

Antimicrobials: Can we continue using them? U.S. Checkoff Programs and Perspectives

Paul Sundberg

Assistant Vice-President, Veterinary Issues, National Pork Board, P.O. Box 9114, Des Moines, IA 50306 USA; *Email:* paul.sundberg@porkboard.org

■ Introduction

The National Pork Board was established by an act of the U.S. Congress in 1985 and is responsible for the collection, distribution, and program accountability for the money generated by the U.S. pork producers' checkoff. A Board led by 15 pork producers creates programs in the areas of promotion, research, and consumer information. These programs, which are directed by producer committees focused on each of the subject areas, support producers by providing them with information on many areas including swine health and pork safety.

Areas of broad responsibility for the National Pork Board Science and Technology Department include pork quality, production research, food safety, swine health, animal welfare, and public health/worker health and safety. The mission of the Science and Technology Department is to provide the scientific support for identifying and addressing issues affecting the health, safety, and quality of the pork industry's animals, products, or people.

The National Pork Board shares the concerns of the public, government agencies, physicians and veterinarians that the use of antimicrobials on the farm could contribute to antimicrobial resistant bacteria being transferred to humans. However, there has been no scientific accounting for the attributable fraction of antimicrobial resistance due to agriculture use.

On behalf of the U.S. pork producers, the National Pork Board has adopted a position statement on the use of antimicrobials in pork production. It reads:

■ National Pork Board Statements

1. To preserve the availability and effectiveness of antimicrobials, a coordinated and appropriate response to the issue of antimicrobial resistance is necessary.
2. Producers and their veterinarians must have the flexibility to responsibly address animal health and production in a timely, cost-effective manner.
3. Producers continue in their science-based commitment to ensure the safety of pork and to maintain consumer confidence.
4. The National Pork Board and the nation's pork producers are supportive of educational efforts to ensure that antimicrobial use does not compromise food safety.
5. The National Pork Board supports a rigorous U.S. Food and Drug Administration process that reviews the scientific data, that evaluates product safety and efficacy and that approves antimicrobials for use in animals.
6. If, based on sound science, additional oversight of antimicrobial use and distribution is considered necessary, stakeholders should discuss the best implementation strategies to achieve the desired result.
7. The National Pork Board supports the development of effective and affordable alternatives to the use of antimicrobials for enhancing production. It has charged its Non-Antimicrobial Production Enhancement Working Group to review the knowledge with regard to the efficacy and economy of the use of non-antimicrobial alternatives to enhance production, to identify the confounding variables that must be controlled to scientifically evaluate the success of these products and/or management techniques, to recommend a research agenda to address knowledge gaps, and to develop a plan of action to educate pork producers about these products and/or management techniques.

■ National Pork Board Position

It is essential to public health and food safety, animal health and well-being, and the environment to maintain the effectiveness and availability of antimicrobials. All decisions affecting the availability of antimicrobials for animal use need to be transparent and based on sound science.

The National Pork Board supports the use of antimicrobials only when they provide demonstrable benefits and urges producers to:

- take appropriate steps to decrease the need for their application;

- adhere to judicious use guidelines;
- assess the benefits and costs of all uses of antimicrobials; and
- complete the Pork Quality Assurance Program and fully implement into their daily operations the management practices described for responsible use of animal health products.

This paper will focus on the U.S. Pork Checkoff's basis for this position from the perspective of the U.S. pork producer.

Statement 1: To preserve the availability and effectiveness of antimicrobials, a coordinated and appropriate response to the issue of antimicrobial resistance is necessary.

A U.S. Interagency Task Force on Antimicrobial Resistance, co-chaired by the Centers for Disease Control and Prevention, the Food and Drug Administration, and the National Institutes of Health, and also including the Agency for Healthcare Research and Quality, the Department of Agriculture, the Department of Defense, the Department of Veterans Affairs, the Environmental Protection Agency, the Health Care Financing Administration, and the Health Resources and Services Administration that was created in 1999. It developed for the U.S. a Public Health Action Plan to Combat Antimicrobial Resistance (U.S. Centers for Disease Control and Prevention 1999).

The Action Plan reflects a broad-based consensus of federal agencies on actions needed to address antimicrobial resistance, which was reached based on input from consultants from state and local health agencies, universities, professional societies, pharmaceutical companies, health care delivery organizations, agricultural producers, consumer groups, and other members of the public. It provides a blueprint for specific, coordinated federal actions to address the emerging threat of antimicrobial resistance. The Action Plan, Part I (Domestic Issues), includes four focus areas: Surveillance, Prevention and Control, Research, and Product Development.

Physicians and their patients and veterinarians and their clients share responsibility to properly use antimicrobials. The Interagency Action Plan calls for increased research, enhanced surveillance, user education and improved diagnostics as ways for the human health community to address antimicrobial resistance. Veterinary medicine and all food animal producers need equivalent initiatives and programs.

Statement 2: Producers and their veterinarians must have the flexibility to responsibly address animal health and production in a timely, cost-effective manner.

One method of delaying and mitigating antimicrobial resistance is to have a variety of products available so any one product does not have to be overly used. Even though there is concern in human medicine about the issue of antimicrobial resistance there is still a very large armamentarium of effective products available to physicians compared to that of veterinarians.

In pork production there are many diseases and conditions that affect our animals for which there is no approved, effective product. We do not now have an adequate arsenal of antimicrobials to address the health needs of our animals. One important available tool is the extra-label use of antimicrobials that can be directed by the veterinarian using his or her professional judgement and knowledge.

The Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA) amended the Federal Food, Drug, and Cosmetic Act to permit licensed veterinarians to prescribe extralabel use in animals of approved human and animal drugs. AMDUCA allows veterinarians to prescribe extralabel uses of certain approved animal drugs and approved human drugs for animals under certain conditions. Extralabel use refers to the use of an approved drug in a manner that is not in accordance with the approved label directions. Three conditions must be met to allow extralabel use under AMDUCA. They are that any extralabel use must be by or on the order of a veterinarian within the context of a veterinarian-client-patient relationship, the use must not result in violative residues in food-producing animals, and the use must be in conformance with the implementing regulations published at 21 CFR Part 530 (USFDA, 2000).

The FDA-CVM continues to reserve the authority to prohibit extralabel use if that use violates its standard of reasonable certainty of no harm. Currently, extralabel use of the following antimicrobials are prohibited:

- Chloramphenicol
- Clenbuterol
- Diethylstilbestrol (DES)
- Dimetridazole
- Ipronidazole
- Other nitroimidazoles
- Furazolidone, Nitrofurazone, other nitrofurans
- Sulfonamide drugs in lactating dairy cattle (except approved use of sulfadimethoxine, sulfabromomethazine, and sulfaethoxyypyridazine)
- Fluoroquinolones
- Glycopeptides

While the prohibition of extralabel use could be an important tool to protect public health in specific instances, it is possible that the Guidance #152 (Draft Guidance for Industry: Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern (Guidance #152); refer to Statement #5) could be used for broad, sweeping extra-label use prohibitions. The body of scientific evidence must support any prohibition of extra-label use.

Statement 3: Producers continue in their science-based commitment to ensure the safety of pork and to maintain consumer confidence.

The National Pork Board has a long history of supporting research that will help the industry base its policies on the best science available on a particular issue. Supported with producer Checkoff funds, research has been conducted into the many questions about the development and selection of antimicrobial resistance, the effective and economical alternatives to the use of antimicrobials and the risk of agricultural uses of antimicrobials. During 2002 over \$365,000 in grants were awarded to researchers studying antimicrobial resistance and the alternatives to antimicrobials. Since 1996 just over one million dollars of Pork Checkoff funds have been used for antimicrobial resistance and alternatives research.

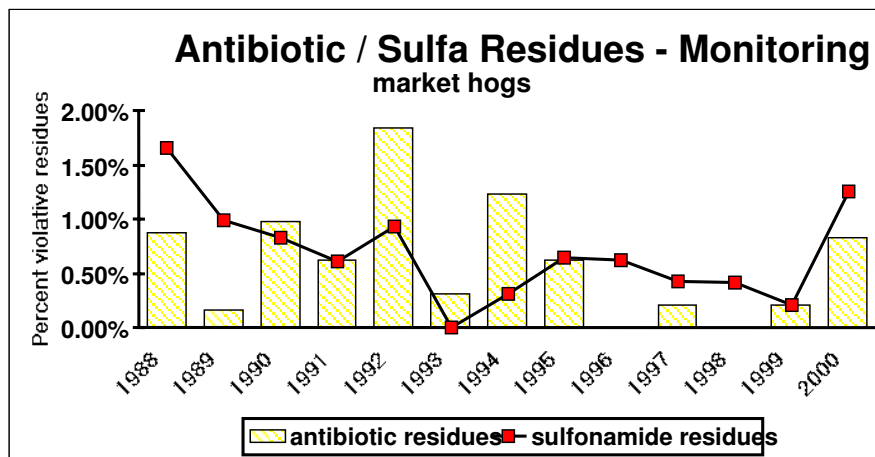
In addition, the Checkoff has formed scientific working groups to review specific issues and advise the National Pork Board's Pork Safety Committee. The Pharmaceutical Issues Task Force, examining pork production's role in the issue of antimicrobial resistance, and the Non-Antimicrobial Production Enhancers Working Group, looking at the scientific basis for the use of antimicrobial alternatives like enzymes, probiotics, prebiotics, immune modulators, etc., are two such advisory groups.

Statement 4: The National Pork Board and the nation's pork producers are supportive of educational efforts to ensure that antimicrobial use does not compromise food safety.

The Pork Checkoff actively promotes educational efforts to ensure that veterinarians and their clients are aware of their responsibilities to use antimicrobial products judiciously. The Pork Quality Assurance Program™ (PQA™) contains a section devoted to specific information about antimicrobial resistance and judicious use. Over 75,000 pork producers have completed the PQA™ Program and have received a judicious use booklet, authored by contract with the FDA-CVM and printed and supplied by the Agency. In cooperation with the American Association of Swine Veterinarians, fact sheets and other informational pieces on antimicrobial resistance and judicious use guidelines for swine veterinarians and pork producers have been developed and distributed.

The U.S. Food Safety and Inspection Service (FSIS) acts to ensure that USDA-inspected meat, poultry and egg products do not contain illegal levels of chemical residues. The FSIS National Residue Program contains a variety of sampling plans and provides for a national database on the occurrence of chemical residues to support risk assessment, enforcement and educational activities (USDA, 2000). The monitoring component of the National Residue Program provides for a random sampling at a rate so that there is a 95% confidence that at least one animal is detected if 1% or more contain violative chemical residues. The surveillance component is a targeted program that samples those animals showing injection marks or chronic febrile conditions. A variety of testing methodology is used for screening and confirmatory testing. All official methodologies are based on microbial inhibition. Figure 1 shows that since the PQA™ began in 1989, the violative residues detected have been consistently in the range of or below the 1% detection sensitivity of the National Residue Program.

Figure 1. Percent violative residues in market hogs. (adapted from the FSIS National Residue Program, 1988 – 2000)



Statement 5: The National Pork Board supports a rigorous U.S. Food and Drug Administration process that reviews the scientific data, that evaluates product safety and efficacy and that approves antimicrobials for use in animals.

The Food and Drug Administration Center for Veterinary Medicine (FDA-CVM) has released a draft guidance (USFDA, 2002) that outlines one method that antimicrobial manufacturing companies might use to show that a new product can be approved for use in food animals without undue risk of antimicrobial resistance affecting human health. The companies are free to use another

method but this is a suggested “guidance” from the Agency. While giving criteria to evaluate antimicrobial resistance safety of new products, Guidance #152 also clearly says that the Agency will be re-evaluating the safety of already approved products. It will affect the future availability of all antimicrobials to producers and to veterinarians.

Although U.S. pork producers support a rigorous, science-based FDA animal health product approval process, there is concern that Guidance #152 sets the bar of acceptance for antimicrobials used in food producing animals so high that it will be unattainable. If implemented to its full potential, Guidance #152 puts at risk timely, cost-effective availability of antimicrobials for animals.

Statement 6: If, based on sound science, additional oversight of antimicrobial use and distribution is considered necessary, stakeholders should discuss the best implementation strategies to achieve the desired result.

Antimicrobials are one tool the producer needs to quickly address clinical and subclinical disease and keep their animals healthy and productive. It is imperative that producers have the timely, cost-effective availability of effective products. Judicious use principles include the involvement of professional veterinary advice whenever a decision needs to be made about the use of an antimicrobial. This involvement can take place regardless of the distribution system for the product. If any additional oversight of antimicrobial use or distribution is considered necessary based on sound science, all affected parties should discuss the best way to implement this to achieve the desired result because it is not yet clear that efforts such as these will ultimately result in the desired effect of reducing risk to public health from agricultural uses of antimicrobials.

Statement 7: The National Pork Board supports the development of effective and affordable alternatives to the use of antimicrobials for enhancing production. It has charged its Non-Antimicrobial Production Enhancement Working Group to review the knowledge with regard to the efficacy and economy of the use of non-antimicrobial alternatives to enhance production, to identify the confounding variables that must be controlled to scientifically evaluate the success of these products and/or management techniques, to recommend a research agenda to address knowledge gaps, and to develop a plan of action to educate pork producers about these products and/or management techniques.

Examining alternatives to the use of antimicrobials for promoting growth and increasing feed efficiency in pork production is one component of a thoughtful,

coordinated response to antimicrobial resistance. Products with these claims are being marketed and there is research and development efforts for new products taking place. For pork producers to make knowledgeable decisions about the use of these products they must have accurate, impartial information about their effectiveness.

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Currently there is not the weight of scientific evidence needed to justify legislative or regulatory prohibition of classes of use of antimicrobials, whether for therapeutic use (treatment, prevention or control) or for improving animal growth and feed conversion. Doing so could have unintended consequences on food safety, animal health and well-being and the environment.

The Pork Checkoff has contributed to the ongoing scientific and technical debate by providing the technical U.S. pork producer perspective to:

- Local county and state public and animal health agencies
- U.S. Department of Agriculture
- U.S. Food and Drug Administration
- Centers for Disease Control and Prevention
- American Academy of Veterinary Pharmacology and Therapeutics
- U.S. delegation to the CODEX Committee on Residues of Veterinary Drugs in Foods
- World Health Organization meetings in Germany, Switzerland and Denmark
- National Academy of Science's Institute of Medicine

- American Veterinary Medical Association
- National and local animal health officials, researchers, veterinarians and pork producers in Sweden and Denmark

U.S. pork producers remain committed to protecting animal and public health in a long-term sustainable manner. This includes using antimicrobials only after an analysis of the operation assesses the relative costs and benefits of their use. It also means that U.S. producers will continue in their efforts to fully implement the Pork Quality Assurance™ Program and judicious use principles on their farms.

■ References

- U.S. Centers for Disease Control and Prevention (1999) Public Health Action Plan to Combat Antimicrobial Resistance, <http://www.cdc.gov/drugresistance/actionplan/index.htm>
- U.S. Food and Drug Administration – Center for Veterinary Medicine (2000) Animal Medicinal Drug Use Clarification Act (AMDUCA), <http://www.fda.gov/cvm/index/amducca/530.pdf>
- U.S. Department of Agriculture – Food Safety Inspection Service. (2000) FSIS National Residue Program Data, USDA-FSIS, Office of Public Health and Science
- U.S. Food and Drug Administration – Center for Veterinary Medicine (2002) Draft Guidance for Industry: Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern (Guidance #152), <http://www.fda.gov/cvm>