founded 1881

November 24, 2008

Office of Information and Regulatory Affairs
ATTN: FDA Desk Officer
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Re: Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Draft Guidance for Industry on Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Drug Listing; 73 *Fed. Reg.* 206 (October 23, 2008); Docket No. FDA-2005-N-0464

Dear Sir or Madam:

The Structured Product Labeling (SPL) Over-the-Counter (OTC) sub-team (the sub-team), under the coordination of Consumer Healthcare Products Association (CHPA)[1] staff, appreciates the opportunity to comment on the collection of information pertaining to the July 2008 Draft Guidance for Industry: Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Drug Listing (the "Draft Guidance"). The SPL OTC sub-team, comprised of manufacturers, consultants, and vendors, was formed in May 2008 to address issues resulting from the new requirement that drug establishment registration and drug listing information be submitted electronically as noted in the Food and Drug Administration Amendments Act of 2007 (Public Law 110-85). More specifically, the sub-team seeks to address the concerns and needs of manufacturers and distributors affected by this change. We respectfully submit the following comments and requests for clarification associated with the estimated annual reporting burdens stated in the notice.

[1] CHPA, founded in 1881, is a national trade association representing manufacturers and distributors of over-the-counter medicines and dietary supplements.

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I. Estimated Reporting Burdens

A. Estimated Man-hours and Resources Necessary to Complete Initial Electronic Submissions

In the October 23, 2008, *Federal Register* (*Fed. Reg.*) notice, FDA outlined its estimated annual reporting burden (see Table 1 in the *Fed. Reg.* notice). While we do not disagree with the estimates provided in the table, it appears the agency did not fully consider the time and resources required to prepare for the initial electronic submissions. This is especially true for OTC Monograph drug product manufacturers who can have more complex manufacturing and packaging contractual arrangements, and who can have multiple sources of active ingredients and less formal control over the registration requirements of facilities producing these active ingredients. Manufacturers represented on the SPL OTC sub-team have various numbers of non-prescription drug products in their portfolios, ranging from a few products to several hundred products (not including different package sizes). Table A below provides examples of the number of products, sites and active pharmaceutical ingredient (API) manufacturers involved in the submission process from a few of the SPL OTC sub-team members. Even now, some companies are still unable to determine the extent of work required in order to comply with these requirements due to the complexity.

Table A: Examples of the Number of OTC Products, Package Sizes, Manufacturing and/or Packaging Sites, and Active Pharmaceutical Ingredient Manufacturers Involved in the Electronic Submission Process

Company	Number of OTC Products Subject to Electronic Submission	Number of Individual Package Sizes or SKUs	Number of Manufactur-ing and/or Packaging Sites Involved	Number of Active Pharmaceutical Ingredient Manufacturers Involved
A	674	N/A	N/A	N/A
B	475	2400	57	15
C	125	600	12	25
D	600-700	2340 +/-	143	N/A
E	450	7500	15+	N/A
F	400-600	~4000	35+	TBD

N/A = Not Available
SKU = Stock Keeping Unit
TBD = To Be Determined (*i.e.*, unable to quantify to date)

In addition to the time companies will now need to spend researching required and recommended information necessary to complete the electronic submission process (*e.g.*, manufacturer, repackers and co-packers, relabelers, establishment/s, identifying foreign company brokers, and importer/s of record plus obtain DUNS numbers for all of these sites), there are several key steps that companies must complete before they can even attempt an electronic submission. Industry activities will include, but are not be limited to:

- investigation of new software programs,
- validation of new computer systems as well as updating and validating existing databases,
- development of new standard operating procedures (SOPs), and
- contacting each manufacturing, contract manufacturing and/or packaging sites, and active pharmaceutical ingredient (API) manufacturing sites to ensure that their electronic registrations have been completed prior to drug listing of the individual products.

Financial resources as well as manpower from corporate regulatory affairs and technology departments will be required to complete these set-up tasks. It is also unknown how quickly and/or time-consuming it will be to resolve any errors that occur with the electronic submission process, potentially delaying a product launch.

B. Estimated Man-hours and Resources Required To Create Drug Listing Submissions for OTC Products

Once companies have completed the transition from paper to electronic submissions and are familiar with the software necessary to do so, it is estimated that a minimum of two hours will be needed to create the complete drug listing SPL file. However, there is a huge investment in man-hours and resources needed **prior** to this stage that we believe FDA is substantially underestimating. It is estimated that the conversion process (*i.e.*, paper to electronic submission) for OTC products will cost $200 - $300 per product label if an outside vendor is utilized. In order to identify which software or software vendor is best suited for a company's needs to generate the SPL file, time must be invested to evaluate the various software or software vendors to choose the appropriate long-term approach for the company. Also, some companies have proprietary systems that are fundamentally incompatible with extensible markup language (XML) and will require substantial work and investment to

co-exist with XML. Furthermore, some company OTC drug organizations are investing significant resources to determine the approach needed to convert to electronic submissions by the June 1, 2009, compliance deadline having only learned of the requirement within the past few months. The evaluation process could involve a considerable time investment as there are many software providers to be considered in addition to the time needed to complete internal discussions for selection of the best software for an individual company's needs. The time required for this evaluation will also depend on the difficulty of the task for that company and their prior knowledge of SPL. Additionally, there will be the cost of purchasing the software (and updates) once a decision has been made.

Companies may also incur expenses to obtain DUNS numbers for third parties business entities if they are unable to obtain the information directly from the firms. In order to obtain this information directly from Dun & Bradstreet, it has been proposed that a manufacturer will need to pay an annual fee of approximately $300.00 plus $2.00 per third party DUNS number requested. This added expense could be nominal or quite costly depending on the number of third parties entities involved in completing SPL submissions on a large product portfolio with several different entities involved. We estimate that one SPL file will require a minimum of four DUNS numbers to be included in the submission, with a single electronic submission estimated to contain approximately five DUNS numbers on average.

As an example of the considerable investment needed prior to completing an electronic submission, one sub-team member has been researching DUNS numbers since February 2008 and continues to find errors that must be corrected or resolved. After nearly a year-long process, the company hopes to have all of the nearly 50 DUNS numbers (only numbers needed for electronic registration, not the complete corporate chart of entities) verified by December 2008. Throughout this 10 month process, staff from various departments including regulatory affairs, finance, and legal, have been involved in attempting to obtain or verify the DUNS numbers. Part of the difficulty for many companies is that there is no centralized department or person dedicated to working with Dun & Bradstreet. Additionally, DUNS numbers are financial numbers, and basing a regulatory compliance program on a financial system potentially creates both short-term and long-term issues. In most, if not all, companies, the staff involved with Dun & Bradstreet requirements and with FDA requirements have limited or no contact. Therefore, new internal corporate relationships must be established to

obtain information needed for SPL submissions. A Dun & Bradstreet representative has indicated that it would be best for each company to allocate to an individual, or small group of individuals, the responsibility for upkeep of the DUNs numbers. Unfortunately, this is not a practical or viable solution for major organizations with branches worldwide. We strongly encourage FDA to use its own registration system which already exists rather than rely on the use of DUNS numbers.

Furthermore, it is important to note that FDA is essentially expanding the requirements for manufacturers by requesting additional "recommended" information not previously required or requested. Some of this information, such as DUNS numbers, must be provided or the system may reject the submission. When the data in a SPL submission changes, a new file must be submitted. Therefore, more frequent submissions compared to that required in current regulations will be needed to maintain current and accurate data.

II. Use of Electronic Submission Gateway

In the *Federal Register* notice, FDA lists the items needed to create and submit an SPL file to the agency, specifically:

- computer with internet access
- appropriate software,
- knowledge of terminology and standards, and
- access to the agency's Electronic Submission Gateway (ESG).

While at first glance these items may be readily accessible for most, if not all, OTC manufacturers, we believe the FDA has oversimplified the use of the ESG. For example, it is unrealistic to expect companies to use a public computer to access X-forms. One main concern to companies is the possible visibility of confidential information in public areas (*e.g.*, community centers, libraries, etc.). Additionally, time limits are often associated with use of public computers.

There may be technical issues associated with using the free X-forms available via the internet, independent of whether the submission process occurs in a public or private setting. For example, updates to websites providing free access to the X-forms may result in compatibility issues that could be difficult or impossible for companies to resolve without external technical assistance. Additionally, there is no guarantee that the private company that has developed the X-forms will develop future forms to keep up with new requirements or

provide problem-solving to companies using the "free" forms. Furthermore, because neither the FDA nor the individual companies own the X-forms, companies may have difficulty getting technical support. Issues such as password errors and problems in saving and/or retrieving copies of the electronic file could complicate submissions of SPL documents. We recommend that FDA and the X-form vendor work to develop a toll-free industry hotline dedicated to address technical questions and issues related to the ESG.

The X-forms themselves have inherent problems. Throughout the implementation process so far, it has been indicated that these forms are more than adequate for small companies, but larger companies should find an alternate source for submissions (that is, a private software developer).

It is also important that it be easy for manufacturers to save the data contained in an X-form in a manner that can be reviewed, approved, shared with colleagues (as appropriate), and easily retrieved. Following the initial submission, it will be more efficient if companies are able to modify prior submissions instead of re-entering data. It is not possible to easily save and retrieve information with the current X-forms.

III. Implementation

In light of the information noted above, we are again urging FDA to consider a phased-in approach for SPL submissions. In our previous comments to the agency, submitted on September 9, 2008, we recommended that implementation occur in two phases. The first phase would require that all drug establishment registrations and labeler code verifications be submitted electronically by June 1, 2009. The second phase would require that all drug listings after December 1, 2009, be completed via electronic submission. Most companies are in the process of learning the new requirements, the elements of submitting SPL documents, how SPL will be used for electronic registration and listing, and identifying the best solution for each company. This dual-phase approach will provide sufficient time for companies to identify the SPL solution that best fits the individual needs of each company and to ensure that the solution is fully capable before the compliance date.

The SPL OTC sub-team thanks the FDA for the opportunity to provide comments on the estimated reporting burdens to comply with SPL electronic submission requirements. The sub-team appreciates FDA's efforts to communicate with, and provide educational opportunities for, industry and looks forward to continued collaboration with the agency on this complex issue.

Sincerely;

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Director, Regulatory & Scientific Affairs
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