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IS LIMITED TO MATTERS AND PROCEEDINGS
BEFORE FEDERAL COURTS AND AGENCIES

April 26, 2004

VIA HAND DELIVERY

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

Re: Docket No. 2003D-0478; Supplemental Comments on Draft Compliance Policy Guide On Marketed Unapproved Drugs, 68 Fed. Reg. 60702 (Oct. 23, 2003)

Dear Sir or Madam:

These supplemental comments are submitted on behalf of PFab LP, d/b/a/ PharmaFab®, with regard to the above-referenced draft compliance policy guide. As noted in PharmaFab's December 22, 2003, comment in this docket, PharmaFab is a contract manufacturer of solid dose and liquid formulations for the branded and generic pharmaceutical industry. To date, the company has concentrated on the production of extended-release capsules and tablets. To meet our customers' growing demand for our manufacturing expertise, PharmaFab is currently developing Abbreviated New Drug Applications (ANDAs), in conjunction with our customers, advancing our solid-dose products, and expanding our granulation capabilities. In addition, PharmaFab is now developing and manufacturing liquid formulations.

PharmaFab considers these comments to supplement its December 22, 2003, comments, and in no way wishes to waive any of the issues and questions raised in those comments.

I. PHARMAFAB JOINS COMMENTS FILED BY THE BRANDED PHARMACEUTICAL ASSOCIATION REGARDING ESTABLISHMENT OF A PRESCRIPTION DRUG MONOGRAPH SYSTEM

PharmaFab joins in the supplemental comments filed by the Branded Pharmaceutical Association (BPA) on April 23, 2004, and that organization's request that FDA establish a prescription drug monograph system for older prescription pharmaceutical products. PharmaFab

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agrees with BPA that FDA has ample legal authority to establish and implement a prescription drug monograph system for the reasons detailed in BPA's April 23, 2004, comments. Such a prescription drug monograph would be an appropriate alternative to the draft Compliance Policy Guide (CPG) on marketed unapproved drugs. A prescription drug monograph system would provide for increase regulatory scrutiny of older prescription drug products marketed outside the current premarket approval system, would preserve primary access to affordable physician-supervised healthcare covered by insurance.

Moreover, PharmaFab agrees that agency resources would also be preserved by focusing FDA's efforts on those products most in need of regulatory scrutiny through a prescription drug monograph. Under the draft CPG, the agency has instead determined that in the event that an older prescription drug product marketed outside of the current premarket approval system receives approval, then the agency will expend resources to force competitors off the market. Such effective delegation of decisions regarding particular drug products that should be examined by the agency to competitive forces is not an appropriate public health policy.

PharmaFab supports BPA's proposal that FDA publish a FEDERAL REGISTER Notice of advance notice of proposed rulemaking (ANPR) seeking comment on the development of a prescription drug monograph system.

PharmaFab also wholly agrees with BPA that a prescription drug monograph system is an idea whose time has come. Manufacture of extended release product is much more settled undertaking than when FDA last considered the use of monographs decades ago. Establishment of a prescription drug monograph system would be good for the public health, good for the preservation of health care dollars, good for the conservation of agency resources, and good for the small businesses that manufacture and distribute these products.

II. FDA SHOULD, IN KEEPING WITH ITS PRIMARY MISSION OF PROTECTING THE PUBLIC HEALTH, TAKE PHARMACEUTICAL COSTS AND ACCESS TO PRIMARY HEALTH CARE WHEN EXERCISING ENFORCEMENT DISCRETION

PharmaFab wishes to reiterate its comments regarding how FDA should exercise its enforcement discretion. PharmaFab agrees that when a company obtains approval of an NDA for a product that other companies are marketing outside of the current drug approval process, FDA should set a grace period for those competing products to obtain their own approvals or leave the market. The draft CPG provides that FDA "normally intends to allow a grace period of roughly 1 year from the date of approval of the product before it will initiate enforcement action" against competing products. The draft CPG also provides that this presumptive one-year grace period

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is expected to vary from this baseline based upon the following factors: (1) the effects on the public health of proceeding immediately to remove the illegal products from the market (including whether the product is medically necessary and, if so, the ability of the holder of the approved application to meet the needs of patients taking the drug); (2) whether the effort to obtain approval was publicly disclosed; (3) the difficulty associated with conducting any required studies, preparing and submitting applications, and obtaining approval of an application; (4) the burden on affected parties of removing the products from the market; (5) the Agency's available enforcement resources; and (6) any other special circumstances relevant to the particular case under consideration.

Draft CPG at 5, lines 172-180.

As PharmaFab stated in its December 22, 2003 comments, FDA should retain all of these considerations in the event of finalization of the draft CPG. In addition, FDA should consider that the "effects on the public health" include not merely the availability of a particular drug under these circumstances, but the costs imposed on consumers as well. For example, when a broad competitive market for single entity, extended release guaifenesin was replaced with a single over-the-counter (OTC) product, not only was there an approximately 700% increase in the cost of the product, but insurance reimbursability was lost in the prescription to OTC switch. For some members of the patient population, the practical availability of a product is very closely tied to its affordability. "Effect on the public health" must be read to include whether affected patient populations can afford the approved product.

The effect of this price increase is striking when considering the size of the market for single entity, extended release guaifenesin that was shifted to a single manufacturer. Single entity, extended release guaifenesin was extensively prescribed in the U.S. Department of Defense's TRICARE system. According to the TRICARE website:

TRICARE is a regionally managed health care program for active duty and retired members of the uniformed services, their families, and survivors. TRICARE brings together the health care resources of the Army, Navy and Air Force and supplements them with networks of civilian health care professionals to provide better access and high quality service while maintaining the capability to support military operations. TRICARE is being implemented throughout the U.S., Europe, Latin America and the Pacific as a way to:

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- Improve overall access to health care for beneficiaries;
- Provide faster, more convenient access to civilian health care;
- Create a more efficient way to receive health care;
- Offer enhanced services, including preventive care;
- Provide choices for health care; and
- Control escalating costs.

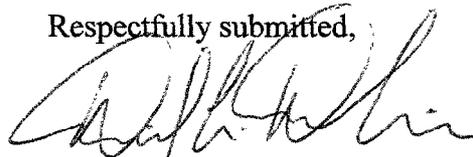
<http://www.tricare.osd.mil/whatistricare.cfm>

The Department of Defense PharmacoEconomic Center (PEC) maintains databases regarding prescriptions written in the TRICARE system. One database available is the TRICARE Retail Pharmaceutical Utilization data by GCN – for Calendar Year 2002. <http://www.pec.ha.osd.mil/TRRx/MCSC%20Totals%20by%20GCN.xls>. An excerpt from that database is attached to these comments. As can be seen from the attached spreadsheet, over 103,000 prescriptions were written for single entity, extended release guaifenesin (representing over 5.4 million dosage units) for TRICARE beneficiaries. Calendar year 2002 was the last year for which single entity, extended release guaifenesin was widely available for the whole calendar year. That product is now gone, save for the single approved product in 600 mg dosage form. Whatever is replacing the 103,000 military prescriptions is unclear but what is certain is that a widely prescribed therapeutic choice for doctors and patients is gone.

* * * * *

PharmaFab has been keenly involved in all of the issues that led to the development of the draft CPG, and appreciates the opportunity to provide comment. As the agency moves forward in this area, it should continue to keep as its primary object preservation of the public health. PharmaFab considers the development of a Prescription Drug Monograph to be a key component of these efforts.

Respectfully submitted,



David L. Durkin
Counsel to PharmaFab

DLD:zkf

Attachment

FOR OFFICIAL USE ONLY
 PDTS - Customer Service Support Center
 Title: MCSC RX Count by GCN
 Date Range: 1 Jan 2002 - 31 Dec 2002
 Report ran on: 01/20/2003
 Report processed by: bspearman

N - Single Source Brand
 O - Multi Source Brand
 Y - Generic

GCN #	Drug/Strength/Form	Generic Indicator	# RX	Total Qty Dispensed	RX Sum by GCN
02487	GUAIFENESIN 600MG TABLET SA	O	591	37186	73104
02487	GUAIFENESIN 600MG TABLET SA	Y	72513	4058128	73104
54932	GUAIFENESIN/P-EPHED HCL 600-120MG TAB.SR 12H	O	3	80	36994
54932	GUAIFENESIN/P-EPHED HCL 600-120MG TAB.SR 12H	Y	36991	1165168	36994
91711	GUAIFENESIN/CODEINE PHOS 100-10MG/5 SYRUP	O	35	6680	30431
91711	GUAIFENESIN/CODEINE PHOS 100-10MG/5 SYRUP	Y	30396	5726204	30431
02483	GUAIFENESIN 1200MG TAB.SR 12H	O	635	27427	25482
02483	GUAIFENESIN 1200MG TAB.SR 12H	Y	24847	1031098	25482
52893	GUAIFENESIN/HYDROCODONE BIT 100-5/5ML SYRUP	O	4	480	23923
52893	GUAIFENESIN/HYDROCODONE BIT 100-5/5ML SYRUP	Y	23919	4065368	23923
53550	GUAIFENESIN/D-METHORPHAN HB 600-30MG TAB.SR 12H	O	68	2713	17122
53550	GUAIFENESIN/D-METHORPHAN HB 600-30MG TAB.SR 12H	Y	17054	695422	17122
13938	GUAIFENESIN/PHENYLEPHRINE HCL 600-30MG TAB.SR 12H	N	1720	48653	11211
13938	GUAIFENESIN/PHENYLEPHRINE HCL 600-30MG TAB.SR 12H	O	2526	86203	11211
13938	GUAIFENESIN/PHENYLEPHRINE HCL 600-30MG TAB.SR 12H	Y	6965	221306	11211
91713	GUAIFENESIN/CODEINE PHOS 100-10MG/5 LIQUID	Y	7842	1469124	7842
89731	GUAIFENESIN/P-EPHED HCL 1200-120MG TAB.SR 12H	O	698	23616	7801
89731	GUAIFENESIN/P-EPHED HCL 1200-120MG TAB.SR 12H	Y	7103	228062	7801
51472	GUAIFENESIN/PHENYLEPHRINE HCL 600-40MG TABLET SA	N	97	2930	6358
51472	GUAIFENESIN/PHENYLEPHRINE HCL 600-40MG TABLET SA	O	3324	107239	6358
51472	GUAIFENESIN/PHENYLEPHRINE HCL 600-40MG TABLET SA	Y	2937	91429	6358
07731	GUAIFENESIN 1000MG TAB.SR 12H	O	576	21317	5093
07731	GUAIFENESIN 1000MG TAB.SR 12H	Y	4517	199801	5093