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

Re: Citizen Petition to Revoke/Amend 21 CFR §310.502(a)(11)

Dear Sir or Madam:

The undersigned submits this petition under §701 of the Federal Food, Drug, and Cosmetic Act (FDC Act), 21 USC §371 to request the Commissioner of Food and Drugs to revoke, or in the alternative, amend a regulation.

A. Action requested

1A. The Petitioner requests that the highlighted portion of the following regulation be revoked (and subsequent numbered items be revised to reflect the deletion):

Subpart E—Requirements for Specific New Drugs or Devices

Sec. 310.502 Certain drugs accorded new drug status through rulemaking procedures.

(a) The drugs listed in this paragraph have been determined by rulemaking procedures to be new drugs within the meaning of section 201(p) of the act. An approved new drug application under section 505 of the act and part 314 of this chapter is required for marketing the following drugs:

...

(11) Sterilization of drugs by irradiation.

...

[62 FR 12084, Mar. 14, 1997, as amended at 64 FR 401, Jan. 5, 1999]

1B. If FDA chooses not to revoke the regulation, Petitioner requests that it be amended as follows (new language in italics):

Subpart E--Requirements for Specific New Drugs or Devices

Sec. 310.502 Certain drugs accorded new drug status through rulemaking procedures.

> (a) The drugs listed in this paragraph have been determined by rulemaking procedures to be new drugs within the meaning of section 201(p) of the act. An approved new drug application under section 505 of the act and part 314 of this chapter is required for marketing the following drugs:
> ...
> (11) *Drugs that are* ~~S~~sterilize*d*~~ation of drugs~~ by irradiation *and that are intended for internal use (injection, ingestion or implant) or ophthalmic use only. Drugs labeled for external use only, e.g., sterile alcohol prep pads, are not subject to this provision.*
> ...

B. Statement of grounds

1. Background

The regulation that is currently designated as 21 CFR §310.502 originated in or about 1955. On December 20, 1955, FDA issued a notice of what it termed a "Republication of Regulations."[1] (Attachment 1). That notice contained the following regulation:

> § 3.45 *Sterilization of drugs by Irradiation.*
> There is a current interest in the utilization of newly developed sources of radiation for the sterilization of drugs. Prior to the marketing of a drug sterilized by such means, it is necessary in the interest of protecting the public health to establish by adequate investigations that the irradiation treatment does not cause the drug to become unsafe or otherwise unsuitable for use. Accordingly, all drug products, including injections, ophthalmic solutions, surgical sutures, and surgical dressings sterilized by means of irradiation are regarded as new drugs within the meaning of section 201 (p) of the Federal Food, Drug, and Cosmetic Act. An effective new-drug application pursuant to section 505 of the act is therefore a prerequisite to interstate shipment of such articles, except as provided by section 505 (i)
> (Sees. 201, 505, 52 Stat. 1042, 1052; 21 U. S. C. 321, 355)

In 1955, it was no doubt accurate to describe the use of gamma or other irradiation to sterilize medical products as "newly developed sources of radiation." And Petitioner, therefore, does not question FDA's 1955 decision to treat any drug sterilized by irradiation as a new drug and to subject it to the full NDA process. But what was the case with irradiation sterilization in the mid 1950's is not the case nearly 60 years later.

2. The Use of Irradiation for Sterilization Is Well Understood

The use of irradiation to sterilize medical products, and FDA's and industry's knowledge of irradiation in that context, has expanded exponentially in the past almost 60 years. Such

[1] 20 FR 9525 (December 20, 1955). Although the title suggests that it is a republication, Petitioner cannot find the provision of relevance in CFRs predating 1956

methods are now the subject of numerous FDA-recognized standards, e.g., ANSI/AAMI/ISO 11137 relating to sterilization of health care products. And certain "drug" products mentioned in the 1955 regulation, e.g., surgical sutures and surgical dressings, were redefined as devices in the 1976 Medical Device Amendments to the FDC Act. No regulation was deemed necessary in the device rulemaking to subject such devices to the PMA process. Why? Because even as early as 1976 irradiation as a sterilization method was a) well understood and b) able to be dealt with by the then nascent CDRH with a 510(k) premarket review much less onerous than the device NDA equivalent – a PMA.

Additionally, quite recently, CDRH further relaxed the pre-marketing requirements for sterile alcohol pads used to disinfect devices. Although these preamendment devices were traditionally subject to 510(k) premarket review, they were exempted from such review in a draft FDA Guidance document issued in early August, 2014.[2] The basis for the relaxation of premarket review was because FDA concluded that such review was not necessary to assure safety and effectiveness:

> "FDA has identified certain Class II medical devices for which FDA believes a 510(k) review is not necessary to assure safety and effectiveness before these devices enter the market place…."[3]

Thus, when labeled for use as a device, alcohol pads sterilized with gamma are subject only to "General Controls," which CDRH feels (and Petitioner agrees) are ample to assure that these products are safe and effective.

The detailed regulatory explanation that was thought to be necessary in 1955 has since been condensed in 21 CFR §310.502 simply to state that sterilization of drugs by irradiation renders them a new drug. Whether or not FDA wants to retain the provision for certain drugs that may be justified (e.g., injections, ophthalmics[4]), there are certain categories of "drugs" for which the provision is an anachronism, and cannot be justified on the basis of public health protection. That class of drugs includes (there may be others) sterile alcohol prep pads intended for external use to prep the skin for injections or incisions.

FDA has recognized the public health risk from non-sterile alcohol prep pads (whether labeled as sterile or non-sterile). The Agency issued a Press Release following a 2011 recall recommending to healthcare professional to use only sterile antiseptics (including alcohol

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[2] The exemption was put in place in August, 2014 via an announced exercise of enforcement discretion until such time as the draft Guidance becomes final. See http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm407292.pdf

[3] Id. at page 2.

[4] There is a distinct regulation that addresses the sterility of ophthalmics in much greater detail than §310.502 (21 CFR §200.50), so the reference to ophthalmics in §310.502 could be removed on the basis of redundancy alone.

applicators, pads, and swabs). (Attachment 2) But to our knowledge no alcohol prep pad labeled for use to prep the skin for injection (i.e., a "drug") has been the subject of an approved NDA.

And gamma irradiation has no detrimental effect on the product. Attached is a test report showing that the 70% isopropyl alcohol in the prep pad is unaffected by the sterilization process.[5] (Attachment 3)

3. 21 CFR §310.502 is Unknown to Many in Industry and Stands as an Impediment to Proper Labeling

The Petitioner knows that many companies in the business are not aware that 21 CFR §310.502 mandates an NDA for an alcohol prep pad sterilized with gamma when labeled for use on the skin prior to injections. The Petitioner and probably FDA know of other companies in the business that became aware of the NDA requirement, and took steps to avoid that result by delisting, removing NDC numbers from the label and repositioning the product as a device or cosmetic.

Those transitioning from drug to device change the intended use to the effect that the sterile alcohol prep pad is used to sterilize medical devices, not skin. Others have transitioned to a cosmetic with an intended use statement to the effect that use of the sterile pad "aids in the removal of oils and residue from the skin." The Petitioner submits that there can be no justification of a public health benefit for a single product – a gamma sterilized alcohol prep pad – to be subject to the new drug application process when labeled for use on the skin, but go through no FDA premarket review when labeled as a device or as a cosmetic.

The inescapable fact is that no manufacturer will invest in an NDA for a low cost, commodity-type item such as a sterile alcohol prep pad when identical products can be marketed as a device or cosmetic with minor labeling chnages. The other inescapable fact is that the most cost effective way to sterilize an alcohol prep pad is by gamma radiation.

4. Information Unfavorable to Petitioner's Position

The Petitioner is aware of a potential FDA concern that gamma sterilization may enable or incent a manufacturer to ease microbiological manufacturing controls, knowing that effective gamma sterilization will negate any microbiological shortcomings during manufacture. That concern can be addressed by drug GMPs and FDA's inspectional oversight of those GMPs. Responsible manufacturers of alcohol prep pads will have in place and continually monitor a validated microbiological control program. Responsible manufacturers will also have data to establish that gamma radiation does not affect the safety, identity, strength, quality, or purity of the alcohol

[5] Company-identifying information has been redacted.

active ingredient or any other aspect of the product. In conclusion, the answer to any concern in this area can be addressed in the context of FDA's existing regulatory authority, which is far preferable from a public health perspective than the movement of manufacturers out of the drug category and into the device or cosmetic category (which now have no FDA premarket review) for this important healthcare product class.

C. Environmental impact

(A) Claim for categorical exclusion under 25.30, 25.31, 25.32, 25.33, or 25.34 of this chapter or an environmental assessment under 25.40 of this chapter.)

This Petition requests FDA to amend or revoke a regulation relating to the submission of an application for approval and is, accordingly, categorically excluded under 21 CFR §25.30(h). That section provides an exclusion for "Issuance, amendment, or revocation of procedural or administrative regulations and guidance documents, including procedures for submission of applications for product development, testing and investigational use, and approval."

D. Economic impact

Not applicable unless requested.

E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the Petitioner which are unfavorable to the petition.

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