Adverse Event Reporting for 351 products

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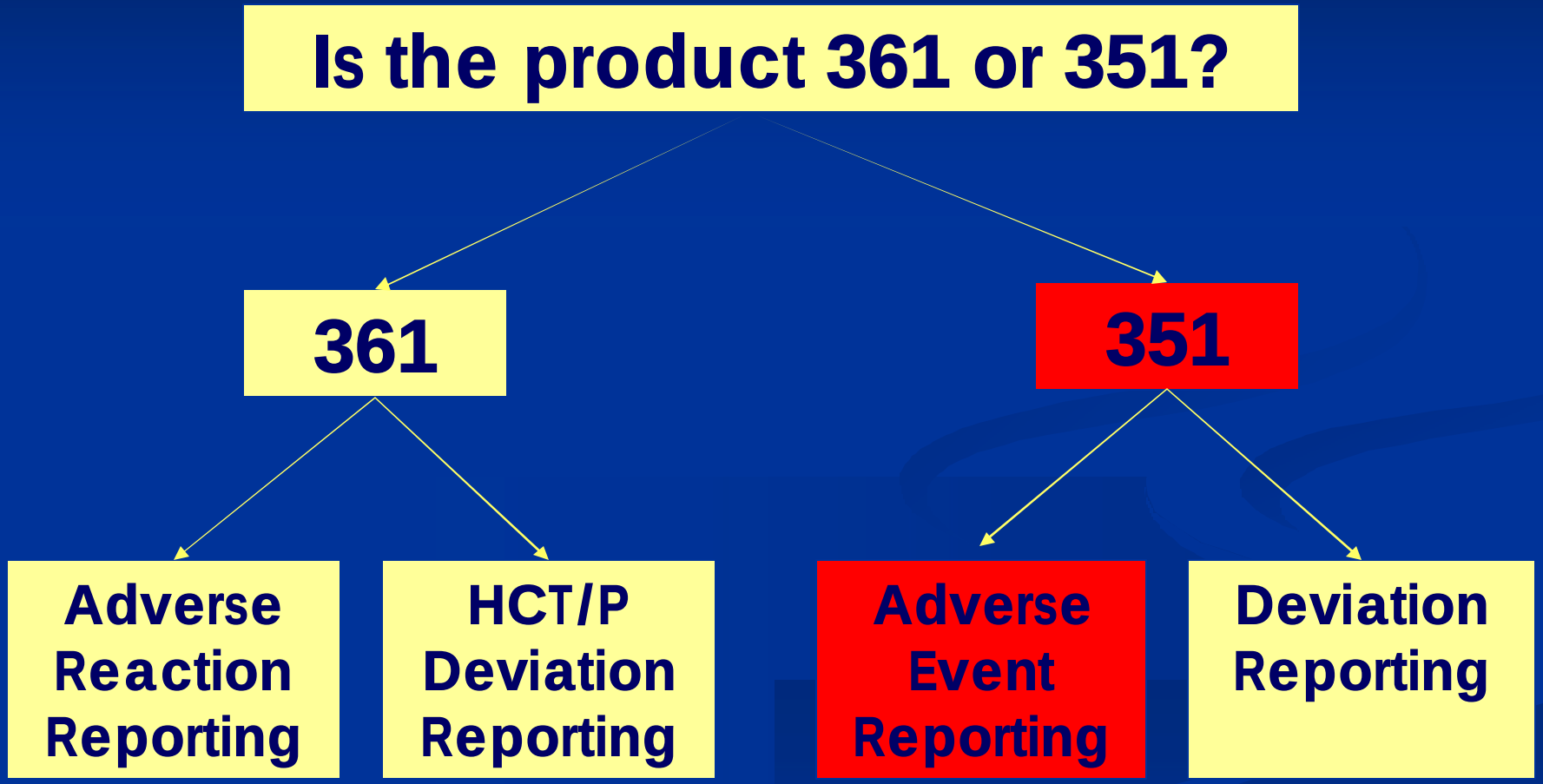
PACT Web Seminar

February 22, 2007

DECISION ALGORITHM FOR REPORTING



361
21 CFR 1271.10

1. Minimally manipulated
2. Intended for homologous use
3. Does not involve the combination…with a drug or a device, except for a sterilizing, preserving, or storage agent, if the agent does not raise new clinical safety concerns
4. Does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function OR

4a. Has a systemic effect… and is for Autologous Use

4b. Has a systemic effect… and is for Allogeneic use in a first-degree or second-degree blood relative

4c. Has a systemic effect… and is for reproductive use

351
21 CFR1271.20

- If you are an establishment that manufactures an HCT/P that does not meet the criteria set out in 1271.10(a), and you do not qualify for any of the exemptions in 1271.15, your HCT/P will be regulated as a drug, device, and/or biological product under the act and/or section 351 of the PHS Act, and applicable regulations in title 21, Chapter I.
- Applicable regulations include, but are not limited to 207.20(f), 210.1(c),210.2, 211.1(b),807.20(d), 820.1(a)

361

- 21 CFR 1271 A,B,C,D,E,F
- Compliance program 7341.002 Inspection of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)

351

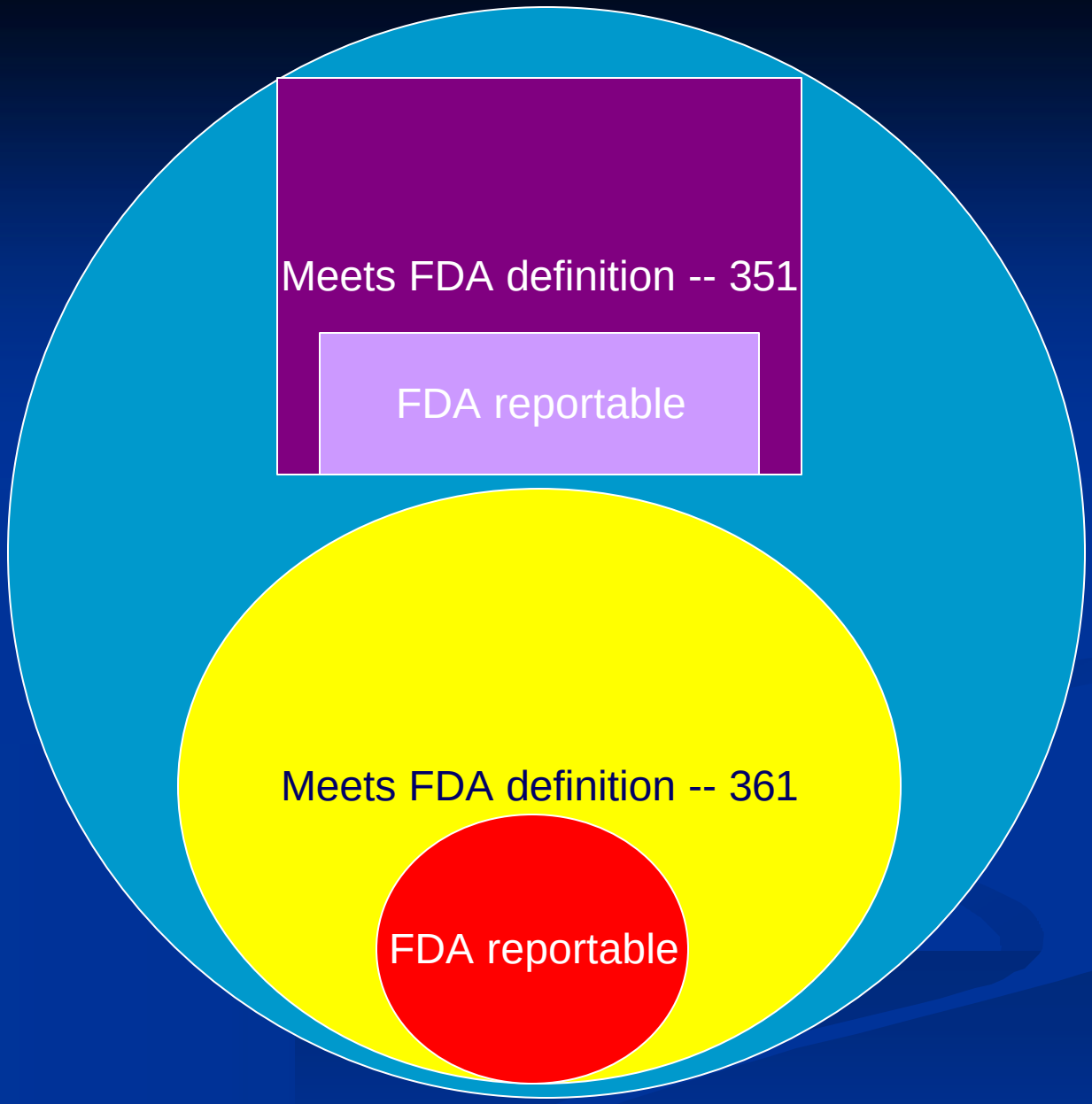
- 21 CFR 1271 C,D
- 21 CFR 207.20 (f)
- 21 CFR 210-211
- 21 CFR 807.20 (d)
- 21 CFR 820.1 (a)
- Compliance program 7345.848 Inspection of Biological Drug Products
- IND – 21 CFR 312

Adverse Reactions

	361	351 pre-licensure	351 post-licensure
Complaint file	CGTP 21 CFR 1271.320	CGMP 21 CFR 211.198	CGMP 21 CFR 211.198
Adverse reaction reporting	CGTP 21 CFR 1271.350(a)	IND Safety Reports & Annual Reports 21 CFR 312.32-.33	Biological Products Post Marketing Reports 21 CFR 600.80
Deviation reporting	CGTP 21 CFR 1271.350(b)	IND CGMP 21 CFR 211.100(b)	Biological Products Deviation Reporting 21 CFR 600.14

All adverse events →

Facility processes and procedures are written for compliance with standards and regs.



21 CFR 312 IND Safety Reports

- (a) Definitions
- (b) Review of safety information
- (c) IND safety reports
  - (1) Written reports
  - (2) Telephone and facsimile transmission
- (d) Follow up
- (e) Disclaimer

351 – 21 CFR 312.32(a) not a single definition

- Life threatening adverse [drug] experience
- Serious adverse [drug] experience
- Unexpected adverse [drug] experience

351 reporting
21 CFR 312 (c)

- Phone or FAX--- unexpected fatal or life threatening experience
  - 7 calendar days
  - Phone or fax; written follow up
  - IND sponsor
- IND Safety Report – serious and unexpected
  - 15 calendar days
  - MedWatch 3500A
  - IND sponsor

Example – Patient A

- If autologous culture expanded T cells
- During manufacture, extended 3 days, use alternative culture media formulation
- Single container of 75 mL.
- Recipient experienced symptoms of fluid overload --- patient had travel difficulties; arrived later than expected; prep regimen caused extreme nausea; had food poisoning; became dehydrated and then was slightly overhydrated.

Example – Patient A

- 351 – more than minimally manipulated.
- Adverse experience --- serious and unexpected
- During investigation --- not labeled "NOT EVALUATED FOR INFECTIOUS SUBSTANCES" (lab practice: no history screening; TTD testing only)
- Meets FDA's definition of adverse experience – not expected. Reportable within 15 days.
- Meets FDA's definition of deviation –
  - Label - reportable because subpart C is not SUBSUMED under cGTP
  - Manufacturing - reportable in IND annual report

    (cGMP – any deviation from the written procedures shall be recorded and justified)

THE END