FTS-HHS FDA CDER

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Coordinator — Good morning and thank you for holding. I would like to remind all parties your lines are in a listen-only mode until the question and answer session of today's conference. This call is being recorded. If you have any objections, please disconnect from the conference at this time.

Ms. Crystal Rice, you may begin ma'am.

C. Rice — Good afternoon, everyone. My name is Crystal Rice; I'm with the Food and Drug Administration. We're here to talk to you this afternoon with regard to the finalization of the generic drug ruling, as well as to discuss some other initiatives with regard to our generic drugs program.

Here at the table today we have Mr. Peter Pitts, our Associate Commissioner for External Relations, who will be leading this call, as well as Mr. Dan Troy, FDA's Chief Counsel, Ms. Jarilyn Dupont, Senior Legislative Counsel, Office of Policy and Planning, and Mr. Gary Buehler, Director of the Office of Generic Drugs. After we have our discussion,

we'll open it up for a Q&A session. If you're ready we'll go ahead and begin. We do have to keep this short, so please keep your questions to a minimum. We'll get started. Thank you.

P. Pitts — Thank you, Crystal. My job as co-leader is to introduce Dan Troy, Chief Counsel, to give a bit of background on what we're talking about today.

D. Troy — Thank you. The President today, the Secretary, and Dr. McClellan, announced two major initiatives today. The first is, we have a final rule with respect to 30-month stays and patent submission that will help speed generic drugs to market, achieving billions of dollars of savings for American consumers, our estimate is approximately $35 billion over ten years. In addition to that, the President's budget has an unprecedented increase of $13 million in FDA resources that are going to be devoted to improving access to generic drugs. This is the largest infusion of resources into this program ever. It increases its size by about one-third. It should enable us to hire about 40 additional experts to help speed the review of generic drugs; so again, we can speed these safe and effective generic drugs to market when the appropriate patents and exclusivities run out.

The rule does three things. It clarifies that there can be only one 30-month stay. This is a change in FDA's interpretation, which previously allowed these multiple, and at times overlapping, 30-month stays. The FTC did an extensive analysis of this and found that in eight or nine cases there were additional delays of blockbuster drugs coming to market, delays of between four and 40 months that they've said cost the consumers lots of money. They recommended a single 30-month stay. So the rule clarifies, changes our interpretation, and says that there will be only one such 30-month stay, which is an attempt to strike an appropriate balance between innovators and generic drugs.

The second thing that the rule does is it clarifies which patents must and must not be listed in what's called the Orange Book, FDA's approved list of therapeutic drugs. There have, in the past, been patents that have been listed in the Orange Book for things like packaging, and metabolites, and intermediates, things that are essentially not the finished drug product. This rule makes much clearer which patents must and must not be listed in the Orange Book. We also substantially tighten up the declaration that the innovator has to file at the time of the NDA, the New Drug Application, and at the time that the New Drug Application is finalized. That information should lead to greater transparency and greater

communication, between the innovators and the generics and FDA, so that the generics can make well informed and appropriate business decisions about what they want to do vis-à-vis the innovators patent protections in terms of entering the market.

Hatch-Waxman is essentially a complex signaling mechanism between the innovators and the generics as to their patents, and it affords the generics, essentially, an opportunity to declare what the status of their product is vis-à-vis the patents that the innovator has listed in this Orange Book, and then the innovator can take certain actions to protect their…. In most cases, this system has worked quite well. Since 1984, when Hatch-Waxman was passed, there's been an enormous explosion in the number of generic drugs that have been available. They are now, I think, more than 50% of all prescriptions are generic drugs, saving the American consumer many billions of dollars. But there were these examples of, let's just say taking advantage of loopholes, that innovators had done, which the FTC very helpfully, usefully, effectively, pointed out. There are other things that the FTC has done to guard against innovator gaming, but we think that this rule is an important element in further plugging loopholes so that we can maintain the appropriate balance between innovation and

safe and effective generic drugs, thus saving American consumers millions and millions of dollars.

The $13 million is, again, going to allow us to – I'm switching away from the rule to the changes to the generic drug program, and I'll let Gary Buehler address those to a greater extent in one moment. There have been approval times for generic drugs that have frankly been too long. It has taken more than 20 months for a new generic drug to be approved by FDA. FDA is committing to get that time down. We are committing to doing more work on bioequivalence and bioavailability. We are also enhancing our public education, as well as, as I mentioned, the scientific study of generic drugs. So we're going to expand our educational programs and partnerships involving generic drugs, because we want to get healthcare practitioners and consumers to ensure that they have accurate information about safe and effective generic drugs. There will be some more expectations of the generic drug industry and generic drug applicants. They have had an unfortunately low rate of approval for applications that are initially filed, something like 7%. They have to go through multiple cycles. We want to cut down on those cycles so that we can, again, ensure that safe and effective generic drugs are made available

as soon as appropriate, and as soon as the appropriate patents and exclusivities are gone.

So with that, I'm going to turn it over to Gary to talk a little bit more about what the $13 million will mean, and what is planned with respect to the public education and scientific study.

G. Buehler The President has proposed an additional $13 million for the Office of Generic Drugs in FY 2004. With that extra funding we hope to hire up to 40 additional experts to speed the review and approval of generic applications through the Office of Generic Drugs.

The number of applications we've received over the past two to three years has been increasing steadily, and we expect to get somewhere around 450 applications this year. This indicates that the generic drug industry is actively submitting applications to us, and we do have to improve our efficiency and our communication with this industry so the applications they send to us are quality and can be processed in the least amount of time possible.

We hope to also use some of the funding to increase our scientific endeavors. We will undertake scientific studies on certain types of generic drugs. These are usually the types of drugs that are not absorbed systemically into the system, and where bioavailability methods have not been adequately developed to make it easy to approve this type of product. Typically of these products are topical products, and meter dosing …. We hope to initiate this research within the next year when we get the funding, and hopefully within a few years we'll be seeing results from this research that will make this type of product more available to the American public.

I think we're ready for questions now?

Question 1: A couple of questions. Can you talk about the assumptions behind the scoring here when you're saying that you'll have savings of $35 billion over ten years? I'm wondering how you arrive at that figure. Are you assuming that each product is indeed going to have a 30-day month stay, or what?

Then you're obviously talking about several different generic initiatives here. Can you spend a little bit of time talking about current thinking on

generic biologics and what progress is being made, and what's the timeframe for seeing more action?

D. Troy I'll start. The rationale for the cost estimates, for the savings estimates, is really set forth mostly in the proposed rule. The economic analysis has not changed very much between the proposed rule, which …. For those of you who are interested in Federal Register Citations, the citation is 67 Federal Register 65448. You can tell I'm a lawyer.

Essentially what we looked at was the universe of drugs that the FTC had identified as drugs that were delays due to 30-month stays, and we looked at their estimated peak sales. Based on the delay in sales information for six of the eight or nine drugs that they looked at, we found that the typical delayed drug had peak annual sales of about $1.36 billion, and was subject to a 23-month delay. According to the FTC report, which had been done about a year and a half, two years ago, there were, again, these eight multiple 30-month stays, but we found-- and they found and we agreed-- that the frequency of these stays has been increasing. Four drugs experienced multiple 30-month stays during 2000 and 2001. So based on this information, we assumed that, absent the proposed rule, there would be two, it would be basically four drugs over two years, situations with

multiple 30-month stays. So in calculating the annual impact of the proposed rule, we multiplied the peak annual sales to the average affected drug by two to account for the frequency. We think it's a reasonable estimate. This methodology that we used is very similar, if not identical, to the methodology that was used by CBO to score S812. The only difference between their numbers and our numbers were the inputs. We think our inputs, which come from CMS, are more accurate.

The $35 billion in savings that is identified in the proposed and final rule do not take into account at all, frankly, the proposed increase of $13 million in FDA resources devoted to improving access to generic drugs. Those should, frankly, save the consumers even more as we implement the changes by getting more reviewers, getting drugs to market faster, having more and better education and scientific exchange.

The initiative we're talking about today has nothing to do with generic biologics, and I would really prefer not to introduce that issue at this point.

Question 2: Good afternoon. Just one question on the initiatives announced today. Will any of these be applied retroactively looking at existing approved

products? What is the process, if there is any, for a company to initiate a review of a product that they think may be in violation of this?

D. Troy The rule is as a legal matter is prospective; it is not retroactive. It could apply, I guess, to products that have been approved beforehand, but it applies only to patents that are filed and listed in the Orange Book after the effective date of the rule, which is August 18th. So as a legal matter it is not retroactive. Particularly since the final is not very different from the proposed, I think people should have altered their expectations and have altered their behavior back in October when we announced the proposal.

If you're asking whether we're going to go back and commence a review of patents that are listed in the Orange Book, the answer is no. The rule makes clear that although we are tightening up on the patent declaration, that is intended largely to be self-executing. If somebody lies to us then the declaration makes clear that under 18 USC 1001 that is a criminal violation. It's a penalty of perjury, you cannot lie to the United States Government; you cannot make false statements to the United States Government. I think all of you know people have gone to jail for that. (I'm not saying you know people who have gone to jail for that). So we are going to continue to ensure that, although we do as much as we can to

make clear which patents must and must not be listed in the Orange Book, we do not intend and we don't believe we have the authority, and we certainly don't have the resources, to get into the kind of patent questions that are raised in litigation. Part of the element of Hatch-Waxman is, frankly, to refer patent questions, questions truly of patent law, to the courts, where the expertise in adjudicating disputes about patents resides. That has been FDA's long-standing position and this rule does not change it at all.

Question 3: Just as a follow-up, on the proposed fines, what will be the calculation? How will those be calculated?

D. Troy I don't know what you mean by proposed fines. There are no proposed fines that are put into this rule.

Question 4: I think in the President's comments he said that there will be stiff penalties and fines, but I may have just misread it.

D. Troy I didn't hear the President's remarks. I'm going to speculate that what he may have been referring to is that if you lie to the United States

Government, then that is a criminal penalty and you can be subject to penalties or fines. That's all I'll say about it.

Question 5: I have a question on types of patents that are eligible for listing in the Orange Book. You make reference to approved uses of drug. I guess my question is, if a company intends to pursue an additional indication, and they already have a patent that's been issued by the PTO, at what point and time could they put that into the Orange Book? At the time of the filing of an SNDA, or would it actually have to be once the new use is approved?

J. Dupont If the company is submitting a supplement to get a new approved use, they are required to file a declaration at the time they file the application. So they can submit it at that time. It would be pending at that time as long as it's a pending method of use. Then if the method of use is then approved in the supplement they file a second declaration that indicates that it is approved.

Question 6: So the new patent wouldn't become effective in the Orange Book until it's actually approved?

J. Dupont — When it's submitted--. You can't submit it before it's approved at the PTO. You have to have an actual patent. You're talking about the approved method. It is submitted, but it's not in the Orange Book until actually it's approved, the indication.

D. Troy — In general, I think we should clarify that we are going to allow patents-- the only patents that could be listed are patents that claim the drug substance, which is essentially the ingredient, the drug product, which is the formulation and the composition, and the method of use, which is what you were addressing. Our new regulations are going to not allow the listing of process patents, which was always the case. We're clarifying the patents claiming packaging, what are called metabolites, which is what the drug product becomes in your body after you take it, or intermediates, which is points along the way before the drug is finished being manufactured, those patents cannot, must not, be listed in the Orange Book.

Question 7: — That actually gets to my next question on metabolites. I'm assuming you're saying you can't use a metabolite patent to protect what we call the pro drug, but if the metabolite then becomes a follow on drug to the original can that metabolite patent then protect the new product?

J. Dupont No, it cannot be submitted for listing.

Question 8: Even if the metabolite becomes a new product?

J. Dupont Right.

C. Rice We have time for one more question.

Question 9: The press notes that there is some performance goals being implemented to speed approvals by the Office of Generic Drugs, and you did mention in your opening remarks that you're looking to reduce the ANDA review time from 20 months. Have you set or publicized any particular targets for that number? Could you disclose any of the other performance goals that you plan to set?

G. Buehler First, let me clarify something I made in my opening statement. I mentioned the $13 million, and that is in the President's *proposed* 2004 budget. I don't know if I made that clear, it is the *proposed* budget.

Now your question about our performance goals, presently it takes about 20 months to approve the average ANDA, and the median time is about 18 months. We hope to reduce that time by two to three months over the next three to five years. We hope to begin that process as soon as we can with the efficiency that we hope to initiate in the communication with the generic sponsors to improve the quality of the generic application, and also to improve the efficiency of our own review process so that we can actually process these applications faster.

Question 10: Also, you mentioned that 93% of generic ANDAs fail on the first review. Can you just disclose what the most common reason for that failure is? Is it CMC or bioequivalence?

G. Buehler Well it really runs the gamut. Usually it has to do with the manufacturing and controls of the particular product and the specifications. Understand that we don't really communicate directly with the generic sponsors through the first cycle. What we do is we review the application as we see it, and we communicate in writing to the sponsor what the deficiencies are. So many of these applications, they're not really that deficient, it's just that our communication policies right now don't allow us to talk to them about the deficiencies that they have right now in the first cycle. So what

we hope to do is be able to increase this communication in the future so that many of these reviews can be finalized during the first cycle and not have to go into the second cycle.

C. Rice — We actually do have time for maybe two or three more questions.

Question 11: — I'm just wondering if the Administration, as a result now of this new rule, has a position on the Senator Gregg compromise in the Senate? Or does Dr. McClellan's earlier statement issue before the Senator Appropriations Committee remain the official position, in which he indicated that he didn't feel further legislation was necessary?

D. Troy — I think that Dr. McClellan is correct that we don't necessarily believe that further legislation is necessary. That said, we are encouraged by the efforts in the Senate on a bipartisan basis to try and codify in legislation what we've done today, which is to say make clear that there can only be one 30-month stay. We don't think it's necessary, but we applaud the efforts to try and do this. This is a very technical area of law, and it's really important to get it right. We want to make sure that anything that comes out is workable. We are committed to and are working with both the Republican and the Democratic staff to try and make sure that any

legislation that goes forward is correct, and actually achieves the goals that are sought to be achieved.

The proposed legislation does at least one other thing that our rule does not address, which is to say it gets into the issue of 180-day exclusivity; our rule does not address that issue.

Question 12: In terms of the issue on whether the patent listings actually cover or claim the marketed product, what's going to be the process for making those kind of evaluations versus what's being done today, since my understanding is that the FDA doesn't always have the resources to make those evaluations?

D. Troy We are not going to get into the business, as we've said before, of policing patents and the patent judgments that are made. The declaration is really meant to be self-effectuating and there are a lot of yes and no questions, I urge you to take a look at it. It's certainly more extensive than it was before. The declaration forms were not in the proposed rule. By making it as yes/no as possible we are hoping that, plus the fact that you're not supposed to lie to the United States Government, will provide a lot of clarity and will encourage people, let's just say, to make the right kinds of

judgments and be straightforward and honest with us. We are not going to establish any kind of process for delisting of patents. If people think the patents are not properly listed, they have recourse in the courts.

C. Rice — We're going to have to end the call, but we do appreciate the opportunity to talk with you today. Again, our material is on our Web site at www.fda.gov. Thank you very much and have a great afternoon. Goodbye.