DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

JUL 25 2006

James Q. Maloy
23 Carol Street
Clifton, NJ 07014

Re: Docket No. 2006P-0159/CP1

Dear Mr. Maloy:

This responds to your citizen petition dated April 6, 2006 (Petition), concerning the use of prescription scales with a pill-counting feature to count pills by weight. You request that the Food and Drug Administration (FDA) recommend changes to the National Institute of Standards and Technology (NIST) Handbook 44, "Specifications, Tolerances, and Other Technical Requirements for Weighing and Measuring Devices," and to the U.S. Pharmacopeia (USP), to reflect pharmacy quality control practices regarding the use of these scales. Your petition is a follow-up to a petition you submitted in November 2003 concerning a change to NIST Handbook 44 to allow for the use of prescription scales with a pill-counting feature (2003P-0531/CP1), which we denied in August 2005.

For the reason stated below, your petition is denied.

I. BACKGROUND

In your 2003 petition, you requested that we issue a report to NIST and the National Council on Weights and Measures (NCWM) providing information on pill weight tolerances and/or variations caused by reformulations. The information was to include (1) the typical range of single-batch and batch-to-batch tolerances on pill weights based on information submitted by drug manufacturers and (2) data on predicted counting error rates. Your 2003 petition stated that the report was needed to allow a proper evaluation of the danger to the public posed by a proposal (adopted by NIST effective January 1, 2004) to allow the dispensing of pills based on weight rather than count in pharmacies.

We denied your 2003 petition in a letter dated August 17, 2005 (August 2005 response). We stated that allowing pill counting based on weight could create some potential for errors in pill counting. Nevertheless, we concluded that pharmacy compliance with the procedures and requirements in the standard for prescription scales under NIST Handbook 44, along with pharmacy quality control practices, should ensure reliable dispensing of drug products.[1] We explained that it would not be feasible for us to

[1] August 2005 response at 3.

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provide the information requested in your 2003 petition. We also stated that if we received reports of frequent pill miscounting as a result of the changes to Handbook 44, we would consider contacting NIST and the NCWM to express any appropriate concerns.[2] We have enclosed a copy of our August 2005 response with this letter.

In a letter to me dated October 7, 2005 (October 2005 letter), you stated that our August 2005 response had answered implied questions concerning whether it was feasible to count pills by weight accurately given single production lot pill weight tolerances and given batch-to-batch pill weight tolerances. Your October 2005 letter referred to the following statements in our August 2005 response at page 3:

> [W]e believe that the procedures and requirements in the standard for prescription scales under NIST Handbook 44, used in conjunction with appropriate pharmacy quality control practices, are sufficient to allow reliable dispensing of tablet and capsule drug products. For example, the prescription scales standard establishes a minimum number of units for which the counting should be used and a check for linearity for material weights corresponding to higher numbers of dosage units. The standard also requires a level of sensitivity during calibration such that the scale will reject one unit under or over the number of units corresponding to a certain total weight. *To ensure that there is a reliable value for dose unit weight, pharmacies using pill weights for dispensing must, either at the time of receipt of a drug product or dispensing, make a determination of average weight for the product.* This and other quality control procedures, along with the prescription scale standards, should ensure reliable dispensing of drug products. (emphasis added)

You maintained in your October 2005 letter that the statement on determination of average weight would allow the use of an average piece weight based on a sample from within the current supply bottle but would disallow the use of a stored average piece weight from a different supply bottle, thereby eliminating problems of batch-to-batch variance. You stated that because Handbook 44 allowed pharmacies to count pills by weight, the statement on determination of average weight — which you described as a "QC procedure," an "operational directive," and a "requirement" — should be included in Handbook 44 to ensure proper scale usage.[3] We have enclosed a copy of your October 2005 letter for your convenience.

II. DISCUSSION

In your April 6, 2006, petition, you ask that we recommend changes to NIST Handbook 44 and to the USP to reflect what you appear to believe is an FDA requirement concerning pharmacy quality control practices. Specifically, you request that we do the

[2] August 2005 response at 3-4.
[3] October 2005 letter at 1.

following: (1) ask NIST, the NCWM, and the USP to prohibit the storing of preloaded (factory) databases in individual prescription scales and the use of a common shared database in the case of scales that are linked to a server and receive their average piece information over a network; and (2) ask the USP to include the "required" pharmacy quality control practice in the USP section on prescription scales (Petition at 1).

You state that most prescription scales that count by weight rely on a table of average pill weights, cross-referenced to National Drug Code (NDC) numbers, stored in electronic memory. You claim that our August 2005 response indicates that these average weights must be updated at the time of receipt of a drug product or dispensing, thereby eliminating the counting problems posed by lot-to-lot weight tolerances and reformulations. However, you state that many prescription scales are shipped with factory-loaded databases that contain average pill weights referenced by NDC number. You maintain that pharmacies must not use these weights because they are not based on the drug products actually received by pharmacies, although you state that "we cannot find a single regulatory document specifying this requirement" (Petition at 1). You state that NIST Handbook 44 should be modified to reflect this "requirement" and to indicate that the stored average piece weight data can only be derived from drug products received by the pharmacy. You also state that the section of the USP relating to prescription scales should be revised to include the "requirement" for updating average drug piece weight as products are received or dispensed (Petition at 2).

You appear to have misunderstood a statement in our August 2005 response concerning pharmacy determination of average product weights (i.e., "To ensure that there is a reliable value for dose unit weight, pharmacies using pill weights for dispensing must, either at the time of receipt of a drug product or dispensing, make a determination of average weight for the product"). This statement was intended only as a comment about what we anticipated that pharmacies using scales that count pills by weight would need to do to ensure that they obtain reliable dose unit weights. The statement does not reflect an FDA requirement concerning pharmacy quality control practices. The practice of pharmacy is regulated primarily under State and local law; FDA generally does not regulate activities that fall within the traditional practice of pharmacy.

Because there is no FDA requirement with respect to pharmacy determination of average product weights, there is no basis for our making the recommendations to NIST, the NCWM, and the USP that you request in your petition. You might wish to examine whether there are any State laws governing the practice of pharmacy that might be relevant to this issue and, if so, to consider contacting appropriate State authorities about the use of prescription scales with a pill-counting feature. You may also wish to express your concerns to NIST, the NCWM, and the USP.

III. CONCLUSION

For the reason stated above, your request that we recommend certain changes to NIST Handbook 44 and the USP to reflect purported requirements concerning pharmacy quality control practices is denied.

Sincerely,

Steven K. Galson, M.D., M.P.H.
Director
Center for Drug Evaluation and Research

Enclosures (2)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

AUG 17 2005

James O. Maloy
23 Carol Street
Clifton, NJ 07014

Re: Docket No. 2003P-0531/CP1

Dear Mr. Maloy:

This responds to your citizen petition dated November 14, 2003 (Petition), regarding a then-pending proposed change to National Institute of Standards and Technology (NIST) Handbook 44, "Specifications, Tolerances, and Other Technical Requirements for Weighing and Measuring Devices," to allow for the use of prescription scales with a pill-counting feature to count pills by weight. You request that the Food and Drug Administration (FDA) issue a report to NIST, the National Council on Weights and Measures (NCWM), and yourself, providing information on pill weight tolerances and/or variations caused by reformulations. You state that this report is needed to allow a proper evaluation of the danger to the public posed by the proposal to allow the dispensing of pills based on weight rather than count in pharmacies.

We have reviewed your petition and the information you submitted in your letter dated December 7, 2004. For the reasons stated below, your petition is denied. However, if we become aware that significant pill counting errors may be occurring because pills are being counted by weight, we will consider addressing the issue with NIST and the NCWM.

I. BACKGROUND

In 2003, the Western Weights and Measures Association (WWMA) submitted to the Specifications and Tolerances Committee of the NCWM a proposal to amend NIST Handbook 44, 2003 edition, to recognize prescription scales with a feature that counts pills by weight. The WWMA proposal was developed with input from prescription scale manufacturers who maintained that: (1) FDA provides a high level of regulatory oversight to ensure that prescription drug dosages are uniform, unlike other commodities sold by count based on weight; (2) pharmacists are trained professionals in search of an accurate method of dispensing pills; and (3) device technology provides greater accuracy for filling containers when counting by weight rather than by hand.[1] The Specifications and Tolerances Committee adopted a revised proposal on a counting-by-pill-weight

[1] NCWM, Interim Report of the Committee on Specifications and Tolerances, 2003, at 10.

feature for prescription scales and sought input from FDA, the U.S. Pharmacopeia (USP), and representatives from the pharmaceutical industry.[2]

The NCWM adopted the proposed change to allow for pill counting based on weight in July 2003. Effective January 1, 2004, the proposal became part of NIST Handbook 44.

II. DISCUSSION

You claim that allowing the counting of pills by weight could lead to erroneous pill counts for several reasons. First, you state that although the dosage weight of pills is controlled, it is not controlled at a level that would permit using pill weight as the controlling factor for counting pills (Petition at 1-2). You state that the USP has a section on uniformity of dosage that allows for dosage weight tolerances of ± 15 percent.[3] You maintain that this controverts the NCWM's assumption about the uniformity of drug dosages. Second, you question the accuracy of pill weights that are stored in the electronic memory of prescription scales. You state that scales that count by weight store in their memory a table of average pill weights, cross-referenced to NDC codes. Because drug manufacturers do not publish the weight of their pills, this information must be gathered empirically. However, you state that because a relative standard deviation of 6 percent is allowable, the stored average piece weight of a sample of 30 pills would not be accurate. Third, you contend that reformulation of pills (changing the weight of the excipients but not the active ingredients) could result in two versions of the same drug with the same NDC code but different pill weights, further complicating the counting of pills by weight. Finally, you claim that studies of pill counting by hand produced an error rate of about 0.4 percent, significantly lower than the error rate that you claim would result from counting by weight, due to the dosage weight tolerances of ± 15 percent (Petition at 2).

FDA agrees that counting and dispensing pills by weight could potentially lead to errors in pill count. We also agree that the calculation of pill weights and reformulation of pills, if not adequately addressed in pharmacy procedures, could affect pill counts. To ensure that patients receive uniform dosages of a drug product from unit to unit, FDA regulations require in-process controls for each drug product and specifications to assure each product's identity, strength, quality, purity, and bioavailability; reference to the USP or National Formulary may satisfy these requirements (21 CFR 314.50(d)(1)(ii)(*a*)). Under our current good manufacturing practice regulations, manufacturers must establish control procedures to monitor the output and validate the performance of manufacturing processes that may be responsible for causing variability in the characteristics of a drug product, including procedures on weight variation and content uniformity (21 CFR 211.110(a)). One of the principal ways that a manufacturer can meet these uniformity requirements is by ensuring that its drug product meets the acceptance criteria set forth in

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[2] Id. at 12.

[3] Petition at 2 (citing U.S. Pharmacopeia 24/National Formulary 19 (USP 24/NF 19), July 1, 2000, Supplement, 2094-96).

USP <905>, Uniformity of Dosage Units.[4] This test provides for two methods to measure the uniformity of active ingredients in dosage units, weight variation and content uniformity. Generally, when the dosage unit is a liquid-filled soft capsule (other than a soft capsule containing a suspension) or when the dosage unit contains 50 milligrams or more of an active ingredient that comprises 50 percent or more, by weight, of the unit, the weight variation method can be used. This method measures the weight of individual units, and the content of active ingredient in each unit is then calculated, assuming homogeneous distribution of the active ingredient. For dosage units that do not qualify for the weight variation method, the content uniformity method can be used, involving assaying the active ingredient in individual units. The same acceptance criteria apply to both methods, i.e., the amount of the active ingredient in each of the dosage units lies within the range of 85 to 115 percent of the label claim and the relative standard deviation is less than or equal to 6 percent.

It might be reasonable to extrapolate these acceptance criteria for the uniformity of *active ingredient* to the uniformity of *pill weight* (assuming homogeneous distribution of the active ingredient). If so extrapolated, applying these wide acceptance criteria to dispensing pills by weight instead of count might potentially lead to errors in pill count. Nevertheless, we believe that the procedures and requirements in the standard for prescription scales under NIST Handbook 44, used in conjunction with appropriate pharmacy quality control practices, are sufficient to allow reliable dispensing of tablet and capsule drug products. For example, the prescription scales standard establishes a minimum number of units for which the counting should be used and a check for linearity for material weights corresponding to higher numbers of dosage units. The standard also requires a level of sensitivity during calibration such that the scale will reject one unit under or over the number of units corresponding to a certain total weight. To ensure that there is a reliable value for dose unit weight, pharmacies using pill weights for dispensing must, either at the time of receipt of a drug product or dispensing, make a determination of average weight for the product. This and other quality control procedures, along with the prescription scale standards, should ensure reliable dispensing of drug products. However, if we become aware of information suggesting that the use of prescription scales is resulting in significant pill miscounting, we will consider submitting comments to NIST and the NCWM.

You ask that FDA issue a report specifying the typical range of single-batch and batch-to-batch tolerances on pill weights based on information submitted by drug manufacturers to the Agency (Petition at 1). You also state that we could provide data on predicted counting error rates using pill weight data provided to the Agency (id. at 2).

It would not be feasible for FDA to provide the information you request. As stated above, § 211.110(a) requires manufacturers to establish control procedures to monitor the weight variation of pills and to validate the performance of the manufacturing processes that might be responsible for causing weight variation. However, pill weight variation is highly dependent on the formulation, size of the dosage unit, weight of the capsule shell,

[4] USP 28/NF 23 (2005) at 2503-05.

manufacturing process, and equipment used in producing each drug product. Therefore, it would not be possible for us to establish "typical" single-batch or batch-to-batch pill weight tolerances that would be applicable to all drug products. Furthermore, providing information on pill weight tolerances for each individual drug product (without identifying each product) would require too many Agency resources to be feasible. For each strength and formulation of every solid oral drug product, we would have to assess all of the factors listed above that affect pill weight variation, calculate a pill weight tolerance, update the information to reflect product changes, and make this information available to the public; this burden would increase with each newly approved drug product and any subsequent modified formulations. For these reasons, we are unable to grant your requests that we issue a report on pill weight ranges and provide data on expected counting error rates based on pill weight data.

III. CONCLUSION

Because of the reasons stated above, your request that we provide a report on pill weight tolerances to NIST, the NCWM, and you is denied. Although we agree that allowing pill counting based on weight creates some potential for errors in pill counting, this potential might be reduced through pharmacy compliance with the procedures for the use of prescription scales. However, if we receive reports of frequent pill miscounting as a result of the changes to NIST Handbook 44, we will consider contacting NIST and the NCWM to express any appropriate concerns.

Sincerely,

8.17.05

Steven K. Galson, M.D., M.P.H.
Acting Director
Center for Drug Evaluation and Research

2005-7593

October 7, 2005

Dr. Steven K. Galson, M.D., M.P.H.
Department of Health & Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
9200 Corporate Blvd., HFZ-308
Rockville, MD 20850

Dear Dr. Galson:

We would like to thank you for your reply to our petition, Docket No. 2003P-0531/CP1, regarding pill weight tolerances as they relate to counting pills by weight. The detailed and carefully worded reply clearly indicates that considerable thought and effort was put forth and we appreciate your response. While you deny our petition, you have, through your reply, provided us with the conclusions that we would have expected based upon the published weight tolerances as specified in the U.S. Pharmacopeia. We acknowledge your understanding the merits of our request as you so clearly state in the *Discussion* section of your response.

The implied questions we sought answers to, but did not ask directly, were; A). Is it feasible to count pills by weight accurately given single production lot (batch) pill weight tolerances? B). Is it feasible given batch-to-batch pill weight tolerances? You answered both questions in your reply and thereby resolved a significant issue.

The first two sentences of the third paragraph of the *Discussion* section justify our request for information. In the third sentence you state the FDA position on these matters. As stated, the FDA believes that the procedures and requirements of H44, "used in conjunction with appropriate pharmacy QC practices, are sufficient to allow reliable dispensing of tablet and capsule drug products". In the fourth and fifth sentence you outline some supporting H44 requirements for counting by weight. In the sixth sentence (S6), you specified a necessary "pharmacy QC procedure", and you answered our implied questions. It states "To ensure that there is a **reliable** value for dose unit weight, pharmacies using pill weights for dispensing **must**, either at the **time of receipt** of a drug product or **dispensing**, make a **determination of average weight** for the product". This would **allow** the use of an average piece weight based on a sample from within the current supply bottle, and **disallow** the use of a stored average piece weight from a different supply bottle (thereby eliminating the batch-to batch problems). Since H44 allows counting by weight in the pharmacy, a special application, the "QC procedure" (actually an operational directive) as outlined by the FDA should be included in H44 in order to insure proper scale usage. The directive relates directly to a scale function, and there are several ramifications to this "must" requirement of S6. These are detailed in the Attachment No.1.

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We will send copies of your letter along with this letter to both the NCWM and NIST. We will follow up with NCWM and, if necessary, make a presentation to NCWM NE section in order to have the FDA conclusions reflected in H44. The latter process can take several years. We are concerned about informing the pharmacist about the S6 requirement in the interim. Perhaps the FDA could help in this area.

Yours respectfully,

James Q. Maloy

James Q. Maloy

05-1593

Attachment No. 1

Suggested Changes to H-44 to rectify scale related problems based on FDA findings:

1. H44 UR.3.12 Correct Stored Weight states "For prescription scales with a counting feature, the user is responsible for maintaining correct stored piece weight. This is especially critical when a medicine has been reformulated or comes from different lots". This wording should be replaced with the exact words of S6. S6 wording, which is both specific and instructive, precludes improper scale usage and eliminates the reformulation problem.
2. H44 table S.6.3.6 note 13 requires scales with a counting function to be marked "counting function is not legal for trade" except for prescription scales. For prescription scales with a counting feature a marking on the scale should be required in order to prevent improper scale usage. The marking shall inform the user of the "must" requirement in a compressed version of S6, such as "user must, either at the time of receipt of a drug product or dispensing, make a determination of APW". If this labeling were made retroactive it would inform users about the requirement for updating the database, including those in scales that came with stored databases.