Sherman, Aaron

From: Norden, Janet M
Sent: Wednesday, July 16, 2008 1:14 PM
To: Sherman, Aaron
Subject: Print

-----Original Message-----
From: Jenkins, John K
Sent: Thursday, August 09, 2007 2:27 PM
To: Burke, Laurie B; Colangelo, Kim M
Cc: Kweder, Sandra L; Norden, Janet M
Subject: RE: Internal discussion on NDA 22-059, Tykerb (lapatinib)

A little more detail now that I am not thumb typing.

OCC has a high priority proposed rule in which they plan to add a couple of phrases to clarify what they view as our long standing intent for the CBE regulations for labeling changes. This is related to various litigations that are proceeding and may go to the Supreme Court. So, the goal for the publication of the PR is late August with a final before the end of the year. Jane is looking to see if we can get anything added to help with the PLR issue, but we are not optimistic since the impetus for the PLR PAS came from the department and Sheldon did not seem inclined to argue for a change. That is why there is also a parallel track (and a lot of e-mail today) in trying to find a waiver provision that we can apply and "sell" to OCC.

John

-----Original Message-----
From: Burke, Laurie B
Sent: Thursday, August 09, 2007 11:51 AM
To: Colangelo, Kim M; Jenkins, John K
Cc: Kweder, Sandra L; Norden, Janet M
Subject: RE: Internal discussion on NDA 22-059, Tykerb (lapatinib)

In a meeting with OPS and Paula McKeever from Jane's group about the 314.70 reg rewrite yesterday, we learned that OCC/Bradshaw is working on a change in those regs that will redefine CBE submissions and trump our initiative for the time being. They are working with Rachel B on this. I'm hoping that was one of the options you discussed yesterday, John.

-----Original Message-----
From: Colangelo, Kim M
Sent: Thursday, August 09, 2007 9:28 AM
To: Jenkins, John K
Cc: Burke, Laurie B; Kweder, Sandra L; Norden, Janet M
Subject: RE: Internal discussion on NDA 22-059, Tykerb (lapatinib)

John,

We had scheduled an internal meeting (you, Sandy, Laurie, Janet Norden and myself) to discuss this matter as well (August 21 at 2:00). Is there still value in holding this meeting, or are we in a holding pattern again?

Kim

-----Original Message-----
From: Jenkins, John K
Sent: Wednesday, August 08, 2007 9:06 PM
To: Jones, Glen D (CDER); Axelrad, Jane A; CDER SEALD Labeling; Burke, Laurie B; Bernstein, Michael; Rosario, Lilliam; Pierce, William (CDER); Colangelo, Kim M; Sadove, Elizabeth; Kweder, Sandra L; Ray, Seth; Loewke, Sally A; Norden, Janet M

ary, Laura

From: Axelrad, Jane A
Sent: Friday, June 06, 2008 4:16 PM
To: Temple, Robert; Dal Pan, Gerald; Jenkins, John K
Subject: FW: CBE final rule draft

Attachments: CBE051508.doc

I spoke with Janet about this this afternoon and she suggested you all take a quick look at this and tell me if you have issues? This is the rule that was done to shore up the agency's arguments that we are preempting state tort law on failure to warn. The proposed rule, drafted by OCC, said that sponsors cannot use a CBE supplement to add a warning or precaution unless the change is based on new information and the sponsor has established a causal connection between the safety event and the drug. This is the draft of the final rule. If you could look at this quickly, I'd appreciate it, as OCC will be asking for my comments, and it is a high priority agency rule. Thanks.

From: Masoudi, Gerald F
Sent: Tuesday, May 27, 2008 8:46 AM
To: Axelrad, Jane A; Cook, Kate; Midthun, Karen
Cc: Lutter, Randall
Subject: CBE final rule draft

Please find attached a draft final CBE rule.

I know that this is not formatted appropriately for the federal register, but I am sending it now to give you some time to review the substance of what is said. It will later be circulated for clearance in the appropriate format (most likely in a few weeks).

Please send me any comments you have by Friday, June 6 so I can incorporate them into the next version.

Scott Danzis is now recused from this matter, so please direct comments to me for now (I'll let you know when we have someone else assigned).

CBE051508.doc (88 KB)

Axelrad, Jane A

From: Axelrad, Jane A
Sent: Tuesday, June 17, 2008 4:20 PM
To: Jenkins, John K; Bernstein, Michael; Temple, Robert; Dal Pan, Gerald
Subject: RE: CBE Rule Comments

I would be saying I won't concur. Not sure others feel the same way. I was going to discuss with Janet when she gets back and see how far she wants to go.

From: Jenkins, John K
Sent: Tuesday, June 17, 2008 4:19 PM
To: Axelrad, Jane A; Bernstein, Michael; Temple, Robert; Dal Pan, Gerald
Subject: RE: CBE Rule Comments

Jane

I like your comments and I think its good to get them on the record. In essence you are saying that we do not concur with the draft final rule, I wonder if you should be even more explicit in making that point.

John

From: Axelrad, Jane A
Sent: Tuesday, June 17, 2008 1:49 PM
To: Bernstein, Michael; Jenkins, John K; Temple, Robert; Dal Pan, Gerald
Subject: CBE Rule Comments

I am considering sending the attached comments from me. I already sent Bob's markup, Gerald's comments, and John's overarching comments about the responses to the comments not being sufficiently clear. Any comments or objections?

Jane

<< File: CBE Final Rule JAA comments 6-17-08.doc >>

Comments on Final CBE Rule (6/4 draft)

The rule is not, as it purports to be, consistent with the agency's role in protecting the public health. We have not experienced problems with sponsors' use of CBE supplements to over warn, and this rule tips the balance against early warnings by using vague and confusing terms such as "causal association" and "reasonable time" that will be difficult for staff and sponsors to apply.

1. The rule will create confusion about the level of evidence needed to submit a CBE supplement and could discourage companies from quickly adding necessary warnings because of the confusion. The confusion arises because of the use of the term, "causal association" and the further references to 201.57(c)(6), which says that "causation need not have been definitively established." The rule is clearly trying to raise the bar on CBEs to support preemption, and references to 201.57 will not adequately prevent inappropriate reluctance on the part of sponsors to use a CBE supplement to add an important warning. The rule recognizes there may be some confusion by saying that if there is doubt as to whether the standard of 201.57(c)(6) is met, the sponsor should confer with FDA. The rule doesn't say with whom sponsors should confer, or where the resources will come from to support such inquiries. Who does OCC believe will be answering those inquiries?
2. The distinction between whether the newly acquired information was submitted to the agency within a reasonable period of time prior to submission of a supplement creates a vague and unenforceable standard. Neither sponsors nor FDA staff will have any idea what "a reasonable time" means.
3. The rule on p. 4 says that "Expressly requiring that a CBE supplement reflect newly acquired information and be based on sufficient evidence of a causal association will ensure that scientifically accurate information appears in the approved labeling for such products." But there is no evidence that there is a need for any change to the rule or that without these vague and unenforceable standards scientifically Inaccurate information has been appearing in the labeling.
4. The REMS discussion is confusing to anyone not very familiar with REMS and how they work. At a minimum, you should have Heidi Gertner or Lynn Mehler look at this discussion.