M E M O R A N D U M DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research

DATE: March 8, 2001

FROM: Sharon O'Callaghan, CSO,
Division of Inspections and Surveillance (HFM-650)
Office of Compliance and Biologics Quality

SUBJECT: Error and Accident Reports - Summary for Fourth Quarter FY2000

TO: Director, Division of Inspections and Surveillance (HFM-650)
Office of Compliance and Biologics Quality

Between July 1, 2000 and September 30, 2000, the Division of Inspections and Surveillance received 6562 error and accident reports from biological product manufacturers. Blood and plasma establishments submitted 6490 reports and non-blood manufacturers submitted 72 reports. There were 347 (5.3%) reports forwarded to the District Offices for follow-up and evaluation as potential recall situations. Based on the information submitted in the error and accident reports, 138 (2.1%) reports did not appear to meet the threshold for reporting, i.e., products were not made available for distribution or the safety, purity, or potency of a product was not affected.

Between October 1, 1999 and September 30, 2000, the Division of Inspections and Surveillance received 23,528 error and accident reports from biological product manufacturers. Blood and plasma establishments submitted 23,346 reports and non-blood manufacturers submitted 182 reports. There were 1401 (6.0%) reports forwarded to the District Offices for follow-up and evaluation as potential recall situations. Based on the information submitted in the error and accident reports, 644 (2.7%) reports did not appear to meet the threshold for reporting, i.e., products were not made available for distribution or the safety, purity, or potency of a product was not affected.

Tables and charts are included that identify the types of errors and accidents submitted by blood and plasma establishments and by non-blood manufacturers. In addition, a table and graphs representing reportable errors and accidents submitted by blood and plasma establishments are also provided that illustrate the distribution of the reporting time, i.e., time from the date the error or accident was discovered to the date that CBER received the report.

ALL REPORTING ESTABLISHMENTS

FY2000

	NUMBER OF REPORTING ESTABLISHMENTS		TOTAL REPORTS RECEIVED		POTENTIAL RECALLS	
	Fourth Quarter	Year To Date	Fourth Quarter	Year To Date	Fourth Quarter	Year To Date
BLOOD/PLASMA MANUFACTURERS						
LICENSED BLOOD BANKS	125*	162*	5658	20196	264	1184
UNLICENSED BLOOD BANKS	19	52	39	125	2	11
TRANSFUSION SERVICES	5	19	10	53	2	2
PLASMA CENTERS	211	316	783	2972	68	179
SUB-TOTAL	360	549	6490	23346	336	1376
NON-BLOOD MANUFACTURERS						
BLOOD DERIVATIVE MANUFACTURER	9	15	15	34	3	3
IN-VITRO DIAGNOSTIC MANUFACTURER	5	11	6	38	3	7
VACCINE MANUFACTURER	5	8	12	21	4	4
ALLERGENICS MANUFACTURER	2	6	30	57	0	6
THERAPEUTIC MANUFACTURER	7	14	9	32	1	5
SUB-TOTAL	28	54	72	182	11	25
TOTAL	**388**	**603**	**6562**	**23528**	**347**	**1401**

*Number of license holders; may be one establishment or multiple establishments operating under one license.

The following tables and pie charts show the type of errors and accidents reported by blood and plasma establishments:

FOURTH QUARTER – FY2000

BLOOD AND PLASMA ESTABLISHMENTS

TOTAL ERRORS AND ACCIDENTS

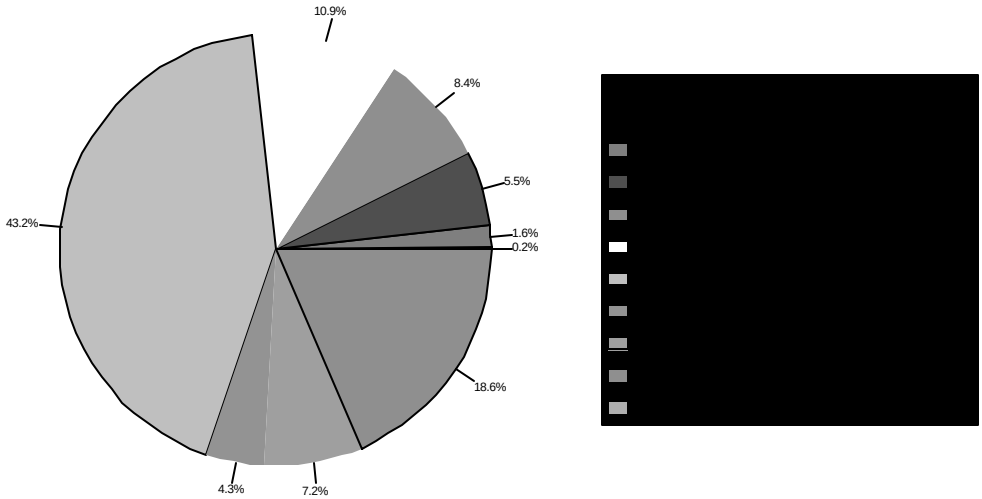
TYPE OF ERROR/ACCIDENT	Licensed Establishments	Unlicensed Establishments	Transfusion Services	Plasma Centers	TOTAL	
POST DONATION INFORMATION	4648	10	0	656	5314	81.9%
STORAGE/DISTRIBUTION	379	8	4	15	406	6.3%
DONOR SCREENING	205	5	0	66	276	4.3%
LABELING	217	12	2	4	235	3.6%
ROUTINE TESTING	66	2	3	0	71	1.1%
MISCELLANEOUS	42	2	0	21	65	1.0%
COMPONENT PREPARATION	44	0	1	0	45	0.7%
COLLECTION	28	0	0	2	30	0.5%
DONOR DEFERRAL	19	0	0	8	27	0.4%
VIRAL TESTING	10	0	0	11	21	0.3%
TOTAL	5658	39	10	783	6490	100.0%

POTENTIAL RECALLS

TYPE OF ERROR/ACCIDENT	Licensed Establishments	Unlicensed Establishments	Transfusion Services	Plasma Centers	TOTAL	
DONOR SCREENING	103	1	0	42	146	43.5%
STORAGE/DISTRIBUTION	50	0	1	13	64	19.0%
LABELING	30	1	0	1	32	9.5%
COMPONENT PREPARATION	30	0	1	0	31	9.2%
DONOR DEFERRAL	15	0	0	7	22	6.5%
POST DONATION INFORMATION	18	0	0	2	20	6.0%
COLLECTION	15	0	0	2	17	5.1%
VIRAL TESTING	3	0	0	1	4	1.2%
ROUTINE TESTING	0	0	0	0	0	0.0%
MISCELLANEOUS	0	0	0	0	0	0.0%
TOTAL	264	2	2	68	336	100.0%

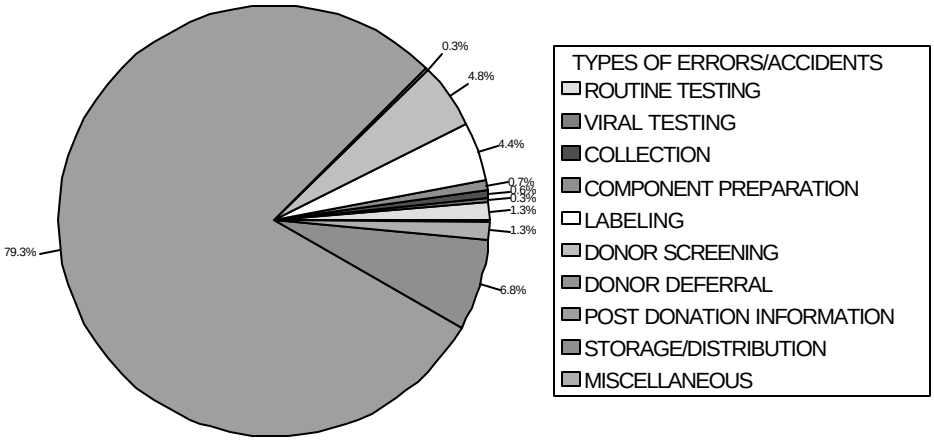
ALL BLOOD AND PLASMA ESTABLISHMENTS FY-2000

POTENTIAL RECALLS



POTENTIAL RECALLS = 1376

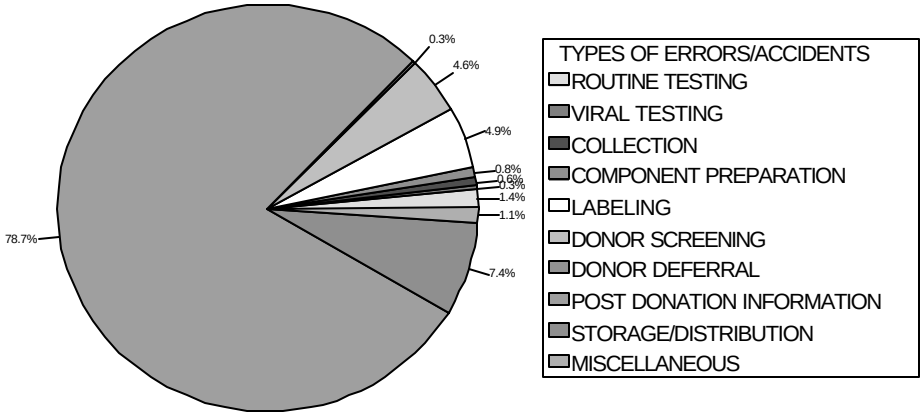
TOTAL REPORTS



TOTAL REPORTS RECEIVED (10/1/99 - 9/30/00) = 23,346

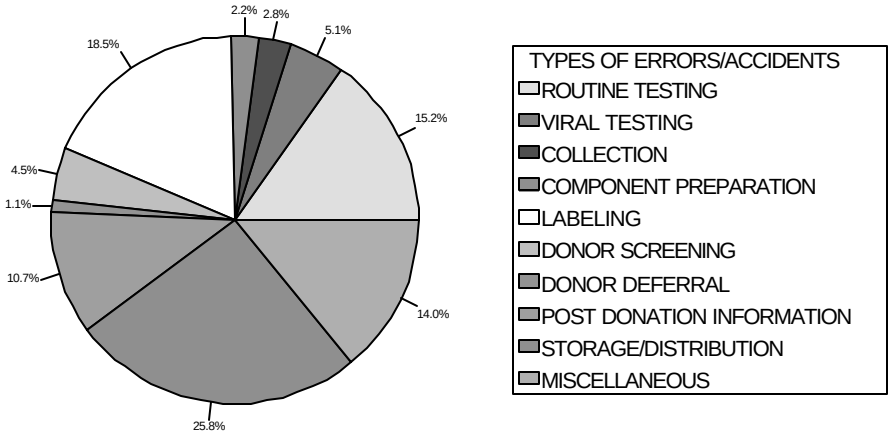
FY-2000
Total Reports

LICENSED BLOOD ESTABLISHMENTS



REPORTS RECEIVED (10/1/99 - 9/30/00) = 20,196

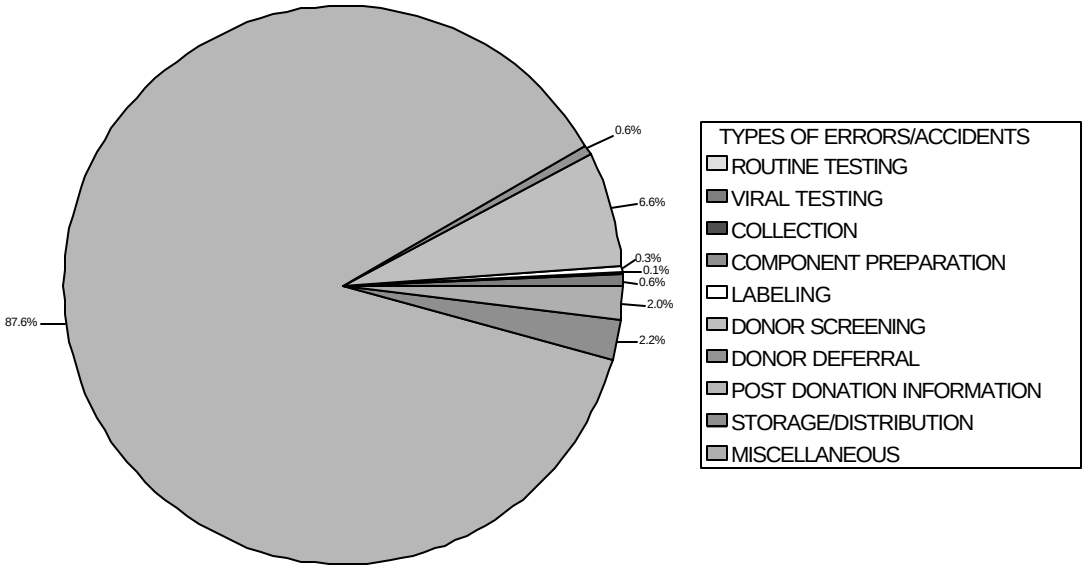
UNLICENSED BLOOD ESTABLISHMENTS



REPORTS RECEIVED (10/1/99 - 9/30/00) = 178
UNLICENSED BLOOD BANKS = 125; TRANSFUSION SERVICES = 53

FY-2000
Total Reports

PLASMA CENTERS



REPORTS RECEIVED (10/1/99 - 9/30/00) = 2972

BLOOD AND PLASMA ESTABLISHMENTS

FY2000

FOURTH QUARTER

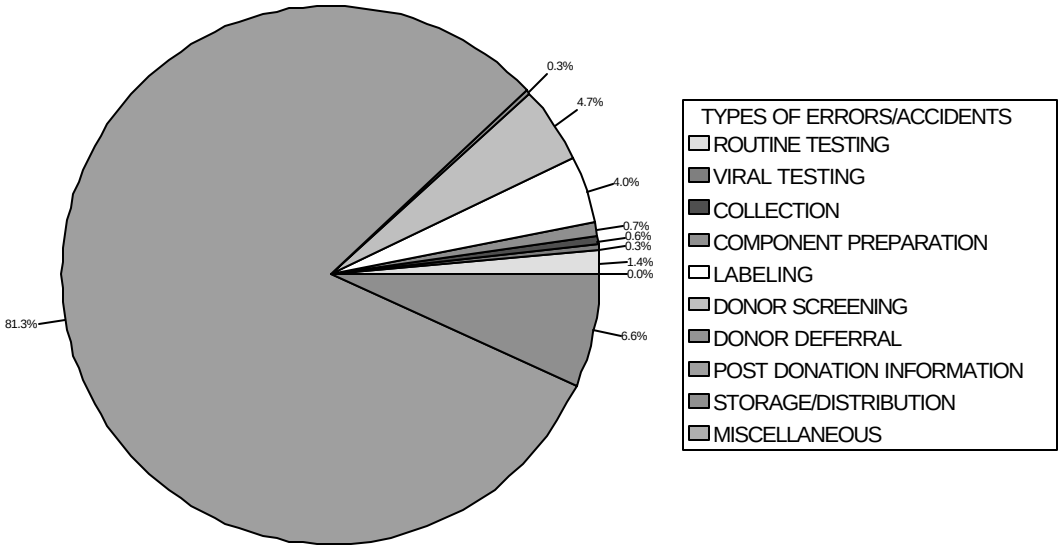
TYPE OF ERROR/ACCIDENT	REPORTABLE	NON-REPORTABLE	TOTAL	%REPORTABLE
POST DONATION INFORMATION	5308	6	5314	99.9%
STORAGE/DISTRIBUTION	375	31	406	92.4%
DONOR SCREENING	270	6	276	97.8%
LABELING	215	20	235	91.5%
ROUTINE TESTING	71	0	71	100.0%
MISCELLANEOUS	0	65	65	0.0%
COMPONENT PREPARATION	45	0	45	100.0%
COLLECTION	27	3	30	90.0%
DONOR DEFERRAL	26	1	27	96.3%
VIRAL TESTING	21	0	21	100.0%
TOTAL	6358	132	6490	98.0%

YEAR-TO-DATE

TYPE OF ERROR/ACCIDENT	REPORTABLE	NON-REPORTABLE	TOTAL	%REPORTABLE
POST DONATION INFORMATION	18471	40	18511	99.8%
STORAGE/DISTRIBUTION	1508	90	1598	94.4%
DONOR SCREENING	1070	59	1129	94.8%
LABELING	908	121	1029	88.2%
ROUTINE TESTING	310	2	312	99.4%
MISCELLANEOUS	5	303	308	1.6%
COMPONENT PREPARATION	165	1	166	99.4%
COLLECTION	127	8	135	94.1%
VIRAL TESTING	79	1	80	98.8%
DONOR DEFERRAL	73	5	78	93.6%
TOTAL	22716	630	23346	97.3%

ERROR AND ACCIDENT REPORTS

ALL BLOOD AND PLASMA ESTABLISHMENTS
REPORTABLE ERRORS/ACCIDENTS
FY2000



TOTAL REPORTS RECEIVED (10/1/99 - 9/30/00) = 23,346
REPORTABLE ERRORS/ACCIDENTS = 22,716 (97.3%)

FY2000
Reports Received 10/1/99 – 9/30/00

REPORTABLE ERRORS/ACCIDENTS – 23,346 (97.3% of total reports)

Top Three Categories of Errors/Accidents:

Post Donation Information – 18,471 (81.3% of reportables)

**Examples:*

Information provided post donation:

- [1]Donor traveled to UK between 1980 and 1996 (nvCJD risk)
- Donor traveled to a malarial endemic area
- Donor received tattoo
- Donor had a history of cancer
- Donor became ill after donation,

  not related to hepatitis, HIV, HTLV-I, sexually transmitted diseases or cold/flu symptoms

[1] *As a result of implementation of the guidance document published November 11, 1999, there was a significant increase in the number of post donation information reports related to CJD risk factors. The guidance recommended deferral of donors who have spent six months or more cumulatively in the United Kingdom from 1980 through 1996. There were 125 reports submitted in FY-99 and 5642 reports in FY2000 related to risk factors for CJD. Of the 5642 reports received in FY2000, 5356 were related to donors who provided information of travel to the United Kingdom.*

Storage and Distribution - 1508 (6.6% of reportables)

**Examples:*

- Release of product that was broken or damaged
- Release of product that contained clots or would not flow through a filter
- Failure to quarantine unit, reason for quarantine:
  - outdated product
  - unit released prior to resolution of discrepancy
  - platelet count or platelet yield unacceptable
  - donor record incomplete or incorrect
- Product was shipped or stored at incorrect temperature

Donor Screening –1070 (4.7% of reportables)

**Examples:*

- Donor provided information that warranted deferral, but donor was not deferred:
  - travel to malarial endemic area
  - history of disease, surgery or cancer
  - received medication

*Examples of errors and accidents represent at least 50% of reports in each category.

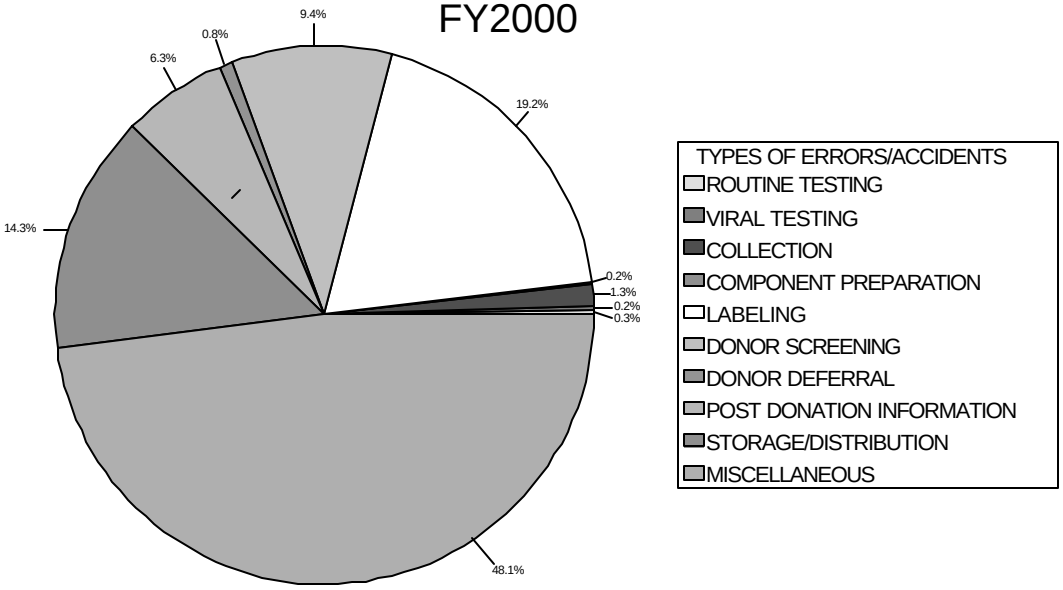
- Donor record incomplete or incorrect – donor history questions

ERROR AND ACCIDENT REPORTS

ALL BLOOD AND PLASMA ESTABLISHMENTS

NON-REPORTABLE ERRORS/ACCIDENTS

FY2000



TOTAL REPORTS RECEIVED (10/1/99 - 9/30/00) = 23,346
REPORTABLE ERRORS/ACCIDENTS = 630 (2.7%)

FY2000
Reports Received 10/1/99 – 9/30/00

NON-REPORTABLE ERRORS/ACCIDENTS - 630 (2.7% of total reports)

Top Three Categories of Errors/Accidents:

Miscellaneous - 303 (48.1% of non-reportables)

**Examples:*

- Recordkeeping error/accident - record is incorrect or not reviewed, testing and labeling acceptable
- No products made available for distribution
- Records destroyed or lost, final disposition unknown; unit determined to be suitable at the time of distribution

Labeling - 121 (19.2% of non-reportables)

**Examples:*

- Unit missing label for ABO/Rh, product, or expiration date
- Unit labeled with incorrect weight, volume, collection date, or facility identifiers; unit acceptable
- Unit labeled with a shortened expiration date
- Directed unit, suitable for allogeneic use, labeled with incorrect name, SSN, or date of birth

Storage and Distribution - 90 (14.3% of non-reportables)

**Examples:*

- Discrepancy between shipping form and shipment
- Irradiated unit requested by another facility, not provided (unit labeled appropriately)
- Failure to quarantine unit after receiving information concerning post donation cold or flu symptoms
- Sterile weld inspection not documented
- Allogeneic unit issued instead of an autologous unit

*Examples of errors and accidents represent at least 50% of reports in each category.

The following table and graphs show the time periods in which CBER received reports from the blood and plasma establishments. The evaluation of timeliness is limited to only reports that met the threshold for reporting.

BLOOD AND PLASMA ESTABLISHMENTS
FY2000

NUMBER OF DAYS FROM DATE E/A DISCOVERED TO FDA RECEIVED

FOURTH QUARTER
Reports received 7/1/00 – 9/30/00

CUMULATIVE PERCENT OF REPORTS	LICENSED (Days)	UNLICENSED (Days)	PLASMA (Days)	TOTAL (Days)
10%	16	20	15	16
25%	22	27	25	22
50%	31	56	44	32
75%	44	113	82	46
90%	72	448	164	82
# REPORTS	5553	45	760	6358
RANGE	3-1648	6-1504	4-977	3-1648

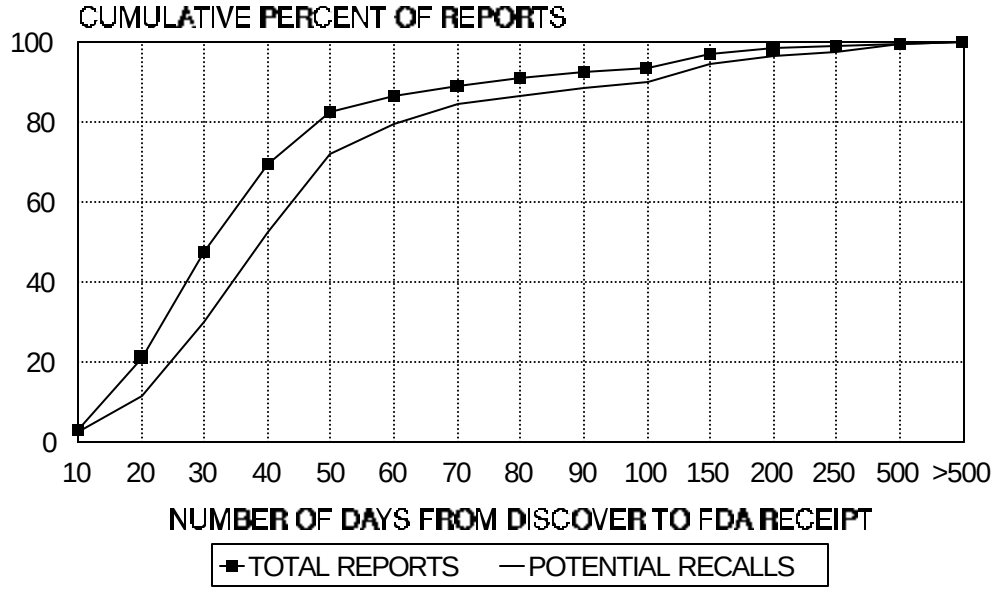
YEAR-TO-DATE
Reports received 10/1/99 – 9/30/00

CUMULATIVE PERCENT OF REPORTS	LICENSED (Days)	UNLICENSED (Days)	PLASMA (Days)	TOTAL (Days)
10%	15	9	14	15
25%	21	19	23	21
50%	30	37	39	31
75%	41	90	67	44
90%	63	223	131	74
# REPORTS	19680	145	2891	22716

RANGE	1-1648	1-1504	8-977	1-1648

REPORTING TIME
FY-2000

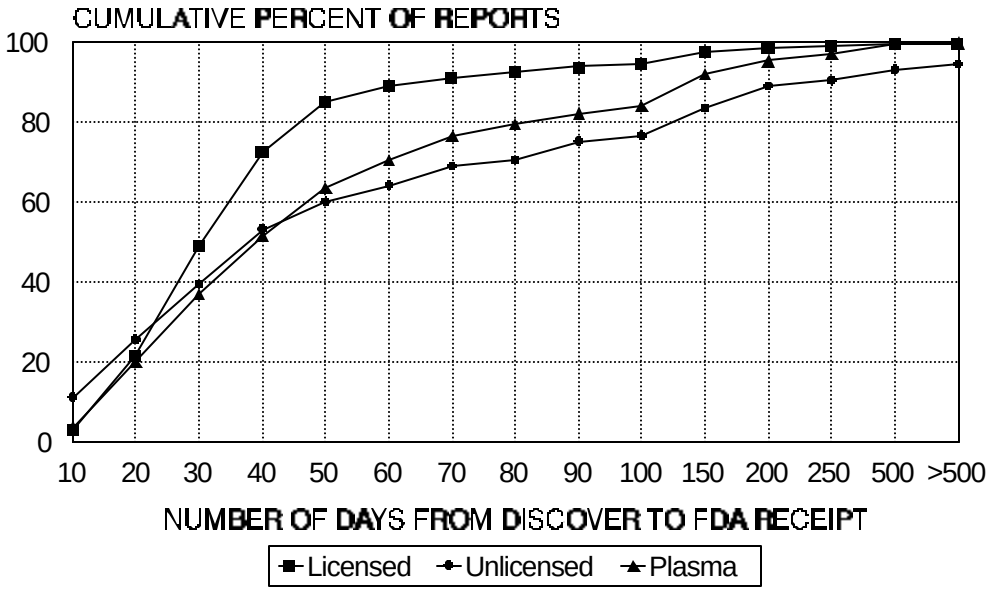
ALL REPORTING BLOOD AND PLASMA ESTABLISHMENTS



TOTAL REPORTS = 22,716
POTENTIAL RECALLS = 1376

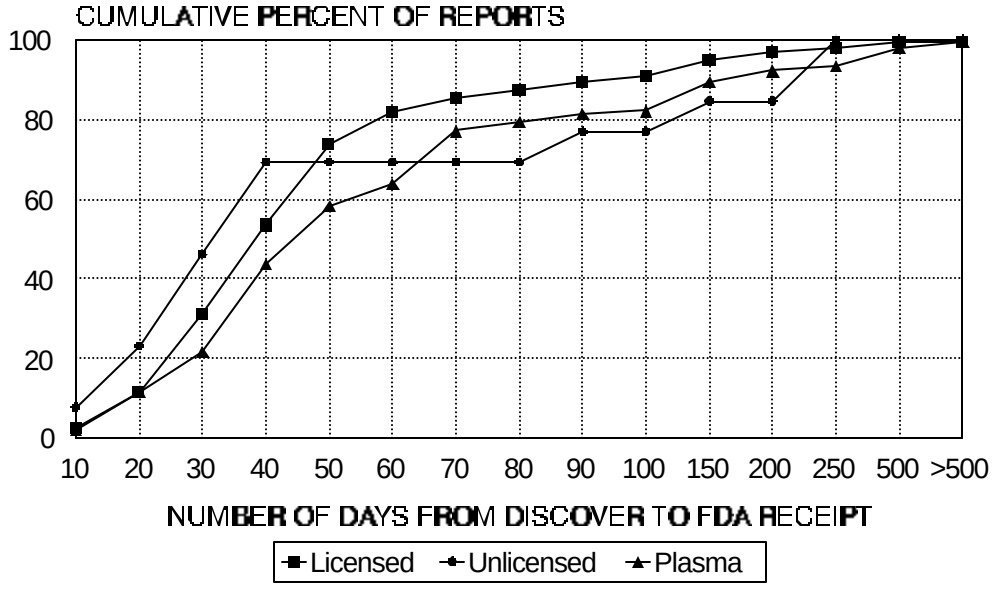
REPORTING TIME
FY-2000

TOTAL REPORTS



TOTAL REPORTS = 22,716
LICENSED BLOOD EST.= 19,680; UNLICENSED BLOOD EST. = 145; PLASMA CENTERS = 2891

POTENTIAL RECALLS



TOTAL REPORTS = 1376
LICENSED BLOOD EST.= 1184; UNLICENSED BLOOD EST. = 13; PLASMA CENTERS = 179

The following tables and pie charts show the type of errors and accidents reported by non-blood manufacturers:

NON-BLOOD MANUFACTURERS
FY2000

FOURTH QUARTER
Total Reports

TYPE OF ERROR/ACCIDENT	DERIVATIVE	IN-VITRO DIAGNOSTIC	ALLERGENIC	THERAPUETIC	VACCINE	TOTAL	
STERILITY COMPROMISED	3	0	22	3	2	30	41.7%
PROCESSING	4	1	0	2	5	12	16.7%
LABELING	0	3	3	1	2	9	12.5%
MISCELLANEOUS	2	0	1	3	2	8	11.1%
STORAGE/DISTRIBUTION	4	1	0	0	1	6	8.3%
NOT REPORTABLE	2	0	4	0	0	6	8.3%
REAGENT PERFORMANCE	0	1	0	0	0	1	1.4%
TOTAL	15	6	30	9	12	72	100%

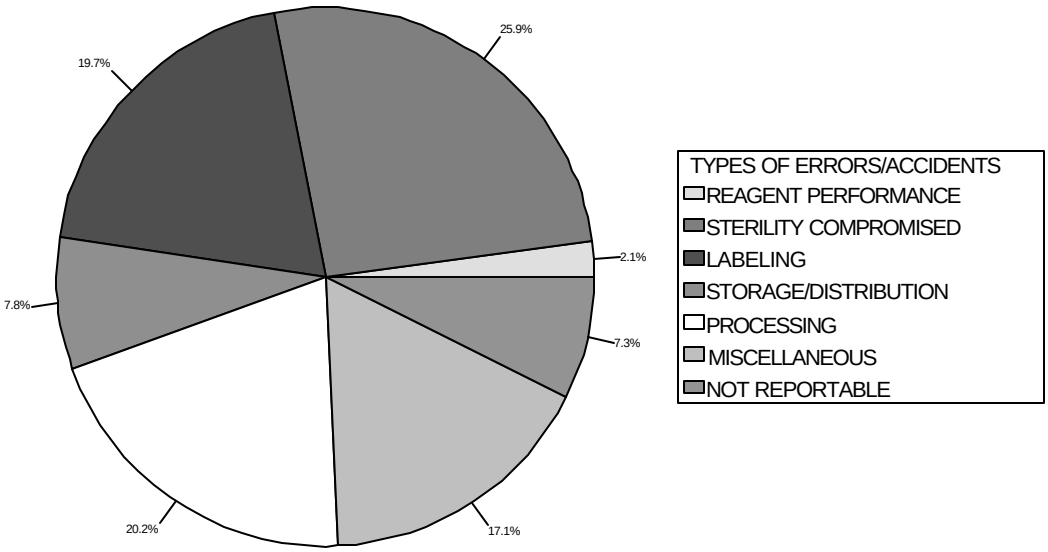
Potential Recalls

TYPE OF ERROR/ACCIDENT	DERIVATIVE	IN-VITRO DIAGNOSTIC	ALLERGENIC	THERAPUETIC	VACCINE	TOTAL	
LABELING	0	2	0	0	1	3	27.3%
STERILITY COMPROMISED	0	0	0	1	1	2	18.2%
STORAGE/DISTRIBUTION	1	0	0	0	1	2	18.2%
PROCESSING	1	0	0	0	1	2	18.2%
REAGENT PERFORMANCE	0	1	0	0	0	1	9.1%
MISCELLANEOUS	1	0	0	0	0	1	9.1%
NOT REPORTABLE	0	0	0	0	0	0	0.0%
TOTAL	3	3	0	1	4	11	100%

ERROR AND ACCIDENT REPORTS

NON-BLOOD MANUFACTURERS

FY2000



TOTAL REPORTS RECEIVED (10/1/99 - 9/30/00) = 182
REPORTABLE ERRORS/ACCIDENTS = 168; NON-REPORTABLE ERRORS/ACCIDENTS = 14

NON-BLOOD MANUFACTURERS
Year to Date

DERIVATIVES

ERROR/ACCIDENT	#REPORTS
STERILITY COMPROMISED	***5***
Precipitate found in product	2
Possible mold contamination	1
Possible residual component	2
LABELING	***2***
Product label incorrect	1
Product label missing	1
STORAGE/DISTRIBUTION	***6***
Product released prior to CBER approval - expiration of CBE submission	1
Product released prior to validation of the lyophilization cycle	1
Product shipped or stored at incorrect temperature	4
PROCESSING	***11***
Source material unsuitable for processing	3
Lypholization cycle interrupted due to an earthquake that caused a power outage	1
Column effluent collected in flexible container rather than stainless steel tank	1
Out of specification volume of fill result	1
Product specification not met	5
MISCELLANEOUS	***7***
Glass defects	1
Water for Injection system was not sampled.	1
Product tested positive for HAV RNA during final container PCR testing, associated products released.	1
Evidence of surface change on stoppers of Normal Horse Serum packaged in the kit	1
Black particles found in WFI system	1
Stability testing failed	1
Decrease in potency	1
NON-REPORTABLE	***3***
Product labeled with missing/incorrect facility identifiers - product acceptable	1
Product not made available for distribution	1
Conflicting information on carton labels, container label correct	1
TOTAL	***34***

NON-BLOOD MANUFACTURERS
Year to Date

IN-VITRO DIAGNOSTICS

ERROR/ACCIDENT	#REPORTS
REAGENT PERFORMANCE	***4***
Indicator Red Cells, used in Syphilis Test System, deteriorating	1
Product giving false positive results	1
A2 cells gave positive reaction when tested with Anti-A1 Lectin	1
B cells gave weak positive reactions	1
STERILITY COMPROMISED	***5***
Microbial contamination	2
Stoppers contaminated with endotoxin	1
Annual revalidation of aseptic dispensing exhibited an unacceptable number of contaminated units	1
Antimicrobial preservative effectiveness test may not have been performed	1
LABELING	***17***
Package insert incorrect	9
Product label incorrect	2
Lot number missing/incorrect and expiration date also missing	4
Lot number, expiration date and bar code missing	1
Insert contains information on the relationship between EU/ml and IU/ml that may be misinterpreted	1
STORAGE/DISTRIBUTION	***3***
Product released prior to completion of required testing	2
Product shipped or stored at incorrect temperature	1
MISCELLANEOUS	***2***
Wrong vial replaced in the 11-cell panel, due to hemolysis.	1
Unacceptable results for linearity in the extended assay protocol	1
NON-REPORTABLE	***3***
Product not made available for distribution	3
TOTAL	***34***

NON-BLOOD MANUFACTURERS
Year to Date

ALLERGENICS

ERROR/ACCIDENT	#REPORTS
STERILITY COMPROMISED	***31***
Loose seal resulted in a leaking vial	1
A piece of rubber from the stopper found in vial	1
Contents leaking out	1
Precipitate found in product	28
LABELING	***13***
Potency not on vial label	2
Product label incorrect	1
Lot number missing/incorrect	1
Concentration missing or incorrect	1
Expiration date extended or missing	7
Labeling did not list all ingredients	1
STORAGE/DISTRIBUTION	***1***
Sterility test cultures may not have been incubated appropriately before products released	1
PROCESSING	***4***
Computer calculation error for preparation of extract	1
Error in correcting calculation error resulted in concentration of 835 PNU/ml instead of 1000 PNU/ml	1
Formula change	1
PNU value incorrectly entered into the computer	1
MISCELLANEOUS	***1***
Stability data indicates increased potency over time	1
NON-REPORTABLE	***7***
Product labeled with missing/incorrect weight or volume; product acceptable	1
Illegible expiration date	1
Expiration date shortened	2
Product not made available for distribution	1
Discrepancy between shipping form and shipment	1
Release of product other than that which was ordered	1
TOTAL	***57***

NON-BLOOD MANUFACTURERS
Year to Date

THERAPEUTICS

ERROR/ACCIDENT	#REPORTS
STERILITY COMPROMISED	***6***
Bacterial contamination	2
Reovirus contamination diafiltered medium	1
Aspergillus flavus found in one roller bottle	1
Particles found in product	2
LABELING	***4***
Expiration date extended	1
Lot number incomplete	1
Concentration missing or incorrect	1
Label missing	1
STORAGE/DISTRIBUTION	***3***
Product released prior to completion of testing	1
Product shipped or stored at incorrect temperature	2
PROCESSING	***11***
Media fill failure	1
Rubber stoppers did not meet specifications	1
Product specification not met	4
BLA ELISA data was identical to that of a previously released lot	1
Purified water mixed into WFI distillate stream	1
Sanitization of the bulking gowning room and gowning room was not performed	1
Out of calibration situation involving the monitoring of solution levels in the processing tanks	1
Leaking ampule from punctures caused by the automatic feeder to the pouching equipment on the packaging line	1
MISCELLANEOUS	***8***
Stability testing failed	4
Lack of vacuum in vials	1
During stability study evaluation, the product demonstrated a new significant band for the SDS-PAGE test (gel electropheresis)	1
Low yield due to gel product adhering to walls of tank	1
Final product vial broke as being opened for cell implantation procedure	1
TOTAL	***32***

NON-BLOOD MANUFACTURERS
Year to Date

VACCINES

ERROR/ACCIDENT	#REPORTS
STERILITY COMPROMISED	***3***
Bulk intermediate failed sterility test at 12-months	1
Sterility testing failed	1
Sterile media fill contaminated with fungi	1
LABELING	***2***
Expiration date extended	2
STORAGE/DISTRIBUTION	***2***
Product shipped or stored at incorrect temperature	2
PROCESSING	***9***
Appropriate testing was not performed	1
Product specification not met	8
MISCELLANEOUS	***4***
Stability testing failed	2
Decrease in potency	1
Stability potency assay not initiated within appropriate time	1
NON-REPORTABLE	***1***
Product not made available for distribution	1
TOTAL	***21***