1

Learning Objectives

After attending this program you should be able to….

- Explain why the manufacturers of blood and blood components have to report errors and accidents in the manufacture to the FDA.
- Describe what is a deviation that must be reported to the FDA.
- Discuss why the manufacture of blood and blood components is subject to the reporting of errors and fatalities to the FDA.

2

WHERE DO I FIND THAT????

FDA's regulations and recommendations *will change*.

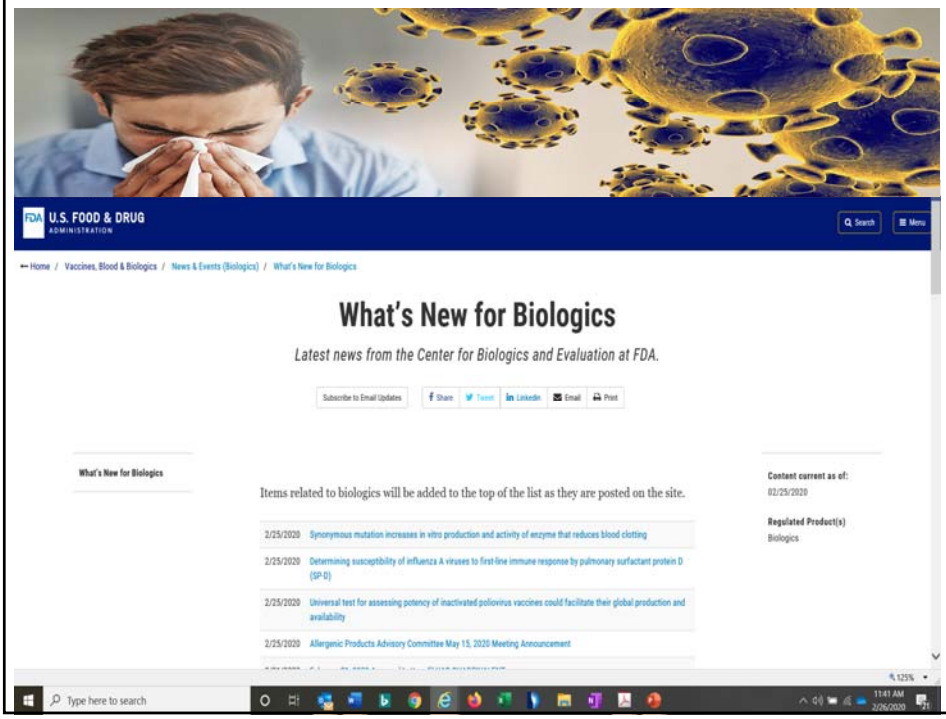
This presentation will also focus on:

- Where to find the FDA resources you need
- Tips to simplify your compliance efforts and
- AABB's supporting resources

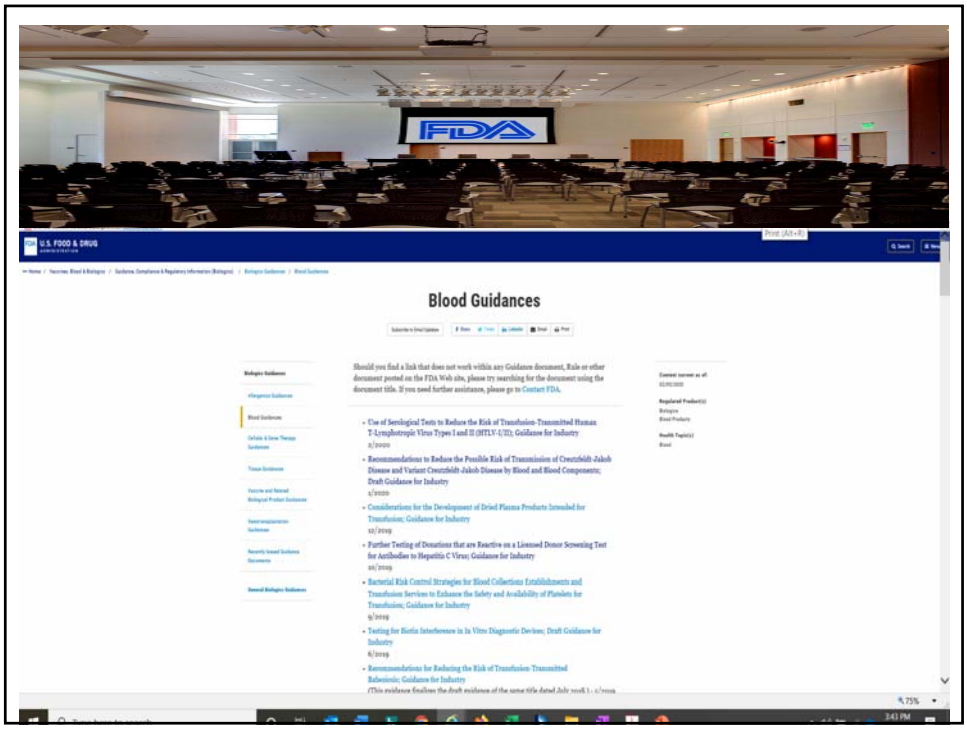
Look for a list of important links!

www.aabb.org 3

3



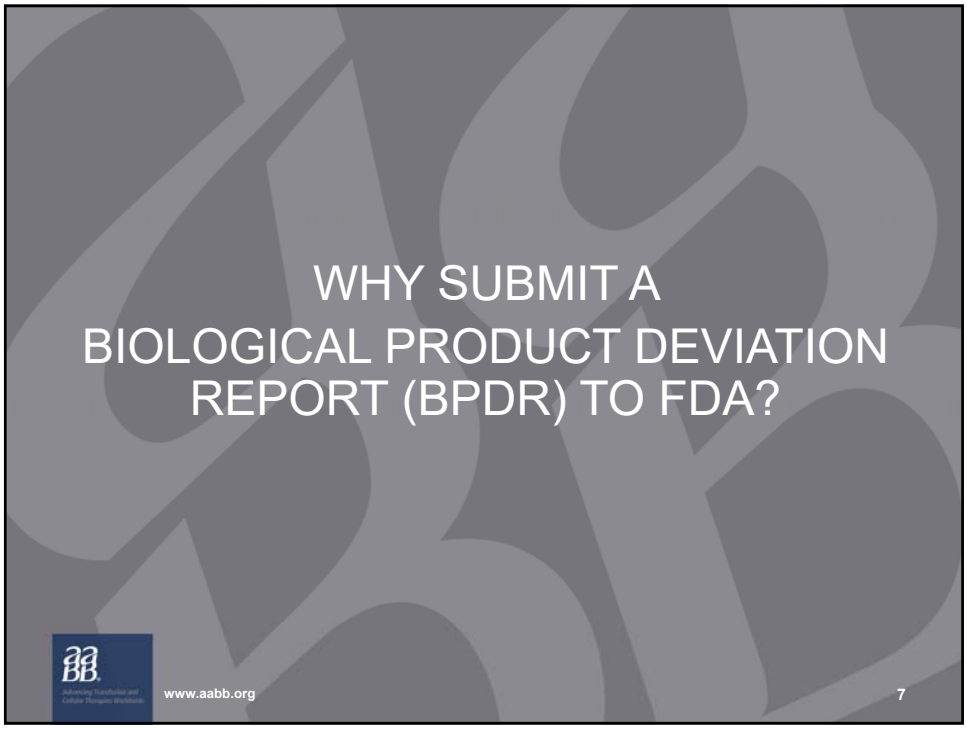
4



5

WHAT REGULATIONS?

6



7

A GOOD PLACE TO START?

FDA's Website!

- **Report a problem to CBER**
- **Biological Product Deviations**
- **Blood Guidances**

Biological Product Deviation Reporting for Blood and Plasma Establishments, October 2006 guidance:

- ✓ **Provides reporting examples**
- ✓ **Provides a flowchart on page 9 ➡ deviation decision chart**
- ✓ **Assists you with complying with current regulations**

www.aabb.org 8

8

WHY SUBMIT A BPDR?

REGULATIONS REQUIRE REPORTING

21 CFR 606.171, effective May 2001:

- Expanded reporting regs to ALL manufacturing blood/blood components:
  - ✓ Licensed blood establishments
  - ✓ Unlicensed blood establishments – including:
    - ✓ transfusion services and
    - ✓ registered blood banks
- Report only events that may affect the safety, purity, or potency of distributed products;
- Establishes a maximum reporting time frame of 45 days from the date the event was discovered.
- No longer Errors and accidents → Now Biological Product Deviations

www.aabb.org 9

9

REPORT WHAT??

Report events associated with manufacturing–including

- ✓ Testing
- ✓ Processing
- ✓ Packing
- ✓ Labeling
- ✓ Storage
- ✓ Holding
- ✓ Distribution

… which may have the **potential*** to affect the safety, purity, or potency of a distributed product as defined in 21 CFR 600.3(p), (r), and (s).

***Potential?! Are you sure?**

Yes – see bottom of page 7 of the 2006 guidance.

www.aabb.org 10

10

WHAT IS SAFE, PURE AND POTENT???

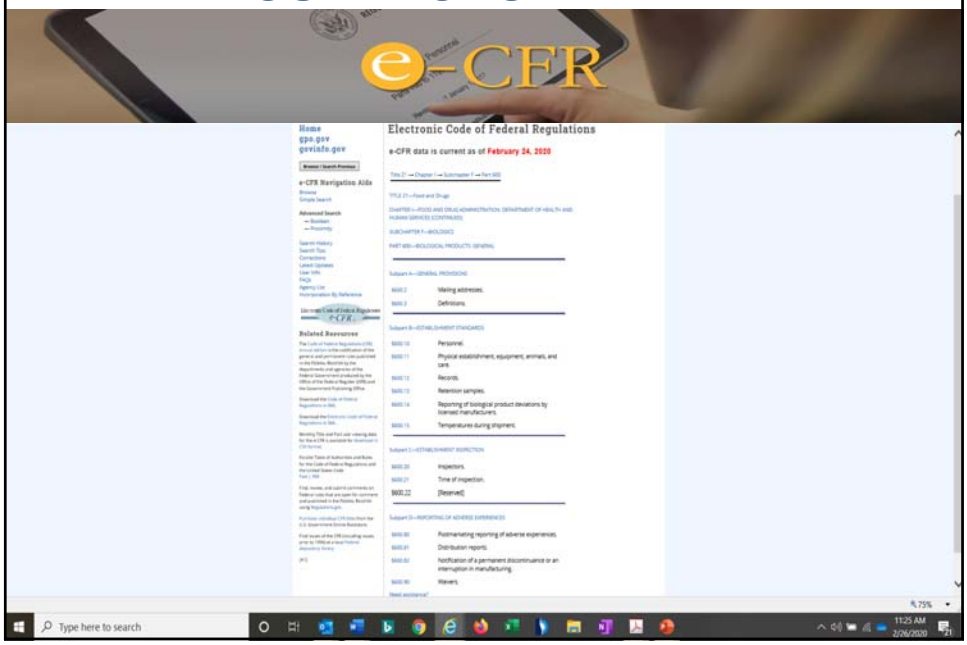
21 CFR 600.3 PROVIDES DEFINITIONS:

- p) The word *safety* means the relative freedom from harmful effect to persons affected, directly or indirectly, by a product when prudently administered, taking into consideration the character of the product in relation to the condition of the recipient at the time.
- (r) *Purity* means relative freedom from extraneous matter in the finished product, whether or not harmful to the recipient or deleterious to the product. *Purity* includes but is not limited to relative freedom from residual moisture or other volatile substances and pyrogenic substances.
- (s) The word *potency* is interpreted to mean the specific ability or capacity of the product, as indicated by appropriate laboratory tests or by adequately controlled clinical data obtained through the administration of the product in the manner intended, to effect a given result.

www.aabb.org 11

11

WHAT REGULATIONS?



12

REPORT WHAT??

EVERYTHING?

No! Just use the flowchart on page 9 of the 2006 guidance to determine if you have a reportable deviation.

Report…**only if** that event meets all of the following criteria:

(1) **Either**

(i) Represents a deviation from current good manufacturing practice, applicable regulations, applicable standards, or established specifications that may affect the safety, purity, or potency of that product;

or

(ii) Represents an unexpected or unforeseeable event that may affect the safety, purity, or potency of that product;

and

(2) Occurs in your facility or a facility under contract with you;

and

(3) Involves a distributed blood or blood component.

www.aabb.org 13

13

REPORT WHERE??

General Instructions for Completing the Biological Product Deviation Report (BPDR) - Form FDA 3486

Instructions for Using the eBPDR System

Electronic Submission of Biological Product Deviation Reports (eBPDR)

Biological Product Deviation Guidances & Rules

Biological Product Deviation Reports Annual Summaries

Links are listed at the end of this presentation

www.aabb.org 14

14

15

WHY REPORT A FATALITY TO FDA?
REGULATIONS REQUIRE REPORTING

Title 21: Food and Drugs
PART 606—CURRENT GOOD MANUFACTURING PRACTICE FOR BLOOD AND BLOOD COMPONENTS
Subpart I—Records and Reports
§606.170 Adverse reaction file.

(a) Records shall be maintained of any reports of complaints of adverse reactions regarding each unit of blood or blood product arising as a result of blood collection or transfusion. A thorough investigation of each reported adverse reaction shall be made. A written report of the investigation of adverse reactions, including conclusions and followup, shall be prepared and maintained as part of the record for that lot or unit of final product by the collecting or transfusing facility. When it is determined that the product was at fault in causing a transfusion reaction, copies of all such written reports shall be forwarded to and maintained by the manufacturer or collecting facility.

(b) When a complication of **blood collection or transfusion is confirmed to be fatal**, the Director, Office of Compliance and Biologics Quality, CBER, must be notified by telephone, facsimile, express mail, or electronically transmitted mail as soon as possible. A written report of the investigation must be submitted to the Director, Office of Compliance and Biologics Quality, CBER, by mail, facsimile, or electronically transmitted mail (for mailing address, see §600.2(a) of this chapter), within 7 days after the fatality by the collecting facility in the event of a donor reaction, or by the facility that performed the compatibility tests in the event of a transfusion reaction.

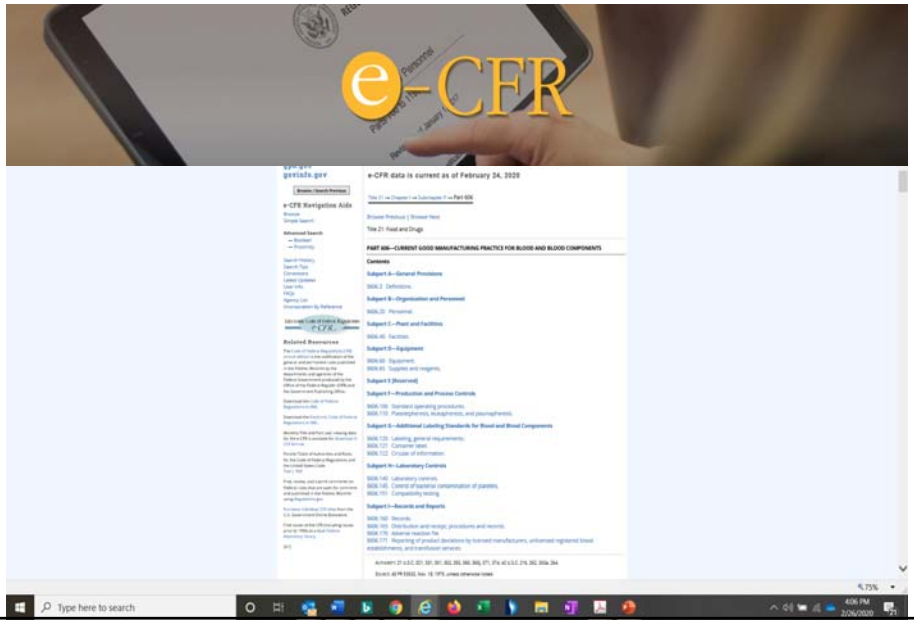
[40 FR 53532, Nov. 18, 1975, as amended at 49 FR 23833, June 8, 1984; 50 FR 35471, Aug. 30, 1985; 55 FR 11014, Mar. 26, 1990; 64 FR 45371, Aug. 19, 1999; 67 FR 9586, Mar. 4, 2002; 77 FR 18, Jan. 3, 2012; 80 FR 18092, Apr. 3, 2015]

Easy to find in electronic CFR

www.aabb.org 16

16

WHAT REGULATIONS?



17

WHERE TO REPORT?

1- TRANSFUSION/DONATION FATALITIES webpage

To report a fatality during regular business hours, call or email our fatality program contact within the Division of Inspections and Surveillance. Outside of regular business hours, you may submit your initial notification by leaving a voice message, or sending an email or facsimile.

Voice-mail: 240-402-9160 / E-mail: fatalities2@fda.hhs.gov / Fax: 301-827-0333

Express mail: See address below

We will contact you as soon as possible to obtain more detailed information. This does not replace the 7-day written report regarding the fatality and all related information that we require pursuant to 21 CFR 606.170(b).

Send your 7-day written report to:

U.S. Food and Drug Administration
Center for Biologics Evaluation and Research Document Control Center
10903 New Hampshire Avenue
WO71, G112
Silver Spring, MD 20993-0002

THIS IS THE CURRENT CONTACT INFORMATION

www.aabb.org 18

18

WHERE TO REPORT?

2- **Blood Guidances webpage**

Guidance for Industry: Notifying FDA of Fatalities Related to Blood Collection or Transfusion, 9/22/2003

HAS OLD ADDRESS

USE ADDRESS ON WEBSITE OR IN CFR:

§600.2 Mailing addresses.

(a) …Food and Drug Administration, Center for Biologics Evaluation and Research, Document Control Center, 10903 New Hampshire Ave., Bldg. 71, Rm. G112, Silver Spring, MD 20993-0002. Examples of such submissions include: Biologics license applications (BLAs) and their amendments and supplements, biological product deviation reports, fatality reports, and other correspondence. Biological products samples must not be sent to this address but must be sent to the address in paragraph (c) of this section.

www.aabb.org 19

19

REPORTING PROCESS??

1-**TRANSFUSION/DONATION FATALITIES:**

- 21CFR 606.170(b) applies
- Notify FDA/CBER/ Office of Compliance and Biologics Quality (OCBQ)
- ASAP after confirming a fatal complication:
  - Collecting facility reports donor fatalities
  - Compatibility testing facility reports transfusion recipient fatalities
- Reporting facility must submit:
  - a written report of the investigation
  - within 7 days after the fatality.
- 21 CFR 640.73 applies to Source Plasma donor fatality

www.aabb.org 20

20

WHERE IS MORE INFORMATION??

2-**Blood Guidances webpage**

Guidance for Industry: Notifying FDA of Fatalities Related to Blood Collection or Transfusion, 9/22/2003

INITIAL REPORT:

- Age and sex of the deceased.
- Date, time, and cause or suspected cause of death (briefly describe what happened).
- If an autopsy was or will be performed.
- Name and address of facility where the fatality occurred if different from your facility.

Plus information related to FATALITY TYPE:

Patient, Donor, Therapeutic Apheresis or Phlebotomies

www.aabb.org 21

21

WHERE IS MORE INFORMATION??
Transfusion/Donation Fatalities

- FDA will contact you as soon as possible to obtain more detailed information.
- This does not replace the **7-day written report** regarding the fatality and all related information that FDA requires pursuant to 21 CFR 606.170(b).

www.aabb.org 22

22

23

BIG FAILURES ARE OBVIOUS!

- **Distribution of a red cell with the wrong ABO type!**
- **Distribution of a component before infectious disease testing is completed!**
- **Component is out of temperature after it was accidently left on the counter overnight!**

24

BUT ARE THEY REPORTABLE?

- **Distribution of a red cell with the wrong ABO type- YES**
- **Distribution of a component before infectious disease testing is completed - YES**
- **Component is out of temperature after it was accidently left on the counter overnight - NO**

It was not distributed

– and discard the unit.

www.aabb.org 25

25

REPORT THIS?

- An double apheresis platelet collection has labels of Container A and B for the two components from that same donation.
- Container A and B are intended for the same patient.
- An error is identified. Labels are switched:

Container A has the label “Container B” and Container B has the label “Container A.”

IS this a reportable deviation?

www.aabb.org 26

26

NO. Why?

Both products are intended for the same patient and this event does NOT have the **potential** to affect the safety, purity, or potency of a distributed product.

www.aabb.org 27

27

REPORT THIS?

- You shipped a product to hospital A collected from a donor who stopped using IV drugs 6 months earlier.
- You notified hospital B within 5 days per your SOP.
- You discovered the notification error and then properly notified the supervisor at hospital A immediately, per SOP, and within 8 days.

What are the reportable events?

www.aabb.org 28

28

WHY?

REPORT?

You collected from a donor who stopped using IV drugs 6 months ago and should have been deferred for HIV risk.

- YES -This failure may effect the safety of the product due to the HIV risk.

You notified hospital A immediately upon discovering the notification error but failed to notify within 5 days as required by your SOP. NO

- You are required to report the improper release of the product
- But not the notification timeline failure in SOPs (which are not required by FDA.)

However, FDA would expect you to also include in the report that consignee notification was not in accordance with your SOP.

The 2006 guidance has several examples to help you!

www.aabb.org 29

29

REPORT THIS?

- An apheresis red cell collection with concurrent plasma collection is completed on the donor's 5th visit to the center.
- At the end of the collection, the donor mentions that he is "motivated to donate based on his own experience with cancer" and "wants to help others."
- The collection is quarantined while the donor records are reviewed.
- There is no record that the donor shared the information about his cancer at the time of prior donations – which were plasma donations.

IS this a reportable deviation based on FDA's requirements?

www.aabb.org 30

30

NO. Why?

In 2005 FDA changed the donor eligibility criteria, removing the donor deferral for cancer.

FDA does not require a BPDR for a collection from a donor with cancer. Period

You do have to follow you own SOP and policy for evaluating the eligibility of a donor following a cancer diagnosis and address this deferral error internally.

31

What should I know about the numbering my BPDR?

FDA instructs facilities to set and follow a procedure to assign a tracking number for each BPDR.

- FDA does not dictate the numbering process.
- Your facility will determine how to number the BPDR and how to use the numbering system.

FDA does require a unique number for each BPDR from your facility – even months later you cannot reuse numbers.

IF you reuse a tracking number, the FDA's system will reject your report.

32

What else should I know about reporting?

Some BPDRs provide a great deal of information but omit key details necessary to evaluate deviation, such as details impacting safety, purity and potency.

IF you report a deviation related to quality control testing:

- Provide a description of the event and the investigation, including the disposition of the product.
- ***Don't forget*** *to identify exactly what type of QC testing was in error.*

www.aabb.org 33

33

What about codes – do they change?

FDA updates BPD codes and issues a document every October to identify the specific changes.

Recall the cancer deferral!

Adjust your reporting accordingly.

Watch for **AABB's Weekly Report** every Friday – we will alert you to changes related to BPD codes and reporting.

Remember the What's New for Biologics webpage!

www.aabb.org 34

34

What is available online?

The following links will assist you:

General Instructions for Completing the Biological Product Deviation Report (BPDR) - Form FDA 3486
https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/general-instructions-completing-biological-product-deviation-report-bpdr-form-fda-3486

Instructions for Using the eBPDR System
https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/instructions-using-ebpdr-system

Electronic Submission of Biological Product Deviation Reports (eBPDR)
https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/electronic-submission-biological-product-deviation-reports-ebpdr

Biological Product Deviation Guidances & Rules
https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/biological-product-deviation-guidances-rules

Biological Product Deviation Reports Annual Summaries
https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/biological-product-deviation-reports-annual-summaries

www.aabb.org 35

35

Important links:

What's New for Biologics
https://www.fda.gov/vaccines-blood-biologics/news-events-biologics/whats-new-biologics?utm_campaign=What%27sNew2019-04-24&utm_medium=email&utm_source=Eloqua

Blood Guidances
https://www.fda.gov/vaccines-blood-biologics/biologics-guidances/blood-guidances

Electronic Code of Federal Regulations
https://www.ecfr.gov/cgi-bin/text-idx?SID=7a644ec9ccf72881518e4a1a64ffb2d0&mc=true&tpl=/ecfrbrowse/Title21/21cfrv7_02.tpl#0

www.aabb.org 36

36

More Important Links:

Report a problem to CBER

https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/report-problem-center-biologics-evaluation-research

Biological Product Deviations

https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/biological-product-deviations

Transfusion/Donation Fatalities

https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/transfusiondonation-fatalities

www.aabb.org 37

37

More Important Links:

Biological Product Deviation Reporting for Blood and Plasma Establishments, October 2006 guidance:

https://www.fda.gov/media/70694/download

Guidance for Industry: Notifying FDA of Fatalities Related to Blood Collection or Transfusion, 9/22/2003

https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/UCM062897.pdf

AABB's Regulatory Affairs Webpage

http://www.aabb.org/advocacy/regulatorygovernment/Pages/default.aspx

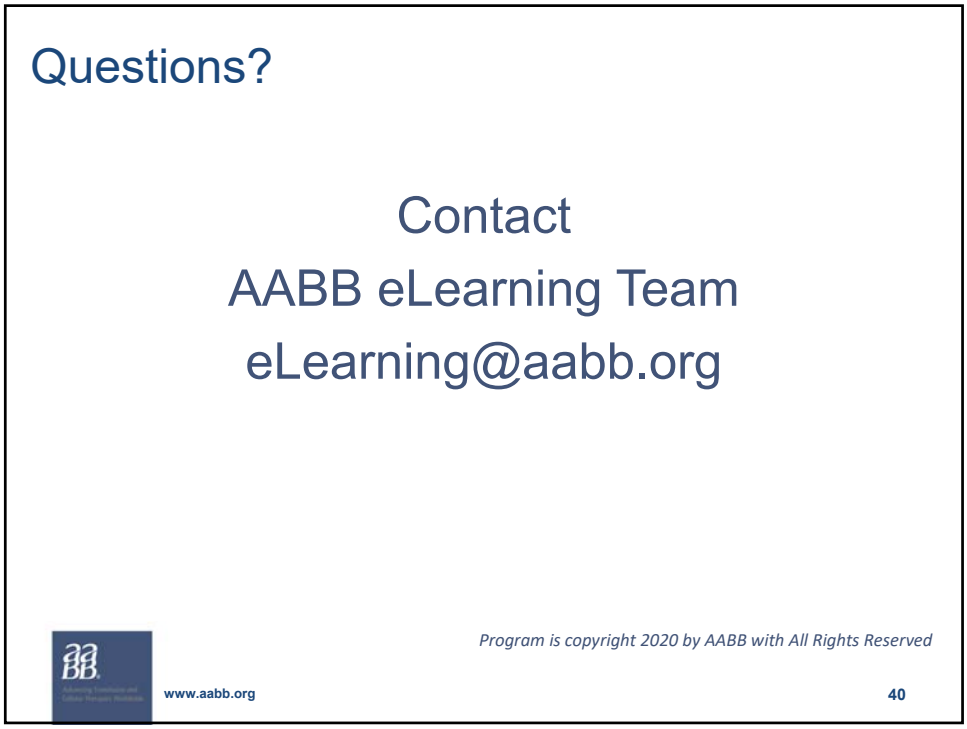
Regulatory Updates for AABB members – Search for updates on any topic dating back to 2017

http://www.aabb.org/advocacy/regulatorygovernment/Docs/regulatory-updates.pdf

www.aabb.org 38

38

39



40