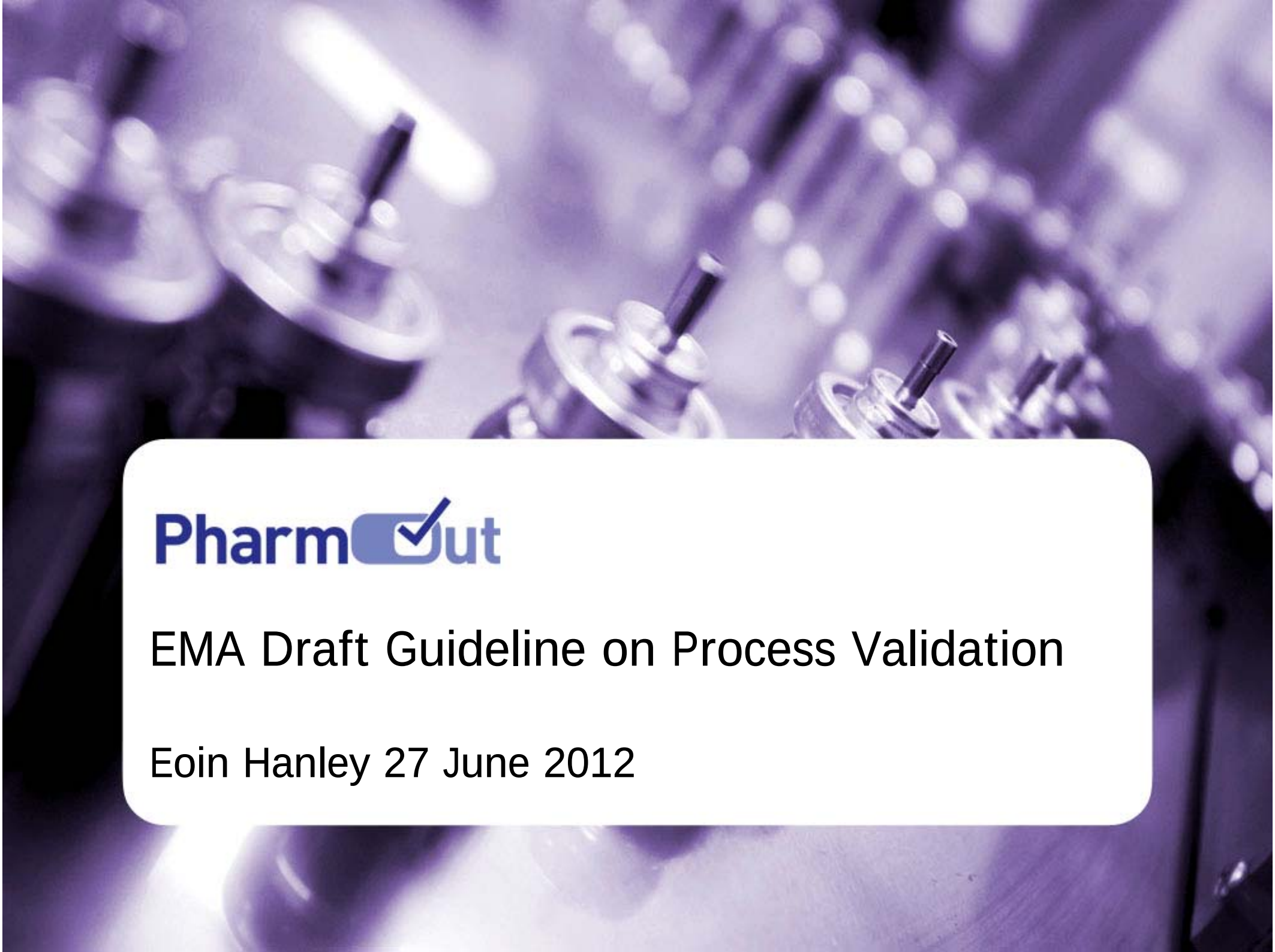

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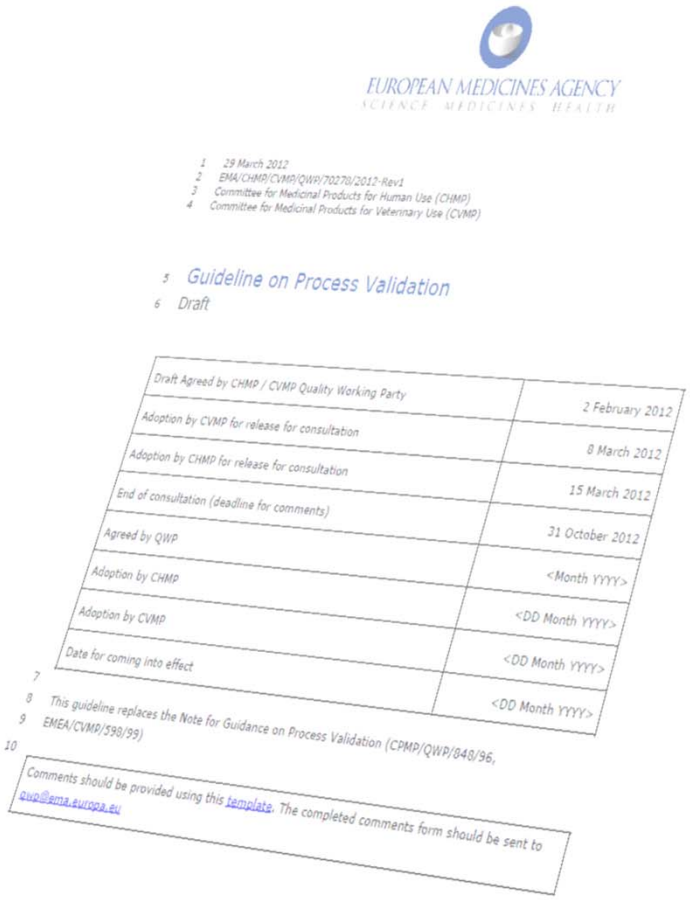
EMA Draft Guideline on Process Validation

Eoin Hanley 27 June 2012

EMA Draft Guideline on PV

- Draft released:
  - 15 March 2012
- End of Consultation:
  - 31 October 2012
- Will Replace:
  - Note for Guidance on Process Validation
- 10 page Guide with 8 Sections



EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

29 March 2012
EMA/CHMP/CVMP/QWP/70278/2012-Rev1
Committee for Medicinal Products for Human Use (CHMP)
Committee for Medicinal Products for Veterinary Use (CVMP)

Guideline on Process Validation
Draft

Draft Agreed by CHMP / CVMP Quality Working Party	2 February 2012
Adoption by CVMP for release for consultation	8 March 2012
Adoption by CHMP for release for consultation	15 March 2012
End of consultation (deadline for comments)	31 October 2012
Agreed by QWP	<Month YYYY>
Adoption by CHMP	<DD Month YYYY>
Adoption by CVMP	<DD Month YYYY>
Date for coming into effect	<DD Month YYYY>

This guideline replaces the Note for Guidance on Process Validation (CPMP/QWP/848/96, EMEA/CVMP/598/99)

Comments should be provided using this template. The completed comments form should be sent to qwp@ema.europa.eu

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EMA Draft Guideline on PV

- Guideline brought into line with ICH Q8, Q9 & Q10.
- No new requirements, but clarifies how companies can take advantage using ICH Q8, Q9 & Q10.
- Possibility of using Continuous Process Verification (CPV) in addition to, or instead of traditional process verification.
- CPV-an alternative approach to PV based on continuous monitoring of batch performance.

EMA Draft Guideline on PV

- Intended to apply to data generated to validate manufacturing process of the intended commercial dosage form only.
- Applies to medicinal products for human and veterinary use.
- Applicable for biological products, however considered on a case-by case basis.
- Provides guidance on the information to be considered for dossier submission.

EMA Draft Guideline on PV

- PV should confirm that the control strategy is sufficient to support the process design and quality of the product.
- PV can be performed in a traditional way or the possibility of implementing CPV.
- A combination of PV and CPV may be employed.
- CPV provides more information & knowledge and might help facilitate improvements.
- Possible to adjust the process during manufacture to maintain finished product quality.

Traditional Process Validation

- PV should focus on the control strategy which primarily includes CPP's and other relevant studies, demonstrating the process is capable of delivering the desired product quality.
- Annex 1 of draft details the process validation scheme that should be provided in the marketing authorisation dossier.
- The number of batches (minimum of 3) should be based on the variability of the process, the complexity of the process/product and experience of manufacturer.

Hybrid Approach

- May use the traditional PV or CPV for different steps in the process.
- Justification for hybrid approach should be in dossier and clear on which approach applies to each part of the manufacturing process.
- Validation requirements in terms of batch size and # of batches would depend on the extent to which CPV has been used.

Continuous Process Verification

- Sufficient knowledge & understanding of the process required to support CPV.
- If design space implemented, CPV may contribute to ensuring its validity through lifecycle.
- Appropriateness & feasibility of CPV strategy should be in development section of the dossier.
- CPV strategy, process parameters, analytical methods in the Validation section of the dossier.
- Applicant needs to define the stage the product is considered validated, with justification.

Continued Process Verification

- Monitor product quality to ensure state of control throughout commercial part of product lifecycle.
- Provides assurance of quality & identifies changes that might improve process.
- Relevant process trends will help verify the original PV or identify changes to the control strategy.
- Extent & frequency of ongoing PV should be reviewed. If appropriate, enhanced sampling & monitoring may help process understanding.

Standard v Non-standard MOM

- Relevant for processes not validated using CPV.
- Lists examples of non-standard methods where production scale validation data might need to be provided in the marketing authorisation application dossier, unless otherwise justified.
  - Specialised dosage forms
  - New technology in conventional processes
  - Highly specialised processes or highly complex processes
  - Non-standard methods of sterilisation

Standard v Non-standard MOM:

- Processes such as lyophilization and aseptic processing are included as highly complex and, upon publication of the full guideline, will warrant full scale validation data to support dossier submission, except where exempted through experience.
- Needs to be justified on a “case-by-case” basis, on the basis of appropriate development data or by reference to similar products.

Similarities to US FDA Guide:

- Incorporates product life cycle, QRM and efficient quality system practices (ICH Q8, Q9 & Q10).
- Emphasis on continued process verification through analysis of pre and post release data to provide confidence of an ongoing valid process.
- Acknowledgement and provision of scope to emerging processing technologies, such as PAT, to assist the validation effort.
- Enhanced detail to provide understanding of regulator expectation on what constitutes an appropriate validation effort.

Differences to US FDA Guide:

- *EMA: "documented evidence that the process, operated within established parameters, can perform effectively and reproducibly to produce a medicinal product meeting its predetermined specifications and quality attributes."*
- *US FDA: "the collection and evaluation of data, from the process design stage throughout production, which establishes scientific evidence that a process is capable of consistently delivering quality product."*

Differences to US FDA Guide:

- The EMA draft guideline states “a minimum of three consecutive batches”, with justification to be provided (there are some exceptions to this statement).
- The US FDA guidance states that the number of batches must be sufficient to provide statistical confidence of the process. It is a subtle, but important distinction in the approaches.

Differences to US FDA Guide:

- The US FDA guidance emphases documenting the development phase as part of PV. The EMA draft encourages the use of the product development activities, but is less prescriptive on requirements.
- The EMA guideline specifically allows the use of CPV to replace traditional validation efforts.US FDA approach does not place high emphasis on CPV, and requires all three stages of process validation to be fully addressed, regardless of whether contemporary or traditional methods are utilised.

Differences to US FDA Guide:

- The US FDA guidance considers equipment and process design, as well as equipment qualification as part of the overall process validation effort.
- The EMA guideline sees process as independent from equipment and facility. Currently, the EMA still relies on Annex 15 of the GMP guide for instruction on equipment qualification.
- It is likely that Annex 15 will be updated in the near future to reflect the changes in process validation guidance.

Impact of this Guide:

- The EMA and the Pharmaceutical Inspection Cooperation Scheme (PIC/S) are closely aligned.
- PIC/S may adopt the guidance in full, or develop its own guidance based on the EMA document.
- Regulatory guidance from the EMA has relevance for Australia and other PIC/S aligned countries.
- Lets see what happens!

PharmOut White Papers

EMA Draft Guidance: Process Validation

Process Capability

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