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REGULATORY AFFAIRS PROFESSIONALS SOCIETY

Preparing for the RAC Exam - Module 3 Marketing/Post Approval, Interfacing

Wednesday, 22 March 2006

12:00 pm–1:30 pm Eastern
11:00 am–12:30 pm Central
10:00 am–11:30 am Mountain
9:00 am–10:30 am Pacific

Upcoming RAPS Programs:

Horizons 2006 RAPS Conference and Exhibition: Innovation to Regulation
29 – 31 March 2006 • San Diego, CA, US

For a complete calendar of events, please visit the RAPS website at www.raps.org

Module 3 Agenda

Premarketing/Regulatory Review and Manufacturing/Quality System

- Practice questions
  - Discuss best answer and rationale
- Content review
- Opportunity to ask questions
  - Via email
  - Via phone line
- Additional references and definitions for you to study later

Audience Poll Question 1

We'd like to know who is in our audience today. Please indicate whether you currently work in Drugs, Biologics or Devices.

1 → Drugs

2 → Biologics

3 → Devices

RAC Test Format

Types of multiple choice questions:

- One correct answer and 3 incorrect responses
- Questions asking for the exception
- Questions with seemingly all good choices
  - ✓Look for key word (eg, IND, IDE, NDA, PMA) to determine context
  - ✓Look for key words like first, except, not
  - ✓Don't over think, go with **best answer**

Recertification

- RAC program requires recertification every 3 years
  - 60 points in 3 year period
  - 40 of 60 points directly related to regulatory affairs
- Recertification is based on participation
  - Attend educational programs
  - Speak at RA education programs
  - Write articles for Regulatory Affairs Focus and professional journals
  - Serve as an officer, director or committee member of a RA professional association
  - Write questions for RAC exam

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Practice Question 1

As the sponsor of an approved drug product, you receive information that your distributed product is exhibiting unexpected properties suggesting chemical, physical, or bacteriological change. You are required to report this information as follows:

A) Within 7 calendar days to the local FDA district office
B) Within 3 working days to the local FDA district office
C) In the annual report
D) Within 15 calendar days to reviewing FDA office

NDA Field Alert Report

Within 3 working days of receipt, applicant must submit to the local FDA district office:

- Information concerning any incident that causes the drug or its labeling to be mistaken for or applied to another article
- Information concerning any incident of chemical, physical, bacteriological change in distributed drug product or any failure of one or more distributed batches to meet established specifications

21 CFR 314.81 (1)

Practice Question 2

The following are objectives of a pre-approval inspection except:

A) Assess cGMP compliance

B) Scientific review of data to assess safety and efficacy

C) Collect samples for analysis by FDA

D) Verify accuracy of data submitted in an application

Pre-approval Inspections

CDER/CBER

- Review data submitted to the agency as part of pre-market new drug applications and generic applications
- Determine whether the specifications in the application meet the agency's standards

Local FDA district office

- Assures GMP compliance via on-site inspections
- Verify authenticity and accuracy of data contained within the applications
- Report on any other data which may impact on the firm's ability to manufacture the product in compliance with GMPs
- May take samples of product during a pre-approval inspection

Reference: Compliance Program Guidance Manual 7346.832

Pre-approval Inspections, Devices

- Office of Compliance may request inspection when making the determination of the firm's ability to design, manufacture or process the device
  - Assessment of the firm's capability to design and manufacture the device as claimed in the PMA
  - Confirm Quality System is in compliance with 21 CFR 820, Quality System Regulation
  - Has firm established a formal QS program?
  - Has firm assured that the approved design is properly translated into specifications via process validation?

Medical Device Premarket Approval Inspections, C.P. 7383.001

Inspections of Medical Device Manufacturers, C.P. 7382.845.

Practice Question 3

Which of the following is not an example of misbranding?

A) An incorrect lot number on the label

B) A drug product without a manufacturer, packer or distributor on the label

C) Font size of established name is 25% of the font size of the trade name

D) Lack of NDC on label

Labeling, Misbranding, NDC Code

- 21 CFR 201.17: Expiration date may appear on carton for single unit packaging
- 21 CFR 201.10: (g) if label bears proprietary name…, (h) requires lot number, manufacturer, distributor or packer, and established name, if exists
- FD&C Act Section 502 (n) font size of established name must be at least half the size of the trade name
- FD&C Act Section 502 (c) prominence of statements
- 21 CFR 201.18 incorrect lot number may be regarded as causing drug to be misbranded
- National Drug Code number (NDC)
  - ✓ **21 CFR 201.2: NDC number requested but not required**
  - ✓ The Drug Listing Act of 1972, amending the FD & C Act, became effective February 1, 1973
  - ✓ Purpose is to provide a current list of all drugs manufactured, prepared, propagated, compounded, or processed by a drug establishment registered under the FD & C Act
  - ✓ Requires submission of information on commercially marketed drugs and is used in the enforcement of the FD & C Act

Practice Question 4

Which of the following examples do not meet the definition of adulteration?

A) A bottle of aspirin (for public retail sale) that is not packaged in tamper-resistant packaging

B) Batch record was accidentally destroyed

C) Incorrect lot number on the label

D) A drug recognized in the USP/NF that does not meet all compendium standards

Adulteration

- 21 CFR 211.132: An OTC product (with few exceptions) for retail sale that is not packaged in tamper resistant packaging is adulterated
- 21 CFR 210.1(b) Failure to comply with any regulation set forth… shall render drug adulterated
- 21 CFR 201.18: Incorrect lot number may be regarded as causing drug to be misbranded
- US Pharmacopeia/National Formulary (USP/NF):
  - Standards, specifications, requirements related to drugs and other articles used in medical and pharmacy practice
  - A drug recognized in USP/NF must meet all compendium standards or is considered adulterated and/or misbranded

Practice Question 5

Which of the following is typically included in a reminder advertisement?

A) Brand and generic names

B) Indication(s)

C) Dose information

D) Statement of efficacy

Reminder Advertisements

- **May contain**
  - Brand and generic names of the product
  - Formulation (eg, tablet, capsule, syrup)
- **Cannot contain**
  - Indication(s)
  - Dosage recommendation
  - Any representation or suggestion relating to the product
- **Cannot use reminder ad if have black box warning in prescribing information**

Reference 21 CFR 202.1

Practice Question 6

Which of the following is a true statement regarding advertising/promotion of prescription drug products?

A) All promotional materials must be approved by FDA prior to use

B) All promotional materials must be approved by the Federal Trade Commission

C) Advertising directing the audience to “see your doctor” for certain medical conditions or diseases” is not regulated by FDA

D) Advertising is not allowed for drugs approved under accelerated approval/Subpart H

Direct to Consumer Advertising

FDA regulates product labeling and prescription drug and restricted device advertising

- Product-claim ads: Make a statement of drug benefit which must be balanced with risks and limitations, ie, “fair balance”.
- Reminder ads:
  - Disclose name of product, may provide dosage form (tablet, capsule, syrup) but may not state indication or make claims
  - Not allowed for products with “black box” warnings

Advertising

- Advertising not regulated by FDA:
  - Help-seeking ads discuss disease/condition and advise audience to “see doctor” (No drug product is mentioned or implied)
- Federal Trade Commission primarily regulates over-the-counter drug and non-restrictive device advertising

http://www.ftc.gov/

Practice Question 7

Which of the following convey “intended use” for a drug product?

A) Prescribing information

B) Verbal statements by sponsor or sponsor’s representative about a product’s use at a trade show

C) Printed promotional materials

D) All of the above

Practice Question 8

You, a regulatory affairs professional, receive a warning letter from DDMAC pertaining to DTC advertising. The first thing you do is:

A) Develop a corrective advertisement

B) Write a response letter to DDMAC

C) Cease dissemination of violative materials

D) Review the marketing application

Response to Warning Letter

- Promptly cease dissemination of violative materials, including materials containing similar claims
- Cross functional response team may include: Regulatory Affairs, Labeling, Medical, Legal, Marketing, Commercial…
- Develop a response to Division of Drug Marketing, Advertising and Communications (DDMAC)
  - ✓ Within timeframe requested in warning letter
  - ✓ Likely will entail reviewing prescribing information and/or marketing application
  - ✓ Describe intent to comply with request
  - ✓ List all promotional materials containing violative claims
  - ✓ Plan of action going forward
  - ✓ Corrective ads
    - Dear Doctor… to alert prescribers to FDA's findings
    - Corrective ad acknowledging FDA's concerns and bringing ad into compliance

Practice Question 9

A label is defined as that which is affixed to the:

A) Carton

B) Shrink Wrapper

C) Shipping Package

D) Immediate Container

FD&C Act Section 201(k): Definition of Label

- *A "label" is a display of written, printed or graphic matter upon the immediate container of any article.[*section 201(k).]

- *"Labeling" includes all labels and other written, printed or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article.* [section 201(m).]

Additional References:

21 CFR 201 Labeling

21 CFR 801 Labeling

Practice Question 10

You, a regulatory affairs professional, are in a situation where an administrative or procedural dispute has occurred between the sponsor and the FDA reviewing division. In attempt to resolve the dispute, on what level would you initially try to resolve the dispute?

A) Review Division

B) Agency Ombudsman

C) Office Director

D) FDA Office of Regulatory Affairs

Dispute Resolution

- Procedural and administrative disputes: first attempt to resolve procedural and administrative disputes within the reviewing division, starting with the CSO
- Scientific dispute: start with supervisory level of individual who made decision and increase levels as necessary
- Office of the Ombudsman: A resource in cases where sponsor is experiencing problems with the regulatory process or with the application of FDA policies or procedures

Guidance: Formal Dispute Resolution Appeals above Division Level

21 CFR 314.103

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Practice Question 11

The FDA wants to develop a new guidance document on electronic submissions. Initially, the best way for FDA to obtain industry input for the preparation of a first draft is to

A) Schedule an advisory panel meeting

B) Announce a public hearing on the issue

C) Conduct talks with a number of trade associations

D) Issue a Federal Register notice of intent to promulgate a guidance document

Industry Organizations

- Pharmaceutical Research and Manufacturers of America (PhRMA)
  - ✓ PhRMA companies are devoted to discovering and developing new medicines that will enable patients to live longer, healthier and more productive lives
  - ✓ Mission: to conduct effective advocacy for public policies that encourage discovery of important new medicines for patients by pharmaceutical/biotechnology research companies

  http://www.phrma.org/
- Biotechnology Industry Organization (BIO)
  - ✓ Biotechnology researchers expand the boundaries of science to benefit mankind by providing better healthcare, enhanced agriculture, and a cleaner and safer environment
  - ✓ Mission: to be the champion of biotechnology and the advocate for its member organizations –both large and small

  http://www.bio.org/

Practice Question 12

Which of the following best describes Advisory Committee meetings?

A) Advisory Committee meetings are always open to the public

B) Advisory Committee meetings only occur in the product approval stage

C) FDA must follow resulting recommendations of Advisory Committee

D) Advisory Committee meetings are a way for FDA to consult with outside experts

Advisory Committees

- Qualifications
  - Advisory committees consist of individuals possessing recognized expertise and judgment in a specific field
  - Ability to evaluate information objectively and to interpret its significance under various, often controversial, circumstances
- Membership
  - Core members appointed by the Commissioner and serve for the duration of the committee or until their terms of appointment expire, they resign, or they are removed
  - Members are subject to conflict of interest laws
  - Core members are usually voting members (exception due to conflict of interest)
- FDA poses specific questions to Advisory Committees
- Final decisions are made by FDA

Guidance for Industry: Advisory Committees, Implementing Section 120 of FDAMA

Practice Question 13

ADEs that do not meet 15-day reporting requirements should be reported by the applicant:

A) Annually, unless alternate reporting arrangement is required by FDA

B) Semi-annually, unless alternate reporting arrangement is required by FDA

C) Quarterly for 3 years after application is approved, annually thereafter, unless alternate reporting arrangement is required by FDA

D) Quarterly for 1st year after application is approved, annually thereafter, unless alternate reporting arrangement is required by FDA

Postmarketing reporting of ADEs

Adverse Drug Experience (ADE):

- Any adverse event associated with the use of a drug in humans, whether or not considered drug related, including event related to accidental or intentional overdose, drug abuse, drug withdrawal, failure of expected pharmacological action
- Report serious and unexpected ADEs as 15-day alert reports (initial and follow-up):
  - Serious ADE: any ADE at any dose that results in death, life-threatening experience, inpatient hospitalization, prolongation of hospitalization, significant disability/incapacity, OR congenital anomaly/birth defect
  - Unexpected ADE: any ADE that is not listed in current labeling for the drug product. Includes events that may be symptomatically or pathophysiologically related to a labeled event but differ because of greater severity or specificity
- Report all other ADEs quarterly for 3 years from date of approval of the application then annually thereafter. FDA may reestablish quarterly reporting, eg, after approval of a supplement, or alternate reporting requirement

21 CFR 314.80

Practice Question 14

As a regulatory affairs professional, you are provided evidence that your firm's product has been the subject of criminal tampering post-distribution which has resulted in 2 known deaths. You assemble the appropriate internal team in order to implement a

A) Class I Recall

B) Class II Recall

C) Class III Recall

D) Market Withdrawal

Recalls and Market Withdrawal

- **Recall:** Action taken by a firm to remove a product from the market. Recalls may be conducted on a firm's own initiative, by FDA request, or by FDA order under statutory authority. Product is viewed as being in violation of the law and FDA would initiate legal action such as seizure.
  - Class I recall: reasonable probability that the use of or exposure to a violative product will cause serious adverse health consequences or death.
  - Class II recall: use of or exposure to a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote
  - Class III recall: use of or exposure to a violative product is not likely to cause adverse health consequences
- **Market withdrawal**: Firm's removal of a distributed product that involves no violation of the law by the manufacturer. Examples: A product removed from the market due to tampering, without evidence of manufacturing or distribution problems or removal of product for purposes of stock rotation. Would not be subject to legal action by FDA.
- **Field correction**: Repair, modification, adjustment, relabeling, of a product without physically removing it to another location

21 CFR 7

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Practice Question 15

Which of the following examples best represents “fair balance”?

A) Risks and benefits are presented in comparable prominence, readability

B) A reminder ad

C) Established name appears next to brand name in type at least 50% of brand name

D) Advertising directed to physicians and consumers

Fair Balance

Fair Balance

- ✓ Between information relating to side effects, contraindications, warnings, and precautions ***vs***.
- ✓ Information related to Effectiveness
- ✓ Contextual Fair Balance: Comparable scope, depth and detail 21 CFR 202.1(e)(5)
- ✓ Physical Fair Balance: Reasonably comparable prominence and readability, accounting for typography, layout, white space, etc. 21 CFR 202.1(e)(7)(viii)

Practice Question 16

Which of the following is not found in the Orange Book?

A) Patent information for approved drug products

B) Exclusivity information for approved drug products

C) Information related to therapeutic equivalence for approved drug products

D) Drug products approved on the basis of safety

Orange Book

- ***Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book)***
  - Drug products approved on the basis of safety and effectiveness by FDA under the FD&C Act
  - Drugs on the market approved only on the basis of safety or pre-1938 drugs are not included in the Orange Book
- ***Therapeutic Equivalents***
  - Drug products that are pharmaceutical equivalents AND
  - Have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling

http://www.fda.gov/cder/ob/default.htm

Practice Question 17

Which of the following is typically included in a reminder advertisement?

A) Brand and generic names

B) Indication(s)

C) Dose information

D) Statement of efficacy

Reminder Advertisements

- **May contain**
  - Brand and generic names of the product
  - Formulation (eg, tablet, capsule, syrup)
- **Cannot contain**
  - Indication(s)
  - Dosage recommendation
  - Any representation or suggestion relating to the product
- **Cannot use reminder ad if have black box warning in prescribing information**

Reference 21 CFR 202.1

Practice Question 18

Which of the following is an example of a "Changes Being Effected" supplement?

A) Add/strengthen a contraindication, warning

B) Change in specifications to comply with an official compendium

C) Editorial change

D) Deletion or reduction of an ingredient to affect color

Practice Question 19

For a marketed product, which of the following is an example of a “Changes Being Effected-30 days” supplement?

A) Deletion or reduction of an ingredient to affect color

B) New analytical method

C) Addition of an alternate analytical method

D) Change in site of testing from one facility to another

Practice Question 20

For a marketed product, which of the following is not an example of a “prior approval” supplement?

A) Manufacturing process change

B) Change impacting product sterility

C) Add a precaution to label

D) Delete specification for drug substance

Post approval Supplements/Changes

- What is potential for adverse effect on identity, strength, quality, purity or potency? You must decide before distributing product made with the change.
  - ✓ Major = prior approval supplement
  - ✓ Moderate = CBE or CBE-30
  - ✓ Minor = annual report
- Annual Report
  - ✓ Delete/reduce ingredient to affect color
  - ✓ Changes to comply with official compendium
  - ✓ Editorial change to label
- Changes being effected
  - ✓ Add/strengthen contraindication, warning, precaution, adverse reaction
  - ✓ Instruction about dose intended to increase safe use of product
  - ✓ Delete false or misleading, or unsupported indications, or claims of effectiveness
- Prior approval
  - ✓ New analytical procedure
  - ✓ Formulation changes
  - ✓ New manufacturing site with no or unsatisfactory GMP inspection
  - ✓ Change in manufacturing process

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Practice Question 21

Which of the following is true regarding ICH guidelines?

A) ICH guidelines represent the joint opinions of regulatory agencies in US, Europe and Japan.

B) ICH guidelines represent the joint opinions of the pharmaceutical industry and regulatory agencies in US, Europe and Japan.

C) ICH guidelines represent the joint opinions of the pharmaceutical industry in US, Europe and Japan.

D) ICH guidelines represent the joint opinions of the pharmaceutical industry and regulatory agencies in US, Europe, Canada and Japan.

ICH Guidance

ICH Mission:

- Ensure that good quality, safe and effective medicines are developed and registered in the most efficient and cost-effective manner
- Consumer and public health, to prevent unnecessary duplication of clinical trials in humans and to minimise the use of animal testing without compromising the regulatory obligations of safety and effectiveness

ICH Steering Committee

- United States
  - ✓ Food and Drug Administration
  - ✓ PhRMA (Pharmaceutical Research and Manufacturers of America)
  - ✓ Pharmaceutical company
- Europe
  - ✓ European Commission
  - ✓ European Federation of Pharmaceutical Industries and Associations (EFPIA)
  - ✓ Pharmaceutical Company
- Japan
  - ✓ Ministry of Health, Labor & Welfare (MHLW)
  - ✓ Japan Pharmaceutical Manufacturers Association (JPMA)
  - ✓ Pharmaceutical Company

Practice Question 22

When an FDA inspector arrives at a facility, he or she must present is

A) Form FDA 482 and credentials

B) EIR

C) Form FDA 483 and Notice of Inspection

D) Form FDA 484

FDA Facility Inspections

- Form FDA 482 – Notice of inspection, presented on arrival with credentials (identification) of investigator
- Form FDA 483 – List of observations, presented at close of inspection
- Form FDA 484 – Receipt for samples
- EIR – Establishment Inspection Report
  - ✓ Includes forms issued during inspection (eg 482, 483, 484)
  - ✓ Investigator's narrative report which provides supportive details to observations documented on FDA-483

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Practice Question 23

Your company wants to conduct a small exploratory study for an alternate dosing regimen for an approved drug/approved indication. As a Regulatory Affairs professional, your first advice is:

A) The results of the study may potentially be useful to support a label change

B) The study must be conducted under an IND

C) You cannot conduct the study unless you intend to pursue a label change

D) Increase the size of the study in order to demonstrate statistical significance

Postmarketing study

- An IND is required if the drug is to be studied “off label”, e.g., alternate dosing regimen, different indication, different formulation (21 CFR 312)
- If the study is conducted under an IND, results of the study may support a supplement for the alternate dosing regimen, i.e., label change
- An exploratory study unlikely to support label change unless safety concern is observed
- Assuming study is conducted under an IND… sponsor’s choice whether to conduct small or large study. A decision based on risk, budget, etc

QSIT (Quality System Inspection Technique)

Quality System Inspection Technique includes**:**

- Moving FDA closer to Global Harmonization guideline for regulatory auditing of quality systems of medical device manufacturers
- Incorporates the seven subsystems concept
- Provides specific guidance on auditing each subsystem

Practice Question 24

Which of the following best represents the Quality Systems Inspection Technique?

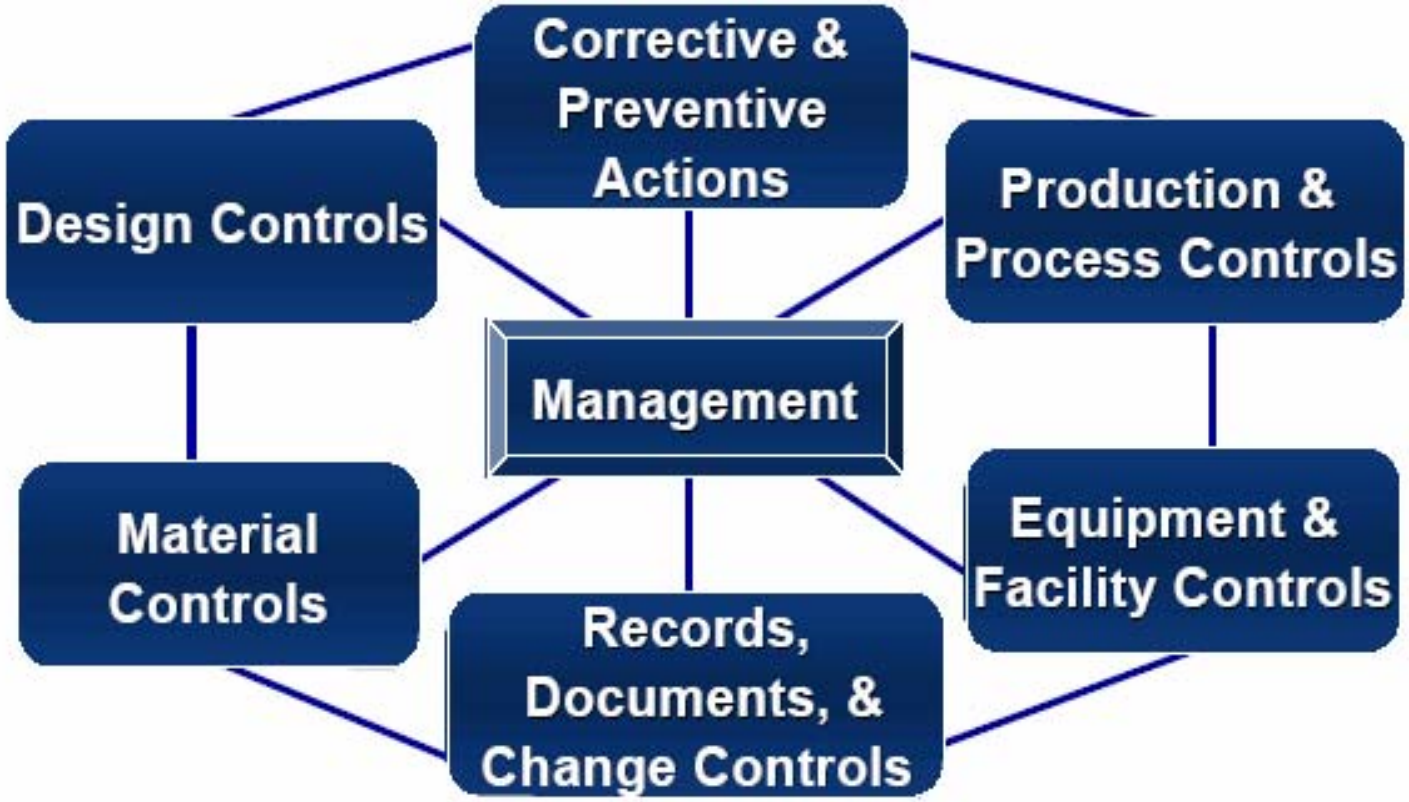
A) Focus on Manufacturing and Manufacturing Processes

B) Focus on QC testing and Product Release

C) Focus on Batch Record Review

D) Focus on Management

Quality System's Sub-systems



QSIT Theme #1 = Management

- Management is responsible for Implementing Quality System
- Start & Finish with Management
- All product, process, design & CAPA problems can be tied to management

The Inspection Approach

- Top-down (versus Bottom-up)
- Sample records (evidence that process being followed)
- Pre- inspection activities (ask for and review documents)
- Start and end with Management

QSIT Progression

1. ***Management Controls***
2. **Design Controls**
3. **Corrective and Preventive Actions**
4. **Production and Process Controls**
5. ***Management Controls***

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Practice Question 25

Which of the following medical device types are not subject to Manufacturer tracking:

A) Life-sustaining or life-supporting device used outside of a device-user facility

B) Life-sustaining or life-supporting device used inside of a device-user facility

C) Permanently implantable device

D) Devices sold to a distributor for ultimate delivery (sale) to end-user

Medical Device Tracking (21CFR821)

Tracking System Includes:

- Current records in accordance with manufacturer's Standard Operating Procedures
- For as long as device is in use or in distribution for use
- Provide for data collection and recording, including when & why required data is missing
- Method for tracking changes to tracking system
- Audit for each device at not less than 6-month intervals for first 3 years of distribution & annually thereafter
- See CFR for exemptions, variances and reporting

Tracking Devices-Distribution

Within 3 working days of FDA request report the following data:

- Name, address and phone # of distributor holding device for distribution and location of device

Within 10 working days of FDA request report the following data:

- Lot, batch, model or serial # providing effective tracking

Date device was shipped from manufacturer

- Name, address and phone # of patient receiving device
- Date device was provided to patient
- Name, mailing address and phone # of prescribing physician
- Name, mailing address and phone # of physician regularly following patient
- If applicable, date device was explanted
- plus don’t forget HIPAA

Practice Question 26

The MDR regulations require that which of the following groups are not required to notify FDA if they become aware of information required to be reported.

A) Manufacturers

B) Distributors

C) Initial importers

D) User facilities

Medical Device Reports (21 CFR 803)

MDR regulation requires manufacturers, importers and user facilities to notify FDA when they receive or become aware of information to "reasonably suggest" a marketed device has:

- Caused or contributed to a death or serious injury **or**
- Malfunctioned and would likely cause or contribute to a death or serious injury if malfunction were to recur

Distributors are required to notify the manufacturer

Medical Device Reports (21 CFR 803)

Reporting is required even if:

- Event is same as, or similar to, one reported previously
- Event is believed the result of one of following actions:
  - User error, Device misuse, Improper service, Improper maintenance

Products are subject to MDR provisions in either of 2 cases:

- Devices manufactured in US sold domestically or abroad
- Imported devices sold in US

Reporting is not required of a US subsidiary not located in the US distributing products exclusive of the US

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Practice Question 27

Which of the following conditions may be expected to lead to a field recall action?

A) Market Withdrawal for correction or removal of distributed devices involving no violation or minor violation of Federal Food, Drug & Cosmetic Act

B) Physical removal of device from point of use to other location for repair, modification, adjustment, relabeling, destruction, or inspection

C) Stock Recovery of a device has not left direct control of manufacturer

D) Routine servicing

Market Correction and Removal (21 CFR 806)

Market Withdrawal

Correction or removal of distributed devices involving minor violation or no violation (i.e., normal stock rotation)

Removal

Physical removal of device from point of use to other location for repair, modification, adjustment, relabeling, destruction, or inspection

Stock Recovery

device has not been marketed or has not left direct control of manufacturer

Routine servicing (meaning regularly scheduled) does not include unexpected repairs or identical replacements of multiple units

Practice Question 28
Name that Device

An OTC denture repair kit (powder and liquid glue) intended for permanent repair of cracks is an example of what type of device?

A) Class 1

B) Class 2

C) Class 3

D) Not a device

(OTC = Over the counter)

21 CFR 872.3570

Practice Question 29
Name that Device

An liquid-filled teething ring (for use by infants) is an example of what type of device?

A) Class 1

B) Class 2

C) Class 3

D) Not a device

21 CFR 872.5550

Practice Question 30
Name that Device

Dental floss is an example of what kind of device?

A) Class 1

B) Class 2

C) Class 3

D) Not a device

21 CFR 872.6390

Practice Question 31
Name that Device

An acupuncture needle is an example of what kind of device?

A) Class 1

B) Class 2

C) Class 3

D) Not a device

21 CFR 880.5580

Practice Question 32
Name that Device

A non-powered microsurgical instrument for use in neurological microsurgery procedures is an example of what kind of device?

A) Class 1

B) Class 2

C) Class 3

D) Not a device

21 CFR 882.4535

Practice Question 33
Name that Device

A female condom is an example of what class of device?

A) Class 1
B) Class 2
C) Class 3
D) Not a device

21 CFR 884.5330

Practice Question 34
Name that Device

Non-prescription sunglasses are an example of what kind of device?

A) Class 1

B) Class 2

C) Class 3

D) No way is this a device

21 CFR 886.5850

Practice Question 35
Name that Device

A male condom is an example of what class of device?

A) Class 1
B) Class 2
C) Class 3
D) Not a device

21 CFR 884.5300

Off-Label Uses

Disseminate nothing about off-label uses with promotional information

Comply with requirements or result may be cessation of dissemination or corrective action deemed appropriate by FDA

Send peer-reviewed article if request comes from an unsolicited practitioner

Remember: You Can't

Adulterate

Misbrand

- with false or misleading labeling
- with reference to having registration number or owner/operator number
- without inviting product detention

Sell banned devices

21 CFR 800.55
21 CFR 807.39

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Questions and Answers

Thanks!
Keep Studying!
Good Luck!

After the exam,
Put it out of your mind, go do something fun
Results by mail in 4 to 6 weeks
Remember to recertify once every 3 years

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Best Answers to Module 1 Practice Questions

Module 1	
Question #	Best Answer
1	C
2	B
3	B
4	D
5	A
6	B
7	B
8	A
9	D
10	B
11	C
12	D
13	A
14	D
15	D
16	D
17	E
18	D
19	C

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Best Answers to Module 2 Practice Questions

Module 2			
Question #	Best Answer	Question #	Best Answer
1	B	19	B
2	C	20	B
3	D	21	C
4	A	22	A
5	B	23	C
6	D	24	B
7	D	25	C
8	B	26	D
9	D	27	E
10	B	28	E
11	D	29	D
12	A	30	D
13	B	31	B
14	A	32	A
15	D	33	A
16	B	34	D
17	D	35	C
18	D	36	C

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Best Answers to Module 3 Practice Questions

Module 3			
Question #	Best Answer	Question #	Best Answer
1	B	19	D
2	B	20	C
3	D	21	B
4	C	22	A
5	A	23	B
6	C	24	D
7	D	25	B
8	C	26	B
9	D	27	B
10	A	28	B
11	C	29	B
12	D	30	A
13	C	31	B
14	D	32	B
15	A	33	C
16	D	34	A
17	A	35	B
18	A		

Code of Federal Regulations

The FDA's portion of the Code of Federal Regulations (CFR), Title 21, interprets the Federal Food, Drug and Cosmetic (FD&C) Act, Public Health Service Act (Section 351 and 352) and related statutes.

Title 21 of the CFR contains most of the regulations pertaining to food, medical devices, drugs and biologics.

Final regulations published in the Federal Register (Final Rule) are collected in the CFR which is divided into 50 titles which represent broad areas subject to Federal regulations.

Regulations have the weight of law.

Electronic CFRs online: http://www.access.gpo.gov/nara/cfr/cfr-table-search.html#

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Study Sheet
Read Later

Code of Federal Regulations

21 CFR Sections for Medical Devices

- Part 801 Labeling
- Part 803 Medical Device Reporting (MDR)
- Part 806/810 Corrections and Removals/Recall Authority
- Part 807 Establishment Registration and Device Listing
- Part 812 Investigational Device Exemption
- Part 814 Pre-market Approval of Medical Devices
- Part 820 Quality System Regulation (GMP)
- Part 821 Device Tracking Requirements
- Part 58 Good Laboratory Practices
- Part 50 Human Subject Protection
- Part 54 Financial Disclosure by Clinical Investigators
- Part 56 Institutional Review Boards

Sources of Information
Title 21 of Code of Federal Regulations

Part 3 Product Jurisdiction

Part 7 Enforcement Policy (and Recalls)

Part 11 Electronic Records & Signature

Part 50 Protection of Human Subjects

Part 54 Financial Disclosure

Part 56 Institutional Review Boards

Part 58 Good Laboratory Practices

Part 99 Off Label Dissemination

Part 201 Labeling

Part 202 Prescription Drug Advertising

Part 203 Marketing

Part 207 Registration

Part 208 Medication Guides

Part 210 cGMP

Part 211 cGMP

Part 312 Investigational New Drug Application

Part 320 Bioequivalence and Bioavailability

Part 314 Applications for FDA Approval to Market a New Drug

Part 600 Biological Products Part 312 Investigational New Drug Application

Part 320 Bioequivalence and Bioavailability

Part 314 Applications for FDA Approval to Market a New Drug

Sources of Information
Title 21 of Code of Federal Regulations

Part 600 Biological Products

Part 601 Biological Product Licensing

Part 606 cGMP for Blood and Blood Components

Part 607 Establishment Registration and Product Listing for Manufacturers of Human Blood and Blood Components

Part 610 General Biological Products Standards Part 606 cGMP for Blood and Blood Components

Part 610 General Biological Products Standards

Parts 640 to 680 Blood

Part 803 Medical Device Reporting

Part 806 Corrections and Removals

Part 807 Establishment Registration and Device Listing for Manufacturers and Initial Importers of Devices (510k regulations)

Part 812 Investigational Device Exemptions for setting up Clinical Study

Part 812 Premarket Approval of Medical Devices

Part 820 Quality System Regulations

Subpart C: Design Controls

International Conference on Harmonization (ICH)

ICH Impact on Drug Development

- Regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions brought together to discuss scientific and technical aspects of product registration.
- Purpose to make recommendations on ways to achieve greater harmonization in the interpretation and application of technical guidelines and requirements for product registration to reduce the need to duplicate the testing
- Objective of such harmonization is a more economical use of human, animal and material resources, and the elimination of unnecessary delay in the global development with regulatory obligations to protect public health.

Sources of Information

- International Conference on Harmonization (ICH) Guidance
  - E2A: Clinical Safety Data Management
  - E4: Dose Response Information to Support Drug Registration
  - E5: Ethnic Factors in the Acceptability of Foreign Data
  - E6: Good Clinical Practice
  - E8: General Considerations for Clinical Trials
  - E10: Choice of Control Group and Related Issues in Clinical Trials
  - M4: Organisation of Common Technical Document (CTD) for the Registration of Pharmaceuticals for Human Use
- RAPS Fundamentals of Regulatory Affairs

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Sources of Information

FDA Guidance Documents:

- General topics such as:
  - Formal Meetings with FDA
  - Special Protocol Assessments
  - Electronic submissions
  - Content and Format of IND
  - Providing Clinical Evidence of Effectiveness
  - Applications Covered by Section 505(b)(2)
  - Consumer-Directed Broadcast Advertisements

Definitions

Device [Section 201(h)]: The term "device" (except when used in paragraph (n) of this section and in sections 301(i), 403(f), 502(c), and 602(c)) means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is–

- (1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,

Definitions (cont)

Device (cont)

- (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or . . .

- (3) intended to affect the structure or any function of the body of man or other animals, and which does **not achieve *its primary* intended purposes through chemical action** within or on the body of man or other animals and which is **not dependent upon being metabolized for the achievement of *its primary* intended purposes**.

Definitions (cont)

Valid scientific evidence [21 CFR 860.7(c)(2)]: Valid scientific evidence is evidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device, . .

Definitions (cont)

Valid scientific evidence (cont)

from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use. The evidence required my vary . . .

Definitions (cont)

Safety and effectiveness [21 CFR 860.7]:

. . . will consider (1) The persons for whose use the device is represented or intended; (2) The conditions of use for the device, including conditions of use prescribed, recommended, or suggested in the labeling or advertising of the device, and other intended conditions of use; (3) The probable benefit to health from the use of the device weighted against any probable injury or illness from such use; and (4) The reliability of the device.

Definitions (cont)

Substantial equivalence [Section 513(i)]: . . . means, with respect to a device being compared to a predicate device, that the device has the same intended use as the predicate device and that the Secretary by order has found that the device

- (i) has the same technological characteristics as the predicate device, or . .
- (ii)(I) has different technological characteristics and the information submitted that the device is substantially equivalent contains information ... that demonstrates that the device is as safe and effective as a legally marketed device and
- (II) does not raise different questions of safety and effectiveness than the predicate device.

Definitions (cont)

Biological Product (21 CFR 600.3(h)): Biological product means any virus, therapeutic serum, toxin, antitoxin, or analogous product applicable to the prevention, treatment or cure of diseases or injuries of man

Biologics are substances derived from or made with the aid of living organisms

What is a Drug?

- article recognized in the official USP, Homeopathic Pharmacopoeia of the US, or official National Formulary
- article intended for the use in the diagnosis, cure and mitigation, treatment or prevention of disease in man or other animals
- article intended to affect the structure or function of the body of man or other animals (other than food)
- article intended for use a a component of the above

Key Reference:

Section 201(g)(1) of the Federal Food Drug and Cosmetic Act

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Prepare for the RAC (US) Exam

David Chadwick, PhD, RAC (US)

Dr. Chadwick was most recently Director, RA/QA for Gyrus Medical in Maple Grove, MN. Dr. Chadwick was responsible for developing regulatory strategy for emerging and marketed products within the company and for regulatory submissions/compliance, and the quality system. He has over 25 years of experience in the medical device industry in such areas as basic research and development, clinical research, and for the past 10 years, regulatory affairs/quality assurance. The scope of his experience includes the product areas of dermatology, periodontology, urology, cardiology, drug delivery and electrosurgery. Dr. Chadwick spent many years in research and development functions and managing clinical trials prior to transitioning into regulatory affairs. Dr. Chadwick received a BS in biology from Albright College and a PhD in anatomy and cell biology from the School of Medicine, University of Pittsburgh.

Prepare for the RAC (US) Exam

Carol Waldo, RAC (US, EU, CAN)
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Carol Waldo, RAC (US, EU, CAN) is an Associate Director in Global Regulatory Affairs at Amgen Inc., where she is responsible for providing expertise on US regulatory requirements to interdepartmental teams and for developing and implementing regulatory strategies to expedite drug development and achieve product registration goals. She has 16 years of experience in pharmaceutical development including drugs, biologics, and multiple therapeutic areas. Prior to Amgen, she has held prior positions in the biotechnology and consulting industries with various responsibilities in Regulatory Affairs, CMC, Quality Assurance and Compliance. She received a Bachelor of Arts degree in Chemistry from North Central College in Naperville, Illinois. Ms Waldo is currently attending UCLA to obtain a Masters in Public Health degree.