

# **Knowledge of FDA Reportable Deviations**

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**Abstract:**

**Background:** As early as 2001, the Food and Drug Administration (FDA) required hospital transfusion centers to report any deviated distributed blood products. Yet between 2001 and 2006, only 472 out of 5134 hospitals actually reported deviations, a mere 9.2 percent. **Study Design and Methods:** Cases were developed and evaluated by the Center for Biologics Evaluation and Research (CBER) and FDA division directors for FDA reportable deviations. A survey of eight Cases was launched in Zoomerang and sent to blood bankers and generalists in Medical Technology. **Results:** There were 176 respondents to the survey. Only 10 (5.6 percent) got all answers correct. Based on job title and place of employment, no group was more knowledgeable than the other. Respondents attached more importance to deviations involving quality control, blood bank identification, unit specification and antibody identification. Less importance was attached to deviations like phlebotomist's initial, not issuing units in computer and crossmatching under previous account. **Discussion:** The people surveyed do not seem to have uniform ideas about FDA reportables. Variations in size of establishment or individual job title did not make any group stand out as more knowledgeable of FDA reportables.

**Abbreviation:** & = and; BPD = Biological Product Deviation; CBER = Center for Biologics Evaluation and Research; CGMP = Current Good Manufacturing Practice; CMV = Cytomegalovirus; DAT = Direct Antiglobulin Test; FDA = Food and Drug Administration; ID = Identification; LA = Labeling; OR = Operating Room; PRBC = Packed Red Blood Cells; QC = Quality Control; RT = Routine Testing.

## **Introduction:**

The main source of information about FDA deviation reporting comes from the FDA website. As early as March 20, 1991, FDA required licensed blood and plasma establishments to report and the voluntary reporting from unlicensed registered blood establishments and transfusion services. Consequently, the regulations proposed on November 7, 2000 by FDA, required all establishments, including unlicensed registered blood establishments and transfusion services, to report deviated products that have been distributed. The term 'error and accident' is replaced with 'biological product deviation'. Error and accident included 'near miss' events<sup>1</sup>. The new term limits what must be reported to distributed products<sup>2</sup>. These events include anything affecting the safety, purity, or potency of distributed products<sup>1</sup>. The term 'may' includes any possibilities of compromising safety, purity or potency of the distributed products. The patient does not need to be harmed in any way. 'Distributed' refers to the biological product that has left the control of the establishment. 'Control' is defined as 'having responsibility for maintaining a product's continued safety, purity and potency and compliance with applicable product and establishment standards and CGMP requirements'. In the 2000 Final Rule, FDA believed limiting reporting to distributed products will ease some of the burden of reporting<sup>2</sup>. The time frame set for reporting is 45 calendar days from the day the event was discovered<sup>1</sup>. The reason behind the change is because of the increase in recalls by unlicensed blood establishments due to lack of reporting<sup>2</sup>.

FDA estimates zero reports per hospital for 6 to 299 bed hospitals and only 1 per hospital reporting for 300 to 500 plus bed hospitals. Of the total of 5134 registered community

hospitals 808 have more than 299 beds<sup>2</sup>. The average of the reporting hospitals from 2002 to 2006 is 472.<sup>4,5,6,7,8</sup> The difference between highest, 499 (in 2003) and the lowest 460 (in 2006), is just 39. The projection by FDA of around one report of product deviation per hospital of more than 299 beds, does not correspond with what is actually being reported. The report average of the 5 years is 1485. That means the 472 hospitals report an average of 3 deviations each. The remaining 334 hospitals of the greater than 299 bed group have not reported. Therefore, some hospitals are more vigilant in reporting deviations than others. The same hospitals probably report year after year with very few additional hospitals reporting deviations. Putting aside hospital size, one can say only 472 out of 5134 (9.2%) hospitals reported.

The purpose of this paper is to determine if the blood banking community would be able to identify FDA reportables using a case study approach. Eight Cases were developed, validated and sent to blood banking related professionals in different size hospital transfusion centers and blood donor centers.

### **Materials and Methods:**

Cases were gathered through past experiences. The Cases were then e-mailed to several FDA regional district offices for guidance and comment. After narrowing the Cases to less than 10, the Cases were sent to CBER for final comment as to which of them would be a FDA reportable deviation. The survey was first piloted to 20 SBB students and instructors then the Cases were put into Zoomerang which is an internet program used for developing surveys. Each person was asked to determine if each Case should be reported to FDA (answer would be yes) or not (answer would be no).

The survey included questions about respondents working locations, their main functions in the blood bank and the numbers of donors processed in the blood donor centers in a month or the numbers of beds in the hospital transfusion centers.

The Cases described in the survey are as follows:

**Case 1:** The phlebotomist's initial was missing from the label on the specimen. A unit of blood was crossmatched and transfused. The missing information was not discovered until the next day when a second unit was crossmatched. The phlebotomist was off on the second day. His initial was added on the fourth day when he returned to work and after the second unit was transfused.

**Case 2:** Red cell reagents (for A1 and B reverse typing, Coombs check cells, 3% screen cells 1 and 2) had expired for three days. The daily QC was done on the expired reagents. 'NC' stands for 'no change' was entered for lot numbers and expiration dates. The QC was all within range. Type and Cross were done using those expired reagents during those three days and units were transfused.

**Case 3:** Two blood bank IDs were on a unit of blood that was dispensed. The unit was first crossmatched to patient whose ID was AAA1111. It was returned to inventory. The technician who did the returning forgot to remove the blood bank ID. It went unnoticed until the unit was examined by two nurses as it was about to be transfused to a second patient whose blood bank ID BBB2222 was also on the unit. The unit was returned to the blood bank.

**Case 4:** The blood bank ID on a PRBC was FTM1234. On the tag, it said FTW1234. It was dispensed and subsequently returned to blood bank for clarification.

**Case 5:** A unit of blood was returned to the blood bank after it was dispensed. The patient needed CMV negative and irradiated blood. The unit that was returned was neither.

**Case 6:** Six units of PRBC and a platelet were issued to the OR. The technician dispensed the PRBC, but forgot to dispense the platelet. The mistake was discovered when OR returned the unused PRBC and platelet to the blood bank.

**Case 7:** A patient was discharged from a hospital, but he returned the next day to the Emergency Room of the same hospital. A type and cross was ordered. The technologist did an add-on two units of PRBC using an old blood bank specimen from the previous admission which had not expired. The patient's blood bank armband from the previous visit was still on.

**Case 8:** A patient's antibody screen was negative. The doctor ordered a DAT which turned out to be positive. The technologist did not request a transfusion history because he thought everything was fine when the screen was negative. The patient was in fact transfused a few days ago in another hospital. An elution was not ordered by the doctor or the technologist. The doctor ordered a unit of blood the next day. The patient had a transfusion reaction. Elution was ordered on the pre and post transfusion specimens because both DAT were positive. Anti-JKa was in the both eluates.

### **Results and Interpretation:**

According to CBER, all the Cases in the survey are FDA reportable deviations:

**Case 1:** The BPD code should be RT6203: routine testing; sample identification; sample used for testing was incorrectly or incompletely labeled.

**Case 2:** The BPD code should be RT6307: routine testing; testing performed using reagents in which QC was unacceptable or not performed, or expired reagents were used.

**Case 3:** The BPD code should be LA8207: labeling; crossmatch tag or tie tag incorrect or missing information; recipient identification incorrect or missing.

**Case 4:** The BPD code should be LA8206; labeling; crossmatch tag or tie tag incorrect or missing information; unit, lot or pool number incorrect or missing.

**Case 5:** The BPD code should be QC9712; quality control and distribution; distribution procedure not performed in accordance with blood bank transfusion service's specifications; product not irradiated and CMV negative as required.

**Case 6:** The deviation code should be QC9719; quality control and distribution; distribution procedure not performed in accordance with blood bank transfusion service's specifications; product not documented or incorrectly documented as issued in the computer.

**Case 7:** The BPD code should be QC9707; quality control and distribution; distribution procedure not performed in accordance with blood bank transfusion service's specifications; product released prior to obtaining current sample for ABO, Rh, antibody screen and/or compatibility testing.

**Case 8:** The deviation code should be QC9310: quality control and distribution; testing not performed, incompletely performed or not documented for: antibody screen or identification.

### **Discussion:**

Every blood banker should have a clear concept of what to report as FDA deviation; this is not shown by this survey. Only 10 out of 176 respondents responded to all Cases correctly. Not one job category appears more knowledgeable. The hospital transfusion centers are not better in deciding deviations than the blood donor centers, or vice versa. The supervisors are not more knowledgeable than the bench technologists. Some of the respondents who responded incorrectly to all eight Cases were supervisors and

directors/managers. The majority of respondents responded incorrectly to Cases one, six and seven. Those Cases involved phlebotomist initial, not issuing platelet in the computer and crossmatching units on a previous account. Respondents tend to see the other Cases as more serious and therefore reportable. Those Cases involved quality control, blood bank identification, unit specification and antibody identification. All reportable deviations can be submitted to CBER electronically or by mail. One can always refer the situation to CBER when one is not sure if a deviation is reportable or not.

The advantages of reporting are not just for FDA to keep track of statistics; it is also beneficial to the blood donor centers and hospital transfusion centers. Any blood banking establishment that vigilantly reports all FDA deviations means it has a stricter Quality Assurance department, more technologists aware of reportable deviations and more supervisors and directors responsible for reporting deviations, and ultimately better patient care. Future surveys can be focused on finding out if an institution has FDA reportable policy and procedures, the number of reportable incidents, the number of deviations actually reported to FDA, the department responsible for reporting, steps taken to ensure all deviation are reported, the personnel in charge of ensuring full reporting and if there is any awareness of benefits of full reporting, such as decrease in reportable deviations. Future studies can also focus on the regulatory agencies to see if they are aware of FDA reportable deviations when they are implementing inspections and how they can assure full compliance.

## References

- 1 Guidance for Industry: Biological Product Deviation Reporting for Blood and Plasma Establishments [on the Internet]. Washington, DC: U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research (CBER); 2006 October [accessed 2008 April 12]. Available from: <http://www.fda.gov/cber/guidelines.htm>
- 2 Federal Register, 65: 66621-66635, Biological Products: Reporting of Biological Product Deviations in Manufacturing, Final Rule [on the Internet]. Washington, DC: U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research (CBER); 2000 November 7 [accessed 2008 April 12]. Available from: <http://www.fda.gov/cber/rules/frbpdr110700pdf>
- 3 Biological Product Deviation Reports, FY 2001 [on the Internet]. Washington, DC: U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research (CBER); 2002 May [accessed 2008 April 12]. Available from: <http://www.fda.gov/cber/biodev/bpdrfy01.htm>
- 4 Biological Product Deviation Reports, FY 2002 [on the Internet]. Washington, DC: U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research (CBER); 2003 May [accessed 2008 April 12]. Available from: <http://www.fda.gov/cber/biodev/bpdrfy02.htm>

- 5 Biological Product Deviation Reports, FY 2003 [on the Internet]. Washington, DC: U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research (CBER); 2004 May [accessed 2008 April 12]. Available from:  
<http://www.fda.gov/cber/biodev/bpdrfy03.htm>
- 6 Biological Product Deviation Reports, FY 2004 [on the Internet]. Washington, DC: U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research (CBER); 2005 May [accessed 2008 April 12]. Available from:  
<http://www.fda.gov/cber/biodev/bpdrfy04.htm>
- 7 Biological Product Deviation Reports, FY 2005 [on the Internet]. Washington, DC: U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research (CBER); 2006 May [accessed 2008 April 12]. Available from:  
<http://www.fda.gov/cber/biodev/bpdrfy05.htm>
- 8 Biological Product Deviation Reports, FY 2006 [on the Internet]. Washington, DC: U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research (CBER); 2007 May [accessed 2008 April 12]. Available from:  
<http://www.fda.gov/cber/biodev/bpdrfy06.htm>

**Table 1. Positive Responses from Blood Donor Centers and Hospital Transfusion Centers with Blood Center**

Facility type by number of Donations	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Blood Donor Center <500	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
Hospital with Blood Center <500	4/7	4/7	5/7	5/7	7/7	3/7	2/7	4/7
Blood Donor Center >500 & <1000	0/1	1/1	1/1	1/1	1/1	1/1	0/1	1/1
Hospital with Blood Center >500 & <1000	3/7	4/7	5/7	6/7	7/7	2/7	2/7	5/7
Blood Donor Center >1000 & <5000	6/7	6/7	6/7	6/7	3/7	4/7	5/7	6/7
Hospital with Blood Center >1000&<5000	5/6	5/6	5/6	6/6	5/6	5/6	2/6	4/6
Blood Donor Center >5000	16/28	19/28	18/28	23/28	17/28	10/28	5/28	13/28
Hospital with Blood Center >5000	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1

Numbers in first column are blood donation per month.  
 Numbers in second to ninth columns are numbers of positive responses per total respondents in a particular category.

**Table 2. Positive Responses from Hospital Transfusion Centers and Hospital Transfusion Centers with Blood Center**

Facility type by number of hospital beds	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Hospital <100	2/6	2/6	3/6	5/6	4/6	2/6	2/6	4/6
Hospital with Blood Center <100	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1
Hospital >100 & <300	24/39	33/39	24/39	27/39	27/39	18/39	17/39	30/39
Hospital with Blood Center >100 & <300	1/3	2/3	3/3	2/3	1/3	0/3	2/3	2/3
Hospital >300 & <500	7/29	15/29	11/29	14/29	15/29	0/29	1/29	16/29
Hospital with Blood Center >300&<500	5/7	6/7	6/7	7/7	7/7	4/7	3/7	6/7
Hospital >500	13/27	21/27	19/27	22/27	22/27	17/27	8/27	19/27
Hospital with Blood Center >500	10/16	11/16	13/16	13/16	15/16	10/16	6/16	16/16

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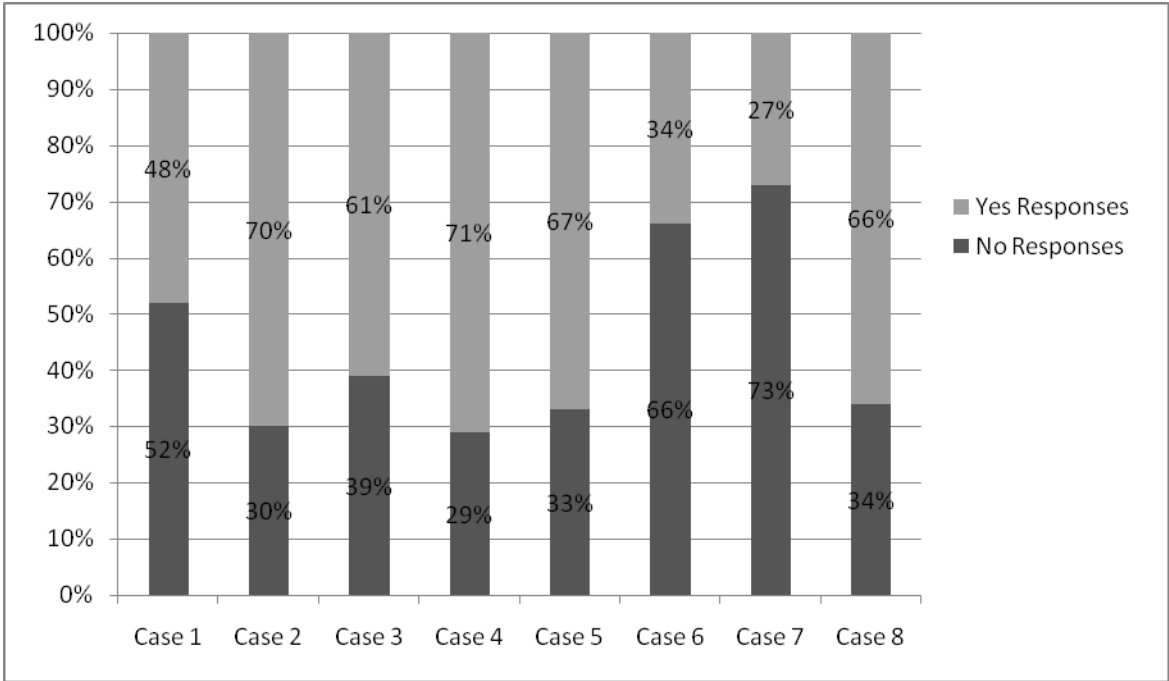
Numbers in second to ninth columns are numbers of positive responses per total respondents in a particular category.

**Table 3. Positive Responses from Respondents of Different Job Titles**

<b>Job Titles</b>	<b>Case1</b>	<b>Case2</b>	<b>Case3</b>	<b>Case4</b>	<b>Case5</b>	<b>Case6</b>	<b>Case7</b>	<b>Case8</b>
Quality Assurance Hospital Transfusion Center	4/5	5/5	3/5	5/5	4/5	4/5	4/5	4/5
Quality Assurance Hospital with Blood Center	1/1	1/1	0/1	1/1	1/1	0/1	0/1	1/1
Quality Assurance Blood Donor Center	7/9	6/9	6/9	8/9	8/9	3/9	0/9	5/9
Director/Manager Hospital Transfusion Center	8/15	10/15	8/15	12/15	13/15	8/15	4/15	5/15
Director/Manager Hospital with Blood Center	3/6	3/6	3/6	5/6	4/6	3/6	1/6	5/6
Director/Manager Blood Donor Center	4/7	6/7	7/7	7/7	3/7	4/7	2/7	6/7
Director/Manager Reference Lab	3/6	5/6	3/6	6/6	4/6	2/6	2/6	1/6
Supervisor Hospital Transfusion Center	13/31	24/31	18/31	20/31	18/31	10/31	6/31	19/31
Supervisor Hospital with Blood Center	8/8	8/8	0/8	7/8	8/8	5/8	4/8	7/8
Supervisor Blood Donor Center	0/1	1/1	0/1	0/1	0/1	0/1	0/1	1/1
Supervisor Reference Lab	2/5	3/5	4/5	4/5	3/5	2/5	1/5	3/5
Lead Technologist Hospital Transfusion Center	8/12	9/12	9/12	10/12	8/12	6/12	2/12	10/12
Lead Technologist Hospital with Blood Center	0/3	2/3	2/3	2/3	3/3	1/3	0/3	0/3
Lead Technologist Blood Donor Center	1/1	1/1	1/1	1/1	1/1	1/1	0/1	0/1
Lead Technologist Reference Lab	0/1	1/1	1/1	1/1	0/1	0/1	0/1	1/1
Bench Technologist Hospital Transfusion Center	5/33	21/33	16/33	17/33	22/33	18/33	13/33	25/33
Bench Technologist Hospital with Blood Center	4/7	5/7	7/7	6/7	6/7	4/7	6/7	6/7
Bench Technologist Blood Donor Center	1/2	2/2	2/2	1/2	1/2	0/2	2/2	2/2
Bench Technologist Reference Lab	0/2	1/2	0/2	1/2	2/2	0/2	1/2	2/2
Education	2/8	5/8	4/8	5/8	4/8	0/8	1/8	7/8
Other	3/8	2/8	4/8	5/8	3/8	1/8	1/8	5/8

Numbers in second to ninth columns are numbers of positive responses per numbers of respondents in a particular category.

**Figure 1: Percentage of Yes and No Responses**



Majority of the respondents answered cases 1, 6 and 7 incorrectly.