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GENERIC ANIMAL DRUG ALLIANCE

The US Veterinary Generic Industry
The 24th CCRVDF Meeting

April 22, 2018

Chicago, IL

Generic Animal Drug Alliance

- An independent professional trade organization that represents the interest of generic animal drug companies within the US.
- Advocate, promote and educate the generic animal drug industry.
- Founded in 1988 following enactment of the Generic Animal Drug and Patent Term Restoration Act (GADPTRA).
- Currently represents the majority of stakeholders in the veterinary generic drug industry.
- Our 20 Sponsor members are focused on development, FDA approval and marketing of high quality generic drugs for livestock and pets.
- Our 10 Associate members provide services and key ingredients to the Sponsor members.

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US Generic Industry - Overview

- Estimate $6 billion annual US animal pharmaceutical market
  - Pioneer = ~$5 billion - Generic = ~$1 billion
- Generics offer cost-effective choices that are as safe and effective as the pioneer products
- Generics shorten the innovation cycle by encouraging pioneer companies to develop new products/technologies
- 10%-15% of pioneer drugs have an approved generic version - (GADA member company review of animaldrugs@fda.gov, Fall 2015)
- ~85% of pet owners and farmers would likely choose an FDA approved veterinary generic if available

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US Generic Industry - Overview

2008 - 2017 Generic Animal Drug Approvals

Number of ANADA Approved	110
Number of Type A Combinations	29
	81

Companion Animals	48 of 81	59%
Food Animals	33 of 81	41%
Approval required Bioequivalence trial	16 of 81	20%
Approval required BE and residue trials	1 of 81	<2%
Biowaiver from HFS granted	32 of 33	100%

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US Generic Industry – What we can do….

Generic Animal Drug and Patent Term Restoration Act - Nov 1988

1. Suitability Petitions – permission for a product that differs from the approved pioneer product as follows:

- Change of one ingredient in combination product or premix
- Change of a dosage form
- Change of a strength of an ingredient
- Change in the route of administration
- Change in use with other animal drugs in animal feed

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US Generic Industry – What we can do….

2. A waiver from the requirement of *in vivo* bioequivalence testing can be granted in the generic product meets certain criteria
    - True solution – completely solubilized
    - Topically applied and intended for a local therapeutic effect

3. When a biowaiver is granted for a food animal product, this typically allows for a waiver from tissue residue studies as well

4. If a biowaiver is not granted, an *in vivo* bioequivalence study is required to demonstrate safety and effectiveness
    - Blood-level study
    - Clinical endpoint study
    - Physiological endpoint study

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US Generic Industry – What we can do…..

5. If a biowaiver is not granted, residue chemistry requirements must be satisfied if the product is for a food animal

- US Tolerances are established by the FDA
- If the Sponsor can demonstrate blood level bioequivalence for the entire withdrawal period of the pioneer, a residue study is not required
- The Sponsor can pursue a shorter withdrawal period to gain a differential advantage over the pioneer
- Sponsor can generate residue data for the generic product as follows:
  - single point confirmation study to confirm pioneer withdrawal
  - set own withdrawal by depletion study using regulatory method
  - set own withdrawal by comparative study with new validated method e.g. sterile injectable/true solution

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US Generic Industry – What we can do….

6. B1 supplements – an NADA process under Section 512 (b)(1)
   - Add a species, route of administration or indication to the generic label that is not on the pioneer label
   - The Sponsor can alter the generic product to gain a differential advantage over the pioneer
   - The approval requirement must address the Human Food Safety Technical Section which would include a residue chemistry component
   - e.g. ANADA 200-008 – sterile injectable - added a route of administration
   - e.g. ANADA 200-221 – Component with Tylan – add a tylosin tartrate pellet to the implant as a local antibacterial

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US Generic Industry – What we can do…..

7. Allowable differences in conditions of use to the pioneer based on generic product data

- allowable labeling differences – trade dress, proprietary name, company information, ANADA number
- storage conditions
- expiration dating
- palatability data
- in-use statement (broaching)

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US Generic Industry – Challenges/Constraints

- Pathways to demonstrate bioequivalence & residue
  - Multi-species labels require studies in each species for initial approval
  - Extend biowaiver opportunities based on physical and chemical characteristics of the finished product
  - Creative regulatory pathway for products that are not waiverable and blood levels cannot be measured (e.g. *in vitro* or clinical endpoint)
  - Tissue residue requirements for certain generic dosage forms
- Increasing regulatory requirements – new interpretations
  - USP monographs intended for human – applied to veterinary
  - CMC – e.g. impurity limits
- Increasing regulatory costs
  - Time from project initiation to approval needs to decrease
  - AGDUFA User Fees

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US Generic Industry – What we want to do….

- Demonstrate bioequivalence to a pioneer in one species and gain approval for that one species even if there are additional species on the label (e.g. obtain a label for cattle only – even if the pioneer is labeled for cattle and swine)
- Reasonable bioequivalence pathway for approval of products that cannot be measured in blood
- If a generic confirms the pioneer withdrawal time – or – if a generic demonstrates a different withdrawal time to the pioneer…..
  - Is this data/information of value to the JECFA process?
  - Since JECFA does not set withdrawal times – how would JECFA use generic testing residue data?

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