3

Quantitative Study

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Introduction

Few studies have systematically examined the volumes, patterns, and quality of pharmaceutical donations. Published reports of drug donation practices in specific countries, including Bosnia-Herzegovina, Mexico, Armenia, the Sudan, and Russia, have reported mixed results.[1–6] An analysis of pharmaceutical products that arrived in Bosnia-Herzegovina between 1992 through mid-1996 found significant problems based upon a review of shipments. The study assessed an estimated volume of 27,800 to 34,800 metric tons of drugs and medical supplies to Bosnia-Herzegovina over the four-and-a-half-year period. The study reported that only 5 percent of those drug and medical supplies that conformed to the WHO *Guidelines for Drug Donations* were considered inappropriate. These products were also reported to have a remaining time to expiration of at least one year. In the same study, about one-third of all donations were considered miscellaneous drugs and other medical supplies. These miscellaneous products did not meet the WHO *Guidelines* criteria or were otherwise considered irrelevant to the medical needs of the geographic area. Eighty-five to 90 percent were assessed as not useful due to poor identification of drugs, expiration, inadequate sorting, or inappropriate packaging. Other country-specific investigations have suggested even higher proportions of donations not considered relevant or useful,[2–6] supporting the criticism that donated products are often near or at expiration or are otherwise inappropriate for the recipient countries.[7] These kinds of concerns about the quality and appropriateness of pharmaceutical donations were among the forces motivating the development of the World Health Organization's *Guidelines for Drug Donations* (see Chapter 1).

This quantitative study of pharmaceutical donations has four specific aims (described in Table 3.1):

1. To describe key cross-sectional dimensions of the pharmaceutical donations process.
2. To characterize longitudinal patterns of time to expiration at the time of shipment from Private Voluntary Organizations (PVOs) to recipient countries.
3. To examine the connection between the dissemination of the WHO *Guidelines* and changes in estimates of median-time to expiration at time of shipment from the PVOs.
4. To identify data management issues that arose in the quantitative analysis.

Cross-sectional and longitudinal analyses of a data base of drug donations were conducted, and the results provide the first systematic information on drug donations to a large number of recipient countries. The analysis and data are intended to contribute to a discussion on drug donations, especially regarding minimal remaining time to expiration at the time of shipment and appropriateness as defined by the WHO Model List of Essential Drugs (WHO-ML) or selected country essential drugs lists (EDLs).

Methods

Data sources

Up to three years of data from two US-based PVOs were used to analyze the profile of drug donations in terms of remaining time to expiration and appropriateness. For these PVOs, we retrieved ASCII receipt and shipment files for the observation period of 1994 to 1997. One PVO was excluded from the analysis due to poor data quality. Of the remaining two PVOs, one had data for approximately two-and-a-half years (January 1994 to May 1996), while the other had three years of data (July 1994 through June 1997).

We used the American Hospital Formulary System to sort pharmaceutical donations into therapeutic categories. This information was retrieved from First Data Bank's (FDB) National Drug Classification (NDC) software,[8] which allowed us to aggregate donations into categories based on chemical entity as well as a more general therapeutic category (based on

TABLE 3.1
Overview of Objectives

Objective	Specific Measures
1. Description of key cross-sectional measures of the donations process	1. Number of shipments and/or shipment items by: (i) PVO (ii) PVO and American Hospital Formulary System therapeutic categories (iii) PVO and donor firm 2. Proportion of pharmaceutical donations shipment items listed on the World Health Organization's Model List of Essential Drugs 3. For Armenia, the proportion of pharmaceutical donations shipment items listed on the country Essential Drugs List 4. Estimates of time to expiration for pharmaceutical donations at the time of shipment from the PVO by: (i) PVO (ii) PVO and American Hospital Formulary System therapeutic categories (iii) PVO and donor firms (iv) PVO and for the three study countries (Armenia, Tanzania, and Haiti)
2. Characterization of longitudinal patterns of time to expiration at the time of shipment by the PVOs	1. Time-series of median estimates of time to expiration at two-month intervals for all pharmaceutical donations, by PVO 2. Regression modeling of the time-series of median time to expiration estimates
3. Examination of the association between dissemination of the WHO *Guidelines* and changes in estimates of median time to expiration at time of shipment from PVOs	1. Interrupted time-series modeling of the two-month estimates of median time to expiration remaining at the time of shipment for one PVO.
4. Process of data use and data quality assessment	1. Examination of key dimensions of data quality, including: (i) uniformity of data files (ii) presence and format of index variables (iii) ease of use of calendar date fields

the AHFS three-byte HIC3 code). In addition, the link between the donations files and the FDB files allowed us to verify the package size (units of active ingredient per package) for a unique NDC as well as the physical form of the product (tablets, injection, and so forth). From the linked file, we were also able to retrieve brand and generic names for a unique NDC. Since the PVO files used both brand and generic names,

we converted all names to generic names in order to link PVO data with electronic files of the WHO-ML (for all donated drugs) and the Armenian essential drugs list (for drugs donated to Armenia).

To establish the identity of unique donors, we linked drug donation files to the Federal Supply Schedule, since donors have multiple numeric identifiers equivalent to the first five bytes of the NDC (which was present in both study PVO data bases).

To construct data sets for analysis and to define secondary variables (such as time between shipment by the PVO and expiration of a donated drug), we first recoded all NDC information into a (5,4,2) format indicating numeric value for donor firm, a firm's chemical ingredient code, and firm-specific codes for package size. One of the two study PVOs had recorded NDC information into a nonstandard format useful for specific operation within the PVO. For example, this PVO had interlocated a one-byte data element between bytes five and six of the NDC and had also added alpha characters at various positions within the NDC. These modifications for the PVO's internal purposes were undone, and the NDC was recoded into standard format.

We recoded all time fields into month, day, year, and century values (MMDDYYCC) for analytic purposes. For example, January 26, 1995, was coded as 01269520. Some date fields had only month and year values. For these observations we chose 15 as a value for the day field, allowing us to code these in the usual MMDDYYCC format without biasing results. Since the PVO data sets contained product donations other than drugs, we excluded all medical supplies (such as needles, syringes, bandages, and dressings) as well as all consumer goods (such as nonmedicated shampoos, baby diapers, and dehydrated soup).

To create analytic files, we constructed delimited ASCII files from the raw data and imported this delimited text into Microsoft Excel 7.0. Fields were formatted as necessary. We then translated EXCEL files into SAS datasets using PROC ACCESS in the SAS software package. Date variables were reformatted in SAS as MMDDYYCC because translation into SAS from EXCEL does not allow for this.

Analysis

Descriptive statistics included median and mean estimates of key study measures, such as time remaining until expiration at the time of shipment by the PVO, proportion of products listed on the WHO-ML, and number of shipments of specific donated products (see Table 3.1). For our analysis, we defined a *shipment item* as one donated drug in a particular

dosage form, strength, and package size that was listed on the PVO's shipment list as a line item. We used this information to construct a metric that measured the proportion of products shipped, defined as the number of times a chemical item in a particular dosage form, strength, and package size was shipped to a recipient, relative to total. We also examined the frequency of shipments by the study PVOs. A *shipment* was defined as all the shipment items sent by a PVO on the same date. Frequency was examined by aggregating shipments into three-month time intervals and reporting the total number of shipments in each period.

We aggregated PVO data into two-month time intervals to observe shifting patterns of drug donations and, in particular, secular trends in the time to expiration of donations. For each of the two-month time periods, we calculated the median times between time of shipment by the PVO and time to expiration for the product, and between the PVO's receipt of the product from the donor firm and shipment by the PVO (to measure the time the product was held by the PVO). After calculation of the median times of interest at each of the two-month intervals, these values were modeled using simple times-series regression models (ARIMA 1,0,0) to estimate any changes in median times that might have occurred over calendar time or as a result of the dissemination of the WHO *Guidelines* in May, 1996. Models included indicator variables for slope and level changes to detect any abrupt or gradual changes in median times.

Results

Description of the PVOs

Table 3.2 provides a summary profile of the two study PVOs. PVO A receives donations from a larger number of pharmaceutical firms than does PVO B. Although its total number of shipments is less than PVO B's, PVO A has a greater product mix, as indicated by the total number of therapeutic categories of drugs shipped to recipients. The distribution of time to expiration remaining at the time of shipment from PVO warehouses is slightly longer for PVO A. PVO B serves a smaller number of countries (67) than does PVO A (117).

Proportions, frequency, and country recipients of donated products

We measured the proportion of donated products shipped by first counting the number of times a chemical item in a particular dosage form and strength was sent to recipients; then we summed counts within the ap-

TABLE 3.2

Descriptive and Shipping Characteristics of PVOs A and B

Characteristic	PVO A	PVO B
Timeframe for data collection	1/3/94 to 5/1/96	7/20/94 to 6/27/97
Total number of shipments	1,017	1,597
Total number of shipment items	11,321	5,245
Total number of recipient countries	117	67
Total number of donor pharmaceutical firms	137	63
Total number of different AHFS-3 therapeutic categories shipped	305	210
Numbers of days between shipping and expiration:		
99th percentile	1,820 days	1,580 days
75th percentile	938	838
50th percentile (median)	599	550
25th percentile	303	321
Mean	655	571

Note: Shipment item = one donated drug recorded on the PVO's shipment list as a line item. Shipment = all the shipment items sent by a PVO on the same date. AHSF-3 = American Hospital Formulary System, general therapeutic category.

propriate AHFS category by aggregating by NDC. For describing the proportions of products shipped, we used two different AHFS categories consisting of (1) a general therapeutic classification (AHSF-3) and (2) the most specific of the AHFS therapeutic classes (AHSF-5).

Table 3.3a lists the results of the more general AHSF-3 therapeutic classification of PVO B's donations. The top ten categories, representing 65 percent of PVO B's drug shipments (N = 5,245 shipment items), are anti-infectives, analgesics, and antipyretics, as well as various cold preparations. Table 3.3b presents the categorization of donations into the most specific of the AHFS classifications (AHSF-5), indicating that the top ten products accounted for 52 percent of shipment items. This list is led by acetaminophen and zinc oxide, a skin protectant, followed by three anti-infectives.

Tables 3.3c and 3.3d present the same analysis for PVO A. Sixty percent of the PVO's shipment items (N = 11,321) are accounted for by the top ten general therapeutic categories (Table 3.3c), including nonsteroidal anti-inflammatories and cardiac drugs as well as anti-infectives, cough/cold preparations, and analgesics and antipyretics. Table 3.3d shows that 39 percent of all shipment items are accounted for by the top ten products, which, like PVO B, are led by acetaminophen.

TABLE 3.3A

Percentage of Shipment Items for PVO B by General Therapeutic Category (AHFS-3)

Ranking	AHFS Description	Percent
1	Penicillins	18.6
2	Miscellaneous analgesics and antipyretic	11.3
3	Sunscreen agents	7.4
4	Antitussives	6.0
5	Expectorants	5.8
6	Antifungals	4.5
7	Iron preparations	3.5
8	Cephalosporins	3.0
9	Antihistamine Drugs	2.6
10	Antitussives, expectorants and mucyolytic agents	2.6
	Total	**65.3**

N = 5,460 shipment items for PVO B.

TABLE 3.3B

Percentage of Shipment Items for PVO B by Specific Therapeutic Category (AHFS-5)

Ranking	Chemical Entity	Percent
1	Acetaminophen	10.1
2	Zinc oxide	7.4
3	Cloxacillin sodium	7.3
4	Amoxicillin trihydrate	5.3
5	Ampicillin trihydrate	4.4
6	Chlorpheniramine	3.7
7	Guaifenesin	3.7
8	Docusate sodium	3.6
9	Pseudoephedrine hydrochloride	3.4
10	Tolnaftate	3.0
	Total	**51.9**

N = 5,460 shipment items for PVO B.

Table 3.3e presents an examination of the number of shipments by both PVOs over the observation period. Over the time period of observation, PVOs A and B sent 1,017 and 1,597 shipments, respectively. PVO

TABLE 3.3C

Percentage of Shipment Items for PVO A by General Therapeutic Category (AHFS-3)

Ranking	AHFS Description	Percent
1	Nonsteroidal anti-inflammatory agents	14.3
2	Cardiac drugs	7.9
3	Antitussives	6.2
4	Miscellaneous analgesics and antipyretic	6.2
5	Anti-inflammatory agents	5.9
6	Antihistamine drugs	4.6
7	Penicillins	4.6
8	Antibiotics	4.0
9	Antitussives, expectorants and mucyolytic agents	3.4
10	Miscellaneous anti-infectives	3.2
	Total	**60.3**

N = 11,321 shipment items for PVO A.

TABLE 3.3D

Percentage of Shipment Items for PVO A by Specific Therapeutic Category (AHFS-5)

Ranking	Chemical Entity	Percent
1	Acetaminophen	7.5
2	Naproxen	6.4
3	Pseudoephedrine hydrochloride	5.8
4	Amoxicillin trihydrate	3.7
5	Naproxen sodium	3.2
6	Trimethoprim	3.1
7	Nicardipine hydrochloride	2.5
8	Ketorolac tromethamine	2.4
9	Dextromethorphan hydrobromide	2.2
10	Digoxin	2.1
	Total	**38.9**

N = 11,321 shipment items for PVO A.

A had a more regular schedule of shipments per calendar quarter than did PVO B. Furthermore, within any calendar quarter PVO A ships donations to recipient countries almost every day (data not shown), which

TABLE 3.3E

Number of Shipments per Quarter for PVO A and PVO B

Time Period	PVO A	PVO B
January to March 1994	178	ND
April to June 1994	172	ND
July to September 1994	113	170
October to December 1994	166	168
January to March 1995	149	76
April to June 1995	130	140
July to September 1995	91	214
October to December 1995	14	377
January to March 1996	4	102
April to June 1996	ND	41
July to September 1996	ND	103
October to December 1996	ND	81
January to March 1997	ND	85
April to June 1997	ND	40

N = shipment of multiple items.
N for PVO A = 1,017 shipments.
N for PVO B = 1,597 shipments.
ND = Data not available.

may be a function of the larger size of this organization compared with PVO B, as well as a larger number of products shipped by PVO A.

The leading recipient countries were calculated according to therapeutic categories. The upper fifth percentile of therapeutic categories included the following countries for PVO B: Croatia, El Salvador, Lithuania, Honduras, Peru, and the Ukraine. For PVO A, the comparable recipient countries were El Salvador, Nicaragua, Honduras, Romania, Russia, and the Ukraine. This pattern suggests some overlap between the countries receiving shipments of donated drugs, although PVO A serves almost twice as many countries as does PVO B (see Table 3.2).

Analysis of donated products by presence on the WHO Model List of Essential Drugs

We compared the list of all shipment items from each of the two PVOs with the WHO's Model List of Essential Drugs to examine whether donated products represented therapies that were listed as essential drugs by the WHO. Since the WHO-ML is a recommended set of essential

drugs and is intended to be adapted for a particular country's circumstances, country-level analyses with national EDLs need to follow this more general analysis with the WHO list.

Only 14.9 percent of PVO A's shipment items (chemical items in a particular dosage form and strength) and 26.1 percent of PVO B's were on the WHO-ML. We also estimated the percentage of all pharmaceutical shipments items to one selected country that were on that country's EDL. For this analysis, we chose Armenia because it represented a relatively high-volume recipient of donations from among the three study countries for which we had detailed EDL information. This analysis suggested that for PVO A, 75 percent of all drug shipment items were found on the Armenian EDL; for PVO B, the similar estimate was 66 percent.

There appeared to be no systematic association between therapeutic category and being (or not being) on the WHO-ML for either PVO, although we did not conduct tests of significance to determine any systematic differences. All therapeutic categories shipped seemed as equally likely to be on the WHO-ML as not. In separate analyses for each of the two PVOs of remaining time to expiration at the time of shipment, there was no difference in time to expiration remaining for items on the WHO-ML compared with those not listed.

Analysis of donated products by time from shipment by the PVO to expiration

The median time from date of shipping to date of expiration for all drug shipment items was 599 days for PVO A and 550 days for PVO B (see Figures 3.1 and 3.2; see Table 3.1 for range of time to expiration values). We stratified the analysis by donor firms, estimating median time between date of shipping and date of expiration. Values of median times for the top ten firms are presented in Tables 3.4a and b for PVO A and PVO B, respectively, together with the percentage of total shipment items accounted for by the individual firms. Four firms are found in both lists of the top 10, while the other firms are unique to each PVO. Two of the three firms found in both top-ten lists have similar median times from date of shipping to date of expiration for both PVOs, while one of the other two firms differs markedly, with median values greater for PVO B.

We next explored the possibility that products with short time to expiration were associated with specific recipient countries. We stratified time from shipment by PVOs to expiration into quartiles, and compared shipment items in the bottom, middle two, and uppermost quartiles. A review of Tables 3.5a and b does not show any systematic shipment of

FIGURE 3.1

Median Time Between Shipping by PVO A and Expiration

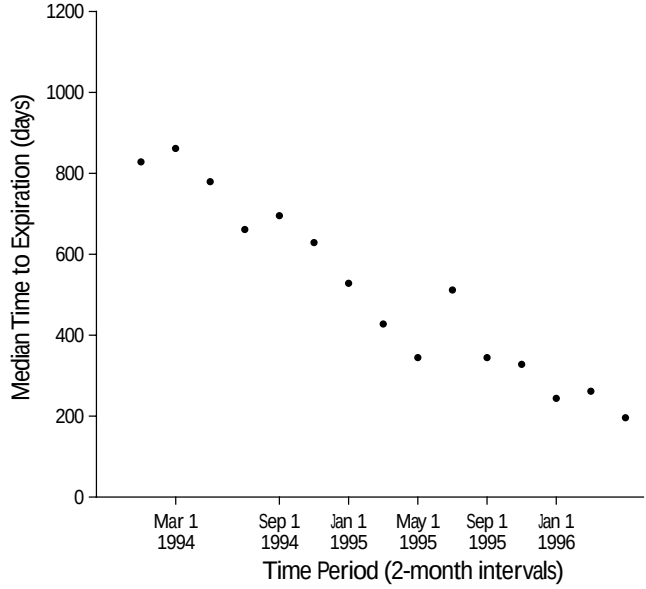

FIGURE 3.2

Median Time Between Shipping by PVO B and Expiration

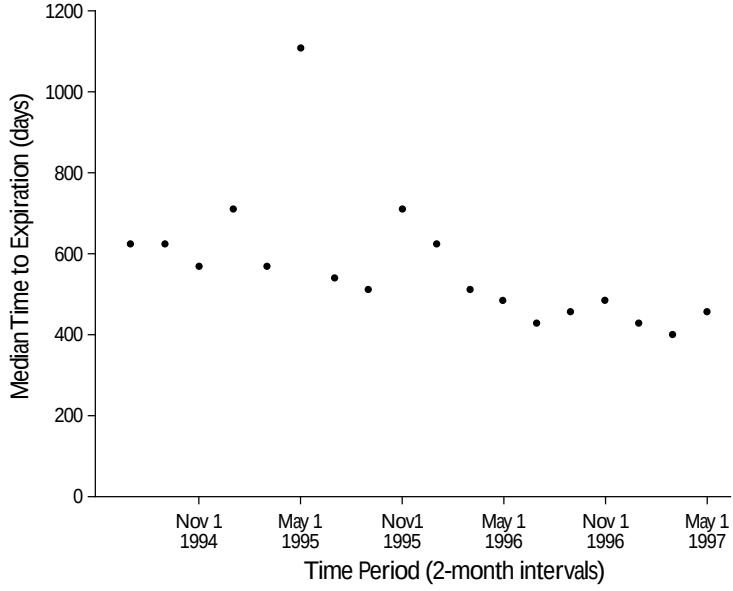

TABLE 3.4A

Median Times Between Shipment and Expiration for the Top Ten Firms Within PVO A

Firm	Median (days)	Percent of Total Shipment Items
A	831	2.7
B	708	3.3
C	625	5.4
D	556	11.1
E	455	14.9
F	451	16.9
G	242	7.3
H	223	2.7
I	140	7.4
J	139	5.2

TABLE 3.4B

Median Times Between Shipment and Expiration for the Top Ten Firms Within PVO B

Firm	Median (days)	Percent of Total Shipment Items
G	1,174	3.4
K	848	5.8
C	830	10.3
L	680	4.0
M	630	16.4
N	609	10.2
D	604	4.7
F	561	5.6
O	492	3.4
P	463	8.8

product with a short time to expiration to any particular country for either PVO A or PVO B. One exception was that three former Soviet countries (Lithuania, Russia, and the Ukraine) received disproportionately high numbers of shipment items from PVO B with a remaining time to expiration of less than 321 days (the lowest quartile of time remaining between shipping by the PVO and expiration).

To assess whether there was a shorter time to expiration for products listed on the WHO-ML compared with those not listed, we conducted

TABLE 3.5A

Number of Shipment Items by Country for the Low, Middle Two, and High Quartiles of Time to Expiration from Shipment (PVO A)

	Quartile			
Country	**Low**	**Middle Two**	**High**	**Total**
Afghanistan	0	1	0	1
Albania	5	23	7	35
Angola	15	32	32	79
Armenia	162	161	116	439
Azerbaijan	0	1	1	2
Bahrain	1	4	4	9
Bangladesh	2	0	0	2
Belarus	71	145	62	278
Belize	4	7	6	17
Benin	1	3	0	4
Bolivia	4	16	14	34
Bosnia	63	66	23	152
Brazil	23	25	8	56
Bulgaria	3	9	4	16
Burkina Faso	1	0	0	1
Cambodia	1	6	1	8
Cameroon	1	17	8	26
Cape Verde	4	2	0	6
Chad	7	30	9	46
China	16	14	7	37
Colombia	10	21	10	41
Comoro Islands	0	1	0	1
Congo	6	6	0	12
Costa Rica	22	45	15	82
Croatia	41	129	99	269
Cuba	5	18	13	36
Djibouti	0	8	5	13
Dominican Republic	16	54	28	98
Ecuador	17	70	17	104
Egypt	7	7	3	17
El Salvador	266	446	221	933
Eritrea	36	69	17	122
Ethiopia	13	48	33	94
Fiji	0	9	10	19
Former Yugoslavia	34	73	33	140
Gabon	0	0	1	1

TABLE 3.5A

Number of Shipment Items by Country for the Low, Middle Two, and High Quartiles of Time to Expiration from Shipment (PVO A) (continued)

	Quartile			
Country	**Low**	**Middle Two**	**High**	**Total**
Gambia	0	4	2	6
Ghana	16	52	24	92
Grenada	1	8	2	11
Guatemala	25	55	43	123
Guinea Republic	0	7	3	10
Guyana	4	25	4	33
Haiti	116	256	112	484
Honduras	131	335	163	629
Hungary	2	1	1	4
India	19	36	15	70
Indonesia	3	7	3	13
Iran	0	7	0	7
Iraq	1	17	3	21
Israel	3	9	8	20
Ivory Coast	33	90	33	156
Jamaica	13	34	32	79
Jordan	2	1	1	4
Kazakhstan	12	20	10	42
Kenya	20	30	11	61
Korea	2	3	0	5
Kosovo	3	25	21	49
Kyrghyzstan	1	2	1	4
Lesotho	14	31	8	53
Liberia	34	73	30	137
Lithuania	23	28	40	91
Malawi	5	16	4	25
Malaysia	4	9	2	15
Mali	1	4	5	10
Mexico	103	186	117	406
Micronesia	9	8	3	20
Moldova	32	41	14	87
Mozambique	16	87	34	137
Myanmar	1	15	13	29
Nepal	15	20	21	56
Nicaragua	222	335	194	751

TABLE 3.5A

Number of Shipment Items by Country for the Low, Middle Two, and High Quartiles of Time to Expiration from Shipment (PVO A) (continued)

	Quartile			
Country	**Low**	**Middle Two**	**High**	**Total**
Niger	3	5	2	10
Nigeria	29	89	44	162
North Korea	17	15	1	33
Pakistan	6	3	0	9
Panama	21	59	26	106
Papua New Guinea	4	14	3	21
Paraguay	0	1	0	1
Peru	12	31	18	61
Philippines	38	90	63	191
Republic of Georgia	15	75	17	107
Romania	223	403	215	841
Russia	234	456	234	924
Rwanda	18	56	9	83
Senegal	0	0	1	1
Sierra Leone	0	7	12	19
Somalia	0	0	2	2
South Africa	0	4	1	5
St Croix	0	2	0	2
St Kitts	3	2	2	7
St Lucia	5	16	14	35
St Thomas	20	21	1	42
St Vincent	7	13	15	35
Sudan	8	38	11	57
Suriname	0	4	2	6
Swaziland	4	4	2	10
Tanzania	21	35	6	62
Thailand	0	1	0	1
Trinidad	2	1	0	3
Turkey	0	1	0	1
Uganda	40	51	7	98
Ukraine	221	338	157	716
USA	4	4	4	12
Uzbekistan	19	28	20	67
Vanuatu	0	6	8	14
Venezuela	3	4	0	7

TABLE 3.5A

Number of Shipment Items by Country for the Low, Middle Two, and High Quartiles of Time to Expiration from Shipment (PVO A) (continued)

	Quartile			
Country	**Low**	**Middle Two**	**High**	**Total**
Vietnam	19	46	10	75
West Bank	22	22	5	49
Yemen	10	18	11	39
Yugoslavia	5	21	11	37
Zaire	12	48	27	87
Zambia	3	17	13	33
Zimbabwe	0	1	0	1
Unknown	10	32	5	47
Total	**2,838**	**5,651**	**2,832**	**11,321**

stratified analyses of remaining time to expiration according to whether a product was on the WHO-ML. We did not observe any significant or systematic differences in values for median time to expiration. For PVO B, the mean time from shipment to expiration for products on the WHO-ML was 512 days, compared with 744 days for drugs not listed. However, the variation around these estimates of the mean remaining time to expiration was very large. The estimated mean time to expiration and standard deviations was 512 ± 227 days for products on the WHO-ML and 744 ± 277 days for drugs off-list. For PVO A, the comparable mean and standard deviations of remaining shelf lives were 380 ± 309 (off-list) and 695 ± 431 (on-list).

Finally, only one of the two PVOs had data on the length of time that donated products were held in the PVO warehouse. We estimated PVO B's median time from receipt of product from donor firms to shipment to recipient countries. The estimated median time that donated drugs were held by this PVO was 113 days, which did not, on average, affect the quality of the product in terms of remaining time to expiration, since the median time to expiration at shipment from PVO B was estimated at 550 days. At the time of receipt by the PVO, pharmaceutical products had an estimated median time to expiration of 663 days and, after warehousing, 550 days.

TABLE 3.5B

Number of Shipment Items by Country for the Low, Middle Two, and High Quartiles of Time to Expiration from Shipment (PVO B)

	Quartile			
Country	**Low**	**Middle Two**	**High**	**Total**
Antigua/Barbados	1	0	1	2
Armenia	23	19	27	59
Belarus	18	4	0	22
Belize	0	1	3	4
Benin	1	41	11	53
Bolivia	22	49	33	104
Bosnia	51	39	21	111
Brazil	3	17	10	30
Bulgaria	2	2	0	4
Burkina Faso	1	35	157	193
Burundi	9	1	0	10
Cambodia	0	1	2	3
Cameroon	4	35	26	65
Chad	0	2	0	2
Chile	2	4	0	6
Croatia	83	229	2	314
Cuba	63	81	38	182
Dominican Republic	41	33	120	194
Ecuador	62	67	34	163
Egypt	0	83	9	92
El Salvador	25	260	16	301
Equatorial Guinea	5	71	49	125
Estonia	30	31	3	64
Ethiopia	0	26	62	88
Gambia	44	22	10	76
Ghana	0	1	5	6
Guatemala	7	53	14	74
Guyana	4	24	4	32
Haiti	6	14	6	26
Honduras	22	141	97	260
India	4	67	12	83
Jamaica	10	15	6	31
Kenya	0	17	5	22
Laos	0	4	4	8
Lebanon	1	2	0	3

TABLE 3.5B

Number of Shipment Items by Country for the Low, Middle Two, and High Quartiles of Time to Expiration from Shipment (PVO B) (continued)

	Quartile			
Country	**Low**	**Middle Two**	**High**	**Total**
Lesotho	0	82	18	100
Lithuania	344	123	31	498
Macedonia	0	31	4	35
Madagascar	0	36	6	42
Malawi	3	9	10	22
Mexico	95	75	53	223
Micronesia	2	6	4	12
Morocco	0	19	5	24
Nepal	0	0	1	1
Nicaragua	4	90	7	101
Nigeria	9	26	21	56
Pakistan	4	0	0	4
Palestine	0	2	0	2
Panama	1	7	10	18
Papua New Guinea	1	4	2	7
Peru	70	180	54	304
Philippines	6	41	25	72
Poland	2	0	0	2
Romania	25	2	1	28
Russia	2	9	7	18
Rwanda	2	20	2	24
Senegal	12	23	13	48
St. Lucia	29	10	1	40
St. Thomas	0	3	3	6
Tanzania	7	50	110	167
Togo	9	59	31	99
Uganda	2	8	0	10
Ukraine	160	107	38	305
Vietnam	25	44	30	99
Zaire	9	68	7	84
Zambia	2	87	48	137
Zimbabwe	0	12	48	60
Total	**1369**	**2724**	**1367**	**5460**

Analysis of the effect of dissemination of the WHO *Guidelines* on trends in time from shipment by PVOs to expiration

Figures 3.1 and 3.2 illustrate the time trends in the median time of remaining time to expiration at the date of shipment from the two PVOs. A times-series regression modeling of the data presented in Figures 3.1 and 3.2 suggests a downward trend over time, indicating a decline of approximately 15 (± 42) days every two months for PVO A. The time-series illustrated in Figure 3.2 for PVO B also shows a downward trend of 17 (± 5) days every two months. This pattern of decline, if it persists for the future, would suggest that this measure of quality (time to expiration) is declining, although reasons for this secular trend remain unknown.

After controlling for this secular trend of decreasing time to expiration at the date of shipment by the PVO, we attempted to estimate any association of the dissemination of the WHO *Guidelines* in May 1996 with median time to expiration. We were unable to detect any significant changes associated with the publication of the *Guidelines* for PVO B. When we set the dissemination date to the first quarter of 1996, to model "anticipatory" effects (which often occur prior to the official implementation date of a policy), we were also unable to detect changes in remaining time to expiration for PVO B. Because we did not have sufficient follow-up data for PVO A (that is, data were available only for the first six months of 1996 for PVO A, which is insufficient to test any effects of the *Guidelines*), we were unable to test the possible effects.

Conclusions

An examination of the patterns of pharmaceutical donations to recipient countries by the two PVOs in this study indicates a product-mix of therapeutic categories dominated by anti-infectives, analgesics, cold preparations, cardiac drugs, and steroidal and nonsteroidal anti-inflammatory agents, all of which are represented on the WHO-ML. (See Chapter 2 for further discussion of the appropriateness of substitution of drugs within a therapeutic category.) The profiles of the top ten therapeutic categories for the two PVOs indicated more similarities than differences. For both PVOs, acetaminophen represented the leading chemical entity donated by firms and shipped by PVOs. The top ten AHFS therapeutic categories accounted for 60 percent of all shipment items for PVO A and 65 percent for PVO B. Only 15 to 26 percent of specific shipment items shipped to all recipient countries were listed on the WHO-ML. However, country-specific EDLs are likely to differ from the WHO-ML. So we compared

products shipped to Armenia to this country's EDL to see if more than 15 percent (PVO A) and 26 percent (PVO B) of shipment items were found on the Armenian EDL. We found that for both study PVOs, nearly three-quarters of all shipment items were included on the Armenian EDL.

The median time between date of shipment from the PVO and date of expiration of product was 599 days for PVO A and 550 days for PVO B for all therapeutic agents shipped to all recipient countries. About 30 percent of the products shipped had one year or less shelf-life remaining at the time of shipment (27.2 percent for PVO A and 28.5 percent for PVO B).

An examination of median time to expiration at shipment date identified a small number of therapeutic categories with median remaining shelf-life of less than 100 days for the two PVOs. For PVO A, the therapeutic categories with median time to expiration of less than 100 days included vitamin preparations, antitubercular agents, and topical antifungals; for PVO B, they included antiarrhythmics, parasympathetic agents, and antiparkisonian drugs. However, these therapeutic categories with median remaining shelf-life under 100 days represented low-frequency donations, ranging from one shipment item for topical antifungals (<0.01%) for PVO A to a high of 27 shipments items of parasympathetic agents (0.5%) for PVO B. Overall, the products with remaining shelf-life under 100 days at shipment date represented 5.6% of all shipment items for the two PVOs.

Although we had data from only one of the two PVOs suitable for estimating the duration of storage time, estimated time between receipt of donation and shipment by PVO was approximately four months (113 days). Since the median time to expiration remaining at the date of shipping was over 550 days, the time that product was held by the PVO does not seem inappropriately long, on average. However, for shipment items with less than one year to expiration on arrival at the PVO, a storage time of four months would represent a significant delay and could affect the usefulness of the product. While we observed an approximate four-month storage time at PVO B, we also observed a downward trend in storage time over the observation period.

The longitudinal regression modeling of time to expiration at the time of shipping demonstrated a trend toward decreasing time to expiration for both PVOs of 15 days (PVO A) and 17 days (PVO B) every two months, although the reason for this downward trend remains unknown. We were unable to demonstrate any association between the dissemination of the WHO *Guidelines* on remaining time to expiration of donated drugs

even after controlling for the strong secular trend toward decreasing time to expiration.

This study identified a lack of standardization in the PVO information systems for drug donations. The two study PVOs record information in a variety of formats, including ASCII, DBASE, spreadsheets, and even word processing files. The lack of a standard information system makes external analysis of donations difficult. For purposes of further study of drug donations, we would recommend that PVOs record drug donation information in standard spreadsheets, so that data are transportable, easily interfaced with other software, and easily analyzed with arithmetic calculations and graphical presentation. For research and routine monitoring purposes, it would also be important to allow a linkage of files at the time of receipt (with information including standardized date formats and national drug codes) with files at the time of shipment. These data could be stored within a unified receipt-shipment data base, as was the case for one of the study PVOs.

Not all PVOs record drug donation information in standardized format and/or with standardized data elements. Of the two study PVOs and one non-study PVO, one had complete NDC information, another had NDC codes that were modified from standard format, and a third indexed its data on the basis of drug brand and/or generic name with limited NDC information. The standard NDC in a 5-4-2 format (donor firm's identifier-chemical entity-package size) should be the cornerstone of a drug donations data base for all PVOs engaged in drug donations. Donors and/or PVOs should also include a separate field in the data base representing the unique chemical entity.

Data elements that are crucial to a donations monitoring system are fields for receipt, shipping, and expiration dates. For analytic purposes, dates need to be in a format that can allow for arithmetic operations, such as time intervals between shipping and expiration, aggregating data by time periods, and so forth. A recommended format would be a MMDDYYCC form (for example, 09220121 would represent September 22, 2001).

Several limitations of the quantitative analysis need to be noted. Most importantly, we studied only two PVOs, which may not represent typical organizations. The lack of generalizability of the results, therefore, needs to be kept in mind, and general conclusions regarding the performance of donor firms or PVOs cannot be made at this time. The results we report, however, are the first systematic analysis of patterns of drug donations received and shipped by a small number of PVOs to a large number

of countries. This analysis needs to be followed by larger, more generalizable studies.

A second limitation of the quantitative analysis is that we studied only those products shipped and did not examine the important question of the usefulness of the *supply* of donated drugs in terms of the demand or need of recipient countries. For example, the leading shipment item for both PVOs was acetaminophen, which may be in high demand by many recipient countries and is typically on national EDLs as well as the WHO-ML. It remains unknown, however, if the volume of acetaminophen shipped matches the need and/or demand in recipient countries.

The major limitation of this study is its lack of data on the volume of donated drugs. Because we do not know if a shipment item contained drug supply for one or for 1,000 patients, we cannot judge the overall quality of donated products or exclude the possibility of "dumping" large volumes of short-dated products.

Using numbers of shipment items as a proxy measure for quantity, we conclude that the majority of drugs donated by the two study PVOs had expiration times largely consistent with the requirements of the WHO *Guidelines*. We recommend further studies to answer questions about drug dumping, to estimate the proportions of donated drugs that can be used by recipients, and to explore the shortening of time to expiration suggested by our analysis.

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