

DRUG RESIDUES IN MILK



BASICS

OVERVIEW

- The US Food and Drug Administration (US FDA) retains responsibility under the Public Health Service Act to assist individual states in assuring the milk supply to the nation is safe for consumption.
- Approval of new drugs for use in lactating animals is accompanied by the setting of a safe-level / tolerance for that specific drug; a concentration below which the drug purportedly does not pose a risk to human health.
- Allowances for drug residues found in milk are regulated by a combination of both federal and state programs and is separate from regulations governing drug residues in food (“Tissue Residues”).
- A list of tolerances of certain drugs in milk (and tissue) for various animals can be found in 21CFR Part 556 (*see Suggested Reading*).

ESTABLISHMENT OF MILK SAFETY AND THE PASTERUZED MILK ORDINANCE (PMO)

- Activities in the beginning of the 1900’s by the US Public Health Service (US PHS) involved investigations on the role of milk in spreading disease.
- The earliest regulation on the sanitization of milk for consumption became known as the Standard Milk Ordinance of 1924. This regulation has been revised more than a dozen times following its inception, ultimately leading to the Pasteurized Milk Ordinance (PMO).
- The PMO establishes standards for milk to be labeled as Grade “A” versus Non- Grade “A” and is used for the certification of interstate milk shipping as well as standards for milk production, animal safety and facility design (*See Suggested Reading*).
- Due to the widespread use of beta-lactam antimicrobials to treat mastitis in dairy cattle, raw milk arriving at milk plants must be tested for at least four (4) of six (6) of the following antibiotics: cloxacillin, amoxicillin, ampicillin, penicillin, ceftiofur and cephalixin.
- The PMO also establishes additional sampling of milk or milk products from a processor and periodic testing standards over the course of the year.
- Other drugs not specifically tested for, however, are permitted to be used provided they are present at or below accepted tolerance levels.
- A number of drugs cannot be used in any amount in animals including: Chloramphenicol, Clenbuterol and others. Standards for the “extra label” use of drugs are identified under the Animal Medicinal Drug Use Clarification Act (AMDUCA) of 1994 (*See Suggested Reading*).
- Permit holders who are in violation of the PMO may be subject to monetary fines, suspension of their permit or permit revocation.

ESTABLISHING OF STANDARDS FOR DRUG RESIDUES IN MILK

- Significant pre-market toxicological testing of drugs (especially antibiotics) for use in food or milk producing animals is performed.
- The USA-EU-Japan trilateral program Veterinary International Conference on Harmonization (VICH), provides guidance on a variety of testing protocols including the evaluation of drug residues in milk (*See Suggested Reading*).
- Drug metabolism studies (e.g.: VICH GL 46; *See Suggested Reading*) are used to identify metabolites and potential residues produced.
- Additional studies including acute and chronic dosing as well as multi-generational and genetic testing are also undertaken.
- Evaluations of drug depletion are also completed to establish withdrawal times (e.g.: VICH GL 48; *See Suggested Reading*).
- The Acceptable Daily Intake (ADI), which is the amount below which a daily consumption over a lifetime does not represent an appreciable risk of harm, is established for each drug.
- The ADI is then used to determine an acceptable “Tolerance” (US) or “Maximum Residue Limit” (Canada) that can be found in a specific media (e.g. tissue, milk).
- Consumption patterns (e.g.: amount consumed daily, monthly, yearly) of the item are used to help establish acceptable amounts.

CURRENT MONITORING FOR DRUG RESIDUES

- The National Milk Drug Residue Data Base (NMDRD) is a voluntary reporting database managed by a non-governmental, third-party, to allow milk producers to report results of their tests (*See Suggested Reading*). Data is confidential to ensure privacy of the submitter.
- The most recent published statistics on drug residues in milk by the NMDRD was published in February 2016 covering the time period of October 1, 2014 – September 30, 2015 and included both Grade “A” and Non-Grade “A” milk (*See Suggested Reading*)
- Forty-Nine (49) states and Puerto Rico (partial) submitted data. Data was not received from Texas.
- During the period, 3,615,460 samples were tested for animal drug residues and of these 579 were positive for a drug residue. These positive results originated from both Grade “A” and Non-Grade “A” milk.
- The source of 371 of the 579 positive results was noted to be from “Bulk Milk Pickup Tankers”, a further 199 from “Producers” with the final nine positive results from “Other”.



MISCELLANEOUS

SEE ALSO

Drug Residues in Milk (www.fiveminutevet.com/ruminant)

ABBREVIATIONS

- ADI: Acceptable Daily Intake
- AMDUCA: Animal Medicinal Drug Use Clarification Act
- HACCP: Hazard Analysis and Critical Control Point
- NCIMS: National Conference on Interstate Milk Shipments
- NMDRD: National Milk Drug Residue Data Base
- PMO: Pasteurized Milk Ordinance
- US PHS: United States Public Health Service
- US FDA: United States Food and Drug Administration
- VICH: Veterinary International Conference on Harmonization; Full name: International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products

Suggested Reading

M-I-05-5: Tolerance and/or Safe Levels of Animal Drug Residues in Milk:

www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/Milk/ucm077350.htm

Grade “A” Pasteurized Milk Ordinance (2011 Revision):

www.fda.gov/downloads/Food/GuidanceRegulation/UCM291757.pdf

National Milk Drug Residue Data Base (NMDRD): www.kandc-sbcc.com/nmdrd/

2013-2014 National Milk Drug Residue Data Base Annual Report:

www.fda.gov/downloads/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/Milk/UCM434757.pdf

21CFR Part 556: www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?cfrpart=556

Veterinary International Conference on Harmonization (VICH): www.vichsec.org

VICH GL 46: Metabolism Studies:

www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM207939.pdf

VICH GL48: Residue Depletion Studies:

www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM207941.pdf

Center for Veterinary Medicine. *Milk Drug Sampling Survey*. United States Food and Drug Administration. March 2015.

Dowling PM. Antimicrobial drug residues in foods of animal origin. In: Giguere S, Prescott JF and Dowling PM (eds). *Antimicrobial therapy in veterinary medicine*. 5th ed. John Wiley and Sons, Inc: 2013. GLH, Incorporated. *National Milk Drug Residue Data Base Fiscal Year 2015 Annual Report: October 1, 2014 - September 30, 2015*. February 12, 2016 (Revised February 18, 2016). GLH Incorporated, Heathsville, VA.

Payne MA, Babish JG, Bulgin M, Lane M, Wetzlich S, Craigmill AL. Serum pharmacokinetics and tissue and milk residues of oxytetracycline in goats following a single intramuscular injection of a long-acting

preparation and milk residues following a single subcutaneous injection. J Vet Pharmacol Ther. 2002 Feb;25(1):25-32.

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