# TIDES 2013: Course 2

## Considerations for Peptide Contract Manufacturing:

## Lessons Learned on Outsource Management

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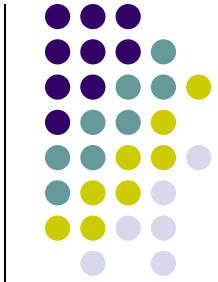
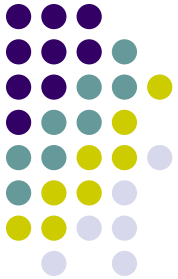
May 12, 2013

# Disclaimer



The views expressed in this presentation are mine and do not reflect those of my past, present or future employers…

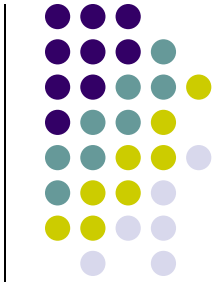
# Why Outsource?



- Access to expertise
- Access to capacity
- Compliance (GMP capabilities)
- Cost-effectiveness

  Internal resources versus project requirements

# What to Outsource?



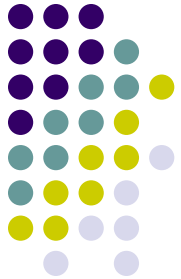
Peptide synthesis

- Requires specialized equipment
  - Automated synthesizers
  - Reactors
  - HPLC purification
- Specialized chemistry
  - TFA or HF cleavage
  - Hybrid synthesis

Analytical characterization

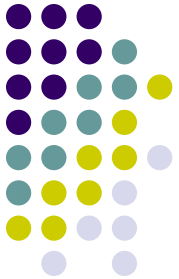
Regulatory oversight

# When to Outsource?



- Discovery support:  Small scale
  - Automated synthesizers
  - Lab bench scale
- Preclinical support:  Medium scale
  - Solid-phase synthesis (specialized equipment)
  - Hybrid synthesis
- Clinical support:  Larg(er) scale
  - Solid-phase/Hybrid
- Commercial:  Large scale
  - Solid-phase/Hybrid
  - Solution-phase

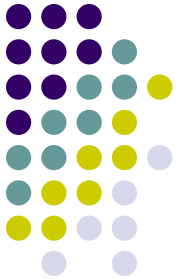
# The Relationship



Managing expectations

- Sponsor
  - Rapid turnaround
  - High quality
  - Lowest cost
- Contract Manufacturer
  - Need to manage multiple projects
  - Flexible resource allocation
  - Constant flow of work
  - Profit

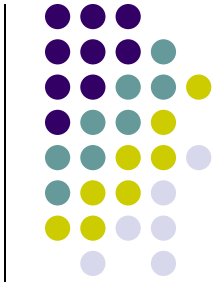
# The Relationship:  part 2



Developing trust

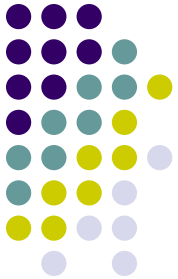
- Communication
- No finger-pointing or playing the blame game
- Root-cause investigation
- Corrective action
- Communication
- Communication
- Communication

# Effective communication



- Critical in early-stage projects
- Type of information
  - Project updates
  - Issues (set expectations of when)
  - Process changes
- Mechanisms
  - Telephone
  - Email
  - Face-to-face
- Quality-Compliance agreement
- Supply agreement

# On-site activities



- Site inspection (tour)
  - Does everything look clean, organized?
  - People?
- Review of SOPs (compliance)
- Meet the team
- Project manager, point-of-contact
- Review batch records

# Agreements

Initial stage (discovery, milligrams)

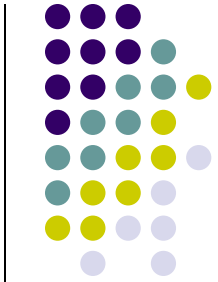
- Quotes-purchase orders
- Quantity and specifications

GMP batches (clinical use)

- Quality agreement
- Development agreement
- Supply agreement

Note: IND/IMPD. Client/sponsor responsible for human safety! Therefore, important to have oversight of manufacturing…

# Quality agreements



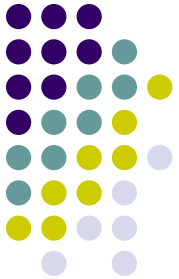
Primary purpose

To delineate the responsibilities (or joint responsibilities) in the manufacture, testing and release of API for clinical human studies or commerce

Compliance

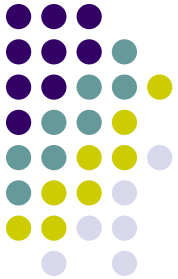
- cGMP
- SOPs

# Elements of a quality agreement



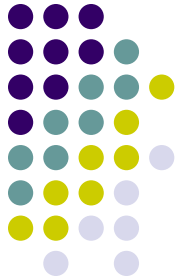
- Responsibilities for review/approval
  - Manufacturing procedures
  - Master batch records
  - In-process, release and stability methods
  - Specifications
- Notifications-approval of changes in
  - Vendors
  - Deviations
  - Out-of-specifications
  - Non-routine findings

# Additional agreements

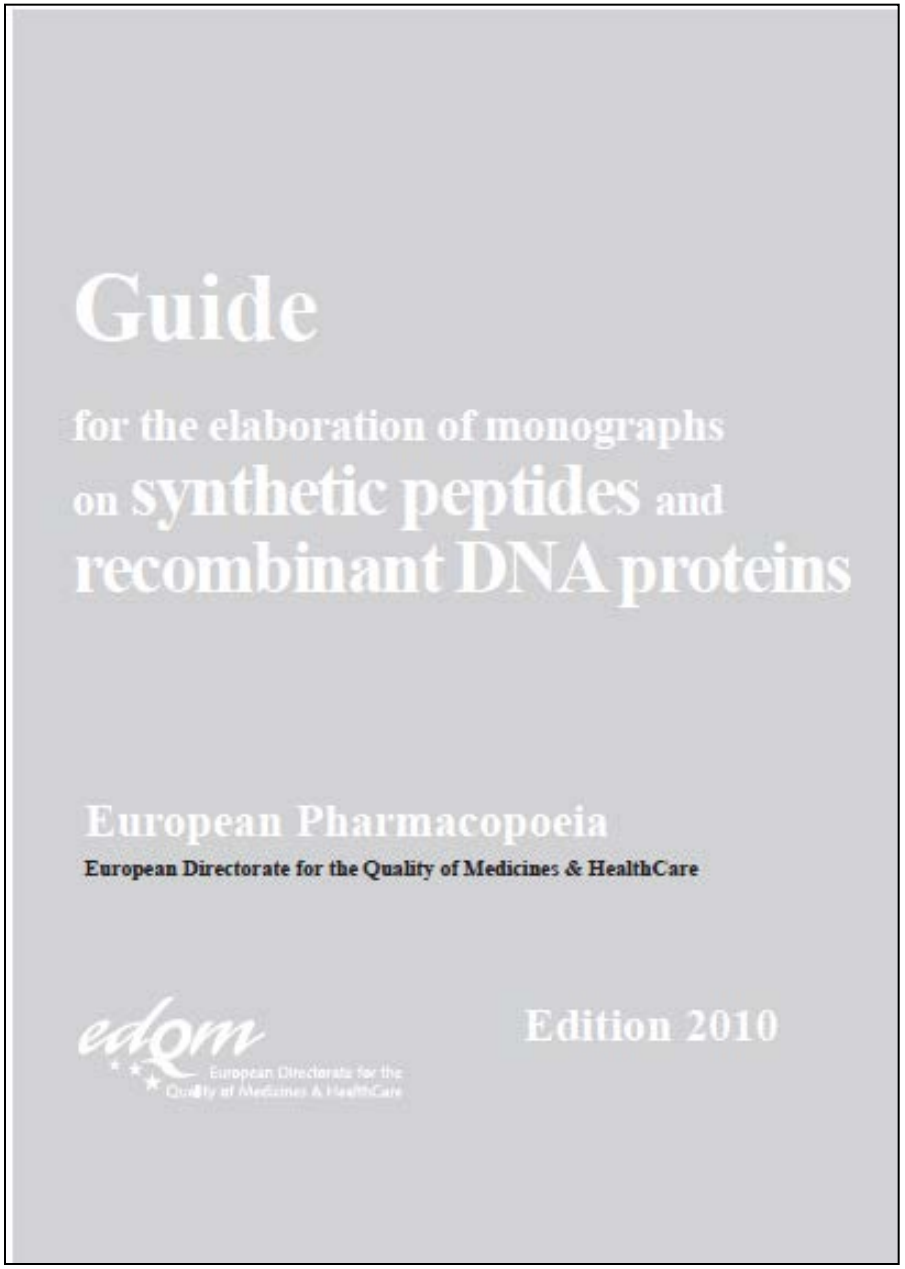


- Process changes
  - How are they documented?
  - Client approval?
  - Impact on toxicology, clinical
- Specification changes
  - Experience with process
  - Feedback from regulatory agencies
- Validations
  - Analytical methods
  - Process

# Final Thoughts

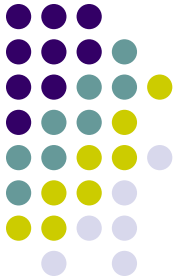


- It is all about the relationship!
- Communication is key
- Agreements help define and set expectations
- Contracts are to protect both sides when the relationship falls apart, so plan accordingly






http://www.edqm.eu/



# Guidance for Industry

## for the Submission of Chemistry, Manufacturing, and Controls Information for Synthetic Peptide Substances

Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

November 1994

Published but withdrawn in 2004

# Withdrawn FDA Guidance

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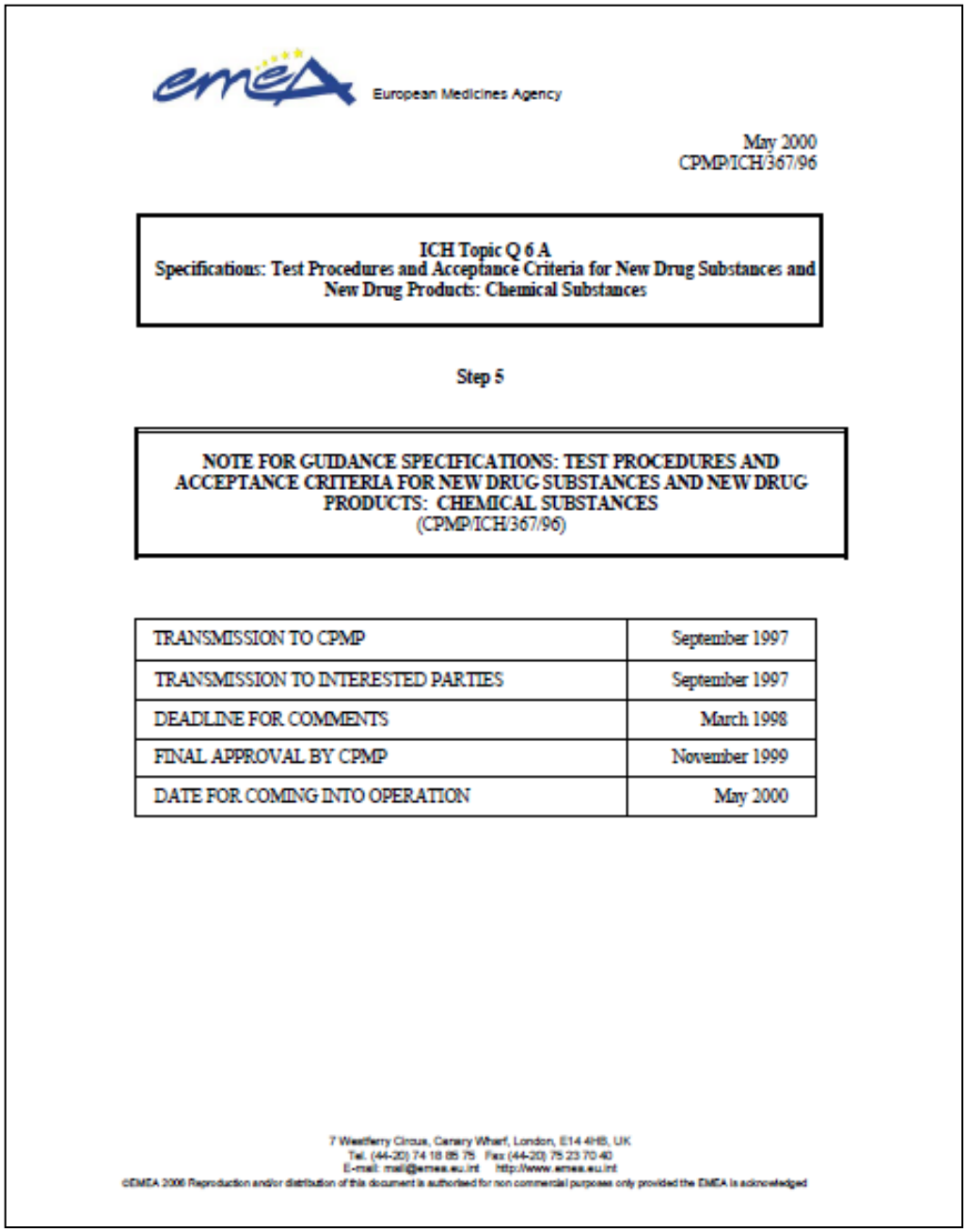

European Medicines Agency

May 2000
CPMP/ICH/367/96

**ICH Topic Q 6 A**
**Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances**

**Step 5**

**NOTE FOR GUIDANCE SPECIFICATIONS: TEST PROCEDURES AND ACCEPTANCE CRITERIA FOR NEW DRUG SUBSTANCES AND NEW DRUG PRODUCTS: CHEMICAL SUBSTANCES**
(CPMP/ICH/367/96)

| | |
|---|---|
| TRANSMISSION TO CPMP | September 1997 |
| TRANSMISSION TO INTERESTED PARTIES | September 1997 |
| DEADLINE FOR COMMENTS | March 1998 |
| FINAL APPROVAL BY CPMP | November 1999 |
| DATE FOR COMING INTO OPERATION | May 2000 |

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Not peptide specific,
but useful guidance

http://www.ema.europa.eu/

Review

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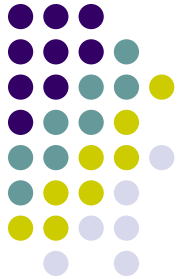
# Quality specifications for peptide drugs: a regulatory-pharmaceutical approach

**Valentijn Vergote,[a] Christian Burvenich,[b] Christophe Van de Wiele[c] and Bart De Spiegeleer[a]***

**Peptide drugs, as all types of pharmaceuticals, require adequate specifications (i.e. quality attributes, procedures and acceptance criteria) as part of their quality assurance to ensure the safety and efficacy of drug substances (i.e. active pharmaceutical ingredients) and drug products (i.e. finished pharmaceutical dosage forms). Compendial monographs are updated regularly to keep up with the most recent advances in peptide synthesis (e.g. reduced by-products) and analytical technology. Nevertheless, currently applied pharmacopoeial peptide specifications are barely harmonized yet (e.g. large differences between the *European Pharmacopoeia* and the *United States Pharmacopeia*), increasing the manufacturers' burden of performing analytical procedures in different ways, using different acceptance criteria. Additionally, the peptide monographs are not always consistent within a single pharmacopoeia. In this review, we highlight the main differences and similarities in compendial peptide specifications (including identification, purity and assay). Based on comparison, and together with additional information from peptide drug substance manufacturers and public evaluation reports on registration files of non-pharmacopoeial peptide drugs, a consistent monograph structure is proposed.** 

**Keywords:** peptide drug substance; quality attributes; acceptance criteria; regulatory affairs; ICH guidelines; *Ph. Eur.* and USP pharmacopoeial monographs; related substances thresholds

Journal of Peptide Science (2009) Vol 15(11), p 697-710



# QUESTIONS?