

# Sample Promotion Under

*Referred to by many as a law in search of a crime, the Prescription Drug Marketing Act (PDMA) has continued to haunt the corridors of pharmaceutical regulatory departments since its enactment in 1988. PDMA was the first in a series of Federal Food, Drug, and Cosmetic Act (FDCA) statutory amendments into which Draconian penalties were injected as a substitute for declining enforcement resources. In addition to the fact that violations can carry \$1 million penalties and criminal sanctions, PDMA also strikes fear because the implementing standards have been so vague.*

LAST MONTH, FDA PROMULGATED LONG-AWAITED FINAL RULES regarding sampling and wholesale distribution. This regulation, presented with almost forty pages of Preamble discussion, corrects many, but by no means all, of the ambiguities created by the 1994 proposed rule.<sup>1</sup> Left unresolved are substantial issues, such as the definition of “significant loss” of samples and the need for bright-line guidance as to when an investigation must be triggered. The regulation also takes strong positions on the PDMA responsibilities of third-party fulfillment houses, coverage of bulk drug transactions, and secondary wholesale distribution.

This article will discuss the most significant of the changes relating to sampling. A second article will address the increased coverage of “wholesale” transactions and the criminal and civil consequences of FDA’s new, stronger stance in that area.

## **“Sample” Definition**

Bid and commercial samples, referring to small bulk drug

# the New PDMA Final Rules

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distributions to manufacturers or distributors for testing, are not samples.<sup>2</sup> Bulk actives (called “bulk drug substances” or “BDS”) are “samples,” meaning that some current distribution practices will have to be drastically revised.<sup>3</sup> Importers/distributors of bulk actives for prescription drugs will have to comply not only with the sample procedures, but also with the wholesale distribution procedures, which can be quite onerous.

The agency also reiterated its position that starter packs, which are distributed free to pharmacies, are *not* samples because they are intended to be sold by the pharmacy.<sup>4</sup> Similarly, vouchers or similar systems that are made available to indigent patients and are to be filled by the pharmacy out of the pharmacy’s stock at the manufacturer’s expense are not samples because the prescription is filled from the store’s stock, which is intended for sale.<sup>5</sup> Although not found explicitly in the rule, a similar logic would seem to permit the distribution of vouchers in lieu of samples to physicians for all patients because the voucher would be processed with products that are intended for sale.

The requirements of PDMA do not apply to the distribution of blood and blood components intended for transfusion. Blood components were initially defined as “that part of a single-donor unit of blood separated by physical or mechanical means.”<sup>6</sup> The final rule delineates red blood cells, plasma, fresh frozen plasma, cryoprecipitated AHF, and platelets.<sup>7</sup> Blood derivatives, such as antihemophilic Factor, Factor IX Complex, and immune globulin products are not exempted from PDMA, nor are recombinant products.

## “Significant Loss”

The agency declined to provide a clearer definition for the phrase “significant loss.” In the proposed regulation, FDA explained that insignificant accounting errors, or small discrepancies in a multimillion dollar company, *may* not be significant, but that the loss of a hundred tablets of a particular drug by a representative *might* be.<sup>8</sup>

No other definition is provided by the final regulation. Instead, FDA adverts to a number of factors that should be considered, including the size of the manufacturer, the number of sales representatives, size and value of sample inventory, the firm’s past experience with sample losses, and “historically validated statistical baselines.”<sup>9</sup> Manufacturers and distributors are thus required to set their own thresholds for determining what losses are “significant” without any further guidance from FDA.

## Investigation and Notification Requirements

Section 203.37(a) of the final rule provides that a manufacturer or authorized distributor of record who has “reason to believe” that any person has “falsified drug sample requests, receipts, or records, or is diverting drug samples,” must:

- notify FDA within five working days;
- immediately initiate an investigation; and
- provide FDA with a written report within thirty days of the initial notification.<sup>10</sup>

Thus, while a company must investigate and report to FDA falsification as soon as there is “reason to believe” it exists, “significant loss” of samples must only be reported to

FDA when the manufacturer or distributor “becomes aware” of the loss or theft.<sup>11</sup>

### **Inventory and Reconciliation Reports**

The final rule clarifies and corrects several open issues in the proposal. First, the agency acknowledges that no “generally accepted inventory practices” exist, and therefore has eliminated that requirement.<sup>12</sup> Second, FDA now requires an annual physical inventory, thereby mandating that each sample pack (in the possession of every sales representative) be examined and accounted for. This distinguishes it from the reconciliation report, in which the company must compare the results of the physical inventory with the most recently completed prior physical inventory and reconcile the two, using records of drug sample receipt and distributions.<sup>13</sup>

Of considerable significance from a manpower perspective is the deletion of proposed section 203.31(d)(3), which required that the inventory and reconciliation reports be conducted and prepared by employees independent of the representative being inventoried, including supervisors, managers, and anyone in their direct line of supervision or command. The intent of the proposed rule — avoiding fraud — was laudable, but was the source of many comments that complained that the requirement of independent auditors was too burdensome, and that there were more cost-effective ways to achieve the same goal.<sup>14</sup> FDA now requires only that manufacturers and distributors take “appropriate internal control measures” to prevent fraud in the conducting of the inventory and reconciliation, and in the preparation of the relevant reports.<sup>15</sup>

Nevertheless, FDA does caution that it “expects” that the internal control measures, including security and audit measures, will be implemented by independent personnel. Section 203.34 thus requires that any company that engages in drug sample distribution “establish, maintain, and adhere to *written* policies and procedures” governing sample inventories, audits, and initiating investigations.<sup>16</sup> This section also mandates random audits (conducted by personnel independent of the representative being inventoried) and for-cause audits.

All third parties that assist in the distribution of samples become “wholesalers” subject to the wholesale requirements of the regulation, and the manufacturer retains ultimate responsibility to ensure that all PDMA requirements are met by the third party.<sup>17</sup>

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### **Drug Samples and Retail Pharmacies**

FDA stated in proposed section 203.40 that drug samples found in a retail pharmacy would be considered evidence that the sample was obtained by the retail pharmacy in violation of section 503(c)(1) of the FDCA (21 U.S.C. section 353).<sup>18</sup> The agency removed this provision from the final rule, but as a practical matter, unless the pharmacy is part of a healthcare entity, the presumption will remain. Samples may be dispensed by a hospital or health care pharmacy to patients at the direction of a physician at a health care organization, but a nonhealth care pharmacy may not do so.<sup>19</sup>

### **Conclusion**

The PDMA is an inherently difficult law to enforce. The proposed rule left many in industry guessing at critical compliance issues. FDA, in the meantime, initiated numerous criminal investigations of sampling and distribution practices, and continues to pursue PDMA infractions vigorously. The final regulation settles some very important disputed issues, and imposes greater burdens on manufacturers across a broader category of products. New training, new internal procedures, and new third-party contractual provisions will provide some safeguards against criminal exposure, but continuing FDA interpretations will be necessary to resolve what remain as significant grey areas.