

AMENDING THE MONOGRAPH

THE HEADLINE above is intentionally contentious considering we still do not have a final monograph (FM) to amend. The tentative final monograph (TFM) is far from sufficient

and yet it is effectively law. In the meantime, we rely upon the mechanism in place to amend the tentative monographs issued since 1978.

1. Advanced Notice of Proposed Rulemaking (ANPR) issued August 25, 1978;

2. Tentative Final Monograph (TFM) issued May 12, 1993; and

3. Final Monograph (FM) not issued yet.

The FM, of course, has not yet been finalized. The FDA did publish the Proposed Final Monograph on August 27, 2007. Calls for the finalization of the FM have escalated to a clamor with a number of recent developments including a bill in Congress and a citizen petition aimed at timely resolution. The citizens' petition, supported by Congresswoman Nita Lowey and filed on Nov. 20, 2008, formally requests the expedition of the process that reviews new UV filters under the Time and Extent Application. The bill by Senators Reed and Dodd (S.1112, entitled The Sun Act) was introduced into the 111th Congress on May 20, 2009 and requires the FDA to issue the Final Monograph on Sunscreens within 180 days of enacting this act.² While many bills have endured years in committee, rumors are that the FM may finally be issued this September. We shall wait and see. See you in September!

Amending the OTC Monograph

A drug manufacturer may wish to alter the conditions of use in an OTC drug monograph. There are three mechanisms by which a drug manufacturer, or any other interested

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party, can amend an OTC drug final monograph:

- New Drug Application (NDA);
- Citizen Petition; or
- Time and Extent Application (TEA).

There are many differences between these three mechanisms.

New Drug Application (NDA):

This is the expensive route to introduce a novel ingredient or formulation. However, the NDA products can be protected from competition from similar products by patent protection, exclusivity or both. On the other hand, an NDA requires costly user fees as well as approval before the sunscreen product can be introduced into the OTC market. Extensive data must be submitted to demonstrate that the product is safe and effective as a sunscreen for use by consumers without the assistance of a health care professional. Any change in formulation, labeling, or manufacturing process that deviates from that in the NDA must be approved by the FDA before the manufacturer can make the change.¹

Citizen Petition: The citizen petition process is described in 21 CFR 10.30. A petition can be submitted to FDA at any time to amend a TFM or



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examining all the OTC drugs in the marketplace to establish whether they are safe and effective. The OTC drug monograph system was designed

FM for any OTC drug category. A petitioner can request that FDA amend any condition of use allowed by an OTC drug monograph. One limitation is that the condition must have existed in the marketplace prior to 1975. After the FDA reviews a petition, it either grants or denies the petition within 180 days. If FDA grants a petition, the appropriate OTC drug monograph is amended by the publication of a rulemaking in the Federal Register. If, on the other hand, the FDA denies a petition, the petitioner receives a letter explaining why the petition was denied.¹

Time and Extent Application (TEA): The TEA is a regulatory process that allows conditions of use not found in the OTC marketplace prior to 1975 to be considered for inclusion in an OTC drug monograph. FDA created the TEA to allow conditions of use to meet marketing “for a material time” and “to a material extent” requirements of Section 201(p) of the Act. The basic requirement for submission of a TEA is that a condition of use be marketed for a minimum of five continuous years in the same country and in sufficient quantity (21 CFR 330.14).

The TEA is essentially a two-step process. One, TEA submission to determine eligibility; and two, submission of safety and effectiveness data and its review by FDA. During the first step, an applicant submits information related to the marketing experience of a condition. Initially, the TEA is considered confidential, similar to an NDA. The FDA reviews the marketing information to determine whether the condition has been marketed for a material time and to a material extent. If the condition does not meet these requirements, the applicant is sent a letter stating that the condition is ineligible to be included in the OTC drug review and explaining the reason(s) for this decision. In this case, the letter is put on public display, but the TEA remains confidential.

If the condition is eligible to be included in the OTC drug review, FDA publishes a notice of eligibility in the Federal Register and a request for data. FDA's review of the TEA is

put on public display. This leads to the second step in the TEA process, which is FDA review of safety and effectiveness data. After FDA reviews the data, it publishes a rulemaking in the Federal Register. The rulemaking contains FDA's conclusions regarding whether the condition is Category I, II, or III for safety and effectiveness. If the condition is found to be GRASE (generally regarded as safe and effective) (Category I), the applicable OTC drug monograph(s) is amended to allow the condition to be marketed.¹

More Filters Under Scrutiny

A public meeting on all TEAs was held at the FDA on May 14, 2009 by Dr. Matthew Holman, deputy director, division of Nonprescription Regulation Development.³ He explained the standing delay in the TEA process. Many had expected a final solution to the issues prematurely. A Proposed Rule (PR) containing five ingredients emerging from the TEA process is expected this fall. Here is the status of all UV filters that have submitted a TEA to date:

1. Amiloxate from Symrise, Enzacamene from EMD and Octyl triazone from BASF were submitted August 2002 and they were the first to receive a notice of eligibility (7/11/2003, 68FR41386).

2. Bisotrizole and Bemotrizinol (Tinosorb M and Tinosorb S), both UVA filters from Ciba, were submitted in April 2005 and received a notice of eligibility seven months later (12/5/2005, 70FR72449).

3. Two other sunscreen actives, Diethylhexyl butamidotriazone (Uvasorb) from 3V was submitted in September 2005 (received eligibility July 2006) and Ecamsule (Terephthalylidene dicamphor sulfonic acid) from L'Oréal was submitted September 2007 (received eligibility September 2008). These last two ingredients will be addressed separately at a date later than September 2009.

According to Dr. Holman, the two major reasons for the delay are:

1. It is the first time that any ingredient will be reviewed via the TEA process. The first PR thus sets

the policy and standard for all followers. They're concerned about setting a useless precedent. Decisions about how to measure UVA are deadlocked pending a resolution of the conflict.

2. Priorities within the FDA. The TEA process has no built-in time line which has proven to be a disadvantage in the allocation of resources.

Dr. Matthew Holman discussed several measures that could improve the situation and explained the procedural steps that will be required after the PR in September 2009. After the 90-day comment period and the review of the comments, there are two possibilities for “final approval.” One, inclusion in the Final Sunscreen Monograph (PR, 27 August 2007) and two, Notice of Enforcement Discretion (NOED).

With the inclusion in the final monograph, or an NOED, marketing of the sunscreen can start at the end of the 90-day comment period assuming no further data is required and no comments surface that may cause delays at the FDA. Thus, realistically, these five ingredients may be approved in early 2010.

So what are the seven ingredients on which we hang our major expectations and hopes to improve the UV protection in the U.S.? They are: Amiloxate, Enzacamene, Octyl triazone, two Tinosorbs, Uvasorb and Ecamsule.

The first three are all UVB filters. The Amiloxate is a cinnamate ester, Enzacamene is methyl benzylidene camphor and Octyl triazone (Uvinul T150) is a powerful UVB filter that has been used in Europe and elsewhere for some time now. None of them would improve the situation with the UVA labeling that has surfaced as a major issue in UV protection in the U.S. The Tinosorbs are UVA filters. Their approval in the U.S. would improve dramatically UVA protection allowing for 3 and 4 star ratings in the Proposed Monograph. The last two ingredients include the Uvasorb from 3V, a powerful UVB filter and Ecamsule, an excellent UVA filter that is patented by L'Oréal and is currently permitted for its use exclusively.

The fact of the matter is that the ANPR and the TFM sunscreen monographs have been amended repeatedly, as shown below:

1. April 5, 1994 UVA claims and testing were introduced.
2. June 8, 1994 five UV filters were removed from the Category I listing.
3. September 16, 1996 Avobenzone was included in the monograph
4. October 22, 1998 Zinc Oxide was included in the monograph.
5. May 21, 1999 the Final Rule was proposed.
6. July 24, 2006 Ecamsule was approved via an NDA.
7. August 27, 2007 The Proposed Final Rule was published.

Adequate Protection Needed

As we eagerly await The Final Monograph and the TEA ruling in the fall, the need for adequate protection remains. Current, compulsory regulations fall sorely behind the latest technological advancements in sunscreen filters. Consumer awareness and incidents of cancer have risen in a manner inversely proportionate to the available coverage when you consider omission of once-approved filters and inhibited growth.

Recently, Will Ferrell, the comedian, launched a range of sunscreen lotions for a cancer charity. He has lent his face to be superimposed onto a naked male body for three sunscreen products called Sexy Hot Tan, Sun Stroke and Forbidden Fruit! All the proceeds will go to the benefit of "Cancer for College Charity," an organization that awards scholarships to former and current patients of the disease.⁴

With celebrity endorsements raising awareness, valuable congress time dedicated, academic standards heightened, business and scientific communities uniting—the time has come for a change. ●

Sunscreens: Regulations and Commercial Development, Third Edition, Ed. Nadim A. Shaath, Boca Raton, FL: Taylor & Francis, 2005, pp.85-94.

2. www.opencongress.org/bill/111-

[s1112/text](http://www.fda.gov/cder/rdmt/s1112/text)

3. Food & Drug Administration Teleconference: Presented by Matthew Holman, May 14, 2009

4. www.allheadlinenews.com/articles/7015397419

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1. Holman, Matthew R. "The Role of FDA in Sunscreen Regulation."