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Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Supplement to the Citizens Petition Docket ID: FDA-2012-P-0617 Filed by the Combination Products Coalition

Dear Sir or Madam:

On June 8, 2012, the Combination Products Coalition submitted a Citizens Petition[1] pursuant to 21 C.F.R. § 10.20 ("Petition") requesting that the Commissioner of Food and Drugs ("Commissioner") take specific steps to improve the transparency of combination product regulation. In that Petition, we outlined the following four steps that are essential to fostering the development of innovative combination products.

1. The Commissioner should improve transparency with regard to combination products by streamlining the internal FDA process for developing combination product guidance and rules and producing more guidance on combination products.

2. The Commissioner should ensure that more FDA records with regard to combination products regulation are released on the Agency's website (e.g., requests for designation, Form FDA-483s, new drug approvals).

3. We recommended a number of ways to improve the FDA's processes and procedures for guidance document development.

4. We provided recommendations in support of transparency in both broad decision-making and also individual adjudication.

Today, we submit a supplement to the original Citizens Petition that outlines additional ways FDA can give guidance to industry. In this supplement, we recommend that FDA look outside the Agency for best practices in managing the sharing of information on complex topics by large enterprises. In this regard, we strongly support the use of new technologies by FDA as communication tools, including the use of social media and electronic knowledge databases.

[1] Citizens Petition Docket ID: FDA-2012-P-0617

Industry needs answers to questions on a timelier basis. By analogy, when policymakers wanted to figure out a way to allow new products to reach the market faster, they analyzed whether they could lessen the premarket obligations and instead strengthen the post-market obligations. We think policymakers should examine the same opportunities when it comes to releasing FDA information: lighten up on the pre-release review and create better mechanisms for ensuring post-release review. To that end, we recommend the Agency push down responsibility for addressing narrow questions and streamline the process to eliminate extensive review and approval by FDA management, but balance that with more robust post-release quality review by the agency and appeal procedures.

Finally, to supplement existing guidance processes, we also suggest FDA consider a process by which the Agency will issue "micro guidance", or guidance on a narrow topic, as well as recognize industry-developed guidance similar to how FDA accepts industry-developed standards.

We file this supplement on behalf of the Combination Products Coalition, but also another coalition we represent called the mHealth Regulatory Coalition (or "MRC"). The MRC believes that the guidance problems are not limited to combination products, and wants to see these reforms adopted more broadly. The MRC is a diverse group of mobile healthcare technology stakeholders focused on promoting the development of an honest, realistic, and thoughtful regulatory policy perspective on mobile health technologies. MRC members include medical device manufacturers, smartphone healthcare application developers, cellular handset manufacturers, network operators, and back end software services and data storage providers, as well as representatives of provider organizations, clinicians, healthcare researchers, and other industry and trade associations. Its members share the common goal of promoting a balanced approach between regulatory policies, and the need for innovation and getting new products to the market for patient's best interests.

If you would like any further information on any of these topics, we would be pleased to help in any way we can.

Respectfully submitted,

Bradley Merrill Thompson
On behalf of the Combination Products Coalition and mHealth Regulatory Coalition

Enclosure: Good Guidance Practices 2.0: supplement to Citizens Petition Docket ID: FDA-2012-P-0617 filed by the Combination Products Coalition

Good Guidance Practices 2.0

Supplement to the Citizens Petition Docket ID: FDA-2012-P-0617
Filed by the Combination Products Coalition

This document is the product of brainstorming. The ideas collected and presented here have not been fully vetted within industry, but rather have been identified simply as possible solutions to the chronic problem of slow and inadequate guidance.

Problems for the industry

1. It takes years for FDA to produce guidance. Unfortunately, that means guidance cannot keep up with the pace of technology and innovation-- the questions that need to have an answer today may not be answered sometimes for years.
2. Proposed guidance becomes outdated as it languishes, waiting to be finalized.
3. Final guidance becomes outdated as the agency falls behind in making updates.
4. Guidance is often very general, when in fact sponsors would often benefit from more specific expectations.

Challenges for the agency

1. The law changes frequently and so any guidance must be kept up-to-date; advice can become out of date if it lingers in a database un-reviewed.
2. The legal issues are complex and fact sensitive. Slight changes in the facts will change the legal conclusion.
3. At a macro level, there are changes in technology and in the public health which lead to changes in policy.
4. There are administrative law complexities around making sure that new requirements are not imposed outside of rulemaking.
5. Guidance needs to be reliable and accurate, which generally means that it must have the support of senior agency management and be given by someone who is trained to do so.
6. In many areas the rules are unsettled without a consensus within FDA.
7. There are established legal mechanisms for giving binding guidance, such as section 513(g).
8. There are enormous resource challenges both with developing guidance, but also with manning telephones to answer questions.

Opportunities

Improving guidance development by--

1. Borrowing best practices from the European Medicines Agency; they have a system of identifying areas where guidance is needed, producing guidance documents within a defined time frame, and managing regular updates so guidance documents reflect the latest thinking, all with complete transparency about the process and accountable parties.
2. Borrowing best practices from how large companies handle customer service and manage compliance to regulations and internal policies and procedures.
3. Using new technologies such as chat room capability, social media, such as Facebook, and the development of electronic knowledge databases, similar to Wikipedia.
4. Looking for opportunities to push responsibility for simpler questions down within the agency, addressed without extensive review and approval by management at FDA.
5. Looking for opportunities to shift the laboring oar to industry; encouraging industry to develop draft guidance to submit to the agency.

Proposal

To address the rather considerable delays in guidance development and in getting answers from the agency, significant changes are required. Proposed changes can be summarized in the following five general principles:

- General principle 1: FDA needs to dramatically streamline the guidance development process, and push authority to write and issue guidance down within FDA so that it is much less burdensome than, for example, promulgating regulations. As compared to regulations, guidance is more informal and therefore should not require anything approaching the review and signoff required for rulemaking.
- General principle 2: Proposed guidance should be finalized within a year, or it becomes obsolete. Proposed guidance should be published within one year of appearing on the agency's guidance development agenda. This is the expectation for the government generally with regard to FDA guidance, including HHS and OMB that review certain FDA guidances. Of course these time limits should not be somehow construed as suggesting that the guidance should be less than the highest quality. Indeed, FDA needs to strive to improve the quality as well along the lines outlined in our citizens petition.
- General principle 3: FDA should push the authority to answer questions in writing down to levels well below that of writing guidance, since in essence this is taking existing guidance and merely explaining it to individual people who have a specific question or who do not fully understand the written guidance. Those responsible for answering questions should be trained at least annually on the current application of the guidance and updates or clarifications based upon any changes in technology, the question and answers submitted during the year, and other Agency experience operating under the guidance.

- General principle 4: To create balance with those reductions in prepublication signoff, the agency should put into place an effective and efficient process through which it can monitor and audit interpretations of the guidance to ensure it remains consistent with the guidance document. The process should include a mechanism to correct any interpretation errors on a go-forward basis. In addition, a member of the public can raise concerns through a feedback loop regarding either guidance or written answers.[1]
- General Principle 5: The guidance process should be focused on providing timely, high quality guidance and continuously improving the guidance provided to industry.

We summarize the appropriate role of the various means by which the agency gives advice and direction to the regulated industry in the following table:

Types of Agency Pronouncements

Types	Group impacted	Binding or not	Public input in development	Level of signoff required[2]	Appeal or feedback loop
Rulemaking/ regulations	Everyone	Yes	Yes	10	Appeal
Guidance	Everyone	No	Yes	6	Feedback loop
Binding answers to questions[3]	Submitter	Yes	No	4	Appeal
Nonbinding answers to questions	everyone	No	No	2	Feedback loop

Basically there are trade-offs reflected in the above table. Quite simply because they are not binding, guidance and nonbinding answers to questions should be offered relatively freely with less signoff required as compared to rulemaking and binding answers to questions and without a formal appeal mechanism. Nonetheless, because they are influential, there needs to be at least a feedback loop so that senior management and other members of the public can be alerted if there are controversial elements that need to be modified.

Process for Nonbinding Answers to Questions

[1] Notice that we deliberately avoided use of the word appeal, because these would not be appeals. Appeals should be reserved for binding decisions that the agency makes. This mechanism should be a feedback loop through which a more senior person would be given the opportunity to correct or modify something that has been written in a guidance document or in an answer to a member of the public.

[2] At a very conceptual level, we have tried to indicate the order of magnitude of what the signoff should be on a scale of 1 to 10, where 10 is extremely high level of signoff and one is extremely low.

[3] Includes such FDA processes as section 513(g).

For decades, in the Center for Devices and Radiological Health, FDA has had an office that responded to industry questions, currently called Division of Small Manufacturers, International and Consumer Assistance (DSMICA). Representatives of that office would field questions that come from the telephone and email and even fax in order to provide assistance with basic questions from members of the public including industry.

While not trying to be unkind, the answers were not always reliable and in fact not always consistent, depending on which person answered the phone. Further, once an answer was given, that answer was lost so to speak, meaning no one else could take advantage of the information learned. So the process was terribly inefficient, with advisers having to answer the same basic questions over and over again.

We think electronic technology allows substantial improvement over that process, with answers being recorded such that other members of the public can find them. This will not only be more efficient from the standpoint of the government's resources, but will also lead to greater consistency as everyone will see the same answer. If that answer is of questionable accuracy, it can also be challenged in a public way to alert anyone else to the ambiguity or potential weakness in the answer.

This proposal addresses both how to interact with the public, but also how to internally manage FDA's participation so that the information is reliable and fresh.

1. FDA establishes a chat room on the agency's website or other interactive medium
2. All incoming questions are put into either of two categories as follows:
    a. Suitable for an answer by an approved FDA expert-- someone who has achieved the designation of associate director of the division within an office.
    b. Suitable for an answer by an FDA manager-- someone who is an office director
3. All answers will be loaded into a public-facing knowledge database that will be subject to annual audit. Any answers that contain inaccurate interpretation will be replaced with a notice that either corrects the answer or indicates that the answer has been removed and a general explanation of why. New answers shall be effective prospectively only after a reasonable period to come into compliance.
4. The Agency will identify a single director-level representative responsible for overseeing the effective interpretation of the guidance and FDA experts and FDA managers responsible for answering the questions. The Agency will provide annual training on how to respond to the questions posed, and create a system for routing the questions to the appropriate FDA expert or FDA manager.
5. There shall be a feedback loop added to the answers given that allow any member of the public to offer feedback on the appropriateness of the answer, and these feedback comments can be rated by other members of the public to establish how useful they are in offering added insight.
6. FDA shall adopt procedures for evaluating this feedback and escalation to appropriate FDA management.

Micro Guidance

FDA seems to struggle most with drafting guidance that covers a wide range of topics. Indeed, that's understandable because it means that FDA has to think quite broadly about a topic and all the different ways that something might go wrong. So another improvement to the guidance process could be the addition of a process for developing micro guidance—guidance on a fairly narrow topic. Among other things, from FDA's vantage point, this would reduce the risk of issuing the guidance because the scope would be so constrained. Indeed, this idea could be coupled with our other suggestion that trade groups play a more prominent role in producing the first draft of documents, so as to leverage FDA's resources as much as possible.

FDA Recognition of Industry-Developed Guidance

In the medical device realm, FDA already has a well-established process for recognizing industry standards. These standards typically address technical specifications that relate to safety and effectiveness, and are developed through an open public process. We think FDA should consider expanding this to include FDA recognition of industry-developed guidance documents on regulatory topics. Industry for decades has had the legal right to propose guidance to FDA, but this goes a step further and allows industry to go through its own public process to fully develop the guidance for FDA.

Obviously such an approach would not cause FDA to lose control over its guidance process because the Agency could simply refuse to acknowledge any regulatory guidance with which it disagrees.

The key to making this successful would be allowing FDA to participate in the development of the guidance, to increase the chances that the resultant guidance would meet FDA's needs. So to make this work, beyond just acknowledging guidance with which it agrees, FDA ought to be specifically authorized to participate in industry driven guidance development processes. That guidance development process could proceed along the following lines:

1. A trade group or other interested party determines where new guidance is necessary.
2. The trade group prepares the guidance, getting informal feedback from FDA along the way.
3. The trade group publishes the draft guidance for comments by any or all stakeholders, including FDA, patient groups, and anyone else.
    - To help ensure that the document is fully vetted, FDA would provide an electronic forum through which trade groups can publish proposed guidance so that patient groups and others can more easily monitor the development of the guidance.
4. The trade organization will publish the final guidance.
5. If the FDA agrees with the guidance, the FDA will point to and endorse the guidance.

Thus, this proposal, like the others, would take advantage of new electronic platforms for centralized development of guidance, whether by FDA or a private party.