Generic Drugs & Promise of Regulatory Science

(3/3)

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All Praise be to
ALLAH

Generic Drugs
Promise of Regulatory Science

Session 4
Emerging Challenges & Radar Navigation

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Generic-A Great Claim

A generic drug is the same as brand name drug

- In Dosage
- In Safety
- In Strength
- The way it is taken
  - The way it should be used
- The way it works
- In Quality

Generic- Perception or Reality

Our drugs are equal quality

Give me Tylenol instead of Panadol

We do not compromise on quality and put in 100% API

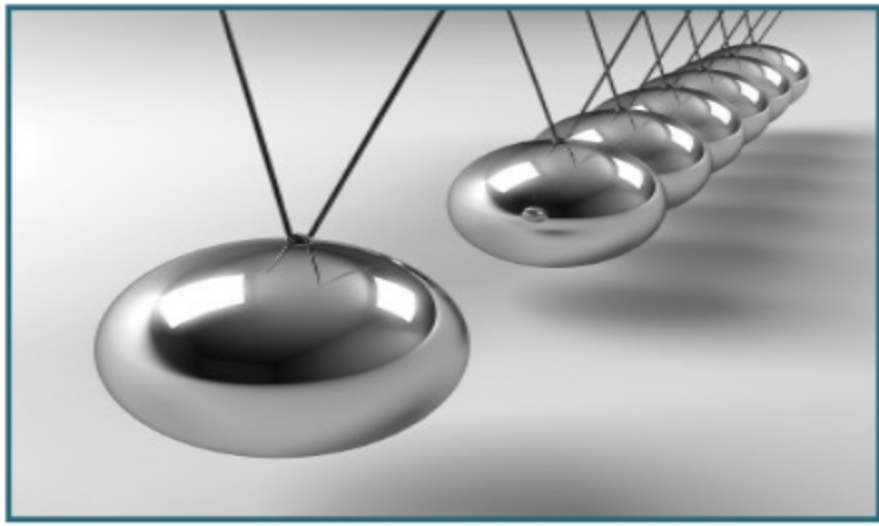
More than 50% drugs are fake

We & our kids use the same drugs, we manufacture

Great Challenge with Generics

1. Manufacturing & Quality Control
2. Product Characteristic & Label
3. Therapeutic Equivalency

80% 125%



Dosage Form Change Over ???

Reference drug is in tablet form

- Can we manufacture injection instead of tablet?

Let's think

- Is there need of any clinical study to go for injection?

Do you think

- Has clinical studies nothing to do with dosage form?

Open for discussion. If you have any reference of any developed country, it will be added knowledge.

Overage

Ergotamine Tartarate

Thyroxine

ACE Inhibitors

Tobramycin

Overage

Generally, use of overage is discouraged. An overage in the drug product, whether it appears in the final product or not, should be **JUSTIFIED** considering the safety and efficacy of the product. Important aspects are

Amount of overage	Reason of overage	Justification for the amount of overage

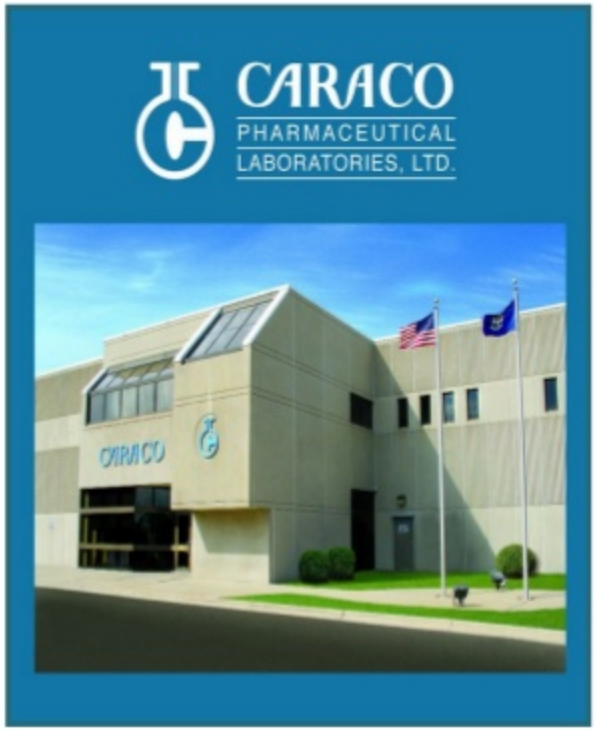
Stability

Caraco Pharmaceuticals, a subsidiary of Sun Pharma

Venlafaxine HCl ER tabs

Failed in dissolution

Stability results went out



Dissolution Failure

Metoprolol Succinate Tabs ER Recall due to dissolution

Tropol XL (Sandoz) approved in 1992

Therapeutic failure reported in 2007

Formulation had not been properly validated (FDA 2008)

2009 Ethex (KV Pharmaceuticals)

2014 Wockhardt & Ranbaxy

Recalled due to dissolution

What do you think?

What should we learn?

Sometimes Maths does not favor

ADHD

- Mallinckrodt
- Methyl Phenidate HCl tab
- 18, 27, 36, 54 mg dose

Failure

- Fasting & fed had two different behavior in extended release

Sometimes Maths does not favor

Bupripion HCl tab

- Study on low dose and waiver on high dose

Failure

- Desired kinetics was not achieved

Teva

- FDA asked to stop distribution in sep 2012

Sometimes Maths does not favor

BUPRIPION

Bupripion (Wellbutrin) IR Tab of SKB 1985

Bupripion SR Tab 1996 & XL Tab 2003

Based on evidence demonstrating BE with low strength

In 2006, Generic version Mfg by Impax/Teva were approved

85 post marketing reports from Jan-Jun 2007

Experienced undesirable effects

Increased side effects, Decreased therapeutic effect

Re-switched on brand

Sometimes Maths does not favor

Temporal relationship under question

FDA re-examined BE data

Conducted study

Withdrawal of Teva drug in Mar 2013 against Sep 2012 FDA advice

BUPRIPION

Also generic of Actavis withdraw their version

A new challenge

General rule will not work always

Its life, please care

Production Scale up

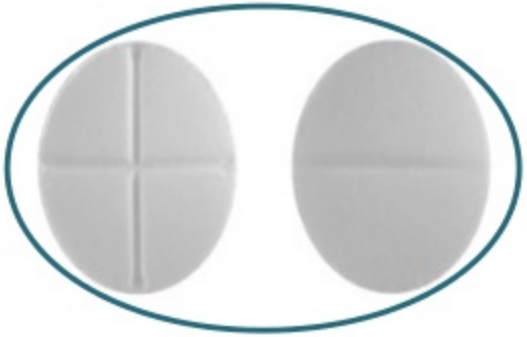
APOTEX
ADVANCING GENERICS

- Apotex Canada
- HTZ capsule 12.5 mg failed upon scale up in assay.

APOTEX
ADVANCING GENERICS

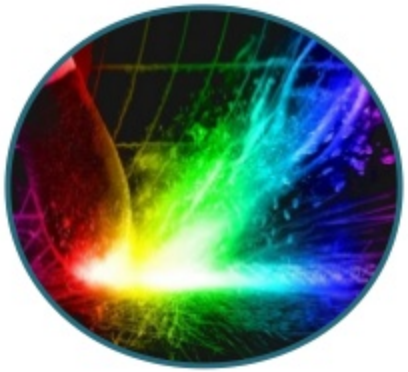
- Failure was limited to some batches
- Root cause was not identified even after a year.

Tablet Scoring



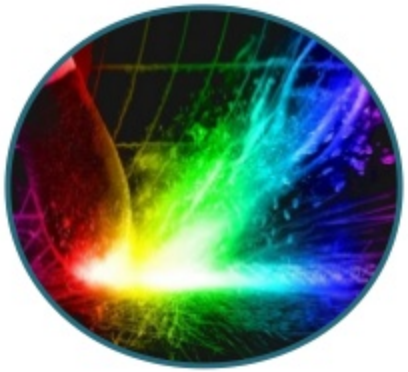
Scoring is not a cosmetic issue
but important …..

Supplier Qualification



Ingredients → Process → Product

Supplier Qualification



Can a drug product manufactured from a non-compliant API ensure safety???

Analytical Method