The science behind **generic drugs**

Norbrook®

Are generics manufactured to the same high quality standards?

Are generics equivalent to the pioneer?

Do pioneer drugs go through more testing?

Should I feel confident with a generic product?

References:

[1] *http://www.hma.eu/uploads/media/CMD_v__GUI-014_Processing_generics_through_MRP-DCP_-_PUBLIC_FINAL-_EMEA-CMDv-262452-2008.pdf*

[2] *http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/document_listing/document_listing_000335.jsp&mid=WC0b01ac0580514d5c*

[3] *bpac, What is Bioavailability and Bioequivalence? – Generics 2009*

[4] *FDA-CVM bioequivalence guidance #35, November 8, 2006*

[5] *VICH GL52 http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm042450.htm*

What is a generic drug?

A generic drug displays pharmaceutical equivalence or bioequivalence to the pioneer product.

The generic product has the same qualitative and quantitative composition of active substances, and the same pharmaceutical form as the reference product (pharmaceutical equivalence). Alternatively, bioequivalence with the reference medicinal product has been demonstrated by bioavailability studies.[1]

Are generics manufactured to the same high quality standards?

Fact 1:
Generic drugs are equivalent to pioneer drugs

According to the European Medicines Agency (EMA) licensing process, the generic manufacturer must show that the generic drug is equivalent in quality, safety and efficacy to the approved pioneer ("Brand") drug in:

- **Active ingredient**
- **Strength**
- **Dosage form**
- **Dosage regime**

In addition:

- **Each ingredient must meet stringent quality standards**
- **The generic must demonstrate stability for the shelf life of the product**

Are generics equivalent to the pioneer?

Fact 2:
EMA regulated manufacturing standards are identical

Pioneer drugs and generic drugs must be manufactured to the same high quality standards set out by the EMA.[2]

Both are manufactured in Veterinary Medicines Directorate (VMD) accredited facilities, to comply with the principles of Good Manufacturing Practice (GMP) in relation to Manufacturing Authorisations (ManA).

www.norbrook.com

Do pioneer drugs go through more testing?

Fact 3:
If a product is not pharmaceutically equivalent, bioequivalence has to be proven

Blood level bioequivalence (BE) studies compare a test product (generic drug) to a reference product (pioneer drug) using parameters measuring and encompassing:

- **Absorption**
- **Distribution**
- **Depletion of the drug concentration over time**

To determine bioequivalence, the generic sponsor completes blood level studies comparing its formulation vs. the pioneer's and reports to what extent the active ingredient concentrates in the blood and for how long. The average or mean results for the generic product must not be significantly different in comparison to the pioneer product.

The EMA considers two products bioequivalent if the mean peak concentration (C_{max}; the maximum serum concentration that a drug achieves) and the area under the curve (AUC; total exposure over time) are not significantly different when applying a 90% Confidence Interval (CI) approach.

The acceptable limits are that the generic product mean must be within *80%-120% (untransformed data) or 80%-125% (log-transformed data) of the mean of the reference product.

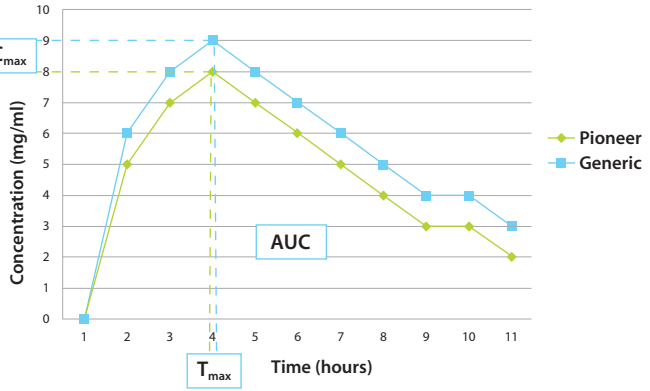
** This does not mean that the generic drug is allowed to have 20% less active ingredient than the pioneer.* ***Both products must be formulated to contain the same amount of active ingredient.***

Did you know?

The excipients of a generic drug can differ, as long as the drug shows bioequivalence during the study.

To conduct the bioequivalence study, the same dosage is used for both the pioneer and generic formulations. Below is a graph of BE study results illustrating the mean blood concentrations of a pioneer drug (green line) and generic drug (blue line). If the two drugs are deemed to be bioequivalent, the products are considered equivalent and interchangeable.[3]

Bioequivalence study results



C_{max} = Maximum or peak concentration that a drug achieves in blood after the drug has been administered

T_{max} = Time at which the C_{max} is observed

AUC = Total area under the blood drug concentration-time curve, or drug exposure over time. AUC is proportional to the total amount of drug absorbed by the body, and thus available to produce a therapeutic effect.[4,5]

It is often not just bioequivalence that has to be proven - in some cases target animal safety and residue depletion for consumer safety testing must be carried out and you must always do a user safety and environmental safety test on generic products.

Should I feel confident with a generic product?

Fact 4:
The quality and monitoring processes continue after the generic drug is approved

EMA's post approval requirements for pioneer drugs and generic drugs are identical:

- **Reporting of manufacturing changes**
- **On-going stability testing**
- **Pharmacovigilance (adverse event monitoring and reporting)**

Did you know?
Designing, conducting and analysing a bioequivalence study can take several years to complete.

Glossary of terms:

Pharmaceutical equivalence:
Generic and pioneer products contain exactly the same ingredients in the same concentration and are manufactured in the same way. This means no animal studies are required.

Bioequivalence:
Generic and pioneer products have the same active ingredients but may have different excipients or concentration of excipients. In this case, bioequivalence studies are required i.e. tests to ensure that the active reaches the same concentration in the blood for the same duration of time as the pioneer products.

Norbrook®

Norbrook®

Norbrook® Laboratories is a leading global provider of veterinary pharmaceuticals enhancing the health of farm and companion animals

About Norbrook

- Norbrook was founded in 1969 in Newry, Northern Ireland. It is one of the largest privately owned veterinary pharmaceutical companies in the world.
- It has world class manufacturing facilities in Northern Ireland, United Kingdom, the Republic of Ireland and Kenya and sales and marketing facilities in nine global locations
- The company exports to 120 countries globally through our own local sales teams and a network of more than 100 distribution partners
- Norbrook is licensed and regulated by the world's leading authorities including the US Food and Drug Administration (FDA), Medicines and Healthcare Products Regulatory Agency (MHRA) and the Veterinary Medicines Directorate (VMD). We adhere at all times to their standards of safety, quality and efficacy.

Norbrook Products

- Norbrook has a portfolio of more than 300 trusted brands
- Norbrook makes sterile and non-sterile products in a variety of dosage forms including parenterals (injectables and intramammaries); tablets; pour-ons; drenches and spot-ons
- It is one of the largest manufacturers of veterinary sterile injectables in the world
- Norbrook manufactures products for other major animal health companies worldwide
- Our strong pipeline of products is a key growth driver for the company

Experience and Quality you can Trust

- Norbrook has been manufacturing and supplying veterinary pharmaceuticals for more than 40 years
- The company produces a number of Active Pharmaceutical Ingredients (APIs) including oxytetracycline dihydrate, flunixin meglumine, oxytetracycline HCL and meloxicam for use in finished goods, ensuring continuity of supply, increased confidence in quality and supporting competitiveness
- Norbrook develops and manufactures generic drugs to the same high quality standards and to attain the same levels of safety and efficacy as pioneer products in the veterinary pharmaceutical market. Norbrook products offer a value alternative with differentiations or enhancements in comparison to pioneer products.

3498-NBK-v2-UK-02/02/17