

# P&G

---

*The Procter & Gamble Company  
General Offices  
1 P&G Plaza, Cincinnati, Ohio 45202*

January 26, 2007

Division of Dockets Management (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

RE: **Docket Number 2005N-0403**

PROPOSED RULE: Requirements for Foreign and Domestic Establishment Registration and Listing for Human Drugs, Including Drugs that are Regulated Under a Biologics License Application, and Animal Drugs

Dear Sir or Madam:

The Procter & Gamble Company welcomes the opportunity to submit comments regarding the Proposed Rule published in the August 29, 2006 Federal Register (FR Vol. 71, No.167 pp. 51276-51357) which would substantively amend the procedures for establishment registration and human and animal drug listing. The Procter & Gamble Company ("P&G") is an international consumer product company headquartered in Cincinnati, Ohio that markets consumer products in over 160 countries around the globe. In the United States, P&G products under FDA jurisdiction include those regulated as human and animal foods, dietary supplements, Rx and OTC drugs, cosmetics, and medical devices. P&G drug products include Crest toothpaste, Prilosec OTC, Head & Shoulders shampoo, Actonel, Old Spice antiperspirant, Metamucil laxative, Pepto Bismol, and Olay sunscreens.

P&G commends FDA's initiative to establish electronic drug listing and establishment registration systems. We believe providing electronic systems will improve the integrity of the US drug supply by helping ensure information provided to and maintained by FDA is current and correct. We believe FDA's proposal to utilize new technology in this process will improve the efficiency of establishment registration and drug listing by allowing direct data entry for facility operators and product manufacturers and improve data accuracy and completeness by detecting errors and preventing omissions. This will benefit stakeholders and the Agency by providing complete, accurate and current information when needed.

2005 N-0403

C93

As FDA sets out to develop electronic systems for drug listing and establishment registration, we strongly encourage the Agency to consider developing a step-wise or tiered approach that focuses initially on the development of an electronic system which facilitates usage of the existing NDC number system. The current NDC number system is highly integrated and intertwined within the US commercial billing, ordering, forecasting, and shipping systems and unilateral changes to the system can have significant far-reaching impacts on consumers, manufacturers, service providers, and other governmental programs. We believe developing the electronic systems for accepting and maintaining establishment registration and drug product listing information should be the Agency's highest priority and the additionally proposed NDC number system changes will only significantly complicate and dilute the initiative, divert substantial Agency and industry resources, and significantly delay the system deployment. We strongly encourage the Agency to focus initially on establishing an operational electronic system for establishment registration and drug listing, and subsequently propose changes as necessary to meet the Agency's further needs with a better and more complete understanding of their impacts on the marketplace.

Where ever possible, we also encourage the Agency to deploy a regulation and process that is objective-based and principle-based, rather than one that mandates redundant or non-value added requirements or procedures. The existing NDC numbering system appears to be serving its many constituents and stakeholders very ably at present and the need for and benefit from a significant system overhaul beyond the establishment of the electronic system is unclear and presently appears unwarranted. At the December 11<sup>th</sup> public meeting, FDA representatives expressed a desire to recast the NDC number system as a system to be used for drug product traceability, claims approval, formulation approval and label approval, despite the already-existing mechanisms currently in place for managing these. Without clear evidence supporting why the existing mechanisms and procedures are broken or in need for upgrade, these changes appear redundant. Further, mandating a specific procedure may impact a much broader target of operations than originally envisioned by the Agency, prompt changes merely for the sake of making changes, limit the incentive for finding superior and/or more efficient ways to achieve a desired endpoint, increase complexity and ultimately increase cost. We believe an objective-based regulation creates incentives that encourage innovation, which can lead to greater future public health benefits.

Our specific comments regarding this Proposed Rule are:

**1. The Proposed Rule imposes significant changes to the OTC Monograph drug system without providing a corresponding benefit.**

The OTC Monograph system was developed by FDA in order to not overburden Agency resources with an excessive number of low risk product reviews and changes. This has allowed the Agency to focus its resources on issues that have higher public health and safety priority and consequences. The OTC Monograph system has worked well in the US for over 30 years. Nationally and internationally, the OTC Monograph system is viewed as an unparalleled success in its ability to assure the safety and effectiveness of OTC drugs, allow manufacturers to provide product forms, doses, flavors and colors meeting consumer needs and preferences, and provide regulatory oversight.

This proposed rule would fundamentally alter this US OTC Monograph system without providing meaningful public health benefits. The Agency is proposing to use NDC number issuance as an opportunity to conduct pre-market product reviews to ensure unapproved new drug claims are not being made (Comments from December 11, 2007; Rockville, Maryland). However, the reinvention of the NDC number issuance system into a pre-market product review process also creates many significant issues for the Agency, product manufacturers, commercial distribution and retailers, and ultimately the consuming public. Among the most significant relate to the significant time difference between when NDC numbers are needed and when product formulations, claims, and labeling are finalized; benchmarks for approval process performance, submission requirements, and Agency resources; and the perceived value and need for making fundamental changes to the existing marketplace.

a. Time differences between when NDC numbers are needed and when product formulations, claims, and labeling are finalized -- Reinvention of the NDC number issuance system into a pre-market product review process creates significant timing issues for product manufacturers. NDC numbers are currently established months before product formulations, product claims and product labeling are finalized. This is done in order to alert retailers of pending new products and to allow product ordering prior to product launch. Since some OTC products are seasonal, establishing and communicating an NDC number 1 year in advance is not uncommon. Generally, at the time an NDC number is needed, the information FDA proposes as required to obtain an NDC number simply does not exist.

b. Benchmarks for approval process performance, submission requirements, and Agency resources -- It is unclear how a pre-market review system envisioned by FDA would be organized and resourced. Would reviews be completed in 5 days or less? Will FDA be able to accept information in the formats each manufacturer currently employs? Will there be a resolution process to resolve differences in interpretation and opinion? Can FDA estimate the staffing levels necessary to manage this system when there will be hundreds, if not thousands of requests per month? This proposal proposes to establish new regulatory review processes without providing the accompanying details.

c. Perceived value and need to make fundamental change to the existing marketplace -- Many of the elements FDA is proposing to incorporate into this expanded NDC pre-market review process are already required or enforced within the marketplace and appear to be working well. Lot number information stamped on each package is already used to track drug products. OTC drug compliance within the Agency has the regulatory authority to act when unapproved new drug claims are made. The OTC drug monographs developed by FDA specify much of the required label information. Drug listing information is required to be submitted to FDA within 5 days of market introduction. FDA establishes part of the NDC codes and the manufacturers set the rest. Net, the information on marketed products is already available to FDA and the new electronic system should improve Agency and public access to this data. Overhauling the commercial marketplace, on the other hand, does not appear warranted in order to implement this new electronic system.

## **2. FDA should permit the existing system for NDC number assignment to continue.**

Retailers and product distributors routinely require NDC numbers for products that are scheduled to launch, but are not yet in production, in order for them to be able to accommodate the products upon market introduction. For seasonal products such as cough/cold products, this information is often needed almost 1 year in advance. Despite this long lead time, the timing on which product NDC numbers are assigned may be very short as manufacturers balance the need to finalize product plans against trade customer deadlines, often working until the last possible moment. The result is often that NDCs must be assigned within very short durations, often within just a few days. At this stage of development, product formulations may not be finalized, product artwork has not been developed, and the product packaging facility may be unassigned. Requiring complete formula, labeling, and manufacturing information prior to assignment of an NDC number would require a complete reversal of commercial systems. Unlike an OTC NDA drug product formulation which may be set years prior to market entry, OTC Monograph drug product formulations can and do change more frequently in order to respond to consumer preferences.

The requirement to make complete formula and label information a prerequisite for an NDC assignment will also create a substantial increase in the rework required for product manufacturers, retailers, and FDA. Under the Proposed Rule, a product change made after initial NDC assignment would require the company's internal records, manufacturing and control documents, and embedded Universal Product Code, or UPC, carrying the first-issued NDC number to be revised. New labels to reflect the updated NDC number would have to be created and previously prepared labels would become obsolete. In addition, companies would have to prepare more NDC number requests, FDA would have to process more NDC number requests, and importantly, trade ordering and billing systems would need to be updated frequently. The incremental manpower to keep these updated would be an immense burden and the consequences of errors would likely be product outages.

The scope for FDA NDC assignment would also cover short term products or special packs which combine 2 or more products together for marketing. Combining 2 different OTC drugs into a single package, combining an OTC drug product with a cosmetic or a paper towel, or a new OTC drug product color for the holiday season would all require prompt FDA NDC review in order for the product to meet its market objectives. A holiday season or Super Bowl promotion approved by FDA in March defeats the purpose of the initiative. Similarly, products like seasonal cough/cold products have an annual trade window they must meet to ensure product availability. The time-based products and time-sensitive promotions are expected to increase in the future, and the marketplace needs confidence in the review process.

Net, the impact of FDA control of NDC number assignments in conjunction with the implementation of an electronic drug listing system will be very substantial, affecting current OTC drug development, existing business practice, company and distribution systems, product availability and cost, promotional activities and events, and the resources needed by industry, the trade and the Agency for system operation. We encourage to Agency to maintain the current system for assigning NDC numbers.

### **3. Submission of inactive ingredient information should not be required for NDC number assignment.**

The Proposed Rule requires OTC Monograph drug products to obtain a new NDC number from FDA each and every time an inactive ingredient change occurs. This provision contrasts with previous FDA positions that both recognize and encourage formula flexibility and a go-to-market capability for OTC Monograph drug products. Formula flexibility was inherent to the development of the OTC Monograph system, is implicitly included within current OTC Monographs, and was affirmed most recently in a 2001 Agency response to a Citizen's Petition.

Requiring submission of inactive ingredient information in order to obtain an NDC number assignment and requiring a new NDC number for each subsequent inactive ingredient change will dramatically increase the number of times NDC numbers will change for OTC Monograph drugs. This will have far ranging effects on those who use NDC numbers for product forecasting, product ordering, and product billing as they will have to increase the size of their databases and the resources needed for data entry. Further, frequent data changes within commercial ordering and billing systems increase the potential for system errors which can lead to shipment delays and product outages. Finally, these systems may not recognize that two NDC numbers can really be the same product formulation packaged at different locations, leading to double ordering. We encourage the Agency to encourage NDC number changes for changes of consequence.

Inactive ingredient changes are made frequently to OTC Monograph drug product formulations for many valid and appropriate purposes to respond to consumer preferences and marketplace dynamics. These changes may be made to change product aesthetics, replace more expensive ingredients, introduce new ingredients, flavors, and/or colors, respond to changes in an ingredient supply chain, or to make a formula compatible in two or more countries. As competition increases, companies and products become more international in focus, and consumer demographics change, OTC Monograph drug products, especially those that are both cosmetics and OTC drugs, must compete in a marketplace that includes both OTC drug products and non-drug OTC products.

Each and every inactive ingredient contained in an OTC drug product is required by FDA regulations to be safe and suitable. Further, all drug product ingredients (both active and inactive) are required to be labeled on the package using a common format mandated by FDA. This regulatory approach minimizes public exposure to unsafe and unknown inactive ingredients while also empowering the US consumer with the ability to self select products to avoid ingredients of personal concern or sensitivity. The success of this approach is readily evident—evidence of unsafe or adulterated OTC drug products is very minimal and the American consumer enjoys a competitive marketplace with many effective product choices.

This proposal also raises the question of when a formulation change becomes an inactive ingredient change that would require a new NDC number assignment. Is a change from to a purer form of the same ingredient an inactive change? Is a new supplier of the same inactive ingredient an inactive ingredient change? Is reducing an ingredient level by 0.01% in a formula an inactive change?

We encourage the Agency to not mandate inactive ingredient information be a requirement for NDC number assignment. Inactive ingredient information is already supplied to FDA as part of the current labeling and drug listing information that must be submitted within 5 days of market introduction. In addition, the label of all OTC drug products must specify the identities of all active and inactive ingredients. Further, Rx drugs provide package inserts which include ingredient statements. Supplying inactive ingredient information for NDC assignments in addition these already existing provisions appears redundant and offers little incremental public health benefit.

#### **4. NDC numbers on packages should correspond to the FPLA mandated responsible party.**

The US Fair Packaging and Labeling Act requires all OTC drugs bear a statement of product responsibility on the package label. This responsible party is generally the organization that is responsible for the product labeling and often knows the most about the product.

The Proposed Rule seeks to redefine the responsibility for NDC assignments to the company that packaged the product rather than leaving the responsibility for the NDC assignments with the responsible party whose name appears on the label. This removes NDC responsibility from the entity that formulated the product, established the product specifications, completed the stability testing, consumer testing and claim support studies, developed product labeling and possibly even manufactured the product in bulk to a contract manufacturer whose product knowledge is minimal. Further, since NDC numbers are printed on the package labeling, package artwork could not be completed until a manufacturing site is selected.

This approach has the potential to cause significant issues in the trade due to increased complexity and supply interruptions. If a company employs any of 4 contractors to package the same product in the same size package, then 4 different NDC numbers would have to be assigned for the same product. This could also mandate 4 different UPC numbers for the same product and require the company to develop and maintain 4 different stocks of packaging materials. Label suppliers would have to make and maintain 4 separate piles of label inventory for the same product, and ensure no labels are made with mismatching UPC and NDC numbers. Shipping the wrong labels to the wrong supplier would have to be minimized. If one contractor were dropped, and a 5<sup>th</sup> company contracted, labels would have to be destroyed. If the products were shipped to a 6<sup>th</sup> company to bundle a 2 of these products together into a multipack, these could not be simply shrink wrapped according to existing regulation because a new NDC number would be required for the package comprised of 2 individual units.

At the end of the spectrum, requiring packager NDC numbers for single site packaging are also an issue. If a local event such as a flood or tornado closes a packaging facility, can a company ship bulk product to another contract manufacturer or must new labels be developed and approved by FDA first—a process that can take up to 6 months to complete. Also, what happens when a contract manufacturer ceases operations?

A number of other scenarios are possible with a very similar result – increased complexity, increased cost, increased chances for errors, increased risk that the packager has little information about the product, no incremental benefit. FDA has stated that they believe this packager specific NDC assignment would be helpful for product traceability, investigations and recalls. However, as stated earlier, better mechanisms for tracing product such as lot codes already exist and the need for using the NDC numbering system to track product is marginalized.

**5. Requiring all OTC drug products to have a mandated common “NDC number” format should not be required.**

Currently all OTC drug products are required to provide copies of labeling and drug listing information to FDA within 5 days of market introduction. This provides a brand name, product indication, statement of identity, active ingredient identification, active ingredient level, inactive ingredient listing, expiration date, lot code information, and other pertinent information.

One requirement that does not apply to all OTC drug products is a requirement to have an NDC number on the package, consistent with the original intent of the NDC number system. In this proposal, the Agency is proposing to reinvent the NDC code in order to require that all drug products carry an NDC number. In some cases, this may not be practical.

Small packages with limited space are one instance where inclusion of an NDC number will result in removal of useful consumer information or a decrease in the size of other important information, making it harder to find and/or harder to read. Professional samples and OTC unit-of-use level such as blister packs are also likely to encounter space and font limitations.

Further, requiring the NDC number on secondary packaging may create additional burdens for the labeling of temporary SKUs, such as multiunit, variety or combination packages and other promotional packages, where two or more immediate containers are repackaged into a single carton. In this situation, each immediate container will have an open stock NDC number, but the promotional SKU may require another, different NDC number as a different packaging configuration.

For these reasons, we do not believe mandatory inclusion of the NDC number on the product label should not be required for OTC drug products, especially those products or SKUs that do not require a bar code label.

**6. Submission of batch size and batch frequency information should be mandated for NDC number assignment or for drug listing.**

Drug product manufacturers should not be required to provide batch size and batch frequency information in order to comply with drug listing or NDC number assignment regulations. Unlike product label information which is contained on every package and is directly relevant to the public, batch number and batch frequency information are not publicly disclosed and not directly relevant to the public. In fact, most manufacturers consider this information to be highly confidential competitive information that should not be disclosed under any circumstance. Many

manufacturers and suppliers have non-disclosure agreements that could be jeopardized by this disclosure.

Further, there is not necessarily a correlation between batch size and lot code. Depending on packaging operations and market need, a lot code can be a subset of a batch or a combination of several to many batches. Batch frequency and size can also be quite variable due to seasonal variations, promotions, and competitive activity. This variability coupled with the general lack of correlation between batch size and lot code size minimizes the usefulness and value of providing this information. The sensitive nature and concerns about disclosure lead us to recommend that it is best not provided.

Finally, the Agency already has access to lot information when needed through NDA applications for Rx and some OTC drugs OTC record access requirements. Finally, since all Rx and OTC drugs are required to meet the current Good Manufacturing Practices (cGMPs) requirements of 21 CFR §211, all drug product manufacturing operations are already subject to FDA oversight and inspection.

**7. Manufacturers should be required to update and drug product listing information when product labels are changed.**

We strongly support the need to ensure drug listing information is up-to-date but also strongly believe there are better approaches for achieving this than mandating certifications every 6 months.

We believe the best approach is to focus on ensuring information is updated when changes in labeling are made to a product. Drug listing information is already required to be provided within 5 days of when a new product is introduced. Allowing manufacturers to enter this information directly into the system would seem to provide the best route to submit this information, to ensure it is accurate and up-to-date, and is accessible. This is perhaps the greatest advantage of implementing the proposed electronic system.

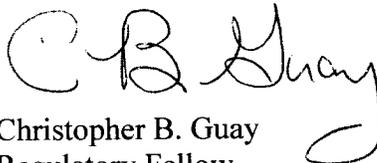
Given the great potential and appeal of this electronic system, we do not support the concept of re-certification each-and-every 6 months. This appears excessive and overly burdensome in the face to the expected benefits of the new system.

Furthermore, the proposals to expand the information required for submission for drug listings and NDC number assignments would only increase the complexity and burden of frequent certification. Broadening the information required to include all inactive ingredients, manufacturing sites, batch sizes, batch frequencies all increase the complexity and increases the likelihood of information being out of date. Just verifying this information for hundreds of products could take at least 6 months. In general, we recommend that the Agency balance the need for periodic re-certifications against the information required and the success of data entry once the new system is in place and running. While 6 month evaluations may be indicated, it is also possible that 2 years would also work.

The Procter & Gamble Company appreciates the opportunity to comment on this proposed amendment and I would be happy to discuss any of these comments in more detail. I can be contacted at (513) 983-0530 or [guay.cb@pg.com](mailto:guay.cb@pg.com).

Sincerely,

THE PROCTER & GAMBLE COMPANY  
North American External Relations

A handwritten signature in cursive script, appearing to read "C. B. Guay". The signature is written in black ink and is positioned above the printed name.

Christopher B. Guay  
Regulatory Fellow  
Regulatory and Technical External Relations