Transcript of Media Briefing on Topical Drug Products Containing Papain and Ophthalmic Balanced Salt Solutions

FTS HHS FDA

Moderator: Rita Chappelle
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Coordinator: Good morning and thank you for standing by.

At this time all participants are in a listen-only mode until the question and answer portion of the conference. During that time if you would like to ask a question please press star 1 on your phone.

I would like to remind all parties this conference is being recorded. If you have any objections you may disconnect at this time.

I would now like to turn the call over to your host today Ms. Rita Chappelle. Ma'am you may begin.

Rita Chappelle: Thank you and thank you ladies and gentlemen for dialing in for this media announcement today.

My name is Rita Chappelle and I work in the Office of Public Affairs for the Food and Drug Administration.

Today you have all received a media advisory announcing that FDA will be taking enforcement action as a part of this unapproved drugs initiative. Today I am joined in the room by Deb Autor, Director, Office of Compliance for the Drug Evaluation and Research at FDA. I'm also joined by Mike Levy,

Director, Physician of New Drugs and Labeling Compliance within the Office of Compliance within CDER and FDA.

Additionally I have Charles Lee, M.D. He is the Medical Officer for the Division of New Drugs and Labeling Compliance and Janice Steinschneider, Regulatory Council for the Office of Compliance. They will be our two technical experts.

Now this call is for credentialed media only and only credentialed media will be able to ask questions. Prior to asking your question I would ask that you state your name and affiliation. You all have received the media advisory as well as the press release that details to you what actions we've taken.

Now after, you will be allowed one question and then one follow-up question, because of the number of callers on the line, and after that we will begin the, we'll do a round up and that will end our call.

So to get us started if there are any media who would like to ask a question now that you have reviewed the press release you may press star zero and ask the operator to assist you with...

Coordinator: Star 1 to ask a question.

Rita Chappelle: I'm sorry, excuse me ma'am, I'm sorry. I'm sorry I made a mistake, I apologize. Before we take questions actually Deb Autor would like to make a statement about the actions that were taken today. Deb.

Deborah Autor: Thank you Rita. Good morning. I'm Deborah Autor, Director of the Office of Compliance of FDA's Center for Drug Evaluation and Research. As Rita mentioned I'm joined today by my colleagues from the Office of Compliance,

Michael Levy, Director of the Division of New Drugs and Labeling Compliance; Dr. Charles Lee, Medical Officer in the Division of New Drugs and Labeling Compliance; and Janice Steinschneider, Regulatory Counsel.

Thank you all for joining us this morning.

The purpose of this call is to talk to you about another proactive FDA step regarding unapproved drugs that present a risk to consumers. Today FDA published Federal Register notices announcing that topical drug products containing papain and ophthalmic balanced salt solutions called BSS, cannot be marketed without approved application.

The notices informed firms that they have 60 days to stop manufacturing these drugs and 120 days to stop distributing them. Those manufacturers and distributors that do not comply with today's notices after the day it's listed will be subject to enforcement action such as seizure or injunction.

Topical papain products are labeled to debride wounds and promote wound healing but the firms marketing these products have not shown them in a reliable scientific way to be safe and effective. In fact, FDA scientists have received and evaluated reports of serious adverse events associated with these products. These concerns include hypersensitivity reactions including anaphylaxis.

Practitioners prescribing these products and consumers who use them should be aware that there are other drugs approved by the agency that have been proven to be safe and effective to treat many of these wounds as well as non-pharmaceutical methods of wound care.

The other products associated with today's action are ophthalmic balance salt solutions used in the eye during ocular surgery. Two firms market FDA approved BSS products. These approved products are not subject to today's action and will remain on the market. There are however several other firms marketing unapproved BSS products that will be removed from the market.

Removing unapproved drugs from the market benefits consumers by enabling the agency to provide greater assurance that these products will be properly made. There have been reports of serious injuries including permanent visual impairment as a result of contaminated or otherwise improperly made BSS products. The application process enables greater agency oversight of the manufacture of these products.

These actions are the next steps in an aggressive FDA initiative to ensure that all drugs marketed in the U.S. are subject to FDA's rigorous evaluation. We renewed our focus on this problem of unapproved drugs in June 2006. At that time FDA issued a Compliance Policy Guide or CPG that outlines our enforcement policies and it efficiently and rationally bring all unapproved marketed drugs into the approval process.

FDA has taken a number of actions against classes of marketed of unapproved drugs and today marks the latest of such actions. We've also issued warning letters to manufacturers that are making unapproved drugs as well as violating other provisions of the Federal Food, Drug and Cosmetic Act. We have also utilized the seizure and injunction provisions of the law and we will continue to take strong effective measures to tackle the problem of marketed unapproved drugs.

The first that market unapproved topical papain drug products and ophthalmic balanced salt solutions have bypassed the requirements of the law and put

consumers at risk. When drugs are reviewed as part of the approval process FDA examines all of the drugs ingredients as well as the drugs labeling and manufacturing process.

Unapproved drugs not subject to this evaluation may not be safe, effective or adequately labeled. They may also be substandard lacking required identity, strength, quality and purity. Today as we take these products off the market we remind firms marketing unapproved products that the FDA drug approval process is an indispensable part of ensuring that consumers in the United States have access to safe and effective drugs.

The agency underscores the expectation that firms marketing unapproved drugs will voluntarily comply with the law and submit required drug applications or cease manufacturing drugs that do not have FDA required approval.

As these actions show, FDA is committed to ensuring that the drugs physicians prescribe and patients take are safe, effective, properly manufactured and appropriately labeled. I look forward to your questions.

Rita Chappelle: Thank you very much Deb. All right, operator again I would like to remind all those on the call that we will only be taking questions from credentialed media and you'll be allowed one question and one follow-up question. And if you have any additional questions you can always e-mail me.

All right (Stacy) at this time we'll take the first question please.

Coordinator: Thank you. Your first question today comes from (Justin Bloom) of (Lindberg) News.

(Justin Bloom): Hi. Thanks for taking my question. The first question is, with each of these two unapproved drugs how many companies are currently making unapproved versions of each one and what are the names of the companies?

Deborah Autor: With the balanced salt solution there are three companies making unapproved BSS products. Those companies are B. Braun, B-R-A-U-N, Baxter and Hospira.

On the papain there are approximately a dozen unapproved products out there. A couple of them are named in our Web site on our Q&A's and Rita could get you a complete list after the call.

Rita Chappelle: Sure (Justin), just e-mail me. Do you have a follow-up (Justin)?

(Justin Bloom): Yes I do. I just, first I just want to make sure I heard right on the first drug B. Braun, Baxter and Hospira are making the unapproved version.

Deborah Autor: Correct.

(Justin Bloom): Okay. So my follow-up question is if in fact these drugs pose such significant dangers the Federal Register notices say that these adverse events go back to the late 1960s. So if these were such a threat to consumers why is it just now that FDA is issuing this order to the companies making unapproved versions and warning consumers about their use?

Deborah Autor: Well as you know (Justin), in June 2006 the agency announced its renewed emphasis on tackling the problem of marketed unapproved drugs and we've continued to work on that initiative swiftly and aggressively and - however it does take time to get through all of these products.

We're using risk-based approach. We are taking off first products that present evidence of safety problem, lack evidence of effectiveness or health (unintelligible) drugs and we continue to do that, and we're glad that we're able to do this after this many years of this problem.

Rita Chappelle: All right. Thank you (Justin). Next caller please.

Coordinator: Thank you. The next question comes from (Ricardo Zalvadar) of the Associated Press.

(Ricardo Zalvadar): Hi. Thanks for taking my question. And could you say again slowly with the spellings the three companies that are making the eye wash?

Rita Chappelle: (Ricardo) this is Rita and we appreciate your question. We'll take that. I think you're speaking a little too closely to the microphone, we're having a little, there's some static and we're having a little difficulty.

Deborah Autor: The approved ones are B. Braun, the name of the company, I'm sorry the unapproved ones, is B. and then Braun, B-R-A-U-N, second one is Baxter, B-A-X-T-E-R and the third one is Hospira, H-O-S-P-I-R-A. The approved products are made by Alcon Surgical, A-L-C-O-N and Akorn, A-K-O-R-N.

(Ricardo Zalvadar): Okay. And a follow-up question on that -- are these Baxter and Braun the, you know, those are big names. Are we talking about the same companies or are we talking about cheap knock offs?

Deborah Autor: You can check with them but I think we're talking about the same companies. There are in fact large pharmaceutical companies that continue to have unapproved drugs in their portfolio. We hope that they will recognize that we

are moving aggressively in this area and they will proactively remove those products from their market share.

Rita Chappelle: Do you have a follow-up (Ricardo)?

(Ricardo Zalvadar): No. That's it for now. Thank you.

Rita Chappelle: Thank you. Next caller please.

Coordinator: The next question comes from Jennifer Smith of FDA Week.

Jennifer Smith: Hi. A couple of months ago FDA met with a bunch of reporters to talk about the unapproved drug initiative but at that time FDA did not have any specifics to the extent which has (unintelligible) affected the market or just how many unapproved drug makers have (unintelligible) sought FDA drug approval. So do you have any updated statistics on that, particularly the 2% figure of prescriptions that are unapproved, especially with this action, I mean any other new data about the market?

Mike Levy: I can give you an update on the number of firms and products we estimate have been affected by...

Jennifer Smith: Okay.

Mike Levy: ...enforcement action. Right now we estimate that over 100 firms have been subject to the seven drug class actions that we've taken so far...

Jennifer Smith: Okay.

Mike Levy: And we estimate that approximately 400 products have been removed from the market if you include those products which will be removed as a result of these two actions.

Jennifer Smith: Okay. So including today's announcement. Okay.

Mike Levy: Right.

Rita Chappelle: Do you have a follow-up Jennifer?

Jennifer Smith: Yeah. So I wanted to double-check the number, the hundred firms that's since 2006 (unintelligible) drug class actions, that's a 2006 or just this year?

Mike Levy: That's 2006.

Jennifer Smith: Okay. All right. Thank you.

Deborah Autor: Right Jennifer, we, this is Deb, we as Mike said we've affected a significant number of products and significant number of companies, we haven't gone back to recalculate. We have estimated in the past that there are roughly 2% of unapproved on the market are unapproved. We have a lot of evidence that we have been making progress.

We have about a hundred companies have called the agency looking for guidance on how to submit applications for unapproved drugs, have a number of companies that have in fact submitted applications for unapproved drugs and a number of companies that have very successfully moved to a legitimate business of selling approved drugs and out of the illegitimate business of selling unapproved drugs and we hope that today's action will again remind companies that they should be taking proactive steps to avoid enforcement,

not waiting for us to issue these Federal Register notices and force their products off the market.

Jennifer Smith: Okay. I just, but when you say though Deb a number companies and then we're talking about kind of a handful or talking more than ten?

Mike Levy: Are you asking who have submitted applications as a result of our...?

Jennifer Smith: Well yeah, you both have, I mean I think yourself and then you Deb just mentioned about like companies that have now moved from selling some of their unapproved products and then moving to the approved status or companies submitted applications, I mean (unintelligible) numbers but our number of companies and what does that mean in number of companies?

Mike Levy: Well I think it's safe to say that dozens of companies have...

Jennifer Smith: Okay.

Mike Levy: ...inquired about submitting applications. As to the number of applications precisely that's probably something that we can't reveal publicly.

Jennifer Smith: Okay.

Deborah Autor: The number of companies have also told us that they will voluntarily take their unapproved drugs off the market and have done so.

Jennifer Smith: Okay.

Deborah Autor: Because they have recognized that that's the right way to do business.

Jennifer Smith: Okay. Thank you.

Rita Chappelle: Thanks Jennifer. And I just want to clarify it was 2% of approved products - of 2% of the products (unintelligible) market are unapproved.

Deborah Autor: We have estimated very roughly that 2% of the prescriptions in this country are filled with unapproved drugs.

Jennifer Smith: Okay.

Rita Chappelle: Thank you. And so we want to make sure you get that correct. Next caller please.

Coordinator: Thank you. Your next question comes from Sue Sutter of Scrip World Pharmaceuticals.

Sue Sutter: Hi. Thanks for taking my question. I think Deb had said that there are about a dozen unapproved papain topical products on the market, but FDA issued a Q&A document this morning that said there were about 35 unapproved topical products containing papain. So I'm just trying to get clarity on the actual number of products out there as well as the number of companies involved in this area.

Deborah Autor: Yeah. I'm sorry, I may have misspoken, there are probably about a dozen firms involved.

Sue Sutter: Okay.

Deborah Autor: Products is higher. The papain market is actually a large one. We estimate that there are over $50 million in unapproved papain products sold per year. There

are no approved topical papain products. So about $50 million of the unapproved ones sold by these various companies, approximately 1.3 million tubes per year.

Sue Sutter: And you said that's over $50 million a year then.

Deborah Autor: Yes.

Sue Sutter: Okay. And do you have a figure for the optical, the ophthalmic market too?

Deborah Autor: I don't have a dollar figure but there are approximately, in 2007 there were approximately 3.2 million units of BSS sold and we estimate that approximately 1% of those are unapproved.

Sue Sutter: Okay. Thank you.

Rita Chappelle: Thank you. Next caller please.

Coordinator: Your next question comes from Jennifer Smith, FDA Weekly.

Jennifer Smith: Hi I'm sorry, I just was reading over what I think you had just said to me and this is about the 400 products that have been I have approved in the market but I think what I meant to write was removed from the market in 2006, I just want to make sure on that.

Mike Levy: Removed from the market, that's right.

Jennifer Smith: Removed market, okay. Thank you.

Rita Chappelle: All right operator?

Coordinator: Yes.

Rita Chappelle: Are there any additional?

Coordinator: Yes. Malcolm Spicer of FDC Reports.

Rita Chappelle: Okay.

Malcolm Spicer: Yes. Thank you. The release today says that the BSS is used during surgeries but I gather from this, your alert today that it in fact the product is available outside of surgical procedures.

Deborah Autor: No I don't, I think it's just used for surgery.

Rita Chappelle: Right.

Malcolm Spicer: So then the product's only in the hands of medical professionals but they perhaps have unapproved products.

Deborah Autor: Correct.

Malcolm Spicer: Okay. So are then, are the BSS products or the topical products, are either of them available over the counter in any places?

Deborah Autor: These are prescription products.

Malcolm Spicer: All prescription products.

Deborah Autor: And the papain products are used both out-patient and in-patient.

Malcolm Spicer: Okay. My follow-up would be that you mentioned earlier about the risk-based strategy. How could you describe how this determining these products to remove from the market how, what the difference and the risk basis was from your previous enforcement action?

Deborah Autor: We've taken a number of actions relating to products that have serious adverse events so why don't we have Dr. Lee describe to you the adverse events associated with the BSS and papain products.

Charles Lee: Right. With regards to the BSS we've had over 300 spontaneous serious events, adverse event reports associated with all of the ophthalmic BSS products, that's over a period of, from the start of (unintelligible) database in 1969 until now.

Some include a condition called toxic anterior segment syndrome and a non-infectious inflammatory condition of the front portion of the eye. Some have included bacterial (endothalmitis), which is basically infection of the globe, or eyeball itself. There's been cases of corneal (pathification) or clouding. Some of these events resulted in loss of eyesight. I guess their database say that there is 16 cases of blindness, one of which also is associated with loss of the eye itself.

We know that some of the events have been associated with contaminants such as bacteria, fungi, endotoxins, particulates and some have also had, been associated with products with improper PH or (unintelligible) strength. In fact one product, contamination of one manufacturers product with endotoxins associated with several hundreds of adverse events including toxic anterior segment syndrome.

So we have a situation where you know, we have approved alternatives on the market and certainly we see loss of vision as being a serious you know, serious problem and when there are alternatives available we want to make sure that the unapproved ones that we're taking action on.

Let me run down the story with adverse events for papain. We had 37 adverse events reported for this. Now that sounds like a small number but four of these were associated with or four of these were anaphylaxis, as you're aware, a life threatening allergic reaction that required treatment with emergency medication, resuscitation, that type of thing.

In addition, and as you're aware, even for approved products we figure there's a ten-fold underreporting, probably substantially higher (unintelligible) for unapproved products. So we're basically looking at a tip of the iceberg on that.

We have also other concerns in the sense that we know that there has been cross sensitization or cross sensitivity to patients who have latex allergy so patients who are sensitive to one potentially could react to the other. In addition papain finds its way into other products as well and there's concern that hypersensitivity events may occur with exposure subsequent to things like (unintelligible) or maybe oral products as well.

In particular in this circumstance too we've got no studies that show that there is any benefit to these products at all. I mean there's no evidence to show that they're effective. So we can't put up with adverse events of this severity where we you know, have a product where we just have no evidence that the product is effective.

Rita Chappelle: All right. Thank you. Next caller please.

Coordinator: Thank you. Your next question comes from (Justin Bloom) of (Lindberg) News.

(Justin Bloom): Hi.

Rita Chappelle: Hi (Justin).

(Justin Bloom): Hi. Thanks for taking my question again. I just want to be clear, are these adverse events with the eye solution also associated with the approved version or the adverse events only associated with the unapproved version?

Charles Lee: That's true. It is, they are associated with, or the database pulls all (unintelligible) solutions. So that figure includes, and the way the database is it makes it very, very difficult to sort out what's approved and what's unapproved which is actually one reason that we want to bring these unapproved products in when we've got actually ability to have better accounting on what's going on with adverse events.

Deborah Autor: Yeah. (Justin) a lot of these adverse events are quality related because this is a product that needs to be sterile when it's used in the eye and so we're especially concerned because with the unapproved products we don't review the chemistry manufacturing controls for them as part of the approval process, so we're concerned about the increased likelihood of these kinds of adverse events, which as Dr. Lee said, can include such things as blindness.

(Justin Bloom): Okay. And second thing, going back to B. Braun, I just want to make sure I'm clear since there are several different versions of this company, you're talking about B. Braun Medical Incorporated?

Deborah Autor: We would need to check specifically in our drug listing to confirm that.

Rita Chappelle: You can e-mail me that question (Justin) and I'll get you a response for that. All right. Thanks (Justin). All right. We have time for one more call and then we will conclude this telecon. (Stacy).

Coordinator: We have a question from (Jared Bovol) of Dow Jones.

(Jared Bovol): Hi. Actually my question was answered so I appreciate you taking the time out.

Rita Chappelle: All right. And what I would like to do is to suggest that all of you log on to our FDA Web site and click onto our new Office of Compliance Web site. We have a lot of information there. We have launched a new video that talks very extensively about what our office does, the various initiatives and actions that we've taken. It's a video that you will find very informative. And additionally you can also read about other actions that we've taken.

Man: Yeah. The easiest way to get to our unapproved drugs Web site is to go onto the FDA.gov Web site and search on marketed unapproved drugs and that will take you directly, the first link will be unapproved drugs, right?

Deborah Autor: Right. And as Rita mentioned we've done a video news release giving some background on the problem of marketed unapproved drugs which we hope will be informative.

Rita Chappelle: Right. And if there are any additional questions, if we didn't get to you, please feel free to e-mail the questions to me, Rita Chappelle. My e-mail address is on the press release and the media advisory and we will respond to you

promptly. And I want to thank all of you for joining us today for this announcement. Thank you (Stacy).

Coordinator: Thank you.

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