QUALITY AGREEMENTS

John J. Vajda
BFC Consultants

SCENARIO

- Contract signed for manufacturing
- Everyone happy
- What do we do next?

HISTORY

- First appeared in UK MCA in 1991 called a Technical Agreement
- Currently it is the “MCA Rules and Guidance for Pharmaceutical Manufacturers and Distributors, 2002”
- Also known as the Orange Book

HISTORY…

- FDA “Guidance for Industry: Cooperative Manufacturing Arrangements for Licensed Biologics” August 1999 best US reference
- Gives some examples of differences between Quality Agreements and business agreements

PURPOSE

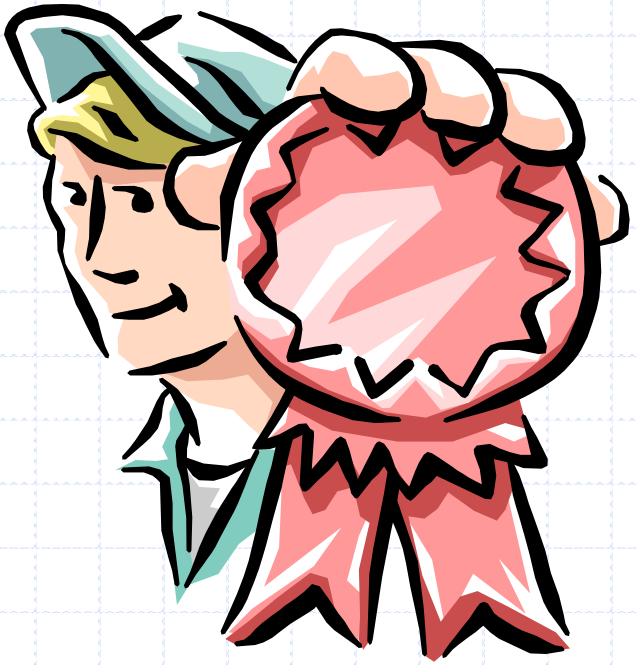
- To define in detail the functional aspects of the relationship
- Establish responsibilities for Quality and Production personnel for each party

YOU MUST

- Assure the Contractor is qualified
- Audit GMP compliance
- Provide ALL information required
- Explain hazards

CONTRACTOR MUST

- Have adequate resources
- Approved raw material sources
- Assure quality
- Not ”farm out”



FDA GUIDANCE SUGGESTS

- Identification and location of contractor
- Defined responsibilities of each party
- Description of materials provided for the Contractor and details of shipment
- Operations to be performed by the Contractor
- Mutually agreed documentation package

FDA GUIDANCE SUGGESTS…

- Contractor must agree to:
  - Provide notification of any changes
    - To facility
    - To manufacturing process
    - To material sources
    - To other products being made
  - Provide notification of deviations
- Agreement on audits

HOW TO STRUCTURE A QUALITY AGREEMENT

- Legal document, needs legal review

STAND-ALONE OR?

- Con
  - Legal objections
  - If product is biologic and sold in Europe
- Pro
  - Can be updated
  - Readily available
  - Available for inspections

WHAT'S THE CONTRACT?

- Written document
- Technically sound
- Defined responsibilities
- Access to
  - Records
  - Premises
  - Samples

WHAT'S THE CONTRACT?…

- Allow visits
- Define release criteria
  - Must meet marketing needs
- Sampling locations

KEY CONTENTS

This is NOT a comprehensive list.

Other points may be added depending on specific needs and corporate cultures.

WHAT DOES NOT BELONG

- Business terms and conditions
- Pricing
- Forecasts and delivery terms
- Confidentiality agreement
- Liability and dispute resolution issues

These belong in a separate Business Agreement!

DISPUTE RESOLUTIONS

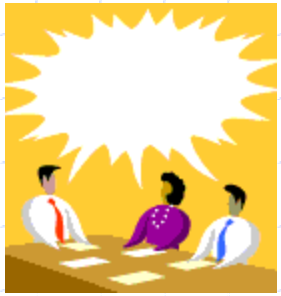
- Refer to in Quality Agreement but keep details in Business Agreement
- Potential issues
  - Testing
  - Release
  - Documentation

RESPONSIBILITIES

- Need to be clearly defined without any ambiguity!
- If in doubt as to what to include follow 21 CFR 211 and assign which company is doing which section

COMMUNICATION

- Will eliminate:
  - " I thought …"
  - " Not sure"
  - " Don't know"
  - " Did not think it was important"
- Assignment of personnel by both parties including contact information



COMMUNICATION…

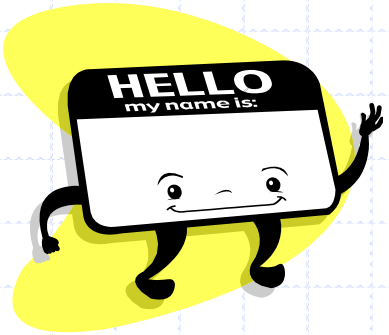
- Timeliness
- Communicating Quality issues
  - We want it NOW! (YOU)
  - We want to investigate first (contractor)

DOCUMENTATION

- Who is writing what?
- Who is approving what?
- What governs if multiple documents apply
- Summaries vs. full reports
- Retention and ownership

BATCH IDENTIFICATION

- Parties will have different systems
- How will product be identified
- Explain all codes to eliminate misunderstandings



DEVIATIONS

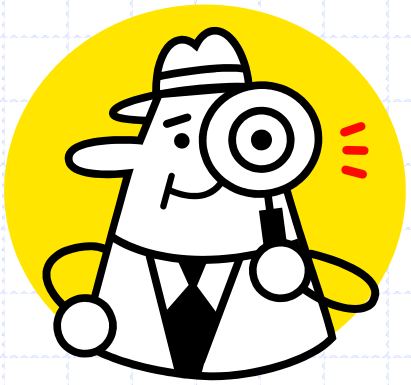
- How to classify? minor vs., catastrophic
- Responsibility for reporting, trending and resolution
- Time is of the essence!
- Who can approve what?

DEVIATIONS…

- Define expectations for communications
- Provide examples of major deviations

AUDITS

- Visit vs. audit vs. inspection
- On- site rep vs. periodic
- Frequency
- Any costs or limitations?
- What to do if FDA comes
  - Will you participate. How?



SAMPLING AND TESTING

- Batch records
- What is acceptable?
  - Purity, stability, expiration
- What method?
- Who is testing what?
- Third party labs
  - Qualifications

SAMPLING AND TESTING…

- Who is approving what?
  - Retention
  - Shelf life
- International requirements

SUBCONTRACTING

- Is it allowed?
- If so, how is it approved?
  - Right to audit

PROBLEMS

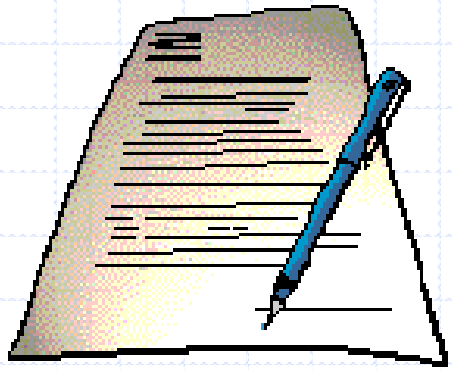
- Complaints
  - How they are:
    - Received
    - Communicated
    - Investigated
    - Reported
- Recalls

ANNUAL REVIEW

- What to include?
- Format
  - Template
- Timing

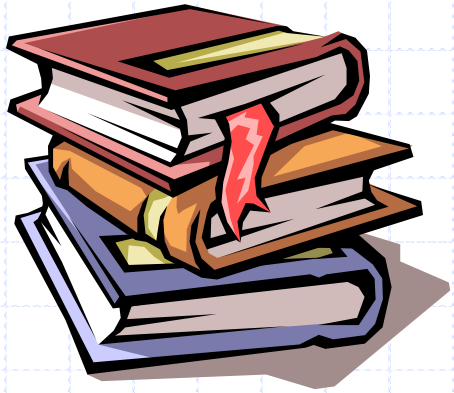
AGREEMENT APPROVAL

- QA for both parties
- Operations
- Legal
- Others
  - Marketing
  - BD



REFERENCES

- "UK MCA Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2002"
- FDA "Guidance for Industry, Cooperative Manufacturing Agreements for Licensed Biologics"
- FDA 21CFR211



CONTACT INFORMATION

BFC Consultants

John J. Vajda

Phone: 408-640-9158

E-mail: jvajda@bfcconsultants.com

Web: www.bfcconsultants.com

QUESTIONS