduced this legislation, I think America can do better.

The CHAIRMAN. Each of you will have an opportunity to expand on your remarks, and all of the members of the committee, as well. The record will stand open for 10 days and there will be an opportunity for some written questions to also increase it, because I actually have more questions now than when I started on this—

[Laughter.]

And we had a whole series of hearings on the FDA and how they operate and concerns that we have with safety within the present operation and we have about 40 suggestions for how we need to change the FDA, and I am mentally trying to figure out how we work that into the entire world.

I appreciate the effort that you have put into this. We will do something on drug importation. I hope that all of you will work with me on it. The amendment that went on the budget bill was an amendment that I submitted and I appreciate the co-sponsor-

ships of a number of people and the unanimous way in which it passed, and one of the key parts of it was that it would go through regular order in the committee. And, of course, the only way it can go through in regular order in the committee is if we are doing something on it. I will be doing something on it and would like to be doing something on it in conjunction with all of the people that have an interest in importation, including the pharmaceutical companies who probably from today have gotten the message that it would be a good idea to have a little lower prices in the United States.

I thank all of you for being on this panel and we will move to the next panel because we have a vote in just a few minutes and we will have to work around that. Thank you.

If I can have the next panel take their place, we will put some name tags there. I will go ahead with the introductions. While I am doing this, I will ask the panel, who I know have already looked at being able to summarize the information that they have, to concentrate on summarizing the information. We have two votes that will take place at 11:45, which means it will be about 12:30 before we can get anybody back, if we can get anybody back, because that then runs into policy lunches, which is where we get to find out what is going to happen the rest of the week as it affects our lives, so that is usually pretty well attended.

Mr. Graham Satchwell is the Managing Director of Proco Solutions, a consultancy in London, the United Kingdom, specializing in brand protection. Mr. Satchwell is a former detective superintendent and has held senior security executive positions within several global corporations. He has recently published a book, *A Sick Business: Counterfeit Medicines and Organized Crime* on parallel trade, counterfeiting, and diversion of prescription drugs in the E.U. He will discuss the security implications of the list of permitted countries in the Dorgan legislation and how this list may not be sufficient to protect against counterfeiting and diversion of pharmaceuticals destined for the U.S. market under a legalized importation scheme.

Dr. Todd Cecil is the Vice President of Standards Development at the United States Pharmacopeia, or USP. USP is a nonprofit, nongovernmental standard-setting organization that advances public health by ensuring the quality and consistency of medicines, promoting the safe and proper use of medications, and verifying the ingredients in dietary supplements. Mr. Cecil will discuss the qualifying drugs provision in S. 334 which allows imported drugs that are not bioequivalent to be substituted for prescribed U.S. label drugs, potentially with very harmful consequences to the patient.

I will invite Senator Isakson to introduce Mr. Thomas Arthur.

Senator ISAKSON. Thank you, Mr. Chairman. It is a pleasure for me to welcome the Dean of the Emory University School of Law, Dean Thomas Arthur, to be with us today. Dean Arthur graduated from the Yale Law School and from Duke University before coming to Emory and he practiced law for 11 years in Washington, D.C. at Kirkland and Ellis. Dean Arthur teaches antitrust, civil procedure, administrative law at Emory University. He has been pub-

lished in the California Law Review, the Tulane Law Review, and the New York University Law Review.

His testimony today will focus on constitutional, intellectual property, and international law, and having realized we were pressing in time, I read it before hearing it and it is awfully good. I commend it to the Chairman.

The CHAIRMAN. Thank you. I have also read the testimony of all of these people and appreciate it.

Dr. David Kessler is the fourth presenter. He is the Dean and Vice Chancellor for Medical Affairs at the University of California, San Francisco School of Medicine. Before joining UCSF in the fall of 2003, Dr. Kessler had been the Dean of the Yale University School of Medicine since July of 1997. Dr. Kessler served as Commissioner of the United States Food and Drug Administration from November 1990 until March 1997. He was appointed by President Bush and reappointed by President Clinton. Dr. Kessler will discuss the implementation of a safe drug importation system.

Mr. Satchwell, you can begin.

STATEMENT OF GRAHAM SATCHWELL, MANAGING DIRECTOR, PROCO SOLUTIONS, LONDON, UNITED KINGDOM

Mr. SATCHWELL. Mr. Chairman and members of the committee, thank you for inviting me to speak here. As you know, I am trying to give a European perspective on these things.

I would like to say this, though, that——

The CHAIRMAN. I don't believe your microphone is on. Sorry. There is a little button there.

Mr. SATCHWELL. Is that better? Can you hear me now okay? Okay now?

The CHAIRMAN. Thank you.

Mr. SATCHWELL. This morning, there was reference to whether you support pharmaceutical companies or the U.S. public on this issue. I can say that from my perspective, I know there are many patient safety groups in the UK that would be advising you in the way that I would, and clearly, they would not be doing that on behalf of pharmaceutical companies.

There was also reference made this morning to what goes on outside of Europe, and Asia was mentioned in particular. China suffered 100,000 deaths from counterfeit medicines the year before last, and about the same number, I think, last year. There are particular initiatives, major initiatives because of public safety fears going on in the Philippines, India, Thailand, Malaysia, and elsewhere in Asia, and in Africa, it is an endemic problem, as you are probably aware.

Turning back to Europe, the UK receives more, far more parallel traded medicine than any other European country because the prices in the UK are so much higher than elsewhere in Europe. But the U.S.A., by comparison, is an even more attractive market to those who would cheat the parallel trading system. So you would be a prime target, just as the UK is now.

Parallel trade has three great pitfalls. First, it provides a perfect way to smuggle counterfeit product into the legitimate chain.

Second, it necessitates repackaging and there is powerful statistical and anecdotal evidence to show that repacking in itself has caused problems, counterfeiting aside.

Third, parallel trade is particularly difficult to police.

Currently, a UK dealer might receive an unsolicited e-mail from a business elsewhere in Europe offering a drug at a particularly attractive price. The UK dealer should ensure that the seller is licensed and ask for evidence of that. The seller will then fax a document that purports to be a license to conduct that business. That is it. There is no one European body that the British dealer can check with to make sure that that is a bona fide license or not, and the UK regulatory agency doesn't see it as their role to do so. In fact, for the UK dealer to accurately be able to check a license that is faxed from Greece or one of the other many European countries and verify its accuracy would mean that each UK trader would need to speak every European language. It is impossible for a UK dealer—oh, I want to stop here.

There is something I wanted to say right up front, and it is very blunt, forgive me, but Dr. Rost, who has been referred to this morning, is provably wrong in his contentions, provably wrong. I want that to go on the record, please, because it can be supported by regulatory agencies, patient safety groups, my own experiences, and so on. Now I will press on, if I might.

A UK dealer doesn't know where the products in his warehouse have come from. They may purport to have come from Greece, but, in fact, they could have come from India or China, Eastern Europe, or elsewhere. There is just no way of his knowing.

It is extremely easy for anyone to find a foreign party willing to counterfeit medicines. I have done it myself on many occasions. It is very easy. And then present those medicines as genuine—that, of course, I have not done—especially when those medicines are repackaged.

The recent Lipitor case is a perfect example of when you import product that you can also import problems. You know, of course, that the Lipitor matter involved drawing in fake Lipitor from other countries, and you all know better than I where those drugs originated. In the U.S.A., there are already real problems and injuries as a result of counterfeit product despite, the achievements of the FDA.

In relation to what has gone on in Europe and the provable evidence that Mr. Rost is wrong, the FDA, of course, can access that evidence themselves.

Parallel trade in Europe has led to a situation where medicines often change hands more than 20 times in the distribution chain. Parallel trade can make fast and thorough product recall practically impossible.

I agree entirely with Senator Burr that the standards that apply in Europe in relation to regulatory control often leave much to be desired and they are not good. There is not standard good practice across Europe when it comes to regulatory control.

The harm that can be caused by a dishonest exporter of pharmaceuticals is extreme. Proper regulation and enforcement are both needed if parallel trade in medicines is to be safe and a clear dis-

tinction needs to be made between the writing of legislation and the practical enforcement of those regulations.

I can say this. It is clear that some of those who are actively seeking to supply, and indeed are now supplying, the U.S. market are dealing with foreign entities that are, known or unknown to them, at least very questionable. Of that, I have evidence.

Some cases of harm have already been recorded in the UK and in the United States. On record, you have cases that involve organized crime in the UK and organized crime in the United States, and I talked about an explosion in the UK of organized crime. The cases that you will see, in fact, only involve international organized crime and some link the UK to the U.S.A. in that regard.

The UK's National Criminal Intelligence Service recognizes the threat—and has done so for 2 or 3 years—that comes from pharmaceutical counterfeiting, and that is reflected also, actually, in the most recent reports of Interpol. So both Interpol and the UK's own National Criminal Intelligence Service recognize the threats.

There have been cases last year in the UK of Cialis and Reductil both being counterfeited and smuggled into the legitimate chain. The method of getting those products into the innocent hands of distributors in the UK was via parallel trade. In fact, we can go back a number of years. I can go back 7 or 8 years to cases involving parallel trade in Italy, where certain GlaxoSmithKline products were actually counterfeited by members of the Cammora, a Naples crime gang, and then smuggled on more than one occasion into UK for distribution.

So there have been a number of significant cases over the years, but it is true to say that there has been a great deal of reluctance to put those cases into the public eye. I don't know why that is, but they are there on the record if you looked for them.

The CHAIRMAN. Thank you.

[The prepared statement of Mr. Satchwell follows:]

PREPARED STATEMENT OF GRAHAM SATCHWELL

Mr. Chairman and members of the committee, I have been asked to comment on the safety of the drug supply from what has been termed, "permitted countries" (as defined) and whether it is possible, given the experience of parallel trade within the EU, to truly limit importation to these "permitted countries."

I understand that under the Bill importation will be allowed, subject to the importation of drugs to the United States not adversely affecting public health.

Perhaps I should first tell you why I think I have been asked to contribute to this discussion. I have been involved in the business of investigating counterfeiting and other intellectual property crime, and its links to organised crime for many years.

In addition—

- In 2004, on behalf of the Stockholm Network, a European based organisation, I completed the writing of a book entitled "A Sick Business—Counterfeit Medicines & Organised Crime." It has been widely reported upon and Interpol have asked to link it to their Internet site.
- I am a member of UK Government's Patent Office Investigative Strategy Group.
- For several years to 1999, I was the official spokesperson (on counterfeiting of branded goods) for Association of Chief Police Officers (ACPO) England & Wales.
- Prior to leaving the Police Service I received personal thanks from four HMG Ministers. I was a detective superintendent for many years in the UK; those thanks included comments from the UK Trade & Industry Secretary in relation to work in anti-counterfeiting of branded goods.
- During my investigative work I have been officially commended by HM Judges, chief constables, the Director of Public Prosecutions and The Lord Lieutenant of London for successful major investigations.

• I have successfully led international and politically sensitive major corporate investigations into counterfeiting, illegal diversion and fraud including the massive re-importation of anti-retroviral drugs from Africa to Europe.

• I was the chief architect and author of the 1999 UK "Memorandum of Understanding" between all police forces in UK, Customs authorities and other law enforcement agencies, brand-owners and industry groups on the investigation of counterfeiting of branded goods.

• For 3 years I was Director of Security (Europe, Middle East & Africa) for GlaxoSmithKline and took the lead on anti-counterfeiting and unlawful diversion.

• Three years ago I created and led an anti-counterfeiting investigative forum in Europe involving the world's leading pharmaceutical companies.

• Between 1994 & 1999 I was the Metropolitan Police "Joint Action Group" leader in relation to counterfeiting of branded goods.

• I am currently providing both anti-counterfeiting and diversion strategic input and operational results to several major corporations and doing research into these subjects for another book on the same subject.

• I have had items published on counterfeiting, diversion and other crime issues in UK and U.S.A.

I should also mention that I am an Honours Law Graduate.

It is about 10 years since the first case involving counterfeit pharmaceuticals came my way. I have specialised in that area for the last 4 years.

It was about 3 years ago that I first developed an interest in the supplies of pharmaceutical products being advertised on the Internet and purporting to come from Canada primarily to serve the U.S market.

I would like to preface my comments by saying that I am in favour of parallel trade. It seems to me right and fair that those who suffer from the highest prices (U.S.A. and Northern Europe) should be able to enter into free-trade with those in less developed countries, to the benefit of both parties and as a result of the differentiation in pricing structures which are imposed.

However, it seems to me to be abundantly clear that in matters such as medicine, special care needs to be taken. It is one thing to buy substandard footwear but quite another to take substandard and potentially life-threatening or life-damaging medicines.

I have read from time to time comments such as, "it can be difficult for the layman to identify counterfeit drugs" or "it would need a trained doctor to examine the package to know whether the drugs were genuine." Such comments completely miss the point and show a lack of experience in handling counterfeit medicines.

The truth is that counterfeit medicines often appear so like the genuine product that no one, not the best specialist can tell the genuine packaging from the counterfeit. And no one, not the best specialist can tell the genuine product from the counterfeit unless the product is subjected to chemical analysis. The result is that everyone, poor, ignorant, rich and smart, all are at risk from counterfeit or substandard products—and they probably won't recognise them when they and if they see them.

Counterfeiters and dealers in substandard medicines do not target particular medicines that we might call "life-style drugs" (such as "erectile dysfunction," or "slimming" products or "steroids") they simply act in their own best commercial interests—they target big selling drugs. A little research into the proportion of the world's top selling drugs illustrates the point perfectly—most have been counterfeited. The threat is therefore neither restricted to those of a certain income, intelligence, nor illness suffered.

The Internet provides an unstoppable market that can, and is, taken advantage of by private and commercial purchasers of firearms, narcotics, pornography, fraudulent deals and all sorts of consumer goods. It cannot be stopped nor easily regulated. Governments make increasing resources available to control the adverse elements of online trading and given that individuals in the U.S.A., UK and elsewhere will buy access to goods and services that are harmful to themselves and others, it is apparent that the Internet market needs to be regulated like any conventional one. Of course such regulation must be commensurate with the level of harm that the particular transaction could be expected to cause.

I have read the draft bill and there are many aspects that I am not competent to comment upon. However, I notice that an important distinction is made between the private individual buyer and the commercial importer; the former risks harming himself, the latter risks harming many others. It seems obvious that regulations on business-to-business transactions should be much more tightly controlled. Thus it is surprising that S. 334 attempts to build a regulatory framework for commercial drug importation via domestic importers and their contracts with foreign companies.

You have invited my specific comments on the safety of the drug supply from those "permitted" countries and whether it is possible, given parallel trade within

the EU, to truly limit importation to these "permitted countries." Based on my experience, I have concluded that the regulatory framework as described in this proposal will not afford your citizens the protections they currently enjoy. As it stands, S. 334 does not afford confidence that a drug from a "permitted country" will have originated there or have been subject to appropriate regulation.

It seems to me that there are two particular issues that this committee will be considering that I might be able to assist with; the experience gained from parallel train of medicines within the Europe Community; and second, what this experience tells us about how the supply from countries outside of the EEC impacts on this more highly regulated community.

The UK now receives some 140 million parallel traded medicines per annum. This is more than 20 percent of the entire consumption of the British National Health Service. The UK receives much more parallel traded product than any other European country; the reason is obvious—the UK is an expensive market in which parallel traded goods offer the best return for any European importer.

Have there been any problems as a result of this trade? There have been many, and there is now a growing awareness of their significance. Currently the UK Serious Fraud Office (A British Government Agency) is conducting a truly massive investigation into the activities of those responsible for the sale of generics to the UK National Health Service, some of those are involved in parallel trade.

The MHRA has recently admitted a problem with counterfeit medicines. Parallel traded medicines are a proven method of introducing counterfeit and other substandard medicines into the distribution chain.

The difficulties surrounding parallel trade arise as a result of several factors:

• The very necessary requirements that medicines marketed in Britain must be packaged in the English language and contain a patient information leaflet in English language—the repackaging of branded goods that follows that requirement (Parallel traded goods will be printed in Spanish or Greek or other language).

• Repackaging standards are not uniformly high and Patient Safety Groups in UK provide many examples of patients being dispensed medicines that "don't look right" or have accompanying patient information that is incomplete, dangerously translated or otherwise different in effect.

• Repackaging is often conducted in the exporting country or some intermediate country. In such cases the UK regulators are blind to the conditions under which these processes are conducted.

• Repackaging is labour intensive. It is often not a mechanised process. The result is that repackaging is often done in those countries with the cheapest labour. It is just such countries of course that often cannot afford proper regulatory control, spend least on hygiene, and frankly, worry least about U.S. or UK concerns.

• Wrappings are taken off, blister packs emptied by hand or cut up (A month's supply in Continental Europe is usually 30 days worth, in UK a month's supply is 28 days worth, traders regularly manually remove 2 days supply from each 30 and put them by to create further packs).

• One survey in 2004 revealed that of 300 parallel traded medicines examined, 25 percent should have failed on "safety reasons," 50 percent because of poor quality of product. In addition, 80 percent failed on legal grounds such as IPR infringement.

• Part of the repackaging process involves the removal of the product from the brand owners packaging including batch numbering and anti-counterfeiting features. This in itself provides an ideal opportunity for sub-standard medicine, counterfeit or otherwise to enter the chain.

• Of course much parallel trade and repackaging is conducted in properly, according to the law. However, in reality, those who choose to buy out of date, counterfeit or otherwise substandard medicines and to have them repackaged or stored in totally inappropriate conditions, can do so in Europe with very low risk of detection.

• One potential risk that has not been adequately researched on either side of the Atlantic, is the potential for counterfeiters to copy lawfully repackaged product. This is a low cost and perhaps the most anonymous method of introducing counterfeit in the chain with lowest risk of detection.

Another very serious concern is to establish that drugs have been distributed legitimately from verified sources.

First and foremost, how can a parallel trader trust the *bona fides* of the trader from whom he purchased his product? If a UK parallel trader wishes to buy from another European dealer then he must first ensure that that foreign dealer is licensed within his own country. The mechanism for doing so is sloppy. It is not sloppy only in UK but elsewhere in Europe.

Currently the UK dealer might receive an unsolicited e-mail from a business which advertises a particular drug at an attractive price. The UK dealer might e-mail back and a price be agreed. The UK dealer should then ensure that the seller

is licensed. He will therefore ask for evidence from the seller. The seller will then fax or post a document that purports to be a licence to conduct such trade. There is no one European body with which the UK dealer can verify his sellers' credentials, and the UK regulatory authority do not see it as their duty.

It should be no surprise that this is seen as something of a loophole. It is impossible for a UK dealer to be aware of the origin of the product in his warehouse. He might have been told that it originated from Greece, but in Greece it could easily have been repackaged from India or Pakistan or China.

In the course of my work I have myself negotiated to buy counterfeit medicines from China, Germany, Poland, India, Pakistan and other countries. It is extremely easy for anyone to find a foreign party willing to counterfeit medicines (without active ingredients) and present those medicines in packaging that will easily pass as genuine.

This is not hypothetical. There have been well-publicised cases in U.S.A. and UK to illustrate the point. In the U.S.A. the recent Lipitor case is but one example amongst many. You will recall that one of the several defendants in that case was a convicted cocaine dealer. Parallel trade in its current form provides ideal opportunities for the unscrupulous. In the UK in 2004 there were several counterfeiting cases but the most informative were those involving the medicines Reductil and Cialis. Counterfeited products entered the legitimate distribution chain in Holland and were shipped to UK dealers for onward sale into the (innocent) market.

Parallel trade in Europe has led to a situation where medicines often change hands more than 20 times before reaching the dispensary. They are manufactured in one country, shipped to the country in which they were intended to be marketed, bought and sold from there by wholesalers and then into the parallel trade market where they typically pass through many hands into the more expensive markets and then frequently moved on again.

No doubt the creation and use of such a long distribution chain is often in itself innocent, but it makes product recall extremely difficult; the manufacturer and regulatory authorities do not and cannot know where the relevant batch is. In addition, such long and convoluted distribution exposes medicines to the increased likelihood of inappropriate storage, provides anonymity for those at the top of the chain, and gives an easy excuse for those downstream should the goods prove substandard (they claim not to know of their origin and movements).

Product recall is of course a vital patient safety issue. In the UK it is currently not working properly and I have no reason to think that things are much better elsewhere in Europe. Apart from the problems that arise from repackaging, we simply do not have a system that can cope with having so many different bodies holding medicines from so many other bodies. Currently, if there is a product recall then a notice is faxed by the MHRA to amongst others primary health trusts, to those listed as having imported the batch if indeed it is a batch rather than whole product issue. However, the overwhelming number of wholesalers and parallel traders are not advised. In a very fluid market such as has been created in pharmaceuticals, this means that those who are in possession of what has become "unsaleable" stock are able, innocently or otherwise, to sell it forward to innocent recipients. Following a product recall in UK last year, incidents occurred where chemists attempted to sell products that had been subject to official recall.

Like any profession, lawyer, policeman, stevedore, parallel trader, there is a dishonest element. The harm that can be caused by a dishonest importer of pharmaceuticals is extreme. Proper regulation and enforcement are both needed if parallel trade in medicines is to be safe. But a clear distinction needs to be made between the writing of legislation (and regulations) and the practical enforcement of the same.

In the UK there are adequate regulations, these are more or less mirrored across the E.U. However, the matter of enforcement of those regulations is another matter. It must be extremely difficult to adequately "police" parallel trade, and the movement of such products within the UK, when the number of licences issued has increased tenfold in 10 years (from 300 to 3000) without any corresponding increase in staff. It currently takes about 18 months to obtain a parallel trade licence. You can imagine the opportunity that this small regulatory agency has to conduct audits on premises (without notice).

Your much larger country will I believe, because of the attractiveness of the U.S. market (both size and cost), face an even more formidable challenge. Without a good number of regulators and inspectors on European soil, it is impossible to conclude that the United States will be able to do any meaningful verifications of drug pedigree, much less in Japan, Australia, New Zealand, or other "permitted countries."

Before the commercial importation is permitted, I strongly urge you to weigh your confidence that you have created and funded a system that not only provides ade-

quate measures to restrict the type of person who can be involved in the supply of those drugs, restricts involvement of particular businesses (by providing criteria for licensing and minimum operating standards), the country of origin of drugs, but also provides adequate inspection and enforcement provisions. Simply relying on the fact that the drugs have come from a European (or permitted country) dealer will not do that.

There is of course great difficulty in relation to enforcement. Importers in U.S.A., should they receive counterfeit or substandard product will no doubt (honestly or otherwise) claim that they had no idea that the goods were other than genuine. It will be for the public authorities to show a guilty mind. The same defence will be offered by those who export from abroad, out of reach of U.S. regulators. Reliance on the law of contract will only extend to "parties to the contract." That is hardly sufficient within a complex and lengthy distribution chain, abroad.

In many countries, including the UK, the involvement of major law enforcement agencies (as opposed to regulatory ones) is something that can be achieved—though it has been only rarely and invariably after the fact. The setting up of thorough investigations after counterfeiting incidents is not a satisfactory means to protect public health, neither will the law of contract (with foreign companies) enforce public safety in the U.S.A. Stronger measures are needed to prevent counterfeiting incidents.

Of course it is impossible to consider the issue of S. 334 without thinking about "Online" sales from Canada. It is a vital experience upon which to call. The opportunities to make a fast buck from the Canadian online pharmaceutical business were quickly pursued by both legitimate businessmen and others. More than 2 years ago advertisements were placed on the Web purporting to come from Canada and yet when drugs were ordered they frequently came from Malaysia, Vanuatu or Eastern Europe. Rates of counterfeiting in such places are high, but that aside, the likelihood of drugs being time-expired or incorrectly stored are extremely high.

I have maintained an interest in this issue and it is clear that some of those who are actively seeking to supply, and indeed now actively supplying the U.S. market are dealing with foreign entities that are, known or unknown to them, at the very least questionable. Of that I have clear evidence.

Even now some Online Canadian business to business traders are actively advertising to supply pharmaceuticals from India and elsewhere.

The pharmaceuticals market is of course a huge one and will no doubt continue to increase. There are fortunes to be made, and I can understand why there is a push toward this type of legislation in order to reduce the cost of drugs to the U.S. consumer.

I have often been asked, Why should the industrialized world worry about drug distribution issues when so few people appear to be hurt by them? To an increasing extent the developed world is becoming more aware of the dangers that counterfeit and other substandard medicines. Cases of harm in the U.S.A. have been recorded. However, if one looks at the global picture it is clear that tens of thousands of people die annually from using such medicines. Those who perpetrate such crime do so for one reason—money. Providing substandard medicines is not a race crime, there is no reason to believe that those who kill those in the developing world by these means would think any more of taking American or European lives, indeed the opposite might be true.

Very often counterfeit drugs contain some active ingredient but in lower dosage, or contain an alternative active, in both cases the user of those drugs might suffer gradual deterioration of health as the disease overcomes the lesser treatment. The results might be simply greater suffering or death. No one knows, and there is little chance of finding out.

The UK's Criminal Intelligence Service recognises these threats, so too does Interpol.

It has only been 5 months since I published (via the Stockholm Network) my book on this subject, and there has been a great deal of interest since. Still however, despite all the evidence some people fail to see the potential for widespread harm. For those who wish to see the dangers, they are clear. Those who call upon Europe in support of allowing easier access to the U.S. market ignore the evidence most blatantly.

Before legislation is introduced in the U.S.A., given the potential for serious public harm, it is fundamentally important that the risks are fully understood and weighed, and then an importation system designed and properly policed in order to achieve and maintain compliance. I would most strenuously recommend that you consider establishing an international framework with regulators, law enforcement, and public health officials of the "permitted countries" in order to establish a system that affords adequate protection.

The CHAIRMAN. Dr. Cecil.

STATEMENT OF TODD CECIL, VICE PRESIDENT OF STANDARDS DEVELOPMENT, UNITED STATES PHARMACOPEIA, ROCKVILLE, MD

Mr. CECIL. Good morning, Mr. Chairman and members of the committee. I am Dr. Cecil. I am a chemist, and I am the Vice President of Standards Development, USP——

The CHAIRMAN. Microphone again. Is the little light on? If the light is on, then you have it on.

Mr. CECIL. It is on.

The CHAIRMAN. Thank you.

Mr. CECIL. In consideration of time, I will be brief. USP is a not-for-profit group that develops standards, chemical standards, for comparison and control of drug substances and drug products in the United States and is written into law in a number of different places. We want to talk about three major key principle components that we want you to look at. One is public standards. The second is pharmaceutical equivalents. And the third is bioequivalents, and let me skip on.

Based on USP's experience and long history ensuring consistency and quality of drugs, we have the following observations.

First, USP believes that any medicine imported without the benefit of the submission of a New Drug Application, or BLA, Biologics Licensing Application, or an ANDA, an Abbreviated New Drug Application, to FDA and subsequent agency review must conform to a USP–NF monograph. Lacking this conformity, the imported medicine should indicate where it differs from the public standard and should state so clearly on the label. The science and regulatory basis for these requirements is the foundation for ensuring quality drugs in the United States and has been for over 185 years.

USP believes that the success of any drug importation program implemented in the United States must recognize the critical role of public standards and required adherence to the official U.S. compendia, that is the USP–NF. Adherence to the public standard in the USP–NF can achieve, via testing to the standard of a monograph or the use of USP reference standards, the consistency and uniformity sought by the initial founders of USP in 1820 and equally critical today in ensuring good quality pharmaceutical care.

Second, through intense science-based deliberations on the part of the USP, the FDA, and the manufacturers, the United States has led the world in considering various issues of bioequivalence for over 50 years. This consideration has many origins, but it certainly began in part to the failure of tablets containing cardiac glycosides, digitalis and its congeners, in the early 1970s. These issues led to national efforts to better define bioequivalence and determine appropriate procedures for assessment.

In the United States, the Congressional Office of Technology Assessment, or OTA, issued a key report in 1974. Many recommendations of the OTA report were subsequently adopted by the FDA and were published in 1977 as regulation. These regulations set the stage for passage of the 1984 Drug Price Competition and Patent Term Restoration Amendments to the FDCA, which established the

comprehensive system of interchangeable, multi-source products in the United States.

Following these major scientific and legislative advances, FDA published a number of guidances that further addressed the many and various complicated bioanalytical and bioequivalent studies that may be needed for both the pioneer and certainly for the generic manufacturers to allow market access. The end result of these science and legal endeavors is a coherent system of interchangeable pharmaceutical dosage forms.

The USP requests that Congress consider carefully whether this multi-decade effort, beginning through substantial marketplace problems and moving to Congressional action through the OTA, can be assumed to have occurred in other countries. The U.S. regulatory, academic, and manufacturing communities have worked to great mutual benefit with their counterparts in other countries. However, these collaborative efforts, no matter how successful, do not guarantee the regulatory systems of other countries will impose the same rigor of bioequivalence that does the FDA.

And third, the USP believes that drug importation programs should carefully consider public health impact of allowing dosage forms from other markets in the treatment of patients and consumers in the United States. Bioequivalence is a concept. It is not just a single clinical study performed by a generic applicant as part of documentation required for an ANDA. Rather, it is a complicated science and policy approach that requires equivalent performance between multiple iterations of both the pioneer and, at the appropriate time, interchangeable multi-source generic products. Both pioneer and generic manufacturers are required under law to initially establish bioequivalence and then assure continuing bioequivalence through careful post-approval changes—change control, pardon me.

USP wishes to emphasize the importance of the pre- and post-approval change control to patient health. In today's environment, where appropriate health care cost control is critical, substantiation of therapeutically equivalent dose forms can occur frequently as health care systems and practitioners try to achieve the most efficient treatment at the lowest cost.

Given the strength of the FDA regulatory system, patients and their practitioners can be reasonably assured that the patient is getting the same medication time after time and dose after dose. Introducing a dosage form for another market has the possibility of substantially disturbing the finely tuned equilibrium, so that without some assurance of bioequivalence, the participating patient would have no way of knowing that the patient is receiving a therapeutically equivalent dosage form.

USP looks forward to working with Congress and other stakeholders in ongoing work in this area, and I would like to thank Mr. Chairman and members of the committee for allowing us this opportunity to speak to you.

The CHAIRMAN. Thank you.

[The prepared statement of Mr. Cecil follows:]

PREPARED STATEMENT OF TODD CECIL, PH.D.

I. Introduction

The United States Pharmacopeia (USP) is a private not-for-profit organization whose mission is to promote the public health by establishing and disseminating officially recognized standards to ensure the quality of medicines and other health care products. USP achieves its mission through the contribution of volunteers representing, pharmacy, medicine, and other health care professions, as well as science, academia, the U.S. Government, the pharmaceutical industry, and consumer organizations.

USP was created in 1820 by practitioners who wished to promote the quality of therapeutic products. The first pharmacopeia was published in 1820 and began as a "recipe" book to promote uniformity in drugs (a drug includes its active ingredient(s) and excipients) that were generally available in the United States at that time. Prior to the publication of the first pharmacopeia, the quality of drugs varied between cities and regions. The practitioners recognized that by setting public standards for drug products, they would help ensure the consistency and quality of drugs used in this country.

Ensuring drug quality through public standards remains USP's core mission. Today, USP's drug standards are developed by its Council of Experts and Expert Committees, a group of 650 nationally and internationally recognized scientists and practitioners in medicine, pharmacy, the pharmaceutical sciences and many other healthcare professions. USP's standards are widely recognized in the United States and elsewhere because they are authoritative, science-based and developed through a transparent and credible process with established integrity.

USP's standards are made public through the United States Pharmacopeia (USP) and the National Formulary (NF). Together the two compendia are published as a combined text annually (USP-NF) with two Supplements. Originally a book of process standards (recipes for preparations), USP-NF evolved over time into compendia containing primarily product standards. These standards are expressed in public monographs for drug substances, excipients, dosage forms and other articles, and in General Chapters, which are dedicated to procedures widely used throughout the compendia. The USP-NF monographs contain specifications (tests, procedures, and acceptance criteria) that help ensure the strength, quality, and purity of the named items. The purpose of the USP-NF is to provide a single standard for medicines used in the United States to ensure product uniformity and quality.

Closely allied with public monographs in USP-NF, and equally important in many respects, is the availability of an official USP Reference Standard. USP Reference Standards are chemical substances used by the pharmaceutical industry to test conformity to the USP-NF. USP Reference Standards are highly characterized chemical materials used in quality control laboratories to carry out tests for strength, quality, and purity described in the USP-NF. USP Reference Standards and USP-NF monographs are complementary tools to ensure these critical attributes for pharmaceutical substances and products.

Over the years, Congress has relied on USP on many occasions and has repeatedly recognized USP's expertise as a standard-setting organization. Initially, in the Import Drug Act of 1848, Congress turned to USP for public standards for imported medicines. Today, principal recognition occurs as a result of Congress' recognition of the USP-NF as official compendia of the United States. The Federal Food, Drug, and Cosmetic Act (FDCA) makes the official compendia, the USP-NF, enforceable by the Food and Drug Administration (FDA).

For over 185 years, USP's activities have supported the availability of safe, effective, good quality therapeutic products for patients and consumers. USP believes it can play a leading and helpful role, working with this committee and Congress, the Federal Government, and other relevant organizations and stakeholders, in evaluating the scientific issues surrounding drug importation and continuing to help ensure the availability of safe, effective, good quality therapeutic products.

II. Science Issues

USP commends Congress for its efforts in attempting to address the issues of drug importation and acknowledging the important role science has in helping ensure that the importation of drugs to the United States will not adversely affect public health. The issue surrounding drug importation calls into question many scientific issues that merit full consideration. This testimony will discuss two science issues—pharmaceutical equivalence and bioequivalence—that USP believes are key considerations in allowing importation of drugs into the United States. USP will also address the need for public standards and the public health impact that imported drugs may have on patients and consumers.

A. Public Monographs in USP-NF and Official USP Reference Standards

USP believes that any medicine imported without benefit of submission of a New Drug Application (NDA), Biologics Licensing Application (BLA), or Abbreviated New Drug Application (ANDA) to FDA and subsequent Agency review must conform to a USP-NF monograph both for its ingredients, including and most importantly the drug substance and the dosage form. Lacking this conformity, the imported medicine should indicate how it differs and should so state clearly on the label. The general approach accords with the FDCA, which states that a drug shall be deemed to be adulterated if it purports to be or is represented as a drug, the name of which is recognized in an official compendium and its strength differs from, or its quality or purity falls below, the standards set forth in such compendium. Such determination regarding strength, quality, or purity shall be made in accordance with the tests or methods of assay set forth in such compendium.

The science and regulatory basis for these requirements is the foundation for ensuring quality drugs in the United States and has been for over 185 years. Specifically, in the Import Drug Act of 1848, the U.S. Government turned to the United States Pharmacopeia for public standards for imported medicines. With passage of the Pure Food and Drug Act in 1906 and in the following almost 100 years, USP has provided public monographs for ingredients and dosage forms, working collaboratively with the FDA and manufacturers of medicines legally marketed in the United States. With passage of the Federal Food, Drug and Cosmetic Act in 1938, USP and subsequently NF were named as official compendia of the United States.

The USP science-based and public process for developing an official monograph for the USP-NF and official USP Reference Standards is a well evolved system that works in concert with efforts of U.S. manufacturers and the FDA to assure the public trust. Speaking simply, the public monograph in the USP-NF for a dosage form and its ingredients is the public *Quality* document, which allies with the *Safety* and *Efficacy* information expressed in product labeling. In offering a USP-NF monograph and, where needed, official USP Reference Standard, USP is part of a comprehensive quality system that helps assure practitioners and patients—and the public at large—that a medicine is "fit for purpose," i.e., is safe and/or effective in the maintenance of health and treatment of disease. Testing to a public monograph in USP-NF supports the Nation's historical objective, through many laws and through actions of FDA itself, in ensuring the identity of an article via the test procedures and other standards of the monograph, regardless of who is manufacturing the article, who is testing it, and when or where it is tested.

In establishing a drug importation program, it is critical for the U.S. Government and other independent testing laboratories to have the capability to test the medicine and its ingredients. The most transparent and effective way this testing can be achieved is via a public monograph in USP-NF, allied with an official USP Reference Standard when needed. Without this capability, the U.S. will ultimately be relying on testimonials from manufacturers vending their products in other countries or on private and/or public specifications that have not undergone the stringent analytical processes conducted either by FDA or USP.

The USP-NF has for 185 years provided public standards for medicines. These standards provide information on the quality, strength, and purity of the ingredient or product and ensure consistency in the medicines taken by the public. USP feels strongly that the success of any drug importation program implemented in the United States must recognize the critical role of public standards and require adherence to the official U.S. compendia—the USP-NF. Adherence to the public standards in the USP-NF can achieve, via testing to the standards of a monograph and with the use of USP Reference Standards, the consistency and uniformity sought by the initial founders of USP in 1820. The failure of such recognition will result in the lack of consistency and uniformity that existed prior to 1820.

B. Pharmaceutical Equivalence

A critical part of the legislation speaks to the definition of pharmaceutical equivalence (PE). The definition alludes to when the drug substance in two duplicate dosage forms is the same or not. Assurance of "sameness" can be readily demonstrated through conformance to a modern monograph in USP-NF. Thus, if the drug substance meets the specification (tests, analytical procedures, and acceptance criteria) specified in the monograph, its identity is established, irrespective of the source of the drug substance, and pharmaceutical equivalence for this specific substance is established.

A modern monograph in USP-NF must account for important characteristics of the drug substance and its impact on safety and efficacy. The drug substance includes impurities and physical characteristics such as particle size. The active pharmaceutical ingredient (API) is itself only one component in the drug substance. Fur-

thermore, the API can take on many forms that at times affect—"dramatically"—the safety and efficacy of the dosage form containing the drug substance. The active pharmaceutical ingredient may differ in terms of crystalline form (different arrangements and/or conformations of the molecules in the crystal lattice), amorphous forms (disordered arrangements of molecules that do not possess a distinguishable crystal lattice), and solvates (crystal forms containing either stoichiometric or nonstoichiometric amounts of a solvent, such as water). Critical risks to public health have arisen based on U.S. experience for virtually all these important characteristics of the drug substance. These risks have related to both sub- and super-potency, risk from impurities, risk from changes in polymorphic form, and risk from change in particle size. Although less well studied, many of these risks are likely to extend to a dosage form's excipients, given that these ingredients frequently form the major part of a dosage form.

C. Bioequivalence

Through intense science-based deliberations on the part of USP, FDA, and manufacturers, the United States has led the world in considering the various issues of bioequivalence (BE) for over 50 years. This consideration has many origins, but it began in part with failure of tablets containing cardiac glycosides (digitalis and its congeners) in the early 1970's. These issues led to national efforts to define BE and to determine appropriate procedures for assessment. In the United States, the Congressional Office of Technology Assessment issued a key report on July 15, 1974 (OTA Report). The OTA Report recommended the importance of bioavailability and bioequivalence studies and indicated further steps to ensure that this information became part of the drug development and regulatory processes. Many recommendations of the OTA Report were subsequently adopted by FDA and were published in 1977 as regulations entitled Part 320-Bioavailability and Bioequivalence Requirements, which contain Subparts A (General Provisions) and B (Procedures for Determining the Bioavailability or Bioequivalence of Drug Products). These regulations were themselves a seminal event and have stood the test of time, with only minor revisions, and have established firmly the general approach to assuring PE and BE for all dosage forms over time. The regulations set the stage for the passage of the 1984 Drug Price Competition and Patent Term Restoration amendments to the FDCA, which established a comprehensive system of interchangeable multi-source products in the U.S. This legislation has also stood the test of time, again undergoing only relatively minor revisions.

Following on to these major scientific and legislative advances, FDA expended considerable energies in the 1990's and thereafter to come to a better understanding of how to document interchangeability for many different types of ingredients and dosage forms. The general approach is established in FDA guidances that address the many and various complicated bioavailability and bioequivalence studies that may be needed both for the pioneer and certainly for the generic manufacturer to allow market access. They ally with the scale up and post approval change (SUPAC) documents created by FDA in the same timeframe. While this work is incomplete, it remains a beacon to the world on the information needed to assure a system of fully interchangeable pioneer and generic dosage forms.

The end result of both these seminal scientific and legislative endeavors discussed above is a coherent system of interchangeable pharmaceutical dosage forms. This system has worked to great success, based on sound legislative, regulatory, and scientific approaches involving a broad constellation of stakeholders. USP requests Congress to consider carefully whether this multi-decade effort, beginning with substantial marketplace problems and moving to Congressional action through the Office of Technology Assessment, can be assumed to have occurred in other countries. The U.S. regulatory, academic, and manufacturing communities have worked to great mutual benefit with their counterparts in other countries. However, these collaborative efforts, no matter how successful, do not guarantee that regulatory systems in other countries impose the same rigor for bioequivalence as does the FDA.

D. Patient Care Issues

USP believes that any drug importation program should carefully consider the public impact of allowing dosage forms from other markets in the treatment of U.S. patients and consumers. Bioequivalence as a concept is not just a single clinical study performed by a generic applicant as part of the documentation required in an ANDA. Rather it is a complicated science and policy approach that requires equivalent performance between multiple iterations of both a pioneer and, at the appropriate time, interchangeable multi-source generic products. Thus, bioequivalence per se exists as a challenge that must be documented for dosage form continuously throughout the life of any medicine irrespective of the company that is manufac-

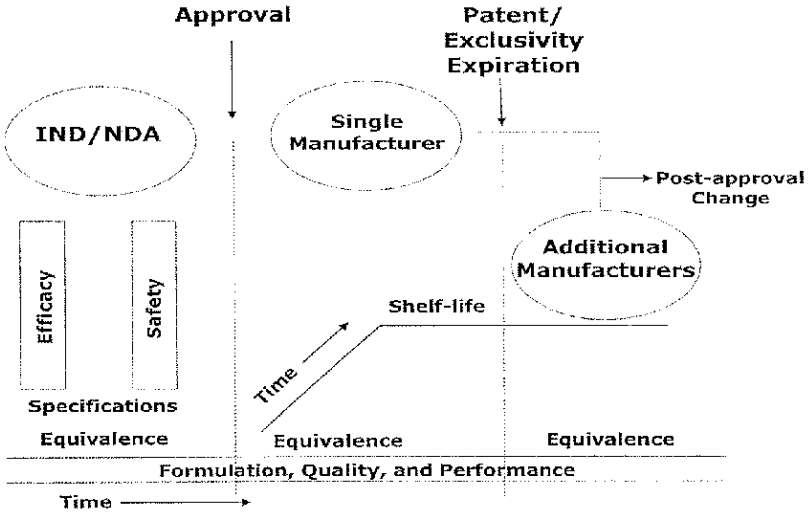
turing it. To gain a glimpse of the general challenge, USP wishes to review briefly an entire and comprehensive series of pre- and post-market series of regulatory and compendial controls.

(i) Pre- and Post-Market Change Control

For the first-entry pioneer manufacturer, a careful series of approaches are needed to assure that the clinical trial material on which safety and efficacy are based is equivalent to the to-be-marketed dosage form. This is a highly resource intensive enterprise executed by U.S. innovator companies who must satisfy FDA requirements for careful product development in a regulatory filing. Many laws, regulations, and guidances provide specific and detailed requirements and recommendations for a pioneer manufacturer in this endeavor. It is a risk based approach that can intensify even for relatively simple, orally administered dosage forms, depending on the complexity of the drug substance—the active pharmaceutic ingredient, excipients, and the dosage form itself.

After approval, the NDA holder must provide continuing assurance to FDA that the approved dosage form remains both pharmaceutically equivalent and bioequivalent to the originally marketed dosage form—even in the presence of multiple changes in method of manufacturing, components, and composition. These same approaches are also critical for U.S. generic manufacturers who have, in principle, the same requirements to initially establish bioequivalence and then assure continuing bioequivalence through careful post-approval change control. Compliance with the general requirements for both pioneer and generic manufacturers over time is a daunting task. The general manufacturing and regulatory set of approaches even now, after many years of study, is not fully resolved for all dosage forms. Below is a chart that sets forth the science and regulatory process for drug approval (Figure One).

FIGURE 1 – Process for Drug Approval



While much remains to be done in this area, USP commends FDA and the U.S. pharmaceutical industry for coming to a much clearer understanding of how to assure, in the presence of pre- and post-approval change, stable quality and performance characteristics of a dosage form and its ingredients over time. These tasks are critical to the U.S. patient and the consumer. The U.S. Congress itself emphasized the importance of post-approval change control with passage of the Food and Drug Administration Modernization Act in 1997, which legislates three types of changes and the need for associated filing requirements. This legislation was subsequently adopted by FDA in changes in regulation at 21 CFR 314.70 and associated regu-

latory guidance. This important legislation followed on to the FDA's careful delineation of the types of information needed by dosage form in the presence of certain changes (SUPAC documents). Again while much more work needs to be done, the SUPAC documents and the FDA's subsequent revisions of both regulation and guidance put the United States and FDA and its regulated industry in the forefront of post-approval change control.

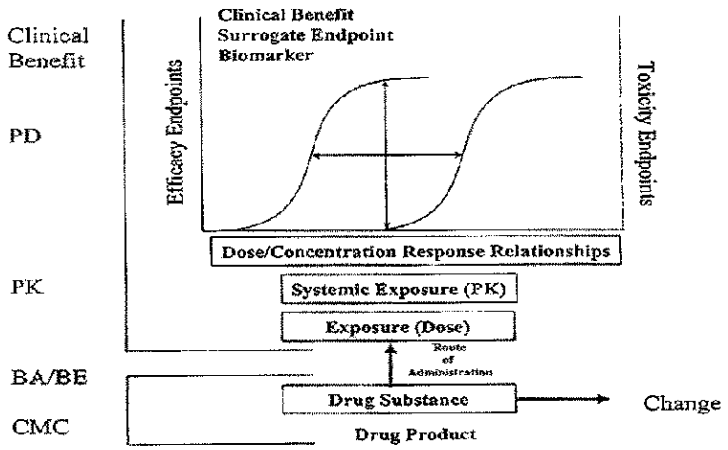
USP has a long and honorable history of supporting approaches that assure optimal dosage form performance. This is expressed most prominently in the USP dosage form monograph, which frequently includes a performance test such as dissolution or disintegration. Dissolution acceptance criteria are usually set in private negotiations between an applicant and a regulatory agency. These subsequently can enter the public dosage form monograph in USP-NF based on decisions of the USP Council of Experts. Based on the relationship between the regulatory decisions and information voluntarily submitted by a pharmaceutical manufacturer to USP, the USP dissolution procedure links to the regulatory judgment about bioavailability and bioequivalence and, ultimately, to a judgment about safety and efficacy. For imported medicines, conformance to a USP dissolution test would be critical to an understanding of product performance.

(ii) Importance to the Patient

USP wishes to emphasize the importance of pre- and post-approval change control to the patient and consumer. The U.S. system generally allows interchangeability based on the ratings set forth in FDA's Approved Drug Products with Therapeutic Equivalence (also known as the "Orange Book"). The Orange Book identifies drug products approved on the basis of safety and effectiveness by the FDA under the FDCA and provides guidance on drug interchangability. This means that in all 50 states and territories, substitution of appropriately rated (e.g., AB rated oral dosage forms) may occur at the pharmacy level. In today's environment, where appropriate healthcare cost control is critical, substitution of therapeutically equivalent dosage forms from one manufacturer to another can occur frequently, as healthcare systems and practitioners try to achieve the most effective treatment at the lowest cost. In practice, this might mean that a patient would receive a dosage form from many different manufacturers over the course of a year's treatment. Given the strength of the U.S. system, this patient—and his/her practitioner team—can be reasonably assured that the patient is getting the same medication time after time and dose after dose. But this assurance is based on FDA's rigorous control of both pharmaceutical equivalence and bioequivalence through careful pre- and post-approval change. Introducing a dosage form from another market has the possibility of substantially disturbing this finely tuned equilibrium so that, without some assurance of bioequivalence, the practitioner and patient would have essentially no assurance that at any point in time they were receiving a therapeutically equivalent dosage form. For both the patient and practitioner, this is an especially critical point. Health and disease have their own inherent progression. Medicines are not like cars, where breakdowns are usually readily apparent but rather may be attributed to the course of a disease or other factors. This challenge in assessing causality impedes understanding that absence of progress or unexpected toxicity may in fact be attributed to the failure of a medicine.

Through careful safety, efficacy, and quality pre-market studies, the U.S. system requires a pioneer to gain some understanding of the dose/response relationship for a medicine. This dose/response relationship allows the concept of a therapeutic window, as demonstrated by the following figure (Figure Two).

FIGURE TWO – Optimal Dose Therapeutic Window



The therapeutic window refers to the point at which efficacy begins to be lost, if the dose administered is too low or too high or is unacceptably toxic. A dosage form should deliver the same amount of drug at the same rate to a patient with each dose time after time to maintain optimal safety and efficacy. If a dosage form under- or over-performs, as may happen with bioinequivalent products, then the optimal safety/efficacy profile may be lost. It is important also to note that concepts of bioequivalence and therapeutic equivalence are applicable to the individual. Thus a patient/consumer must receive a dosage form that reliably delivers the right amount of the drug at the right time, day after day, in order to assure optimal safety and efficacy over time.

Furthermore, while all regulatory systems produce drugs based on population studies, the concept of generic substitution relates also to the therapeutic window for a single patient. At this time we have little or no understanding of this therapeutic window in an individual or how it might change in different populations such as the elderly, children, women, or the infirm. As a specific example, the therapeutic window for a narrow therapeutic range drug such as warfarin might range between 2 and 10 or more milligrams/day in the population. But in an individual, such a wide dose range would produce intolerable loss of efficacy, manifested in excessive coagulation, or unacceptable toxicity, manifested by bleeding. Careful attention to bioequivalence both within and between manufacturers is designed to prevent such occurrences. Even small differences between bioinequivalent dosage forms—in terms of amount of drug delivered and the rate at which is delivered—can thus produce dangerous outcomes in individual patients.

Congress, FDA, USP, the pharmaceutical industry, and many other stakeholders have been addressing the issue of bioequivalence and its impact on patients for over 50 years in the United States. The result is a vigorous regulatory process that provides reasonable assurances to patients and practitioners. Any drug importation program must provide patients and practitioners in the United States the equivalent assurance in order to not to adversely impact public health. USP believe that adherence to public standards in the USP-NF is one mechanism to help achieve such assurances.

III. Conclusion

USP commends Congress for its efforts in attempting to address the issues surrounding drug importation. USP looks forward to working with Congress and other stakeholders in the ongoing effort to ensure that patients and consumers are not adversely affected by the importation of drugs into the United States. USP is ready to assist you by making available our scientific expertise and experience. Specifically, USP believes it can play a leading and helpful role, working with this committee and Congress, the Federal Government, and other relevant organizations and stakeholders, in evaluating the scientific issues surrounding drug importation.

Thank you Mr. Chairman and members of the committee for providing USP the opportunity to provide input on the scientific issues surrounding drug importation.

ANNEX 1.—USP AND ITS PUBLIC HEALTH MISSION

1. HISTORY

USP is a not-for-profit organization that was created in 1820 by 11 practitioners who wanted to promote the quality of therapeutic products. The first pharmacopeia was published in the United States in 1820 and began as a "recipe" book to promote uniformity in drugs (a drug includes its active ingredient(s) and excipients) that were generally available in the United States at that time. Prior to the publication of the first pharmacopeia, the quality of drugs varied between cities and regions. The practitioners recognized that by setting public standards for drug products, they would help ensure the consistency and quality of drugs. Ensuring drug quality through public standards remains USP's core mission.

2. VOLUNTEER BASED ORGANIZATION

USP's governing bodies include its Convention, which meets every 5 years, and a Board of Trustees, which provides direction to staff in the years between Convention meetings. Standards-setting activities are conducted by the USP Council of Experts. Membership in the Convention (representing approximately 400 associations), on the Board (11 members representing Convention constituencies), and on the Council and its Expert Committees (approximately 650 members) is entirely voluntary. To support the activities of these bodies, USP maintains a staff of approximately 350 in its Rockville offices.

3. PUBLIC MONOGRAPH IN THE USP-NF AND OFFICIAL USP REFERENCE STANDARDS

USP's drug standards are developed by its Council of Experts and Expert Committees, a group of 650 nationally and internationally recognized scientists and practitioners in medicine, pharmacy, the pharmaceutical sciences and many other healthcare professions. USP's standards are widely recognized in the United States and elsewhere because they are authoritative, science-based and developed through a transparent and credible process with established integrity.

USP provides standards for more than 4,000 prescription and non-prescription drugs, dietary supplements, veterinary drugs, health care product, and excipients. These standards are presented in a combined text consisting of two compendia—the United States Pharmacopeia (USP), to which the National Formulary (NF) was added in 1975. Together the two compendia are published as a combined text annually (USP-NF) with two Supplements.

USP's standards, which are presented in monograph form, contain specifications (tests, procedures, and acceptance criteria) that help ensure the strength, quality, and purity of the named articles. Closely allied with public monograph in the USP-NF, and equally important in many respects, is the availability of official USP Reference Standards. USP Reference Standards (chemical specimens) are used in the pharmaceutical industry to test conformity to such monograph standards. USP provides approximately 1,750 USP Reference Standards that are specifically required in many Pharmacopeial assays and tests.

USP's official Reference Standards are highly characterized materials used in a quality control laboratory to carry out tests for strength, quality, and purity described in the USP-NF. Such tests help to determine whether a batch being released to the market conforms to its USP-NF specification as required by law and will continue to conform throughout its shelf life. The Reference Standards are typically used to conduct the analytical procedures set forth in the USP-NF.

USP Reference Standards also are used as calibrators—for dissolution, particle count, melting point, and standardization of titrants and as blanks and controls (negative control plastic, lanolin, and methylcellulose). Reference Standards are used for measurements required to obtain accurate and reproducible results in chromatographic and spectrophotometric procedures. USP has Reference Standards for drug substances, dosage forms, dietary supplements, excipients, impurities, and degradation products, as well as performance calibrators.

4. REFERENCE STANDARDS DEVELOPMENT PROCESS

When USP identifies the need for a new Reference Standard (based on monographs in the USP-NF that require its use), it requests bulk materials from pharmaceutical manufacturers. USP subjects the candidate materials it receives from man-

ufacturers to rigorous analysis and review. USP tests the materials in its own laboratories, and requests collaborative testing by FDA and independent laboratories. The goal of the collaborative testing is to confirm the identity and assess the purity of the material, to confirm its homogeneity, to determine its suitability for use in the official applications, to provide the user with all the necessary information and directions for use, and to acquire time-zero information for future continued-suitability-for-use studies. USP compares and analyzes the results of this collaborative testing and prepares a report for its Reference Standards Expert Committee (RS-EC). The RS-EC comprises experts from industry, government agencies, and academia from the United States and from abroad. The RS-EC determines whether the candidate material is suitable to be established as an official USP Reference Standard. USP Reference Standards are established and released under the authority of the USP Board of Trustees upon recommendation of the USP RS-EC.

5. PUBLIC PROCESS

During the past 185 years, USP has played an important role in developing standards for medicines, including drugs, devices, biologicals, and dietary supplements. USP standards are developed and continuously revised by a unique public process, involving expert volunteers from academia, industry, government, trade associations, and consumers, and are subject to public comment.

USP's public comment process occurs via the Pharmacopeial Forum (PF) and is similar to the Federal Government's Federal Register. The PF is the working vehicle of the USP Council of Experts (CoE). The PF provides interested parties the opportunity to review and comment as the CoE develop and/or revise standards for the USP-NF.

6. LEGAL RECOGNITION

The USP-NF is recognized in Federal laws regulating drugs, food, devices, and dietary supplements. Initially, in the Import Drug Act of 1848, Congress turned to USP for public standards for imported medicines. Thereafter, the USP was incorporated in the 1906 Pure Food and Drug Act, which stated that drugs included all those medicines and preparations in the USP and stated that a drug was considered adulterated if it differed from the standard of strength, quality, or purity described in the USP. The current law, the Federal Food, Drug, and Cosmetic Act (FDCA), was enacted in 1938 and recognizes the USP-NF in several sections. The FDCA defines the USP-NF as official compendia, specifically stating that "official compendium" includes the United States Pharmacopeia, the National Formulary or any supplement to any of them. The FDCA also incorporates the 1906 adulteration provision, by stating that a drug is adulterated if it is recognized in the USP-NF and fails to meet the strength, quality, or purity set forth by compendial standards. In addition, the FDCA integrates USP-NF standards in the misbranding provisions for drug products, saying that drugs are considered misbranded if they fail to adhere to USP-NF standards for packaging and labeling. Section 502(e) requires that the established name of a drug appear on the label and states that the established name of a drug or ingredient is the one designated by the Secretary of the Health and Human Services or the name appearing in the USP-NF.

Congress also has recognized USP-NF standards for dietary supplements but has made adherence to them voluntary. Specifically, § 402(s)(2)(D) provides that a dietary supplement is considered misbranded if it states conformance to an USP-NF monograph and fails to so conform. Thus, if a dietary supplement manufacturer asserts conformance to the USP-NF monograph, the product must conform to the monograph requirements or the product will be deemed misbranded.

The Social Security Act (SSA) recognizes the USP-NF in the provisions regarding Medicare. According to the SSA, Medicare provides reimbursement for drugs that cannot be self-administered, such as those drugs administered in a physician's office. The SSA then defines drugs to be those that are included or approved for inclusion in the USP, NF, United States Homeopathic Pharmacopeia, or in New Drugs or Accepted Dental Remedies or approved by the pharmacy and drug therapeutics committee. As a practical matter, drugs administered in a physician's office are generally not subject to approval by a pharmacy and drug therapeutics committee so the drugs must be in the USP-NF or approved for inclusion in them. USP has a process whereby a drug can be readily approved for inclusion into the pharmacopeia.

Most recently, under the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, the Secretary of the Department of Health and Human Services is required to request USP to develop, in consultation with pharmaceutical benefit managers and other interested parties, a list of categories and classes that may be used by prescription drug plans in developing their formularies. USP is to revise

this classification from time to time to reflect changes in therapeutic uses of covered drugs and addition of new covered drugs. In December 2004, USP provided the Centers for Medicare and Medicaid Services (CMS) the USP Model Guidelines as set forth under the MMA. USP is working with CMS to determine the revision process for the USP Model Guidelines.

7. OTHER RELATED USP ACTIVITIES

a. USP—International

The international market for manufactured pharmaceuticals is changing at a rapid pace, leading to an especially challenging global environment where the likelihood of counterfeit and substandard drugs is of increasing concern. Like early practitioners in the United States, modern practitioners in many parts of the world beyond the United States may confront a bewildering array of poorly named therapeutic ingredients and products, with uncertain safety, efficacy, and quality. In a recent publication, USP proposed the creation of a separate official USP compendium, clearly distinguished from USP-NF, to support international needs and, as feasible, national interests as well. The approach allows availability of useful public analytical information to all constituencies of USP throughout the world. USP believes this general approach to assure optimal quality of medicines irrespective of their market sphere of authority might be especially useful in considering issues of importation.

b. USP's Verification Programs

USP has established a Dietary Supplement Ingredient and Product verification program. USP is considering expansion of the approach to excipients, drug substances and perhaps even dosage forms. USP believes that this type of program could be used by the Federal Government to help assure the quality of medicines entering the U.S. market from another country or region. USP has enclosed additional information on its Verification Programs.

The CHAIRMAN. And again, I will reiterate that all of your testimony will be a part of the record and I really do appreciate all the work you went through. There are more pages there than we could possibly handle in a hearing, but there is a lot of good information. I have been through it all.

Mr. Arthur.

STATEMENT OF THOMAS C. ARTHUR, DEAN, EMORY UNIVERSITY SCHOOL OF LAW, ATLANTA, GA

Mr. ARTHUR. Thank you, Mr. Chairman. Mr. Chairman, members of the committee, I am honored to be asked to come before you today to discuss some of the issues with the statute. The issues that I would like to discuss haven't been discussed so far, except that they have been alluded to by Senator Isakson.

This is not just a bill to provide—to permit imports by people who wish to import drugs into this country. It also contains provisions to coerce people to import drugs into this country that do not wish to, and along with that, it has provisions which are intended not just to permit free importation and free trade, but also to create by indirection foreign price controls over American drugs and have them imported into the United States.

Now, the way the bill does this is it requires U.S. manufacturers selling abroad and foreign manufacturers who sell drugs in the United States to make available in the quantities—at unlimited quantities and at prices regulated by foreign price controls supplies to be imported back into the United States, or in the case of American producers, reimported back into the United States. It also has provisions which regulate the prices at which these companies can sell drugs to exporters, even drugs that are not intended to be sent

back to the United States, and other various regulatory provisions for companies overseas.

Now, that presents four problems. The first problem is that it raises questions with the appropriate constitutional scope of foreign commerce. The power to pass this bill and these provisions regulating what foreign nationals do in their own countries comes from the power of the Congress over foreign commerce. This power, according to the Supreme Court, also extends to acts taken abroad that affect U.S. commerce.

Now, in one sense, any act, even a decision not to trade with the United States, arguably can affect the foreign commerce of the United States. For example, we have learned recently that oil consumption in China affects American gas prices. But if effects of that indirect sort can justify American regulation of foreign economies, it proves too much. It would allow the Congress to regulate the entire world.

Second, it raises a question about international law. International law permits countries to regulate extraterritorially to protect their own interest. But again, that is a matter of whether there are direct effects intended to cause effects in the United States, not whether there are intentions not to affect the United States which may indirectly affect it.

Now, this is a two-way street. To the extent that we can say that decisions not to sell in the United States authorize us to regulate and coerce people to do so, it would also under international law allow other countries to regulate our citizens for their benefit. It is a two-way street. And because intrusive extraterritorial regulation can be such a problem, nations have voluntarily imposed what is known as the rule of comity in which they stay their hands. They voluntarily write statutes which regulate extraterritorially only to the extent absolutely necessary. The Supreme Court has announced that it interprets statutes with a canon of construction to suggest that they read statutes narrowly, as Justice Breyer wrote for the unanimous Court last year in the *Empagran* case, to ensure that we intrude as little as possible in the ability of other countries to run their own affairs. Now, we don't do this just to be nice. We do this because what goes around comes around. If we can regulate other countries' activities, then they can regulate ours.

Therefore, it leads me into my third point, which is this point made by Senator Isakson. If regulating drug prices is a good idea in the United States, why don't we do it directly in the United States? If we do it directly in the United States instead of importing other countries' drug and price controls, we don't interfere with their business. We don't try to give command and control regulations to foreign companies. We don't raise any of these issues. But in addition, we would have a regulatory regime which would be produced by an American Congress and responsive to American needs for the benefit of American consumers, done to be imposed by an American regulatory agency using American processes and procedures, which are not the same as they are in the rest of the world, as we have learned sometimes to our dismay, and subject to Congressional oversight and judicial review in American courts.

By importing regulations of drug prices that are done by other countries for the benefit of their consumers and their voters, regu-

lated and overseen by their legislative committees and reviewed in their courts, I don't understand why we would want to import their sovereignty into our country rather than doing it ourselves, which leads to my fourth point, and I will conclude, sir.

I think the reason we haven't done it directly is it is not probably a good idea. There has been a lot of discussion about whether drug prices are too high and so forth and so on, but nonetheless, American policy through the patent laws, which have been visited time and again by this Congress, has been to provide the incentives to the patent system for the development of new drugs, and that is something which the Congress could change if it wants to, but so far, it has not seen that to be a good idea.

The CHAIRMAN. Thank you.

[The prepared statement of Mr. Arthur follows:]

PREPARED STATEMENT OF THOMAS C. ARTHUR, L.Q.C.

Mr. Chairman and members of the committee, I am pleased to be here today to discuss with you the important constitutional, international law and public policy issues raised by S. 334. The views expressed herein, of course, are strictly my own and not those of Emory University or its School of Law.

To summarize my views at the outset, I have four objections to S. 334 (the Dorgan Bill). First, to the extent that it seeks to regulate the exclusively foreign operations of foreign drug manufacturers in foreign markets, the Dorgan Bill may be unconstitutional. Second, even if assumed to be constitutional, the bill's extensive and heavy handed regulation of foreign drug manufacturers in foreign markets threatens to raise drug prices abroad and otherwise violate the fundamental principle of comity by undermining the policies of other countries. Not only will this violate principles of international law and create animosity toward the United States, it will also invite other countries to regulate conduct in the United States for the benefit of their economies, regardless of adverse effects on American interests. Third, the purpose of the bill's intrusive provisions is to impose other countries' drug price controls on drugs consumed in the United States. But if drug price controls were a good idea, they could be imposed directly in this country without interfering with other countries' regulation of their own pharmaceutical markets. In that case, they would not be imposed by foreign governments under foreign legal standards unchecked by either Congressional oversight or judicial review. Instead, they could be imposed by an American regulator under American legal standards, subject to oversight by the Congress and review in the courts. Fourth, drug price controls are not a good idea, whether imposed directly by new legislation or indirectly by the Dorgan Bill. If the bill operates as its sponsors hope, it will seriously undermine the incentives to innovation in the drug industry that the patent laws currently provide.

CONSTITUTIONAL ISSUES

Congress' Constitutional authority to enact the Dorgan Bill must come from the Commerce Clause, particularly the "Power . . . To regulate Commerce with Foreign Nations." U.S. Const. Art. I, § 8. cl. 3. This provision empowers Congress to regulate our international trade. Several provisions of S. 334 seek to coerce foreign manufacturers which produce drugs that are not for sale in the United States to supply those products for export to the U.S. against their will. See S. 334, § (n)(1) at 72–86. These provisions also impose a duty to supply exporters with other drugs that will not be exported to America, but rather consumed abroad, and regulate the prices for those coerced sales. See S. 334, §§ (n)(1)(A), (C), & (D). But when foreign manufacturers choose not to ship certain products to this country or agree with third parties to stay out of that trade, it is hard to see how Congress can legitimately regulate those decisions under the guise of regulating the foreign commerce of the United States.

One can argue that their decision not to export to the United States affects the foreign commerce of this country. As globalization proceeds, output and consumption decisions in other countries will increasingly have some economic effects on the prices and quantities of goods exported to the United States. For example, it has been reported in the press that the growing demand for petroleum products in China and other developing nations has diverted supplies from the United States, causing higher gasoline prices here and around the world. In a manner of speaking,

then, the consumption decisions of Chinese industries and consumers are affecting petroleum exports to the United States, a part of our "foreign commerce."

But this argument proves too much. It would provide a rationale for Congress to regulate the entire world economy. This certainly was not intended by the Framers, nor can it be justified as a reasonable expansion of Congressional power to fit modern conditions. The provisions of the Constitution must be given a reasonable interpretation. A reading of the commerce clause extending the legislative jurisdiction of the United States to virtually the entire world economy cannot be reasonable.

INTERNATIONAL LAW AND COMITY ISSUES

Under current international law a nation may regulate conduct outside its territory that has significant effects within its territory. This is the principle that justifies, e.g., the extraterritorial application of our antitrust laws to foreign nationals for conduct in their own countries *and,* as most dramatically seen in the EU's prohibition of the GE/Honeywell merger, the extraterritorial application of other countries' laws to the activities of Americans taken in the United States.

To the extent that provisions of the Dorgan Bill would attempt to coerce foreign manufacturers, who are directly or indirectly engaged in commerce, to export to the United States and to sell in their own countries other drugs, which will not be exported to the U.S., at controlled prices to exporters, the legislation's extraterritorial effect would violate international law.

The "significant effects" test permits very intrusive extraterritorial regulation, as the GE/Honeywell decision illustrated. To moderate such effects, nations traditionally have voluntarily followed the principle of *prescriptive comity,* which counsels against regulation that unreasonably interferes with other countries' efforts to regulate their own affairs. Thus legislatures and courts have foregone opportunities to regulate within other countries to avoid undue interference with those countries' self-governance. For example, the Supreme Court "ordinarily construes ambiguous statutes to avoid unreasonable interference with the sovereign authority of other nations." *F. Hoffman-LaRoche Ltd.* v. *Empagran S. A.,* 159 L.Ed. 2d 226, 236 (2004) (Breyer, J.); *see also Hartford Fire Ins. Co.* v. *California,* 509 U.S. 764, 812–19 (1993) (Scalia, J., dissenting) (discussing use of prescriptive comity to construe statutes). Indeed, the statute construed in *Empagran,* the Foreign Trade Antitrust Improvements Act of 1982, was passed in 1982 to ensure that the Sherman Act would *not* be unreasonably applied extraterritorially. *Empagran,* 159 L.Ed. 2d at 240.

Nations do not follow the comity principle just to be nice. They do so as a matter of enlightened self-interest, in the realization that extraterritorial regulation is a two-way street. A nation that extends the extraterritorial reach of its laws unreasonably can expect the same treatment in return. Legislatures and courts around the world have exercised self-restraint as a matter of mutual self-interest.

The provisions of S. 334, even if assumed to be constitutional and valid under international law, violate these principles of prescriptive comity. In essence, the bill intrusively regulates drug manufacturers in other countries, both as described above and in a myriad of other ways. These provisions are remarkably intrusive into other countries' affairs. At the least, they will stir up resentment toward the United States. It is hard to believe that the presence of FDA inspectors abroad will not be seen as a slur against other countries' drug regulations and yet another example of American exceptionalism and "imperialism." Other provisions add injury to this insult and may provoke more than mere resentment. The most glaring example is the requirement to sell for export to the United States at local prices. In many cases companies that sell both in this country and abroad, the primary targets of the bill, will raise foreign prices or even forego sales in other countries altogether rather than lose U.S. revenues.

In response to these injuries, other countries will be tempted to retaliate against the American interests by adopting similar requirements where their products are sold for less in this country than at home. For example, Japan could require its camera and electronics firms to sell in the United States at (higher) Japanese domestic prices.

Even if other countries do not retaliate in kind, the Dorgan Bill would set a bad precedent that erodes the principle of comity, to the detriment of American sovereignty and interests. In today's interdependent global economy many nations can justify extraterritorial regulation of American conduct under the effects test used in international law. If the United States aggressively and insensitively promotes its own interests via the extraterritorial application of its laws, it can hardly expect other countries to exercise self-restraint. This is already a serious problem in antitrust, as the confusion and conflict caused by the worldwide application of over 100

countries' competition laws has led to calls, in America as well as abroad, for a supranational competition law under the auspices of, e.g., the WTO.

FORM OF DRUG PRICE CONTROL REGIME ISSUES

The bill is clearly aimed at drug companies that sell in both the United States and in other countries, most notably Canada, where foreign price controls force them to charge lower prices. By forcing these companies or their foreign affiliates and licensees to supply the American market from abroad, especially from Canada, the bill seeks to import these foreign price controls into the United States.

But if drug price controls are a good idea, they should be directly imposed by our Government in a straightforward manner, rather than in this backdoor, Rube Goldberg fashion. Under the Dorgan Bill the price controls of any of the foreign governments in the bill's list of "permitted countries" may be imposed indirectly on American manufacturers. These controlled prices will be imposed by foreign governments which do not answer to American voters. They will be imposed under foreign legal standards by foreign regulatory bodies using foreign administrative procedure. If subject to judicial review at all, it would be available only in foreign courts. These agencies and their regulations will be beyond the checks and balances of Congressional oversight and judicial review in American courts.

By contrast, direct controls under a regulatory regime adopted by our Congress would be authorized by a statue enacted under the constitutional and political constraints of our system of government, by the U.S. Congress responding to the policy preferences of American voters. It would be implemented by an agency of the U.S. Government, pursuant to U.S. statutory standards, under the procedural and judicial review procedures contained in the enabling legislation, the Administrative Procedure Act and the Constitution.

In short, an American price control system would be an action of the U.S. Government, operating for the sole benefit of American consumers under American legal and constitutional principles, subject to American political and legal controls. These are the benefits of any regulatory regime created by our sovereign Government. If drug price controls are a good idea, why would we delegate this task to foreign governments, rather than to our own?

INNOVATION ISSUES

If the Dorgan Bill operates as its sponsors intend, it might well remove the incentives to innovation, provided by U.S. patent policy, that have made the American drug industry the leading provider of new medications. This is why there has been no serious move for drug price controls. Instead, public policy has gone in the exact opposite direction, giving the creators of new drugs patent rights that protect them from competitive pressures for a limited statutory period. This patent protection is justified as a reasonable inducement for innovation.

The economic theory of the Dorgan Bill appears to be that the profit incentives currently provided by drug patents are excessive, not necessary to induce the research and development of new drugs. This thesis is based on the fact that drug companies make enough in Canada and other price controlling countries to justify production and sales there.

This theory is wrong. Once a new drug has been developed, the expenses of developing it have already been incurred. They are what economists call sunk costs. A rational seller will sell, if need be, at a low price that does not allow it to recover these sunk costs, so long as the sales do permit it to cover the current costs of production. This is especially true if the seller can charge enough in other markets to recover its sunk costs.

We see this all the time in the travel industry, as hotels rent rooms and airlines sell seats at very low prices rather than see them go empty. As long as the hotel or airline recovers its immediate out of pocket costs, the low price makes sense. But as we are now seeing in the airline industry, a carrier cannot survive if too many of its seats go at these low prices.

A similar principle applies to the drug industry. It makes business sense to sell in Canada as long as the controlled prices cover the out of pocket costs of producing and distributing the drugs there. But this does not mean that Canadian price levels would be sufficient to induce the research and development necessary to produce new medications.

This is not just a theoretical argument. If Canadian and European drug prices are sufficient to induce innovation, why do those countries depend on the American drug industry for new drugs? Why don't their domestic drug companies match ours? Canadians may argue their population and GDP are too small to support a domestic drug industry, but Europeans cannot. The European Union's population and GDP

are as large as our own. Yet most new drugs continue to be developed in the United States.

In sum, the Dorgan Bill raises serious issues of constitutional and international law, would subject American interests to foreign regulatory regimes, and would threaten the incentives that make this country the leading developer of lifesaving new medications. It should not be adopted.

The CHAIRMAN. Dr. Kessler.

STATEMENT OF DAVID A. KESSLER, M.D., DEAN, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO SCHOOL OF MEDICINE, SAN FRANCISCO, CA

Dr. KESSLER. Mr. Chairman, I am pleased to be here to address the important issue of the safety of our drug supply.

During my more than 25 years as a physician and particularly in my role at FDA, assuring the safety of prescription drugs has been one of my greatest concerns. I am here today to ask you to take important steps to protect American consumers from our current system of unregulated drug importation. The current system presents uncontrolled risks to the American public.

With the explosion in shipments from Canada in the last several years, FDA has seen a growing number of counterfeit and questionable drugs. The current system is out of control. There is virtually no reliable way for consumers to know whether an Internet pharmacy outside the United States is legitimate and sells authentic, safe, and effective drugs.

FDA currently lacks the jurisdiction and resources to verify that legitimate pharmacies in Canada or elsewhere are delivering safe and effective drugs to people here in the United States. The existing framework in Section 801(a) of the Federal Food, Drug, and Cosmetic Act effectively ties FDA's hands.

Mr. Chairman, the choice before you is not the choice of imports or no imports. We already have a system of importation of drugs that jeopardizes public health. Congress, I believe, has a responsibility to fix this serious problem.

The Pharmaceutical Marketing Access and Drug Safety Act of 2005 includes provisions that would address these problems. This legislation goes farther than previous attempts at addressing this issue. The bill would allow FDA to implement safeguards to stop dangerous imports that currently reach American consumers. The bill gives FDA a way to assess whether drugs distributed in other countries meet FDA standards and it assures that FDA reviews drugs before they are imported. The bill gives FDA authority to verify that imported drugs are made in legitimate, FDA-inspected plants.

And yes, today in the United States, manufacturers submit manufacturing changes every day. If you change a color of a capsule or the capsule supplier, that is a manufacturing change. FDA has a long history of handling these kind of changes.

The bill anticipates and accommodates various anti-counterfeiting technologies that are now or will become practical. This bill, through user fees, gives FDA the resources it needs to inspect facilities and verify their product. The bill assures that imported drugs will be labeled appropriately for patients. The bill gives FDA and other agencies better authority to police the importation of

drugs from dangerous, illegitimate, and scrupulous Internet sites and suppliers overseas.

The bill also addresses domestic Internet pharmacies. American citizens who choose to buy their drugs from another country or via the Internet can have confidence that they are getting FDA-approved drugs from FDA-inspected manufacturing plants if they work within the safety system created by this legislation.

Mr. Chairman, as Congress debates this legislation, there are some important points I would ask you to keep in mind. The proposed regulatory system that would permit importation of safe and effective prescription drugs should be implemented in a carefully phased manner. S. 334, in effect, creates a safe system, a validated system for drug importation. I commend the bill's sponsors for including provisions to limit the number of authorized pharmacy wholesalers and drugs in the first 2 years. Congress should consider whether similar limits should be included in the legislation in subsequent years in order to keep the program manageable and of the highest quality.

Mr. Chairman, I believe that implementing these provisions in a phased manner and with sufficient resources would be an important step to protect the public from the uncontrolled risk of imported drugs that exists today. The American public will be safer with a regulated system than with the current system of uncontrollable risk.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you.

[The prepared statement of Dr. Kessler follows:]

PREPARED STATEMENT OF DAVID A. KESSLER, M.D.

EXECUTIVE SUMMARY

The recent exponential increase in unregulated prescription imports amounts to uncontrolled risk to American consumers. The existing framework in section 801(a) of the Federal Food, Drug and Cosmetic Act effectively ties the FDA's hands so that it cannot halt packages containing questionable drugs on their way to U.S. consumers. Congress must act to protect the public from dangerous imports. S. 334 would allow FDA to implement safeguards to effectively and efficiently stop dangerous imports currently reaching American consumers and to assess the manufacturing source of imported drugs according to the same standards used for domestic drugs. Implementing these provisions in a phased manner and with sufficient resources would be an important step to protect the public from the uncontrolled risk of imported drugs that exists today.

Mr. Chairman, members of the committee, my name is David Kessler. I was Commissioner of the Food and Drug Administration from 1990 until 1997. Currently, I am vice chancellor of medical affairs and dean of the School of Medicine at the University of California, San Francisco. I am pleased to be here today to address the important issue of the safety of our drug supply.

During my more than 25 years as a physician and particularly in my role at FDA, protecting the public health and assuring the safety of prescription drugs has been one of my greatest concerns. I am here today to ask you to take important steps to protect American consumers from our current system of unregulated drug importation that presents uncontrolled risks to the American public.

In the past couple of years, there has been an exponential increase in the number of prescriptions brought into the United States from Canada and other countries. The Department of Health and Human Services has estimated that the number of shipments has grown from 2 million packages in 2001 to 10 million in 2004. With this explosion in shipments, FDA has seen a growing number of counterfeit and questionable drugs. Currently, FDA is unable to adequately assure that the imported drugs reaching American consumers are safe and effective because the agen-

cy lacks both the resources and an effective statutory framework to regulate or stop the shipments. The continued increase in prescription drug prices, the ease of setting up what looks like a legitimate pharmacy on the Internet, and the absence of regulation all contribute to this worrisome trend.

I am sure that most American consumers making these purchases truly believe they are getting the drugs that their doctors prescribed to keep them healthy. And the low prices offered on Web sites and by e-mail may be hard to resist.

But the current system amounts to uncontrolled risk. Consumers have no way to verify whether the drugs they receive measure up to U.S. standards for efficacy and safety. Even worse, the FDA lacks the regulatory structure to efficiently police the marketplace.

The current system is out of control.

There is no reliable way to know whether an Internet pharmacy outside the United States is legitimate and sells authentic, safe and effective drugs, although some cities and States have identified legitimate Canadian pharmacies from which consumers can order Canadian drugs.

The existing framework in section 801(a) of the Federal Food, Drug and Cosmetic Act effectively ties the FDA's hands so that it cannot halt packages containing questionable drugs on their way to U.S. consumers. Currently, if an FDA inspector identifies a questionable drug shipment, the agency must conduct a detailed inspection and send a specific notice to the addressee detailing the violations before it can take final action.

FDA currently lacks the jurisdiction and resources to verify that legitimate pharmacies in Canada or elsewhere are delivering safe and effective drugs to people here in the United States. The FDA does not have the authority or the resources to inspect pharmacies, wholesalers or manufacturers in Canada or anywhere else outside the United States. The agency's current ability to inspect manufacturing plants producing drugs for the U.S. market does not extend to facilities manufacturing drugs for Canada or anywhere else.

Mr. Chairman, the choice before you is not the choice of imports or no imports. We already have a system of importation of drugs that jeopardizes public health. Congress has the responsibility to fix this serious problem.

The risk to consumers in the current scenario is not just theoretical. FDA investigators ordered prescriptions from one Web site purporting to be selling approved drugs. Although the site advertised what it said were Canadian generic versions of Viagra, Ambien, and Lipitor, none of the drugs that were delivered measured up to the minimum U.S. standards. All three of the drugs had the wrong amount of active ingredients; the Lipitor and Viagra pills also were contaminated and failed dissolution tests. Simply put, these prescriptions were not safe and not effective.

While that Web site may no longer operate, there are literally hundreds of other Web sites that exist today without any regulatory oversight whatsoever.

As I understand it, the Pharmaceutical Market Access and Drug Safety Act of 2005 includes provisions that would address these problems. This legislation goes farther than previous attempts at addressing this issue. This bill would allow FDA to implement safeguards to effectively and efficiently stop dangerous imports that currently reach American consumers. American citizens who choose to buy their drugs from another country or via the Internet will have confidence they are getting drugs that are indeed safe and effective, if they work within the confines of the safety system created by this legislation. The health benefits of modern pharmaceuticals are possible only if patients get the right doses of the right medication.

S. 334 would enable FDA to determine where a drug comes from and whether it truly is the drug that the seller claims. By requiring FDA inspection and approval of both the manufacturing source of the drug and the chain of custody of the drug, the act allows consumers and commercial entities to buy prescription drugs from Canada and certain other countries with reasonable assurance that the drugs are safe and effective.

S. 334 gives the FDA the authority to assess the manufacturing source of drugs according to the same standards used for domestic drugs and to ban the importation of any drug it finds inadequate. Furthermore the bill gives the FDA the authority to inspect and verify the "chain of custody" of the drugs all the way back to the source of manufacture.

It also bars imports from countries known to be major sources of counterfeit pharmaceuticals.

In addition to assuring the safety and efficacy of the supply of imported drugs, S. 334 would increase the safety of drugs purchased via domestic Internet sites. Legitimate pharmacies require a doctor's prescription. This bill makes that rule apply to online pharmacies, and it authorizes State Attorneys General to go to Federal court to shut down rogue pharmacies.

The provisions of S. 334 make it possible for consumers to safely import drugs for their own use and enables American pharmacies to obtain safe and effective drugs from other countries for the benefit of consumers here. It also anticipates and accommodates anti-counterfeiting technology that is now or may become practical.

Mr. Chairman, as Congress debates this legislation, there are some important points I would ask you to keep in mind.

First, the proposed regulatory system that would permit importation of safe and effective prescription drugs should be implemented in a carefully phased manner. S. 334, in effect, creates a safe system for drug importation. I commend the bill for its provisions that limit the number of authorized pharmacies, wholesalers and drugs in the first 2 years. Let me suggest that Congress consider whether similar limits should be included in the legislation for subsequent years, in order to keep the program manageable and of the highest quality.

Second, creating a safe environment for drug importation also means giving the FDA clear jurisdiction and sufficient resources to do its job effectively. S. 334 gives FDA the authority to take strong regulatory action against questionable imported prescription drugs, while at the same time, creating a program for safe and effective imports.

Implementing this program will require significant resources. The bill provides funding through user fees, but these should be periodically evaluated to make sure this funding is sufficient to assure the safety of the drug supply.

Mr. Chairman, I believe that the American public will be safer with a regulated system than with the system of uncontrolled risk that we allow today.

The CHAIRMAN. I appreciate the brevity of all of the members of this panel. I apologize again that we are more than halfway through a vote, so we won't have much time, but since you have testified, I hope you will be open to written questions that any member of the committee may submit, and many were planning on doing that anyway, and we would appreciate your quick response on those. The record will stay open for another 10 days. You can expand on anything that you get in questions or anything in addition to the statement that you have given.

I do have from Dr. Kessler a couple of letters that he wrote, one that he wrote in 1999 and one in 2000, as well as his letter last year supporting the Dorgan legislation, and I would ask unanimous consent that all three of those letters be a part of the record preliminary to some of the questions that I will need to ask. I do appreciate your comments, Dr. Kessler, about a phased-in implementation of S. 334.

[The letters of Dr. Kessler follow:]

May 19, 2004.

Hon. EDWARD M. KENNEDY,
U.S. Senate,
Washington, D.C. 20510.

DEAR SENATOR KENNEDY: Thank you for the opportunity to respond to your questions about S. 2328, the Pharmaceutical Market Access and Drug Safety Act of 2004. As a former Commissioner of Food and Drugs, and a current leader of one of the Nation's leading centers for medical research and treatment, I share your concern over the affordability of prescription drugs, and support your efforts to ensure that less costly prescription drugs purchased overseas are safe and effective.

Question 1. Does S. 2328 ensure the safety of drugs imported to the United States? In particular, are there adequate assurances that drugs imported by registered pharmacies and wholesalers and exported to individuals from registered pharmacies in Canada will not be counterfeit and will meet the conditions of approval of the Food and Drug Administration?

Answer 1. It is essential that prescription drugs purchased by Americans are safe and effective. I am certain that FDA, given the proper authority, mandate, and support can ensure the safety of drugs imported into the United States. S. 2328 provides a sound framework for assuring that imported drugs are safe and effective. Most notably, it provides additional resources to the agency to run such a program, oversight by FDA of the chain of custody of imported drugs back to FDA-inspected plants, a mechanism to review imported drugs to ensure that they meet FDA's ap-

proval standards, and the registration and oversight of importers and exporters to assure that imported drugs meet these standards and are not counterfeit. As the legislation progresses, I'm sure that adjustments to this sound framework can be made to accommodate legitimate concerns of FDA or other experts and ensure that the legislation works as intended.

Question 2. Will the user fees provided for in S. 2328 provide adequate resources for FDA to police the importation of drugs under the bill?

Answer 2. FDA must be given new and adequate resources to carry out the responsibilities it would have under S. 2328. As commissioner, I oversaw the implementation of the 1992 Prescription Drug User Fee Act (PDUFA). PDUFA has proven that users fees can be an effective means of funding critical agency programs. User fees capped at 1 percent of the value of imported drugs as provided in S. 2328 would give substantial resources to FDA to police drug imports. For example, using CBO projections that 10–15 percent of drugs used in the United States might come in through imports, and assuming that the drugs will be half the price of domestic drugs, the user fee proposal in S. 2328 could result in up to $100 million in new resources for FDA, which would enable FDA to double the center for drugs field budget. It will be important, however, that the Congress work with FDA to ensure that as the drug import program evolves that FDA receives adequate, new funds to support the program.

Question 3. Does S. 2328 provide adequate protections against efforts by drug companies to stop drug importation, such as cutting of supply of drugs to those entities that export drugs to the United States or changing drugs distributed overseas so that they do not meet the conditions of approval of FDA?

Answer 3. U.S. prescription drug companies have made their products available at substantially less cost in highly developed countries such as Canada, but have then acted to prevent U.S. citizens from importing these less costly versions of their products. The steps you have taken in S. 2328 are effective tools to prevent some of the industry practices that have been documented to date.

Question 4. Do you believe that innovation in the pharmaceutical industry will cease because of drug importation? How will it be affected?

Answer 4. Research and development funding is an expense that should be shared equally by the citizens of wealthy countries throughout the world. Innovation is the heart of the prescription drug industry. The leaders of the industry, its stockholders, and the continuing enormous investment in biomedical research that is occurring at leading institutions around the world will ensure that drug innovation not only continue but accelerates.

Again, thank you for the opportunity to assist you with this important endeavor.

Sincerely,

DAVID KESSLER, M.D.,
Dean, UCSF School of Medicine.

September 13, 2000.

Hon. BYRON DORGAN,
719 Hart Senate Office Building,
Washington, D.C. 20510.

DEAR SENATOR DORGAN: Thank you very much for your letter of September 12, 2000. I very much applaud the effort that you and your colleagues are making to assure that the American people have access to the highest quality medicines. As you know, my concerns about the re-importation of prescription drugs center around the issues of assuring quality products. The Senate bill which allows only the importation of FDA approved drugs, manufactured in approved FDA facilities, and for which the chain of custody has been maintained, addresses my fundamental concerns. The requirement that the importer maintain a written record of the chain of custody and batch testing to assure the product is both authentic and unadulterated provides an important safety net for consumers.

Let me address your specific questions. First, I believe U.S. licensed pharmacists and wholesalers—who know how drugs need to be stored and handled and who would be importing them under the strict oversight of the FDA are well positioned to safely import quality products rather than having American consumers do this on their own. Second, if the FDA is given the resources necessary to ensure that imported, FDA-approved prescription drugs are the authentic product, made in an FDA-approved manufacturing facility, l believe the importation of these products

could be done without causing a greater health risk to American consumers that currently exists. Finally, as a nation we have the best medical armamentarium in the world. Over the years FDA and the Congress have worked hard to assure that the American public has access to important medicine as soon as possible. But developing life saving medications doesn't do any good unless Americans can afford to buy the drugs their doctors prescribe. The price of prescription drugs poses a major public health challenge, While we should do nothing that compromises the safety and quality of our medicine it is important to take steps to make prescription drugs more affordable.

I applaud your efforts to provide American consumers with both safe and affordable medicine.

Sincerely,

DAVID A. KESSLER, M.D.

June 29, 1999.

Hon. JOHN D. DINGELL,
2328 Rayburn House Office Building,
U.S. House of Representatives,
Washington, D.C. 20515.

DEAR REPRESENTATIVE DINGELL: You may recall that there has been a continuing controversy about the reimportation into the United States of prescription drugs manufactured here and exported abroad (so-called "American Goods Returned"). As you know the Prescription Drug Marketing Act of 1987 (the PDMA), P.L. 100–293 (Apr. 22, 1988), of which you were the principal sponsor in the House prohibits such reimportation. As the former FDA Commissioner who oversaw the implementation of many of the provisions of the PDMA, I wanted you to know of my concerns about this issue.

I believe the prohibition on reimporting exported drugs serves two critical public health purposes: (1) preventing the introduction into U.S. commerce of prescription drugs that may have been improperly stored, handled, and shipped overseas, and (2) reducing the opportunities for importation of counterfeit and unapproved prescription drugs. I know you will recall that the Energy and Commerce Committee described these purposes in its report accompanying the bill that became the PDMA.

Specifically, the existence and method of operation of a wholesale submarket, herein referred to as the "diversion market," prevents effective control over or even routine knowledge of the true sources of merchandise in a significant number of cases. As a result, pharmaceuticals which have been mislabeled, misbranded, improperly stored or shipped, have exceeded their expiration dates, or are bald counterfeits, are injected into the national distribution system for ultimate sale to consumers. . . .

A significant volume of pharmaceuticals is being reimported to the United States as American Goods Returned. These goods present a health and safety risk to American consumers because they may have become subpotent or adulterated during foreign handling and shipping. The ready market for reimports has also been a catalyst for the perpetration of a continuing series of frauds against American manufacturers, and has provided the cover for the importation of counterfeit pharmaceuticals in several cases. Moreover, the hazards associated with reimports have forced the Food and Drug Administration and U.S. Customs Service to spend inspectional and other resources that are solely needed in other areas.

H.R. Rep. No. 76, 100th Cong., 1st Seas. 6–7 (1987).

In 1986, the Oversight and Investigations Subcommittee of the Energy and Commerce Committee, which you chaired, described the public health and safety concerns of allowing "American Goods Returned" as follows:

[T]he clear and present danger to the public health from reimported pharmaceuticals is the threat that subpotent, superpotent, impotent or even toxic substances labeled as U.S.-produced legend drugs will enter the distribution system. The foremost danger comes from so-called "generic" drugs produced in developing countries that do not provide product patent protection for pharmaceuticals.

Uncertain Returns: The Multimillion Dollar Market in Reimported Pharmaceuticals, 99th Cong., 2nd Sass. 23 (Comm. Print 99-GG 1986). One well-publicized example involved importation of more than 1 million counterfeit birth control pills, complete with counterfeit packaging and labeling. Id.; Dangerous Medicine: The Risk to American Consumers From Prescription Drug Diversion and Counterfeiting, 99th Cong., 2nd Sess. 22 (Comm. Print 99-Z 1986).

In my view, the dangers of allowing reimportation of prescription drugs may be even greater today than they were in 1986. For example, with the rise of Internet pharmacies, the opportunities for illicit distribution of adulterated and counterfeit products have grown well beyond those available in prior years. Repealing the prohibition on reimportation of drugs would remove one of the principal statutory tools for dealing with this growing issue.

I know one argument now being made for allowing reimportation is that this would make lower priced prescription drugs available to U.S. consumers. But, your committee effectively rebutted that argument in 1986, in terms that seem to me to be equally applicable today.

Pharmaceuticals reimported by diverters displace full price sales in the wholesale market. Moreover, prices to ultimate consumers are generally not lowered as a result of diversion. Rather, the profits go to the various middlemen, here and abroad, while consumers bear the risk.

Uncertain Returns, supra, at 32 (emphasis added). See also Dangerous Medicine, supra, at 25–26 ("there is little or no significant benefit to consumers from pharmaceutical reimportation, and there are obvious costs in terms of health and safety risks and the utilization of scarce FDA resources").

I know of no changed circumstances that require either a shift in FDA policy or the passage of legislation to repeal PDMA's prohibition on reimporting drugs. Furthermore, I believe that such a repeal or change in policy would re-create the substantial public health risks PDMA was designed to eliminate, I would welcome your analysis and comments on this matter.

Sincerely,

DAVID A. KESSLER, M.D.

The CHAIRMAN. Senator Burr.

Senator BURR. Thank you, Mr. Chairman. Let me thank this panel for your willingness to be here, but more importantly, for your expertise, your interest, and your passion for this.

Mr. Satchwell, I can't thank you enough for your willingness to point out, hey, we have tried some of this. It doesn't work. I think listening to people who have either willingly or unwillingly become part of something is important. That you look up and say those that claimed that this would happen, in fact, were wrong. It does create a nightmare when you try to blend together a group of individual regulatory regimes into one where you haven't changed the regulations, you have just said, we will ignore ours and accept yours because there has to be some greater good, and I think that the European Union will revisit that at some point. I think that is enough of a warning that we shouldn't join into it as a full-fledged partner and blindly accept the standards of other countries. I know that shortly after we did FDAMA, that was an issue that was on the table for the United States as it related to harmonization.

Mr. Cecil, the labeling issue is quite important. Labeling should clearly state differences in equivalencies. The problem is that these bills that are on the table inject bulk purchasing into the United States for the first time. This is not an individual prescription that is being accessed from Canada. This is opening up the United States to a bulk market of foreign products. We have to hope that labels follow these products.

Mr. Arthur, I think that this proposal ignores U.S. code in total as it relates to patent protection, and intellectual property rights. Now, I understand that the Dorgan bill surgically opens the Code up and says, in this particular case, reimportation of drugs is ok. Will you address the precedent that we are setting by doing that?

Mr. ARTHUR. Well, Senator, I agree with you. It seems to me it is completely opposite from the provisions of the patent laws, par-

ticularly the ones that appertain to drugs, because there is a very careful statutory scheme that provides patent protection for people who actually come up with new drugs which have never been made before and which are not obvious and all the other protections of the patent code to make sure there has been real innovation, and the whole basis of that system is one of incentives. That is, it allows you to, for a limited term of years set by the statute and authored to deal with the problems of getting it through the FDA, a period in which you can be the exclusive seller.

Now, it is intended, in other words, to take ordinary business incentives, and that incentive basically is the one to make money, to use it as an incentive to get companies to innovate and produce new drugs and invest into a risky system, because prices of drugs don't only represent the price of the actual drug, its manufacture, or even its R&D, but also the ones that fail.

Senator BURR. Well, the authors of this bill might suggest that their intent is not to eliminate patent protection for new therapies. They are not here and that may be a question that we need to ask them, because they know that you need that incentive for those new therapies to be developed. The problem that we have today is that we are not overpriced on generic drugs. As a matter of fact, the U.S. market is underneath all foreign markets as it relates to the price of generics. So if they kept the patent protection for the new therapies, they haven't done anything. So I have got to think that their intent is to eliminate the patent protection, the incentive for research and development for new therapies as well as those that still have some patent life in them.

Mr. ARTHUR. Oh, absolutely. I mean, what it would do, if I understand the bill, I think the key is reimportation. It is interesting, we have only heard that word reimportation during this hearing without anybody talking very much about it. A normal trade matter, a normal trade law would be one that applies to importation, voluntary importation. Reimportation suggests that a drug be made in the United States, sent to Canada, and then sent right back again. The only thing that is imported is the Canadian price——

Senator BURR. And we——

Mr. ARTHUR [continuing]. As a way to, in effect, artificially lower the price. It is almost—it is like driving your car with one foot on the accelerator and one foot on the brake.

The patent law gives American companies, and European companies, for that matter, any company that innovates and gets an American patent, the right to set the price at what it chooses to. Price controls go in the opposite direction. So to say on the one hand, you can charge whatever you want to in the United States. That is your reward for innovation. But you are under legal obligation, if you sell in any one of these other countries, to provide enough to any exporter in that country to resupply the United States market at a lower price. It basically gives with one hand, takes away with the other.

Senator BURR. The Chairman and I have to leave, and I apologize, but I do want to ask Dr. Kessler one or two questions. You said in your testimony that you were glad to see that the legislation initially limits the number of pharmacies, the number of

wholesalers, and the number of drugs participating in reimportation. Can you envision how that is going to happen, how we are going to limit the number of pharmacies, the number of wholesalers, the number of drugs?

Dr. KESSLER. Certainly, Senator. I strongly support that. As the Chairman said, I think a phased approach makes sense.

Senator BURR. But understand, we can't determine whether something is adulterated today at Dulles Airport without bringing a biologist in and going through some type of process where we can determine the active ingredients because the knock-off is so good. Are we now going to ask these individuals to only let the blue pills in, but not the red ones, and only if they come from this pharmacy and not that one, and only if it came through this wholesaler and not the 12 other ones that we excluded?

Dr. KESSLER. I think what S. 334 does is create, in essence, a safe environment. It tries to create a safe environment by dealing with 50 to 100 pharmacies, the top selling drugs. And, in fact, I think by keeping it small and keeping it focused on those drugs that are the most important, we have the greatest ability to assure the American people that their drugs would be safe——

Senator BURR. And we rely on a paper trail, a paper chain to assure us that it went through the right wholesaler, that it came from the right manufacturer. Now, let me just ask you this. In the 7 years that you were at the FDA, you were an advocate for safety. You understood the letter of the law as it related to the FDA process. Would the FDA have ever accepted a regulatory scheme in the United States where companies weren't inspected, they just had to have paperwork that said that they met the FDA standard, paperwork that said that the ingredients that they got were, in fact, from where they said they were and not necessarily tested?

Dr. KESSLER. Senator, it is an excellent question, and, of course, FDA would not only require the paperwork, but as S. 334 contemplates, FDA would have to be able to go in and inspect. So it is paperwork and inspection. I think if you ask career officials at FDA today, they would much prefer the ability to have jurisdiction and the resources to be able to have the paperwork and the ability to inspect rather than have the uncontrolled system that they are currently dealing with——

Senator BURR. We have had U.S. drugs manufactured abroad for well over a decade. When you were FDA Commissioner, were there facilities from which we brought drugs into the United States that were not inspected by the FDA?

Dr. KESSLER. We inspected facilities all around——

Senator BURR. Were there any that were not inspected by the FDA that manufactured drugs for U.S. consumption?

Dr. KESSLER. For counterfeit? There were certainly counterfeit. There have always been counterfeit. There will continue to be counterfeit.

Senator BURR. I am talking about authorized manufacturers. Did we get to every manufacturer in the world——

Dr. KESSLER. We did not have—it is an excellent point, Senator. We did not have the resources in order to be able to do foreign inspections as much as we would like. That is why S. 334 requires

the user fees to do those inspections and requires—in some ways, it is ironic. The inspections would be every 12 months.

Senator BURR. You were required before.

Dr. KESSLER. You didn't give us the—I mean, not you, Senator—[Laughter.]—but the resources weren't there. I apologize.

The CHAIRMAN. The Senator's time——

Dr. KESSLER. You always did. You were the friend of the agency.

Senator BURR. But my point is this.

Dr. KESSLER. It is a good point.

Senator BURR. You had it in law. It said it had to be done, and the resources meant that you couldn't do it. What blind faith should we leap into this with a new bill that proposes a whole new regulatory acceptance on our part and say, well, we just have to trust that it is going to work?

Dr. KESSLER. No blind faith, Senator.

Senator BURR. So we have to trust——

Dr. KESSLER. Set up the right system. Give the agency the right resources. Give the FDA the right jurisdiction, as this bill tries to do, and then I think you can have the assurances.

Senator BURR. David, in the absence of——

The CHAIRMAN. The Senator's time has expired and so has the vote.

[Laughter.]

Senator BURR. Last one. In the absence of the next Congress, who may or may not fund, and you know how the budget process goes up here, everything that the FDA wants, have we not set up a regime then that allows inspections not to happen because somebody says, we didn't get funding, and the American consumer is then the recipient of adulterated, counterfeit, illicit drugs, and FDA just says, well, we didn't have the money. You didn't give it to us.

I think we have always erred on the side of making sure that didn't happen. You did it when you were there. I think the Congress, since I have been involved, wouldn't have done it. There is an easy way out. That is, give everybody what they want. But we make decisions based upon the safety of the entire population.

I thank you for your service. I thank all of you for your time. I yield back.

The CHAIRMAN. I will allow each of you to answer that last one in writing and him to submit other questions, as well as everybody else.

This hearing is adjourned.

[Additional material follows.]

ADDITIONAL MATERIAL

S. 334: A Different FDA Standard for Imported Drugs That Would Compromise the Safety, Effectiveness, and Quality of the American Prescription Drug Supply

On February 9, 2005, Senator Dorgan introduced S. 334, the Pharmaceutical Market Access and Drug Safety Act of 2005. This bill legalizes commercial and personal importation of unapproved prescription drugs from foreign countries, thereby opening a closed system designed to protect the health and safety of the American public. S. 334 makes sweeping changes to the Federal Food, Drug, and Cosmetic Act (FDCA). It creates an entirely new statutory regime to govern the importation of "qualifying" prescription drugs from "permitted countries." It exempts imported drugs from sections 501 and 502 of the FDCA, which set forth the prohibitions on adulteration and misbranding that apply to domestic products. Moreover, imported foreign drugs are not subject to the rigorous "gold standard" approval mechanisms/requirements of section 505 of the FDCA. **Rather, the bill creates a new standard of "approval," a "manufacturing changes" standard, for these foreign products.** Under this approach, manufacturers would be mandated to submit "notices" describing the differences between their foreign product and domestic product as though they were making a change in the manufacturing process and thereby removing one product from the marketplace. But in fact, this process would result in the availability of both products in the United States. The bill would require an order from the Food and Drug Administration (FDA) to ensure that importation of unapproved foreign products will not begin. This inverts the rule applicable to domestic products that distribution of the new version of the product is prohibited until FDA issues an approval. Finally, the bill replaces the refusal-to-admit mandate in section 801 of the FDCA with a permissive authority. Other provisions of the bill are fundamentally flawed, as well. These include, for example, the attempt to exclude imports from certain European countries and the lack of any effective funding mechanism. The sweeping changes S. 334 makes to the FDCA, will put American patients at serious risk of receiving dangerous and counterfeit prescription drugs.

I. THE CURRENT SYSTEM ENSURES THE SAFETY AND EFFECTIVENESS OF PRESCRIPTION DRUGS MARKETED IN THE UNITED STATES

Since 1938, section 505(d)(1) of the FDCA has prohibited the marketing of any new drug unless it has been shown to be "safe for use under the conditions prescribed, recommended, or suggested" in its labeling. In 1962, Congress amended the FDCA and section 505(d)(5) now requires proof of the effectiveness of marketed drugs and gives FDA authority to stipulate the specific tests required before the agency will approve the drug for marketing. Since that time, FDA's authority has been expanded, strengthened, and refined by the Hatch-Waxman Act of 1984 and the Prescription Drug Marketing Act of 1987 (PDMA). As a result of these enactments, FDA now regulates virtually every stage in the life of a prescription drug, from pre-clinical testing in animals and human clinical trials before the drug can be marketed, to manufacturing, labeling, packaging, and advertising when the drug is marketed, as well as to monitoring the safety of a drug after its sale to consumers.

The key to FDA's ability to protect the safety, effectiveness, and quality of prescription drugs is its authority to review and approve new drug applications before a new drug may be sold. A new drug application (NDA), filed under section 505(b), must contain full reports establishing with substantial evidence the safety and effectiveness of the proposed product. An abbreviated new drug application (ANDA), filed under section 505(j), does not contain data on safety and effectiveness. Instead, an ANDA applicant may "piggyback" on the safety and effectiveness data which has been previously submitted to the FDA by the innovator of the product. However, an ANDA applicant must submit data described in section 505(j)(2) which establishes—among other things—that a proposed generic drug must have the same active ingredient as and be bioequivalent to the innovator drug. When FDA approves an application under section 505, the approval is specific to the product formulation and labeling, as well as the manufacturing process and facilities, described in the application.

After approval as stated in section 506(A), FDA retains regulatory authority over both the manufacturer and the drug product. For example, the holder of an approved application must validate any change to any aspect of the approved product (including changes in the manufacturing process) and must notify FDA of that change. Further, it must submit a supplemental application to FDA for all but the

most minor changes. And it must seek prior approval of significant changes with the potential to affect safety, effectiveness, or quality. The manufacturer must continue to ensure that the drug, and the methods used in, as well as the facilities and controls used for, its manufacture, processing, packing, and holding comply with current good manufacturing practice (GMP) as described in section 501(a). Section 502(n) of the FDCA mandates that the drug not be misbranded, so—for example—the manufacturer and distributor must include in their advertisements for the product a "brief summary" of the product's side effects, contraindications, and effectiveness.

In short, sections 501, 502, and 505 form the foundation of FDA's regulation of pharmaceuticals in the United States by prohibiting the introduction into interstate commerce of an adulterated, misbranded, or unapproved new drug. Importation of a prescription drug results in the introduction of that drug into interstate commerce and therefore imported drug products are subject to sections 501, 502, and 505. A drug manufactured in a facility not listed in the approved application, and a drug that is not manufactured according to the specifications described in the approved application, is unapproved—even if made by the NDA or ANDA holder. It cannot be imported or otherwise introduced into interstate commerce. Moreover, section 801—added by the PDMA—prohibits the importation (sometimes called "reimportation") of a drug manufactured in the United States in full compliance with the approved application and then exported abroad. There is an exception (section 801(d) for the original manufacturer, who is an integral part of this closed regulatory system and subject to FDA authority and oversight at all times.

II. UNSAFE PRODUCTS.—S. 334 WRITES SECTIONS 501, 502, AND 505 OUT OF THE FDCA, CREATING FOR UNAPPROVED FOREIGN PRODUCTS A NEW REGIME THAT IS FUNDAMENTALLY INCONSISTENT WITH U.S. DRUG LAW

S. 334 permits the importation of foreign products that do not comply with any approved NDA and that are not bioequivalent to any approved U.S. drug. It also exempts these products from most of the adulteration and misbranding provisions that apply to domestic products. In sum, it writes sections 501, 502, and 505 out of the statute ending decades of consumer protection. It also effectively exempts imported drugs from section 506A, which governs manufacturing changes made to products approved under sections 505. And it eliminates the tough refusal-to-admit standard that applies to imports under section 801(a). Finally, it repeals the PDMA, amending section 801(d) to permit the "reimportation" of approved drug products that have been outside the jurisdiction of the FDA and beyond the control of the manufacturer.

A. S. 334 Writes the Section 505 Approval Process Out of the FDCA

FDA's ability to protect American patients from unsafe and ineffective drugs depends on its authority under section 505 of the FDCA to review and approve new medicines prior to their distribution in commerce. The Dorgan bill, however, creates an alternative route to market for foreign drugs, one that wholly bypasses section 505. It expressly permits the importation of foreign drugs that are different from and not bioequivalent to any FDA-approved drug, raising serious safety concerns. It permits these products to enter the United States pursuant to FDA review of a "notice" (rather than an application) using the "manufacturing changes" standard of section 506A. In addition the new pathway to market contained in S. 334 threatens the balance between encouraging innovation, on the one hand, and ensuring timely generic competition, on the other hand.

1. S. 334 Replaces the Uncompromising Approval Standard in Section 505 with Speculation About a Hypothetical "Manufacturing Changes" Submission

Proposed section 804(g)(2)(A) of S. 334 provides that an imported drug must "comply with the conditions established in the approved application under section 505(b) for the U.S. label drug as described under this subsection." Subsection 804(g) of S. 334, however, does not really require the foreign drug to comply with either section 505 or the approved NDA. Rather, it requires the manufacturer of any "qualifying" drug to submit a "notice" to FDA.

A product is a "qualifying" drug if it is a drug for which there is a "corresponding U.S. label drug." This, in turn, is a "prescription drug" that (1) has the same active ingredient or ingredients, route of administration, dosage form, and strength as the qualifying drug, (2) is manufactured by or for the person that manufactures the qualifying drug, (3) is approved under section 505(c) of the FDCA, and (4) is not a controlled substance, biological product, infused drug, inhaled drug, or drug for which there are two marketed generics. The "notice" must identify each difference

in the qualifying drug from a "condition established in the approved application" for the corresponding U.S. label drug. (The notice need not identify variations provided for in the U.S. drug's labeling or differences in the labeling, except ingredient labeling.)

It must include "the information that the Secretary may require under section 506A," although section 506A applies only to "a drug for which there is in effect an approved application under section 505 or 512 or a license under section 351 of the Public Health Service Act" (i.e., not an import), so this requirement may be meaningless. It must also include "any additional information the Secretary may require," which in turn may—but need not—include data on bioequivalence. Finally, the notice must include (1) the date on which the qualifying drug was or will be introduced for commercial distribution in the foreign country, (2) a demonstration that the manufacturer has notified the foreign government about the notice to FDA, (3) the foreign marketing application in original and in translation, and (4) various certifications as well as a filing fee in many cases.

This "notice" submitted to FDA is nothing like a new drug application. FDA regulations and dozens of FDA guidance documents, lay out the content and format requirements for any new drug application filed with FDA. Among other things, the NDA must include a chemistry, manufacturing, and controls (CMC) section that describes the composition, manufacture, and specifications of the drug substance and drug product, including its physical and chemical characteristics; its stability; the process and controls used during manufacturing and packaging; and analytical methods to assure its identity, strength, quality, and purity. Every step in the manufacturing process must be described in exhaustive detail, and the entire process must be "validated" (i.e., the company must document that it consistently produces a product meeting pre-determined specifications and quality attributes). The NDA also includes a nonclinical pharmacology and toxicology section, a human pharmacokinetic and bioavailability section, a microbiology section (if the product is an anti-infective drug), a clinical data section, a statistical section, labeling, case report forms, and patent information. An NDA can exceed a hundred thousand pages in length. The CMC section itself can exceed thousands of pages in length. Although proposed section 804(g) would require manufacturers to provide FDA with English translations of the relevant foreign marketing applications, these applications will not comply with 21 CFR § 314.50 or with accompanying agency guidance documents. The foreign regulator may have required different information, in a different format, and in a different order.

Under S. 334, the Secretary must treat the difference described in the notice as a "manufacturing change to the U.S. label drug under section 506A." He must "review and approve or disapprove the difference . . . using the safe and effective standard for approving or disapproving a manufacturing change under section 506A." If FDA concludes that it would approve a supplement for the U.S. drug if the difference were presented as a manufacturing change to the NDA for the FDA-approved product, it must allow the foreign product to be imported. There would be no such supplement, however, and it is not clear how FDA could determine what data this non-existent supplement would contain and whether the supplement would be approvable under "the safe and effective standard" of section 506A of the FDCA. When an NDA-holder makes a manufacturing change, it supplements an existing document (the NDA) that is both highly detailed and very specific to the FDA-approved drug. The "difference" between two drugs, one that is the subject of this document and one that is not, cannot plausibly be reviewed as a "change" to that document—any more than the edits to one piece of legislation can be grafted onto a different piece of legislation. So while the Dorgan bill purports to apply the "safe and effective standard" in section 506A, the standard is meaningless in this context: it in essence lowers the existing standards.

The new "notice" provisions also reverse the presumption in section 505. Under current law, the burden is on the manufacturer—whether innovator or generic manufacturer—to satisfy the legal standards of section 505. Absent approval of an application filed under section 505(b) or 505(j), the new drug in question cannot be distributed. If the Dorgan bill became law, however, the FDCA would not automatically prohibit the distribution of qualifying foreign drugs, even if they were significantly different from FDA-approved drugs. Instead, FDA would have to affirmatively issue an order that importation not begin until the agency's review of the manufacturer's notice was complete.

2. Eliminates the Bioequivalence Standard.—S. 334 Permits the Importation of Non-Bioequivalent Drugs for Which There Would be No Assurance of Safety or Effectiveness

While the Dorgan bill putatively incorporates the sameness requirements of section 505(j) by requiring that imported drugs have the same active ingredient, route of administration, dosage form, and strength as the corresponding FDA-approved drug , it does not require that these unapproved drugs be bioequivalent to any FDA-approved product. Nor does it require pre-market submission of detailed manufacturing information. So in addition to exempting imported drugs from the NDA requirement, it exempts them from the alternate requirement of bioequivalence applicable to generic drugs in the United States. The risk to patients from nonbioequivalent therapies would be amplified for certain classes and categories of drugs, including those with a narrow therapeutic index. The Surgeon General's Task Force concluded that, "even slight changes in the dose and/or amount of drug in the blood could potentially have dangerous effects" for persons taking drugs with a narrow therapeutic index such as digoxin, lithium, phenytoin, theophylline, and warfarin. If a patient switches from a U.S. drug to a nonbioequivalent foreign drug, the change could cause his clinical condition to recur or lead to toxicity.

Currently under section 505(j) of the FDCA, when an applicant seeks to market a "generic version" of an innovator product, the applicant must establish that the product is the same as, and bioequivalent to, the innovator drug which has already been approved through the NDA process before it can be presumed to be as safe and effective as that innovator product. A sponsor must also provide as required in 505(j) full chemistry, manufacturing, and controls information regarding the "generic" drug and product manufacturing. Bioequivalence concerns are real and the lack of equivalence has prompted the FDA and the World Health Organization (WHO) to remove a number of drugs from the marketplace and its list of pre-qualified medications respectively. (See WHO, "Removal of Antiretroviral Products from the WHO List of Prequalified Medicines," at <<http://www.who.int/3by5/news22/en/>>).

If S. 334 were adopted there would then be three pathways to the U.S. prescription drug market—a new drug application under 505(b), an abbreviated new drug application under 505(j), and *a "notice of manufacturing change" under the Dorgan bill.* This eviscerates the important balance struck by Congress in 1984 and in 2003, when it drafted and then amended the Hatch-Waxman amendments to the FDCA. Under S. 334 a foreign drug product might be permitted on the U.S. market on the strength of the U.S. innovator product's NDA safety and efficacy data, even if the products are different, made differently, and not bioequivalent. The Dorgan bill authorizes the Secretary to exclude non-bioequivalent foreign drugs if he determines that the availability of both versions "would pose a threat to the public health." But the Secretary could not make this determination in time to exclude the foreign drug entry into the United States market: it would require clinical data assessing the effect of a switch or post-approval data from a country in which both were approved and marketed. Such drugs are not eligible for approval through the ANDA process, and they should not be eligible for import into this country.

The likely result is a glut of non-bioequivalent foreign drug products will enter the U.S. market. The FDA has expressed concern about this "needless proliferation of pharmaceutical alternative drug products." For each FDA-approved drug product, there could be dozens of nonbioequivalent foreign versions. Such an influx of nonbioequivalent drugs will be confusing to both patients and practitioners. The Secretary may—but is not required to—add to the U.S. labeling (which, of course, is specific to a different product) an advisory that the drug is "safe and effective" but "not bioequivalent" to the FDA-approved product. When the product is dispensed to a consumer, the pharmacist must include that advisory. The advisory is likely to be meaningless to consumers, however. And nothing requires that this information be provided to the healthcare provider who prescribed the drug. A physician will thus have no way of knowing that his patient has received a non-bioequivalent drug. Even if the advisory is provided to the physician, it will be meaningless without an explanation of how the imported product differs from the approved product, i.e., is it super potent as the result of greater bioavailability or sub potent due to poor bioavailability.

B. S. 334 Exempts Imported Foreign Drugs From Adulteration Provisions in Section 501

Section 501 of the FDCA defines the situations in which a drug is deemed "adulterated" and its distribution therefore a prohibited act. Among other things as stated in section 501(a)(1) & (a)(2), a drug is adulterated if it "consists in whole or in part of any filthy, putrid, or decomposed substance" or if it "has been prepared,

packed, or held under unsanitary conditions." It is also adulterated, according to section 501(a)(3) if its "container is composed, in whole or in part, of any poisonous or deleterious substance which may render the contents injurious to health." Finally a drug can be considered to be adulterated if the "methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice."

Rather than requiring that imported drugs comply with section 501 of the FDCA, however, S. 334 writes that provision and the associated hundreds of pages of Federal regulations and code out of the existence. Under proposed section 804(g)(4), an imported drug is "considered to be in compliance with section 501 if the drug is in compliance with" proposed section 804(c). In turn, section 804(c) requires merely that the following be true: (1) the drug was manufactured in an establishment required to register under the FDCA and inspected either by FDA or by a permitted country whose regulatory system FDA recognizes as equivalent under a mutual recognition agreement; (2) the establishment manufactured the drug for distribution in the United States or one or more permitted countries; (3) the drug meets minimal chain-of-custody and paper pedigree requirements; (4) the drug is imported from a permitted country; (5) if ever outside a permitted country, the drug was under the control of the manufacturer; and (6) the registered importer or, in the case of personal importation the registered exporter, retains a sample of each lot sufficient for testing. Provided these minimal requirements are met, the drug is deemed to comply with section 501.

This means, in short, that an imported drug may consist "in whole or in part of any filthy, putrid, or decomposed substance." Its container may be composed of a "poisonous or deleterious substance" that renders the contents injurious to health. It may contain an unsafe color additive. As discussed more fully below, FDA will no longer be instructed to interdict such a drug at the border. And because the drug will be exempt from the adulteration provisions of section 501 that apply to domestic products, FDA may be without authority to seize it once it enters the stream of commerce. Indeed, even if the drug becomes adulterated after entering the country (for example because it is held in unsanitary conditions, causing it to become contaminated with filth), FDA will arguably be powerless to seize it under section 304.

C. S. 334 Effectively Writes the Misbranding Provisions of Section 502 Out of the FDCA

The Dorgan bill exempts unapproved foreign drugs from 8 of the 12 basic misbranding provisions that apply under section 502 to brand and generic drugs currently authorized for distribution in the United States. Specifically, the bill provides in proposed section 804(g)(3) that a commercially-imported drug will be considered "in compliance with section 502" if it bears (1) a copy of the labeling approved for the corresponding U.S. drug, (2) the name and location of the manufacturer, (3) the lot number assigned by the manufacturer, (4) the name, location, and registration number of the registered importer, and (5) the National Drug Code (NDC) number assigned to the drug by the Secretary. A personally imported drug will be considered "in compliance with section 502" if its packaging and labeling comply with all applicable regulations promulgated under sections 3 and 4 of the Poison Prevention Packaging Act, and if its labeling includes (1) directions for use by the consumer, (2) the lot number assigned by the manufacturer, (3) the name and registration number of the registered exporter, (4) if required by the Secretary, an advisory that the product is safe and effective but not bioequivalent to the U.S. label drug, (5) if the inactive ingredients are different from those in the U.S. label drug, an advisory regarding allergies and a list of those ingredients, and (6) a copy of any "special labeling" that would be required by the Secretary if the U.S. label drug were dispensed in the United States. Section 502 itself, however will not apply.

Not only does the Dorgan bill exempt foreign drugs from the misbranding provisions of section 502, but it affirmatively requires that these products bear inaccurate labeling.

Specifically, it requires that the FDA-approved labeling for the corresponding U.S. drug accompany any commercially imported unapproved foreign drug—even though the foreign drug may not be bioequivalent and even though some of the information in the labeling may be incorrect. Although the labeling may be amended to include a brief statement if the drugs are not bioequivalent and must include information about variations in inactive ingredient, the rest of the labeling will pertain to a different drug and could be inaccurate. The foreign drug, for example, may have been studied in different clinical trials than those summarized in the FDA-approved labeling. As a result of a change in the inactive ingredients, information on storage conditions and stability may be inaccurate. FDA-approved labeling distills the

mountain of data submitted to FDA about a particular drug, including data from all clinical and pre-clinical studies, into a set of instructions that permits physicians to use the drug product safely and effectively. The Dorgan bill slaps this carefully crafted labeling onto a different drug, undermining the FDA-approved labeling and interfering with the ability of physicians to make thoughtful prescribing decisions.

D. S. 334 Repeals the PDMA Prohibition on Reimportation

Congress amended the FDCA in 1988 to prohibit the reimportation of FDA-approved drug products that have circulated overseas outside the control of the manufacturer and beyond the jurisdiction of the FDA. Congress added this provision to seal a dangerous hole that had allowed the introduction of counterfeit medicines in the 1980s.

In 1984, nearly 2 million counterfeits of G.D. Searle's Ovulen 21 birth control pills were found to have been shipped to Miami and New York from Panama. In June 1985, the staff of the Subcommittee on Oversight and Investigations of the House Committee on Energy and Commerce published a report discussing the incident and launching the legislative effort that would culminate in the PDMA provision prohibiting reimportation of American-made and FDA-approved goods that have circulated overseas. In 1985, 1,800 bottles of Eli Lilly's antibiotic Ceclor capsules entered Miami and Boston from Singapore. The products contained Eli Lilly's active ingredient, but the capsules, labels, lot numbers, and packaging were all fake. The subcommittee convened the first of eight public hearings on drug diversion and counterfeiting on July 10, 1985. Over 2 years, the Energy and Commerce Committee heard from State and Federal law enforcement officers, private investigators, State drug and narcotic agents, Customs officials, Food and Drug Administration (FDA) officials, pharmacists, diverters, U.S. attorneys, pharmacy and pharmaceutical trade associations, pharmaceutical sales representatives, and senior enforcement officials from State regulatory agencies.

After this elaborate investigation, the House Energy and Commerce Committee concluded that permitting reimportation of U.S.-origin goods "prevents effective control or even routine knowledge of the true sources of merchandise in a significant number of cases." As a result, "pharmaceuticals which have been mislabeled, misbranded, improperly stored or shipped, have exceeded their expiration dates, or are bald counterfeits, are injected into the national distribution system for ultimate sale to consumers." Congress amended the FDCA to prohibit the reimportation of approved drugs that have left the United States. The prohibition was not controversial, and it has been a significant component of our country's defense against the surfeit of counterfeit medicines on the global market.

The Dorgan bill reopens the American drug supply to drugs sent overseas, shipped from country to country, passed from party to party, and then imported to the United States by third parties that are not affiliated with the manufacturer. If it becomes law, the Dorgan bill will return us to a time when counterfeits entered this country under the guise of "American goods returned" and jeopardized the health of American patients.

E. S. 334 Eviscerates the Tough "Refuse to Admit" Rule That Applies to Obviously Dangerous Drugs at the Border

Under section 801(a) of the FDCA, FDA must refuse entry to a drug at the border if it appears from examination or otherwise that: (1) the drug "has been manufactured, processed, or packed under unsanitary conditions," (2) the drug is "forbidden or restricted in sale in the country in which it was produced or from which it was exported," or (3) the drug is "adulterated, misbranded, or in violation of section 505." By mandating that FDA refuse admission to obviously violative drug products, this provision too is an important element in the defense of our drug supply. Yet the Dorgan bill effectively repeals it.

First, proposed section 804(g)(1) states that an imported drug must comply with the standards in section 801(a) "subject to paragraphs (2), (3), and (4)." These paragraphs, in turn, effectively delete the requirement of approval (paragraph 2), prohibition of misbranding (paragraph 3), and prohibition of adulteration (paragraph 4). Second, proposed section 804(g)(5) states that an import "may" (but need not) be refused admission if—among other things—the drug does not comply with the substitute-501 or the substitute-502 provision, or the Secretary "becomes aware" that the drug (1) may be counterfeit, (2) may have been prepared, packed, or held under unsanitary conditions, or (3) may have been manufactured, processed, packed, or held in facilities that do not conform to GMP. Additional permissive grounds are listed, although some make no sense. For example, the Secretary "may" refuse the drug admission if he has ordered that its importation cease after review of the manufacturer's notice. Inexplicably, it appears he may instead choose to permit that

drug to enter the country. To give another example, the Secretary may refuse the drug admission if he has "withdrawn approval" of the drug under section 505(e). Since imported foreign drugs are not "approved" under section 505 in the first place, this provision may be meaningless.

In short, every ground listed in the new "refuse to admit" provision is permissive. The Secretary may choose—or perhaps by virtue of resource limitations may be forced—to permit a foreign drug into U.S. commerce even if it has been recalled, its markings appear counterfeit, or he is aware that it was not manufactured in accordance with GMP. Moreover, the Secretary lacks even permissive authority to refuse admission of a drug that violates the provisions of section 501 that apply to domestic products. He thus lacks authority to stop a product clearly composed of a "filthy, putrid, or decomposed substance" or held in a container composed of a "poisonous" substance. And, as discussed above, because this product would be exempt from the adulteration and misbranding provisions of sections 501 and 502, FDA may lack authority to seize the product under section 304 after it enters the stream of commerce.

III. UNSAFE SOURCES OF PRESCRIPTION DRUGS.—S. 334 IS FUNDAMENTALLY FLAWED, AND ITS IMPLEMENTATION WOULD PUT THE AMERICAN DRUG SUPPLY AT RISK

The Dorgan bill creates a significant risk that poor-quality and counterfeit drugs will be imported into this country and sold to American consumers. First, in an apparent effort to limit importation from the newest members of the European Union (EU), the bill draws unworkable and unenforceable distinctions between EU member states. Second, the bill's distribution safeguards—intended so FDA may document and monitor the chain of custody and ensure the authenticity of imported drugs—are inadequate. And third, the bill does not provide FDA with enough time or money to implement its provisions safely.

A. The Dorgan Bill Draws an Unworkable and Unenforceable Distinction Between EU Member Countries in its Definition of "Permitted Countries"

S. 334 authorizes commercial and personal importation of qualifying drugs from "permitted countries." It defines "permitted country" to mean Australia, Canada, Japan, New Zealand, Switzerland, and any member of the European Union except those operating under 2003 accession treaties that include "a transitional measure for the regulation of human pharmaceutical products that has not expired." Five of the ten countries that joined the EU on May 1, 2004, have transitional measures of this sort in their accession treaties: Cyprus, Lithuania, Malta, Poland, and Slovenia. The bill's definition of "permitted country" therefore includes the 15 "old" EU member states (Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden, and the United Kingdom) and five of the ten "new" EU member states (Estonia, Latvia, Hungary, Slovakia, and Czech Republic). It does not include Cyprus, Lithuania, Malta, Poland, or Slovenia. At the expiration of the relevant treaty provision, the last in 2008, imports from these last five countries also will be permitted.

This distinction between EU members, however, does not fully overlap with the EU regime, and it draws distinctions between EU products that are contrary to EU law and policy, including a founding principle that goods should move freely between member countries. The accession treaties for the five member states excluded by S. 334 limit the movement of only certain drug products approved for sale prior to accession. Other drugs approved by those members may move freely throughout the EU. These include drugs cleared by those countries after May 1, 2004, as well as drugs approved prior and then reapproved under a regulatory regime that complies with EU-requirements. In contrast, the Dorgan bill prohibits importation of all drugs from each of these five countries until the expiration of that country's transition period. In other words, the EU draws distinctions that the Dorgan bill does not, and the Dorgan bill draws a distinction that the EU does not.

This fundamental asymmetry makes the Dorgan approach unworkable. For example, even if a drug is approved throughout the European Union, section 804(c)(2) of the Dorgan bill prohibits its import if it was actually manufactured for distribution solely in an excluded member state (i.e., and not also a "permitted" member state). While section 804(c)(5) of the Dorgan bill prohibits the importation of a drug that has passed through an excluded member state, unless it was within the manufacturer's control at the time. A drug may thus be imported into the United States if it was manufactured *for* and exported *from* a permitted country, even if it was manufactured in an excluded member state. A product may also be imported if the manufacturer shipped the drug to a distributor in a permitted country by way of an excluded member state. If, however, the *distributor* shipped the product through an excluded member state, the drug is no longer eligible for export to this country. This

effectively imposes tracking and chain-of-custody requirements that do not exist under EU law.

B. S. 334 Does Not Adequately Protect the American Drug Supply From Counterfeit and Damaged Pharmaceuticals

The Dorgan bill provisions intended to ensure that imported drugs are both authentic and traced from manufacturer to patient are inadequate and unrealistic. As a result, with the newly opened border, the resulting glut of imports, and FDA's longstanding resource constraints, the volume of counterfeit and damaged medicines that enter the U.S. drug supply will undoubtedly increase.

In section 804(c)(3) of S. 334 registered importers and registered exporters are required to obtain drugs directly from the manufacturer or from an entity that agrees in a contract with the registered party to meet certain chain-of-custody requirements. Specifically, the contracting party must (1) provide a statement that identifies each prior sale, purchase, or trade of the drug, (2) permit FDA to inspect those statements and related records to confirm their accuracy, (3) permit FDA to inspect its warehouses and other facilities, including records, to determine whether the facilities comply with FDCA standards applicable "to facilities of that type in the United States," and (4) ensure, through contracts if necessary, that the Secretary has the same inspectional authority with respect to prior parties in the chain of custody.

The bill does not give FDA regulatory authority or jurisdiction over foreign parties in the chain of custody. The bill instead relies upon the contractual assurances from those foreign parties that they will honor chain-of-custody statements and permit to the Secretary to inspect records, facilities, and warehouses. This contractual right, presumably, would be enforced by the registered importer or exporter, possibly only under foreign contract law. It is unclear how FDA could enforce the requirement that a registered party "enforce" the contract, under those circumstances. If a foreign party in the chain of custody refused inspection, presumably the registered party could sue for breach of contract. When could HHS deem the registered party to have violated the statutory requirement to enforce the contract? For example, if the foreign court agreed that there had been a breach but ordered money damages instead of specific performance, perhaps then HHS could terminate the registration—or perhaps the registrant could argue it had adequately "enforced" the contract. In any event, in this situation, there is no way for FDA to assert rights directly over the foreign parties in the chain of custody and no recourse for U.S. consumers who may be injured while the registrant and its subcontractors bicker over contract terms and while FDA's hands are tied.

The process outlined in S. 334 does not require the identification of any repackaging or relabeling firm that had the drug product in their custody after the product left the custody of the manufacturer, even though these practices may increase the risk of adulteration and the risk of contamination with counterfeits. Further, nothing in the chain-of-custody provision addresses the risks inherent in transshipment. During movement from permitted country to permitted country, these drugs are out of the manufacturer's control, beyond FDA's jurisdiction, and often exempt from local government regulation. Lax storage, handling, and shipping could degrade the products and endanger the patients who eventually take them.

FDA's lack of authority over foreign parties is exacerbated by the bill's exemption of foreign commercial exporters from its registration requirements. The bill requires two categories of entity to register: (1) licensed pharmacies and wholesalers in the United States who import commercial quantities of drugs "registered importers," and (2) entities in Canada "registered exporters" who ship medicine directly to individuals in the United States. It does not, however, require registered importers to purchase their supplies from registered exporters. In other words, wholesalers and pharmacies will purchase foreign drugs from foreign companies that are not regulated under the FDCA and may not be regulated under foreign law.

Elsewhere the bill relies on unrealistic requirements to ensure that the medicine supply will be protected. For example, it provides that the Secretary must inspect registered exporters and registered importers, and during this inspection "verify the chain of custody" from the manufacturer to that entity. Simply stating that the Secretary must "verify" the chain, however, will not ensure that he has the resources or information necessary to do so. While the bill calls for the use of anti-counterfeiting and track-and-trace technology, it admits that some drugs will lack these features, and it adds that these drugs may not be excluded from the import chain simply because they lack these features. A drug without such features, and with a forged pedigree paper, may be incorrectly deemed "verified" even if fraudulent and dangerous. And although the bill requires the retention of samples, it does not require that products actually be tested—whether for authenticity or for adulteration.

Random sampling and testing will never allow FDA to identify all counterfeit or dangerous drugs. But it would be one means to identify some compromised drugs. Without accompanying testing requirements, the sample retention provision is simply a housekeeping provision in the guise of a safety measure.

C. S. 334 Does Not Provide FDA With Sufficient Resources or Time for Its Implementation

HHS and Customs officials have repeatedly testified to Congress that they lack the personnel and resources to adequately enforce existing law. The Dorgan bill would open the borders to a flood of foreign products, without providing HHS with adequate funding to enforce its provisions. Although the bill requires registered importers to pay a one-time registration fee of $10,000 and thereafter inspection fees assessed twice annually, the latter are capped at 1 percent of the total price of the drugs imported annually under the law. (A matching provision applies to registered exporters.) A fund consisting of 1 percent will be insufficient for FDA to undertake all the tasks assigned to it under the bill. To give just a few examples of new tasks to be undertaken by FDA: the agency must assign personnel to review registration forms and changes to those forms; maintain the Web site and staff the toll-free number that lists registered exporters and lists notices filed by manufacturers; monitor importer and exporter compliance with registration conditions; conduct hearings related to suspension of registrations; conduct hearings related to termination of registrations; conduct onsite inspections of exporters and importers at least 12 times per year per registered party; review notices of import shipments; verify chains of custody; inspect the facilities and records of foreign parties in the chain of custody; inspect shipments to determine whether they should be refused admission; calculate, assess, and adjust inspection fees throughout the year; inspect foreign manufacturing establishments when notices are submitted under section 804(g); undertake consumer education activities; verify that registered exporters are authorized to dispense drugs under the law of the permitted country in which they are located; and monitor the affixing of markings to imported drugs. If the agency lacks sufficient resources to police illegal imports now, how will a 1-percent user fee possibly fund a program of this magnitude?

The bill also fails to provide FDA with adequate time to draft implementing regulations. Under S. 334, regardless of the status of implementing regulations, personal importation from Canada may begin 90 days after enactment. Even if FDA has not finalized implementing regulations, commercial importation from Canada and other permitted countries may begin 1 year after enactment. The Dorgan bill authorizes personal importation from Canada 90 days after enactment, regardless of whether FDA has issued implementing regulations. Commercial importation from Canada and other permitted countries may begin 1 year after enactment, again even if FDA has not concluded a rulemaking. This is not enough time for the agency to complete notice and comment rulemaking or to establish the infrastructure necessary to implement the complex drug importation scheme embodied in S. 334. Even the Bioterrorism law for food security provided 18 months for many parts of the final regulations to be issued, and FDA already had food importation authority and inspection infrastructure in place.

IV. OTHER CONCERNS.—S. 334 DISTURBS THE BALANCE BETWEEN INNOVATION AND GENERIC ENTRY STRUCK BY CONGRESS IN 1984 AND AFFIRMED IN 2003

The Hatch-Waxman Act was the culmination of years of legislative consideration as to the proper balance between making available lower cost generic drugs and creating an incentive for pharmaceuticals innovation. The result was a compromise between the research-based and generic industries whereby generic manufacturers obtained the ability to gain approval based upon proprietary innovator data and to infringe patents prior to expiration in order to conduct tests necessary for FDA approval. In return, pioneers were promised the restoration of a portion of the patent term lost to FDA review, a meaningful opportunity to vindicate patent rights prior to generic approval and market entry, and limitations on generic companies' use of their proprietary data. Congress affirmed this compromise in 2003 in the Medicare Modernization Act (MMA). The Dorgan bill threatens to destroy it.

S. 334 undercuts the very incentive to innovate that Congress sought to provide in the Hatch-Waxman Act and preserve in the MMA. The bill adds a new provision to the Patent Act that would adversely affect patent rights that are an important incentive for innovation. Under the provision, it is not an act of patent infringement to use, offer to sell, sell within the United States, or import into the United States any patented invention under section 804 that was first sold abroad by or under the authority of the owner or licensee of such patent. This overturns settled law. And only the pharmaceutical industry is singled out for this treatment. Indeed, the very

concept of foreign drug importation threatens U.S. innovation. Following approval of an innovative new drug in the United States, there will be immediate market penetration by a price-controlled foreign import. This will eviscerate the market for the innovator product, effectively eliminating the intellectual property protection that otherwise allows innovators to recoup their investment in research and development.

V. UNSAFE INTERNET PHARMACIES.—S. 334'S INTERNET PHARMACY PROVISIONS CREATE AN ILLUSION OF SAFETY WITHOUT FULLY ADDRESSING ROGUE INTERNET PHARMACIES

As the Surgeon General's task force pointed out in December, many drugs sold over the Internet are sold by "rogue" pharmacies, which claim that their products are "FDA-approved drugs," even though the drugs are not. Further, as FDA witnesses testified before Congress last year, some sites falsely purport to be "Canadian" pharmacies. The drugs they sell—which could be counterfeits or even toxic—may in fact be shipped from countries with very ineffective pharmaceutical regulatory systems. The Dorgan bill requires that domestic Internet pharmacies have a "qualifying medical relationship" with their patients and include certain identifying information on their Web sites. But these provisions are inadequate to assure the safety of consumers. The bill does not require Internet pharmacies to be certified as legitimate businesses—let alone require them to register with or seek the approval of the government before operating. It does not ensure adequate tracking of adverse events linked to drugs dispensed over the Internet. It does not require Internet pharmacies to establish systems for addressing consumer complaints. It does not establish a mechanism for effective recalls of drugs distributed through the Internet. It does not address the problematic practice of Internet pharmacies requiring a waiver of liability from purchasers. This timid step toward regulating Internet pharmacy may create the illusion of safety without actually reforming the Internet pharmacy industry and protecting American consumers from unsafe and/or ineffective prescription drugs.

VI. THE DORGAN BILL SHOULD BE REJECTED FOR FAILURE TO ENSURE THE SAFETY OF AMERICAN PATIENTS

The Dorgan bill lacks provisions that would allow HHS to stop importation if it proves dangerous. For example, the bill does not instruct HHS, or anyone else, to evaluate the impact of the importation program on patient safety or drug costs. It appears to be permanent; there is no sunset or opportunity for Congress to assess, modify, and reauthorize its provisions in the light of experience. There is no provision for suspension of the program if patients begin to die. In fact, although the Secretary may impose "other" requirements on registered importers and registered exporters in order to protect "the public health," the bill expressly provides that he must still permit both personal and commercial importation. In other words, even if a particular requirement or standard is essential to protect the public from an imminent danger, if importers and exporters are unable to meet it, the Secretary may not impose it. The Dorgan bill does not even contemplate a pilot program, which might allow HHS to test the impact of importation in a controlled setting before throwing open the borders nationwide. Indeed, even if personal importation from Canada proves unsafe in the first year, the Secretary may not limit the number of permitted countries from which commercial importation begins in the second year.

In light of the evidence in the preceding pages, it is difficult to understand why Congress would even consider passing the Dorgan bill.

[Whereupon, at 12:10 p.m., the hearing was adjourned.]

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