Workshop on PAT for Biologicals

5th EGA Symposium on biosimilars

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Background: Pharmaceutical Quality – A New Vision

" Develop a harmonised pharmaceutical quality system applicable across the lifecycle of the product emphasizing an integrated approach to quality risk management and science."

Brussels July 2003

Q8: Pharmaceutical Development

Q9: Quality Risk Management

Q10: Pharmaceutical Quality System

Background: Pharmaceutical Development

1. **Minimum: conventional approach**
2. **In addition: PAT or QUALITY by DESIGN concept.**

<u>Enhanced knowledge</u> of product performance over wider range of material attributes, processing options, process parameters, can lead to the establishment of a design space, real time release and to more flexible opportunities.

Risk based approach to development

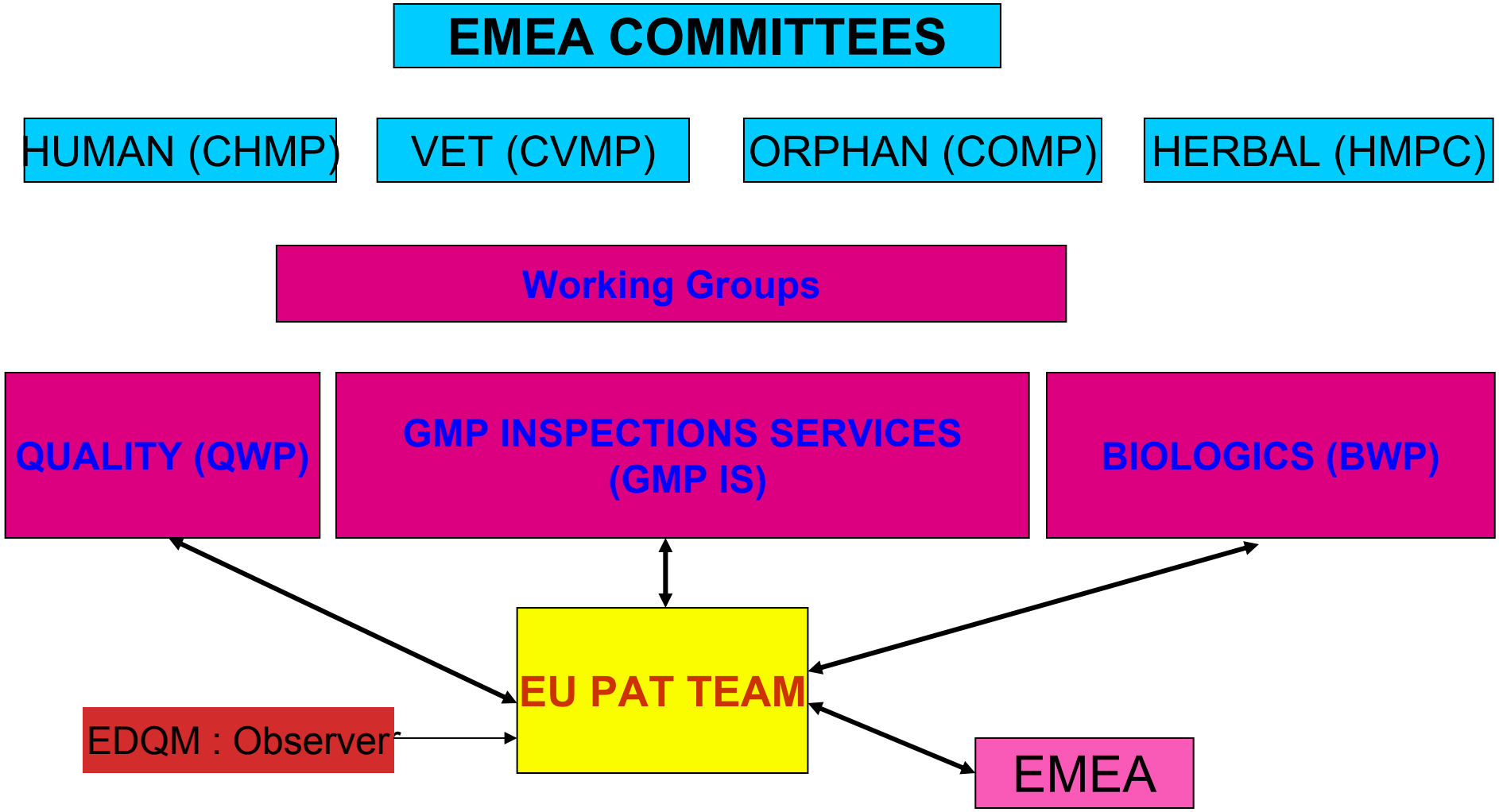
Background:
ICH Q8: Incorporation of new concepts

- Process Analytical Technology
- Real time release
- Design Space
- Formal experimental design
- Flexible (regulatory) approach/opportunities
- Risk based regulatory decisions (reviews and inspections)
- Lifecycle: update to support new knowledge
- Continual improvement
- Knowledge versus data

Format of Workshop

- Introduction - Regulatory (BWP, PAT, QWP, Inspectors)
- General Industry presentations (EGA, EFPIA)
- Confidential Industry presentations
- General Conclusions (all)

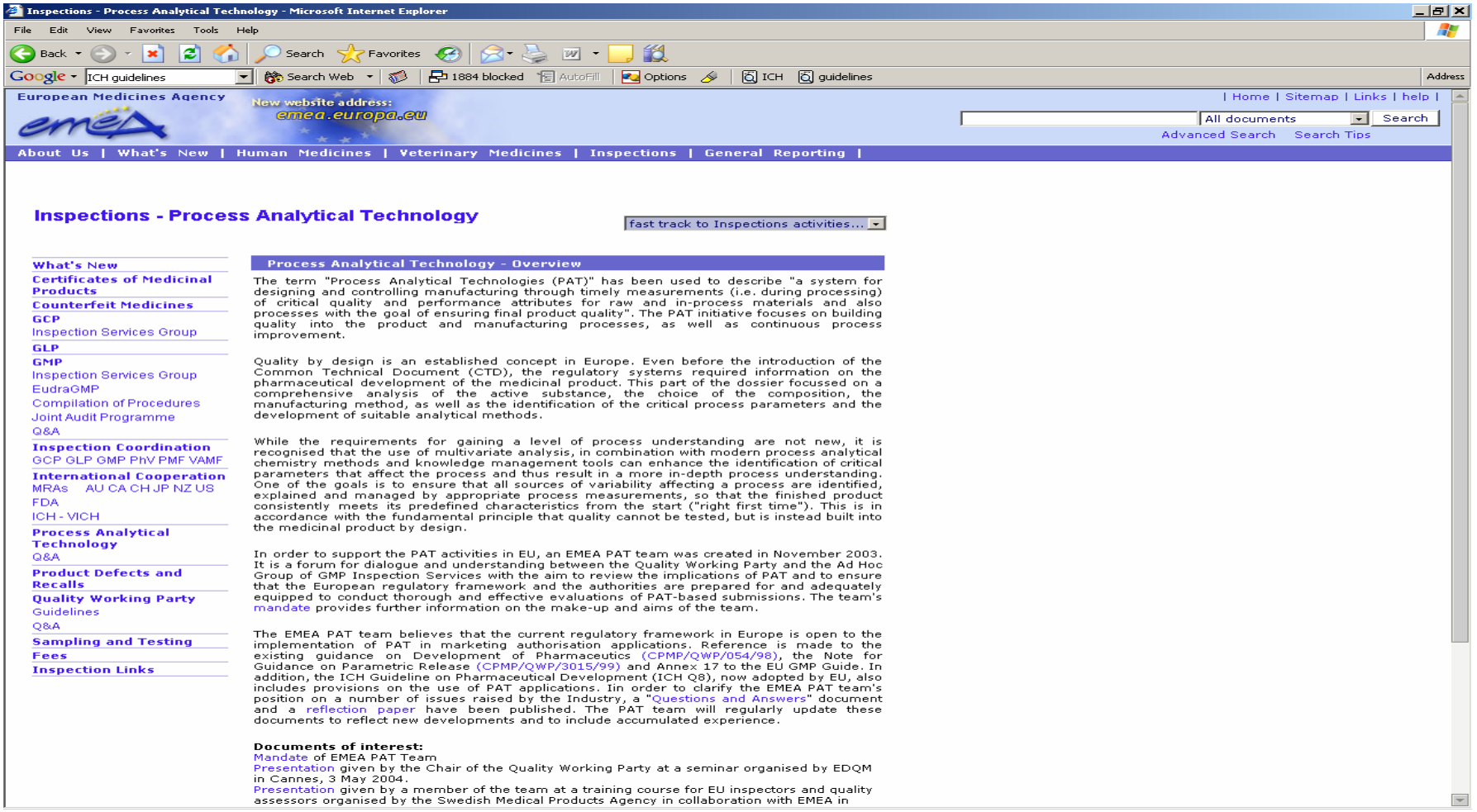
European Regulatory Structure - PAT



Role of BWP

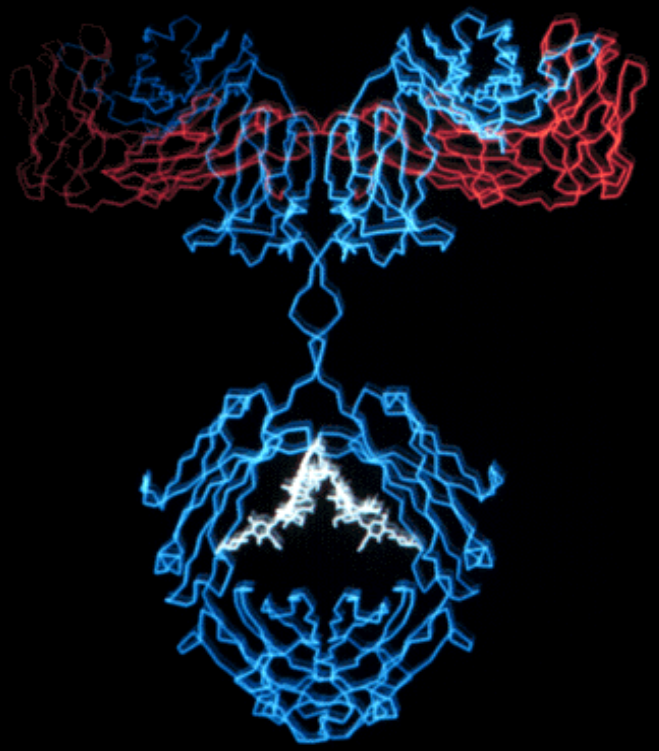
- **In general…**
  - » Assists CHMP in the assessment of new applications.
  - » Assists SAWP in the assessment of request for scientific advice.
  - » Produces guidelines (EU/ ICH)
- **in particular…**
  - » Together with the EMEA PAT team discuss PAT and QbD aspects with interested parties

EMEA Website

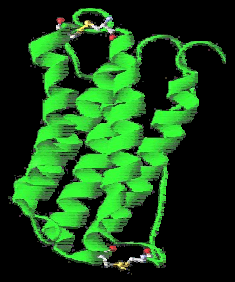


http://www.emea.europa.eu/Inspections/PAThome.html

Specificities of biologicals



IgG
~660AA, MW: ~150 000 Da



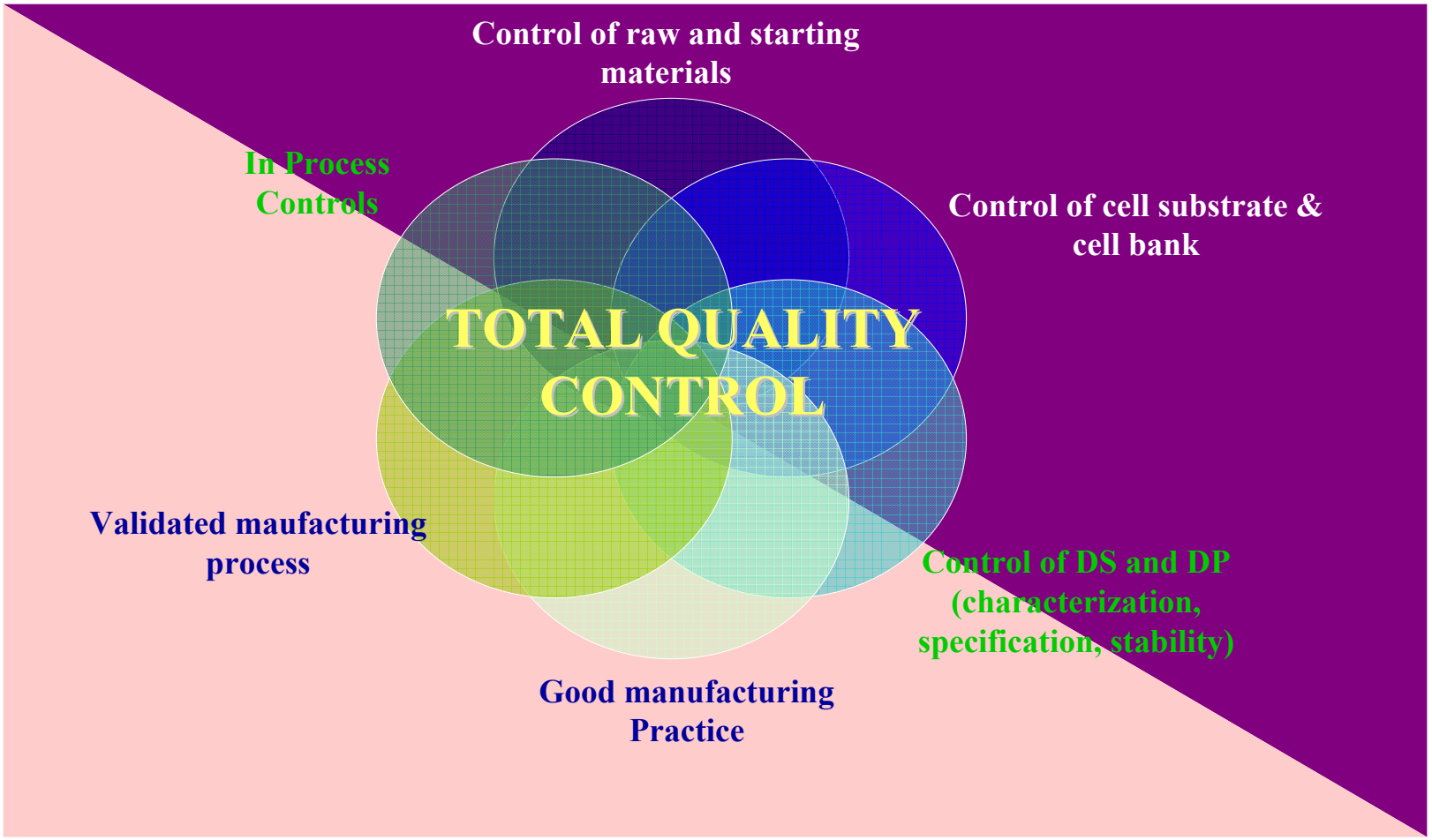
Interferon alfa,
165AA, MW: 19 625 Da

Aspirin,
MW: 180 Da

Specificities of biologicals

- **Process Complexity**
  - » Culture of living organism: genetic stability / mutation, viral safety
  - » Harvest: complex matrix dependant on starting/raw materials and process conditions
  - » Purification adapted to protein of interest, impurities and contaminants
- **Process specificity**
  - » Post-translational profiles
  - » Host Cell Proteins

Specificities of biologicals



Regulatory Aspects

- **Application of PAT on biologics**
  - » *Part or complete process:*
    - – Single module (e.g. bioreactor)
    - – Set of modules (e.g. purification steps)
    - – Globally (e.g. complete process ?)
  - » *Before / after MA*
    - – before MA: validation and demonstration of robusteness
    - – after MA: "knowledge" confirmed by marketing and clinical experience

Regulatory Aspects

- Biotech specificities:
  - » Paradigm for the last 25 years: **Process ↔ Product**
  - » Biotech guidances: mostly address manufacturing issues

- **"Not revolution but evolution" of tools and concepts**
  - » Additional analytical tools, additional tools to treat data, but "spirit" already there for biologics
  - » New words on concepts not clearly defined / applied
  - » Regulatory implications – risk / flexibility

Interaction: Industry - Regulators

- **Informal meetings**
  - » Contact through PAT group
  - » BWP scientific involvement
- **Requests for scientific advice**
- **Applications (variations possible now)**
  - » Stepwise process

Outlook

- **Gaining experience with Q8, Q9 and Q10**
  - » Implementation
  - » Survey of already assessed files
- **Development and manufacturing for APIs**

  Taking into account the principles and concepts outlined in Q8 together with risk management tools.
- **Revision of existing guidelines:**

  e.g. specifications (Q6A/B)
- **Revision of QOS:**

  use as an assessment tool
- **Need for change of the legislation ?**

Thank you for your attention !

- **For your information:**
  - » EMEA Website: http://www.emea.europa.eu
  - » Biosimilars:
    http://www.emea.europa.eu/htms/human/humanguidelines/multidiscipline.htm
  - » Peter.Richardson@emea.europa.eu