Medicines Quality & Interchangeability? How Can We Be Sure?

First Qatar Medication Safety Symposium

It's everyone's concern

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Disclaimer: *The presenting author has no relationship to Disclose*

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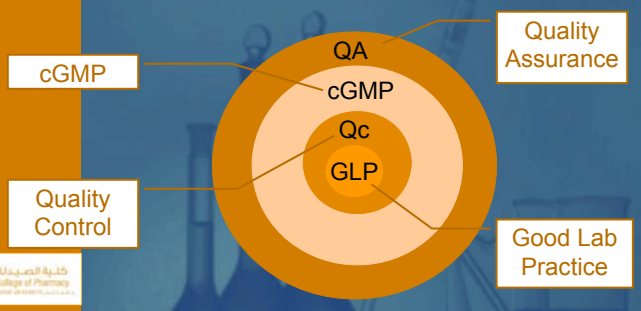
Objectives

- **Introduce key elements of the quality control/assurance process for pharmaceuticals (solid dosage forms)**
- **Highlight the most relevant pharmacopeial and ICH guidelines pertaining to medications safety and quality control.**
- **Present real example(s) representing interchangeability challenges and quality of marketed medications**

QC History/Evolution

- **1900's- Adulterated Food**
  - First purity laws enacted
- **1930's- Sulfanilimide Elixir**
  - Drugs had to be proven safe
- **1960's- Thalidomide**
  - Drugs had to be proven safe and effective through clinical trials
- **1980's- Tylenol Incidence**
  - Controlled Inspection

Pharmaceuticals Quality Management



Why QC is important?

- **They are enforced by laws**
- **Ensure good quality of Pharmaceutical products**
- **Reduce final product rejects & recalls**
- **Ensure Satisfied customers**
- **Maintain manufacturing consistency**
- **Company image and reputation**

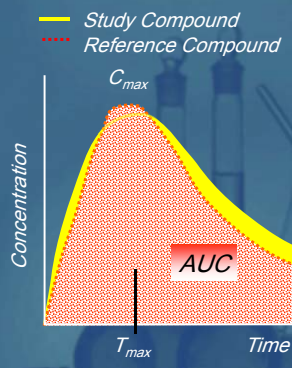
Key Quality Terms

- **CHANGE CONTROL**
  - written procedure that describes the action to be taken if a change is proposed to facilities, etc. used in fabrication, packaging, and testing of drugs or any change that may affect quality or support system operation
- **DEVIATION**
  - Planned or unplanned temporary departure from an approved process, specification or procedure with the ***potential*** to impact product quality

Generic Versus Brand

- **Bioequivalence Studies**

Bioavailability/Bioequivalence Studies

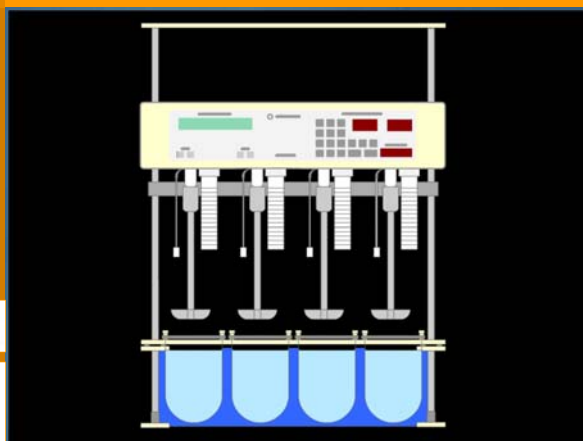


- *AUC*
  - *Area under the concentration-time curve*
- *C_{max}*
  - *Maximum concentration*
  - *A difference of greater than 20% in C_{max} or the AUC represents a significant difference between the study and reference compounds*
- *T_{max}*
  - *Time to maximum concentration*

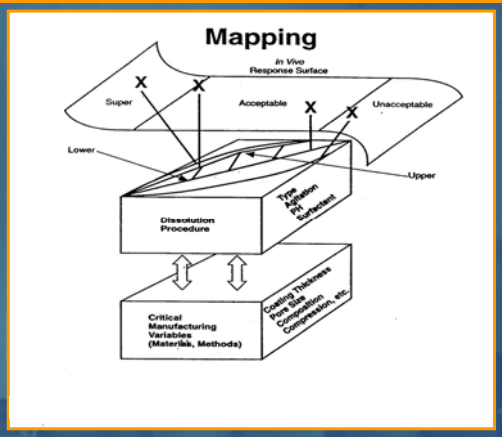
Compendial Testing of Solid Dosages

- **Content Analysis**
  - Dose accuracy and confirmation
- **Dissolution Testing**
  - *in vitro – in vivo* correlation
  - Possible representation of bioavailability
- **Similarity Factor Analysis**
  - Confirm similarity in behavior and release pattern

Dissolution Testing



Mapping Concept



Interchangeable Drug Products

- Pharmaceutical equivalents or pharmaceutical alternatives that are therapeutic equivalents and have the same route of administration of the reference and fall within the conditions of use for that reference product.

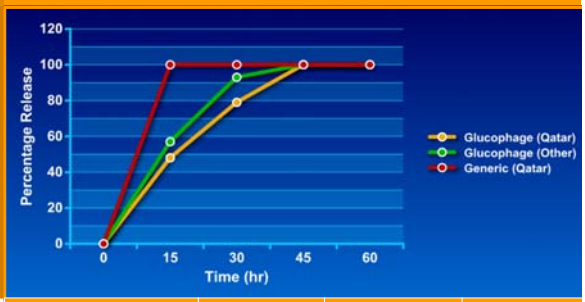
Therapeutic Equivalents

- Pharmaceutical equivalents or pharmaceutical alternatives that have been shown to be bioequivalent to a reference product as demonstrated by bioavailability (based on same molecular species), pharmacodynamic, or clinical studies. and have been deemed to have the same safety and efficacy profile as the reference product.

Metformin Study: What to look for?

- According to the USP 37, Not less than 70% of the label amount of Metformin HCl dissolved in 45 min.
- According to the USP 37, Metformin HCl tablet should not contain less than 95% and not more than 105% of active ingredient.
- According to the FDA and ICH guidelines, dissolution curves of any 2 drugs could be considered similar or equivalence, if the f2 value greater than 50 (50-100).

Metformin Compendial Testing



	Glucophage (Qatar)	Glucophage (Other)	Generic (Qatar)
% Content	97.9	96.6	102
Similarity Factor (f2)		88	32

Conclusions & Recommendations

- Post marketing random sampling and testing is a must!!
- In vitro similarity and testing confirmation does not always guarantee similar in vivo results unless strong (level A) vitro-in vivo correlation is established
- Similarity factor and release pattern should be considered in certain cases of pharmaceuticals.

Questions!