

Antibiotic Residues In Poultry Tissues and Eggs: Human Health Concerns?

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ABSTRACT Antibiotics are used by the poultry industry to enhance the health and productivity of flocks. The use of antimicrobials is strictly regulated by the Food and Drug Administration (FDA) and the USDA to warrant their safety and efficacy. Prior to regulatory approval, the pharmacokinetics and tissue tolerances of an antimicrobial are determined to set the proper dosage. To ensure proper use, both the FDA and USDA have research, surveillance, and compliance programs to develop detection

methods and monitor poultry tissues for antimicrobials. Unfortunately, there is the perception among many consumers that our food supply contains high concentrations of drug or hormone residues causing significant health concerns or problems. In fact, foods produced in this country (including poultry) are very safe and meet the highest standards to exclude chemical contaminants. An overview will be presented on the federal oversight and monitoring of antimicrobial residues in poultry tissues.

(Key words: antibiotic residue, poultry, egg, safety)

2003 Poultry Science 82:618–621

INTRODUCTION

Antibiotics are used by the poultry industry and poultry veterinarians to enhance growth and feed efficiency and reduce disease. Antibiotic usage has facilitated the efficient production of poultry, allowing the consumer to purchase, at a reasonable cost, high quality meat and eggs. Antibiotic usage has also enhanced the health and well-being of poultry by reducing the incidence of disease. Although these uses benefit all involved, unfortunately, consumer perceptions are that edible poultry tissues are contaminated with harmful concentrations of drug residues. In a recent consumer survey, Resurreccion and Galvez (1999) reported that 77% of consumers responding considered animal drug residues in meats to be an extreme health concern (Figure 1). Only 23% responding thought that drug residues were not a problem. These perceptions are supported by popular media including the recent article by Gaskill (2002) recommending “organic produce and chicken, because of the hormones and antibiotics conventional producers use.” These comments were published in the in-flight magazine (AmericanWay) for American Airlines. Although antibiotics are approved for use in poultry, there is extensive regulatory oversight to ensure the safety of our foods (see following section). Furthermore, hormones are not approved for use in poultry, are illegal to use, and are closely monitored

by the federal government to ensure they are not used in poultry.

DRUG APPROVAL PROCESS

The use of antibiotics is strictly regulated by the Food and Drug Administration (FDA) and the USDA. The FDA is the regulatory agency responsible for approval of antibiotic usage in poultry. Once approved, both the FDA and its sister agency, the USDA, have active surveillance and compliance programs to ensure the proper use of antibiotics and the safety of the food supply. The authority to approve drugs (including antibiotics) is granted to the FDA by the Federal Food Drug and Cosmetic Act (1958). As part of this law, the FDA is mandated to ensure the safety and efficacy of drugs prior to approval. The burden of proof to demonstrate safety and efficacy is on the sponsor (usually a pharmaceutical company) and not the FDA. The sponsor is required, with FDA input, to perform scientific research to meet the regulatory standards for drug approval. The FDA’s role is to provide input and proper guidance and evaluate the safety and efficacy data to determine the suitability for drug approval. From a safety standpoint, extensive toxicology and pharmacology studies are required to demonstrate consumers will not be exposed to harmful concentrations of antibiotic residues in edible poultry tissues.

PREAPPROVAL REQUIREMENTS

Prior to approval, the FDA requires several different types of toxicology and pharmacology studies to access the safety of antibiotics in edible tissues (see www.fda.gov/cvm/guidance/published.htm for specific require-

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Received for publication September 26, 2002.

Accepted for publication December 2, 2002.

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Abbreviation Key: FDA = Food and Drug Administration; NOEL = no observable effect level.

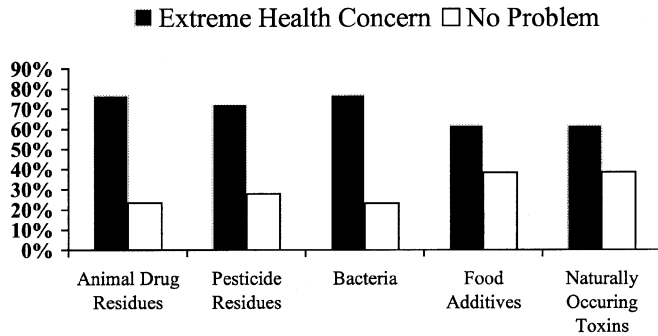


FIGURE 1. Consumer survey: concern about potential food contamination in meat. Reprinted with permission from Food Technology (Resurreccion and Galvez, 1999). [AUTH QUERY: Please provide copyright permissions to the PSA editorial office]

ments). The types of toxicology tests required will depend upon the knowledge and history of use for specific antibiotics. For example, requests to use an antibiotic in broilers, which has a history of safe use in other food-producing animals, will probably require less extensive toxicology testing. For a newer, untested antibiotic, however, extensive safety testing will have to be performed. Thus, the drug approval process can vary for different antibiotics. There are general guidelines, however, followed for all drug approvals.

For toxicology testing, the sponsor has to perform acute and chronic dosing studies. The acute studies evaluate animals for problems such as allergic reactions, whereas long-term chronic studies identify if problems such as cancer are associated with a particular drug. These studies will determine a dose that does not create any health problems. This is called no observable effect level (NOEL) and is the antibiotic dose at which no adverse effect on an animal's health can be observed. Once established, this information is used to calculate a tolerance concentration for the antibiotic in edible tissue. This is accomplished by taking the antibiotic dose at the NOEL, reducing this dose by 100- or 1,000-fold (safety factor), and multiplying by the average daily intake of the edible tissue (e.g., poultry muscle) for a 60-kg adult. A safety factor of 100 is usually used for antibiotics already in use (e.g., other animals, humans) with a known safety record. Otherwise, a safety factor of 1,000 is used.

$$\begin{aligned} \text{Tolerance} &= \text{NOEL (dose, no observable effect)} \\ &\times \text{safety factor (100 or 1,000 times less} \\ &\quad \text{than the NOEL dose)} \\ &\times \text{ADI (average daily intake) } \times \text{60-kg adult} \end{aligned}$$

Once an antibiotic is approved for use, the tolerance is published in the U.S. Code of Federal Regulations. Thus, a person eating a chicken breast from an antibiotic-treated chicken would, at most, consume a dose of antibiotic of 100- or 1,000-fold less than the dose demonstrating no health effects. In other words, based on sound scientific research, the chicken or eggs we consume are extremely safe with respect to residues.

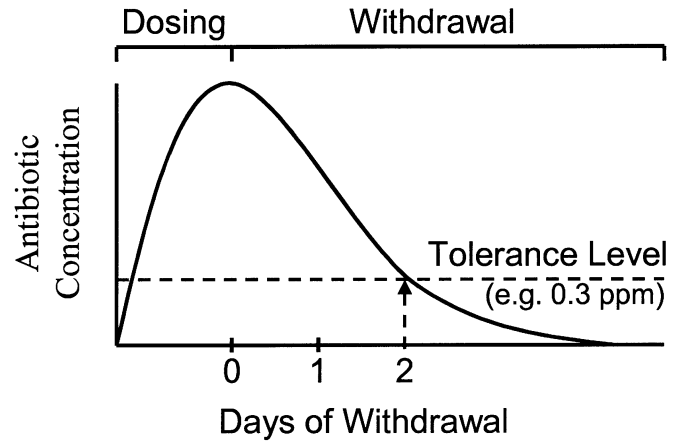


FIGURE 2. Theoretical depletion of antibiotic residues in edible poultry tissue.

Once the tolerance is established for an antibiotic, the FDA requires the sponsor to perform pharmacokinetic studies to ensure the tolerance is not exceeded for the proposed dosing, according to label directions. Usually, a C^{14} radiolabeled-antibiotic depletion study is conducted by the sponsor (www.fda.gov/cvm/guidance/published.htm). Following dosing, edible poultry tissues are evaluated at different time points to determine when total residue concentrations decrease below the tolerance. A theoretical example of a depletion study is depicted in Figure 2. In this theoretical example, a tolerance of 0.3 ppm has been established in poultry muscle (as described previously). Following oral dosing of chickens, total C^{14} radiolabeled antibiotic residues exceed the tolerance during the dosing and the first day of drug withdrawal. By the second day of drug withdrawal, however, the residues in edible tissues are lower than the tolerance. Therefore, the FDA would only approve use of this antibiotic with at least a 2-d withdrawal period. Thus, when the antibiotic is used according to label directions, poultry tissues should not contain harmful residues.

POSTAPPROVAL DRUG MONITORING

Although the FDA requires extensive scientific studies to ensure the safe use of antibiotics by the animal industry, there is the possibility that inappropriate use of antibiotics could cause harmful residues. Inappropriate use could be due to unintentional misuse (not following label directions) or intentional, illegal usage. To guard against these possibilities, both the FDA and USDA have active postapproval monitoring programs for our food supply. This extensive effort requires collection and analysis of samples by field scientists throughout the country. Tissue samples are analyzed for numerous analytes (including antibiotics) to determine if they exceed established tolerances. If a violation is determined, corrective action is taken to prevent recurrence. Usually, violations are due to simple misuse (not following label directions), and education corrects these problems. However, enforce-

TABLE 1. U.S. Food Safety Inspection Service (FSIS) national antibiotic residue monitoring results (1997 to 2000)¹

Production class	Violations 1997 (%)	Violations 1998 (%)	Violations 1999 (%)	Violations 2000 (%)
Young chickens	0.0	0.0	0.0	0.2
Mature chickens	0.0	0.0	0.0	0.4
Young turkeys	0.0	0.0	0.2	0.0
Mature turkeys	0.0	0.0	0.0	0.0
Ducks	0.0	0.0	0.0	0.0

¹Website: www.fsis.usda.gov/ophs/red2000/index.htm.

ment can include legal remedies including criminal prosecution and incarceration. Thus, violations are taken very seriously by the regulatory authorities.

DEVELOPMENT OF METHODS FOR RESIDUE MONITORING

During the preapproval process, the FDA requires the sponsor to develop an official analytical method to test for residue concentrations in edible tissues. These methods can be used by the FDA or USDA to test for violative residue levels of antibiotic in poultry tissues. The FDA cannot, however, require sponsors to develop testing methods for antibiotics (or other drugs) in tissues that are not part of the drug claim. For example, the FDA cannot require a method for enrofloxacin in eggs when the sponsor only requests approval for use in meat-type broilers. Thus, the burden to develop methods to detect antibiotic residues in edible tissues for off-label uses falls on the federal government.

Extensive federal resources are dedicated to development of monitoring methods and research pertaining to the pharmacokinetics of antibiotics in edible animal tissues (including poultry). Results of these efforts allow the federal government to monitor antibiotic residues in tissues for label and off-label usage. There are numerous research scientists at the FDA and USDA involved in these efforts, some of which include the laboratories of the FDA, Center for Veterinary Medicine (Laurel, MD), Office of Regulatory Affairs (e.g., Atlanta, GA; Denver, CO) and USDA/ARS, Microbial Biophysics and Residue Chemistry (Wyndmoor, PA), and Animal Metabolism Agricultural Chemical Research Unit (Fargo, ND).

In addition, veterinary or pharmacokinetic programs at numerous universities or private research facilities also provide research in support of the federal monitoring effort. An example of the extensive effort on the part of the federal government and universities include the author's collaborative research with federal scientists. These collaborations have produced pharmacokinetic models for antibiotic and pesticide transfer into poultry (Donoghue et al., 1996a,b, 1997a,b; Donoghue and Hairston, 2000; Donoghue and Myers, 2000; Donoghue, 2001) and analytical methods for detection of antibiotic (e.g., tetracyclines, sulfonamides, fluoroquinolones, chloramphenicol) and pesticide (e.g., organochlorine, organophosphorus) residues in poultry (Pensabene et al., 1998;

Cohen et al., 1999; Donoghue and Hairston, 1999; Fiddler et al., 1999; Maxwell et al., 1999; Pensabene et al., 1999; Shaikh et al., 1999; Chu et al., 2000; Pensabene et al., 2000; Schenck and Donoghue, 2000; Schneider and Donoghue, 2000, 2001; Lehotay et al., 2001; Heller et al., 2002).

U.S. RESIDUE MONITORING RESULTS FOR POULTRY

Data from the federal monitoring program contradict the perception held by many consumers that harmful antibiotic residues are abundant in meats (including poultry, Figure 1). The most recent 4 yr of monitoring results from the USDA (1997 to 2000) indicate that few if any violative (exceeding tolerances) levels of antibiotics were detected in poultry tissues (Table 1; www.fsis.usda.gov/ophs/red2000/index.htm). In both 1997 and 1998, no violative residue levels were detected. In 1999 and 2000, only 0.2, 0.2, and 0.4% of the samples had violative residues in young turkeys, young chickens, and mature chickens, respectively. These levels of violative residues would not realistically support most consumer perceptions that edible meats contain residues that pose extreme health concerns (Resurreccion and Galvez, 1999). Furthermore, it must be remembered that violative levels of antibiotics in poultry do not necessarily mean they are harmful. This is because the FDA requires the tolerance to be 100- to 1,000-fold below the dose of the antibiotic at which there are no health effects (NOEL). Thus, the safety factor required by the FDA ensures that residues exceeding the tolerance even by as much as 100-fold in edible poultry are still safe to consume.

Conclusions

Both the FDA and USDA provide extensive regulatory oversight to ensure the safety of our food supply. This includes mandatory and rigorous safety (toxicology and pharmacokinetic) studies prior to the approval of an antibiotic for use and monitoring of the food supply to ensure the antibiotic is being used correctly. Furthermore, the federal government, universities, and private research facilities conduct research that allows for monitoring of antibiotics that may be used illegally. Federal monitoring of the U.S. food supply reveals few, if any, violative antibiotic residues in poultry tissues. The intensive efforts of the U.S. government, state agencies (e.g., universities),

and the private sector (e.g., pharmaceutical companies) have arguably produced the safest food supply in the world.

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