1.15

CPMP/QWP/122/02

Stability Testing of Existing Substances and Related Finished Products

Comments for its application

1.1 Objectives of the Guideline

- ❒ Extension of the ICH Q1A(R2)
- ❒ Sets out the stability testing requirements for existing drug substances and related drug Products.
- ❒ An existing drug substance is one that has been authorised previously through a drug product within the European Community
- ❒ The guideline is applicable to chemical drug substances and related drug products

2. Guidelines

2.1 Drug Substance

2.1.1 General

- ❒ For drug substances not described in an official pharmacopoeial monograph (EP or Member State) stability studies are required.
- ❒ For drug substances described with covers the degradation products with suitable limits but no defined re-test period two options:
  - Applicant specifies that the drug substance complies with the specifications of the monograph prior to manufacture of drug product.
  - Applicant fix re-test period based on results of long term testing

2.1.2. Stress testing

- ❒ **Following approaches for drug substance**
  - Drug substance described in an official pharmacopoeial monograph (EP or MS) no stress testing required if degradation products are named under purity test and/or impurities.
  - It is acceptable to provide relevant data published in literature.
  - When no data available stress testing should be performed according to ICH Q1A(R2) and Q1B

2.1.3 Selection of batches

- ❒ **Two options:**
  - Two production batches 6 moths accelerated and long term testing
  - Three pilot scale batches 6 months accelerated and 12 months long-term.

2.1.4-2.1.10 further basic principles according to ICH Q1A(R2)

- Container Closure System
- Specification
- Testing frequency
- Storage conditions
- Stability Commitment
- Evaluation
- Statements /Labelling

2.2 Drug Product

2.2.2 Photostability Testing

Photostability Test on one primary batch

2.2.3 Selection of Batches

❒ **Two options:**

- Two pilot scale batches
  - Conventional dosage forms (e.g. immediate release, solutions)
  - Drug substances are known to stable
  - 6 moths accelerated and long term testing

- Three primary batches, two pilot scale one smaller
  - Critical dosage forms (e.g. prolonged release form)
  - or drug substance are known to be unstable
  - 6 months accelerated and 12 months long-term

- Drug substance considered stable if within specifications when stored at 25°C/605 two years and at 40°C/75% 6 months.

2.1.4-2.1.10 further basic principles according to ICH Q1AR

- Container Closure System
- Specification
- Testing frequency
- Storage conditions
- Stability Commitment
- Evaluation
- Statements /Labelling

❒ **Extrapolation of data**

- Normally extrapolation to twice the length of the real time studies
- Maximum extrapolation should not exceed 3 years