

Public Meeting Introduction --- Prepared by Tim Cote, MD MPH

Good morning and welcome to FDA's open public meeting on the topic of the review of "articles" (that is, drugs, biologics and medical devices) used in the treatment of rare diseases. My name is Tim Cote, and I serve as the Director of FDA's Office of Orphan Products Development in the Office of the Commissioner. Additionally, I serve as Chairman of the expert committee mandated by Section 740, which was an amendment to FDA's 2010 appropriations bill. That law mandates that FDA convene a committee of expert FDA employees to consider the ways the Agency reviews articles to treat people with rare diseases, and consider policy improvements that might help people with rare diseases get better treatments faster. While the law says nothing about the expert committee receiving public input, we are gathered here today because such policies would affect everyone: patients and their families and the advocacy groups that represent them, the biotech industry and the academics that they partner with. So it is only natural that we set aside a time to hear the reflections of those engaged in the endeavor of making miracles and those desperately awaiting them, to hear your concerns about the process as it now stands and your visions of how it could or should be.

Today I am joined by Dr. Elizabeth McNeil who serves as the Executive Secretary to the Section 740 Committee. It is she who will actually draft the Commissioner's report to Congress and the guidance document that flows from its contents. I am also joined by representatives from each of the Agencies major review division Centers; the Center for

Drugs Evaluation and Research, the Center for Biologics Evaluation and Research, and the Center for Devices and Radiologic Health. The representatives of these centers may change over the course of these two days of meetings, but those chairs will remain occupied by an active listener.

This meeting is being conducted under the rules of Part 15, which is an official mechanism for soliciting public input. Beyond these introductory comments, I and my colleagues from the Agency will contribute very little to the content of the next few days; though we may offer the occasional question of clarification, it is basically your meeting. We're not here to answer questions, but to hear from you how you believe we as an agency should proceed towards a review process that yields more and better new drugs for people with rare diseases. From the agenda it seems we will have quite a lot to listen to; there are a wide variety of speakers ranging from patients and advocates to industry and other interested parties, many who are long established members of the rare disease community and a few who are less mainstream. This is good; I expect the Committee will hear both conventional and innovative ideas on the topic.

Before we get started, please permit me to make a few comments on where we've come from and the current state of affairs in making drugs for people with rare diseases. Then it will be you who answer the question of where we should be going.

In 1982 the world was a much different place for people with rare diseases---over the preceding 10 years fewer than a dozen new drugs had been developed for people with rare diseases. The basic model for the pharmaceutical industry was that you create a new drug and then sell it to patients to recoup your development costs, battling it out with whoever else was also trying to get in on the new market you'd just created. This market scenario was very unattractive, hence hardly any companies undertook the development risks. The Orphan Drug Act of 1983 changed all of that, most importantly by establishing a 7-year marketing exclusivity period that made the business model work. Over the subsequent 27 years FDA has designated more than 2200 products with promise as "Orphan Drugs", and from these our review divisions have approved 358 for marketing because they were found be safe and effective.

Credit for these successes must be given where it is due. First and foremost, this was driven by patients and those who struggle on their behalf; there are none among us so unstoppably motivated as a parent seeking a cure for their sick child. Secondly, a whole biotechnology sector grew up around the past 27 years of implementation of the orphan drug act, the drugs have not come from government programs but from independent genius, innovation and willingness to take risk. And lastly, the FDA review divisions have been populated by people of extraordinary sensitivity and sensibility who have flexibly applied the same regulations that govern all FDA-approved drug, that is, the requirement that they be clearly shown to be safe and effective, to these orphans, approving drugs sometimes on the basis of experience with extremely small numbers of study subjects but still demanding credible evidence of safety and effectiveness. Abby

Meyer, that housewife and grassroots organizer from Danbury Connecticut who went on to pass the Orphan Drug Act and lead a movement called NORD, always held that as a matter of civil rights, rare disease patients are entitled to drugs that are safe and effective just like common disease patients. It was for this reason that the Orphan Drug Act's yield of new drugs was based on a change in marketplace math, not on a change in the standards of FDA approval.

And so now we arrive at the crux of today's meeting, for there are some 7,000 rare diseases, the vast majority still with no therapies at all. The FDA policy regarding the review of drugs and biologics for rare diseases is no policy at all---they are held to those same standards of safety and efficacy mandated for all pharmaceutical. And while we've accumulated a large collection of new therapies for rare diseases, and the basis of their approvals has exemplified flexibility and reasonableness in FDA's evidentiary demands, this have been done on a case-by-case basis. The process has been practical and very productive, but the policy remains no policy.

So the questions we put to the public, albeit more eloquently written in the Federal Registrar notice, which we on the Committee are asking ourselves and which you all will answer today is this: is it working? Do we need a policy? If so, then what? In one of her first publications after becoming FDA Commissioner, Dr. Margaret Hamburg related that the Agency has been oft accused of approving drugs at only two speeds---too fast or too slow. How do we find the right balance for drugs for rare diseases? Today, FDA's marketing approval means we know a drug really works, not that we think it might work,

and that it's reasonably safe. How do we defend that standard while reckoning with the great urgency of now experienced by the parent of a sick child?

The answers to these questions are found not only in regulatory science but in the will of the people. Gratefully, you have answered our call to democratic participation in this process as we prepare our report for the Commissioner to Congress. We cannot do it without you. We'd best get down to our long day of listening. Can we have the first speaker?