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REGULATORY RESEARCH PERSPECTIVES

Impact on Public Health

Human Health Impact and Regulatory Issues Involving Antimicrobial Resistance in the Food Animal Production Environment

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Abstract: Reports of antibiotic-resistant bacteria isolated from farms and animal carcasses are raising concerns that antibiotic use in agriculture may play a role in selecting for antibiotic resistance among foodborne bacteria. Emergence of antimicrobial resistance is a very controversial issue. Some contend that the indiscriminate use of antibiotics in agriculture creates a reservoir of resistant microorganisms in the environment that could infect humans through the food chain. Others contend that the abuse of antibiotics in human medicine may instead be largely responsible for the increase in antibiotic resistance. Animal drug industry representatives feel that there is not enough evidence to conclusively demonstrate a link between the use of antibiotics in food animals and the emergence of antibiotic-resistant bacteria. The research and regulatory issues on antimicrobials used in food-producing animals are of great importance to the Food and Drug Administration (FDA). This report will cover recent developments and describe some of the collaborative research (Table 1) that is being conducted in the Division of Microbiology at the National Center for Toxicological Research (NCTR).

Introduction

Antibiotics are the "miracle drugs" that are extensively used for the treatment and prevention of infectious diseases in humans and pets, as well as in food-producing livestock, poultry and fish. The Centers for Disease Control and Prevention (CDC) estimates that 50 million pounds of antibiotics are produced in the United States alone each year, with roughly 40 percent used in agriculture. Antibiotics have greatly enhanced human life expectancy, reduced mortality, improved quality of life. and almost won the war against many infectious diseases. However, to avoid possible extinction, the bacteria have adapted their own defenses against antibiotics (1). Thus, the development, proliferation, and persistence of antimicrobial resistance are major public health concerns (2). Furthermore, ingested antibiotics may affect the microbial dynamics of the gastrointestinal (GI) tract of the consumer. The resultant decrease or elimination of susceptible bacteria, or overgrowth by foreign microorganisms, may contribute to antimicrobial resistance within the human GI microflora (1).

Another trend that has contributed to the widespread prevalence of antimicrobial resistance is the use of antimicrobials in food-producing animals (Figure 1). Antimicrobials are mixed in chicken and turkey feeds for the prevention and treatment of colibacillosis and staphylococcosis. They are also used for the treatment of mastitis and respiratory diseases of cattle. However, a significant percentage of antibiotics are used, not as therapeutics to treat infections, but in subtherapeutic concentrations as "antibiotic growth promoters" (AGP) (3-4). AGPs enhance meat production; however, they can also increase the prevalence of drug-resistant bacteria. Residues of some of these antibiotics are also known to linger in farm products (4-6). Very little is known about the effects of long-term exposure of humans to these residues.

From an environmental standpoint, the discharge of antibiotics and their metabolites in farm wastes could create a reservoir of resistant microorganisms in the environment. Several antibiotics enter aquatic and terrestrial ecosystems through the discharge of effluents from farms (7). Drug residues in aquatic environments have gained much interest because pharmaceutical

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compounds can frequently be found in effluents from fishpond and river waters at concentrations of up to several micrograms per liter (8). In addition, residues of antibiotics and their metabolites bind to organic matter and persist unchanged for long periods of time in soils. The human health implications of these drugs in aquatic and terrestrial ecosystems are still unknown. Studying the effects of effluents containing antibiotics on the natural microflora may help to reduce the occurrence of drug resistance and provide a basis for regulating the use of drugs in the future.

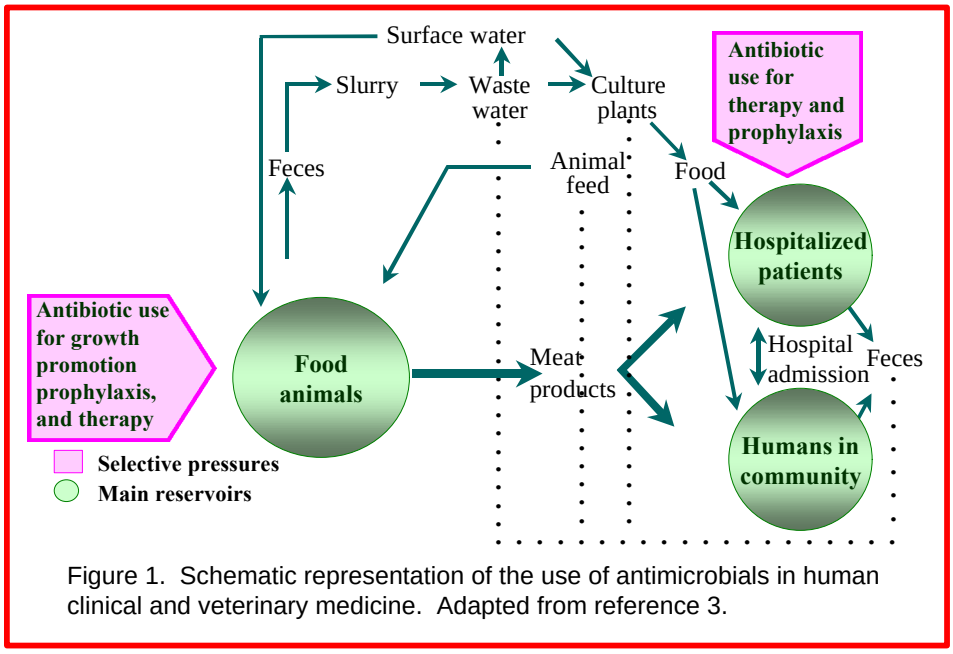

Figure 1. Schematic representation of the use of antimicrobials in human clinical and veterinary medicine. Adapted from reference 3.

Key Regulatory Issues

The FDA Center for Veterinary Medicine (CVM) reviews and approves the use of antibiotics in veterinary practice. The agency reviews data submitted in support of New Animal Drug Applications (NADAs) and Food Additive Petitions (FAP) to assure product efficacy, target-animal safety, human food safety, and environmental safety. Nevertheless, several public health agencies and private citizen groups attribute the occurrence and prevalence of numerous drug-resistant pathogenic bacteria (*Salmonella*, *Campylobacter* and *Listeria*) in food-producing animals to the use of antibiotics in veterinary practice (2-4). Use of these drugs as AGPs may have played a major role in selecting for increased resistance among bacteria pathogenic to humans that are transferred to humans primarily through consumption or contact with contaminated food, thus compromising the clinical treatment of infections. Higher rates of salmonellosis, campylobacteriosis and listeriosis have been observed in people with compromised immunity, and infections are more likely to be severe, recurrent, or persistent in those individuals (9).

Table 1. Research protocols in the Division of Microbiology concerned with antimicrobial resistance.

- Validation of *in vitro* culture systems to measure the effects of antimicrobial compounds on the human intestinal microflora. [Dr. Bruce D. Erickson]
- Studies on mechanism of fluoroquinolone resistant *Salmonella* spp. isolated from animal feeds (poultry), animal production and the development of molecular methods for screening the drug resistance genes. [Dr. Ashraf Khan]
- Molecular screening methods for the determination of vancomycin resistance in selective competitive exclusion product bacteria. [Dr. Saeed A. Khan]
- Studies on the fluoroquinolone resistance in *Campylobacter* sp. isolated from poultry. [Dr. Mohamed S. Nawaz]
- Microbial degradation of drugs and feed additives used in fish farming (aquaculture). [Dr. Jairaj V. Pothuluri]
- Mechanism of antimicrobial resistance in bacteria from the human intestinal tract. [Dr. Fatemeh Rafii]
- Microbial models for biotransformation of fluoroquinolones. [Dr. John B. Sutherland]
- *In vitro* model and molecular analysis of competitive exclusion products. [Dr. R. Doug Wagner]

Bacteria resistant to several antibiotics, including ciprofloxacin and vancomycin, have been isolated from poultry and beef (10). In poultry, infections can arise by transmission from infected breeder birds at the hatchery, by the use of contaminated feed, or by exposure to *Salmonella* spp. from a variety of environmental sources, including wild birds, rodents, insects and inanimate objects. Farm personnel, too, may introduce the organisms into poultry houses when adequate precautions are not observed. The FDA is most concerned about the increase in multiple fluoroquinolone and vancomycin resistance in pathogenic bacteria, especially *Staphylococcus aureus*, *Escherichia coli*, *Campylobacter* spp., *Salmonella* spp., and *Listeria monocytogenes* (11,12). The potential for transfer of fluoroquinolone-resistant bacteria from animals to man presents a risk to public health and could limit the choice of antibacterial therapy for pathogenic bacterial infections. Since this is a safety issue, as defined by the Federal Food, Drug and Cosmetic (FFD&C) Act, the FDA needs adequate information on the prevalence of drug-resistant bacteria and the factors that contribute to their spread.

On October 26, 2000, the CVM

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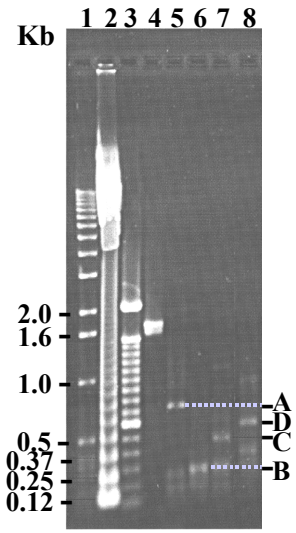

Figure 2. Restriction fragment length polymorphic patterns of *Dde*I digested flagellin (*fla*A) gene from different fluoroquinolone-resistant *Campylobacter* spp. Lanes 1, 1.0 kb ladder; 2, 123 bp ladder; 3, 100 bp ladder; 4, undigested *fla*A PCR product; 5-8, *Dde*I digested *fla*A amplicons.

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proposed withdrawing the approval of the animal drug application (ADA) for use of a fluoroquinolone antimicrobial, enrofloxacin, in poultry. This action was based on the CVM's determinations that (a) the use of fluoroquinolones in poultry causes the development of fluoroquinolone-resistant *Campylobacter* spp. in poultry, (b) this fluoroquinolone-resistant *Campylobacter* is transferred to humans and is a significant cause of fluoroquinolone-resistant *Campylobacter* sp. infections in humans, and (c) fluoroquinolone-resistant *Campylobacter* infections are a hazard to human health. CVM's conclusions were based on data from the National Antimicrobial Resistance Monitoring System (NARMS), a national surveillance program, a case-control study on campylobacteriosis in humans conducted by the CDC and published literature.

To estimate the risk posed by the use of antimicrobials, the CVM conducted a quantitative risk assessment that modeled the human health impact of fluoroquinolone-resistant *Campylobacter* spp. attributed to the consumption of chicken. Risk assessment included a review of how surveillance data are collected and the identification of measurements that are most relevant for linking drug-resistant foodborne pathogens to human disease.

The CVM recently released a draft quantitative-risk assessment that modeled the human health impact of fluoroquinolone-resistant *Campylobacter* spp. and factors associated with the consumption of chicken. They used data from NARMS, CDC's case-control studies, FoodNet, and other sources. The preliminary results indicate that there is an impact on human health from fluoroquinolone-resistant *Campylobacter* spp. that is associated with chicken consumption.

Virginiamycin has been used as an animal growth promoter (AGP) in Europe and North America for more than 20 years. Last year, a structurally related antimicrobial, Synercid® (quinupristin/dalfopristin) was approved in the U.S. for use as a last-resort weapon against antibiotic-resistant enterococci and other bacteria in humans. However, Synercid®-resistant bacteria are being found in patients who have never been exposed to this drug combination before, suggesting a non-human source (13). The use of virginiamycin in food-producing animals may have selected for resistant enterococci, which can contaminate food, enter the human gastrointestinal (GI) tract, and pass the new resistance genes to enterococci of the human intestinal microflora (14). A second risk assessment is being conducted to assess both the plausibility of a link between the use of virginiamycin in animals and quinupristin/dalfopristin resistance in humans and the human health impact attributable to use of virginiamycin. Ultimately, the FDA wants to ensure that significant human antimicrobial therapies are not compromised or lost due to virginiamycin use in production of food animals.

Since there has been concern about the indiscriminate use of antibiotics in agriculture, other approaches are being developed to minimize contamination of animal products with foodborne human pathogens. Reducing colonization of animals by pathogenic bacteria by using competitive exclusion treatment, phage therapy, vaccines, and farm hygiene is being considered as an alternative to antimicrobial feed additives (15).

The extensive use of antibiotics in animal production to promote growth, increase feed conversion efficiency, and, for the prevention of intestinal infections, has led to an imbalance in the beneficial intestinal flora and the appearance of resistant bacteria. The use of probiotics to competitively exclude colonization by intestinal pathogens has been proposed for poultry, especially after the European Commission (EC) banned certain antibiotics that are frequently included in poultry feed as growth promoters (16).

For widespread commercial use, it is essential that any competitive exclusion preparation for poultry be free from all known human and avian pathogens and from any organisms with unusually high resistance to antimicrobials (17). Competitive exclusion products are applied to newly hatched chicks as soon as possible at the hatch-

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ery or on the farm. The FDA has approved a competitive exclusion product designed to prevent the colonization of chicken intestines by pathogenic bacteria, such as *Salmonella* spp., *Campylobacter* spp. and *E. coli*, and also to reduce the use of antibiotics in farm animals and the spread of antibiotic-resistance genes (17). However, the product itself contains several bacteria resistant to vancomycin, an aminoglycoside antibiotic. Clinicians have expressed serious concerns about the prevalence of vancomycin-resistant bacteria because vancomycin is considered the "silver bullet of last resort" (7). Thus, the FDA is concerned about the spread of vancomycin-resistant bacteria to the human food supply via competitive exclusion product use in poultry.

In recent years, there have been questions concerning the consumption of trace levels of antimicrobial residues in foods from food-producing animals and the effects of these residues on the indigenous human intestinal microflora (18). Bacteria from the human gastrointestinal (GI) tract are exposed to antimicrobial agents during treatment for diseases and also through the consumption of food products from antibiotic-treated animals that contain low concentrations of drug residues (1-4). The effects of therapeutic doses of antibiotics on bacteria have been documented, but the effects on the intestinal microflora of low levels (i.e., ppb or ppm) of antibiotics in food from treated animals, especially on selection for resistant organisms, are not well defined (18). The CVM is concerned about the effects on the human intestinal microflora of antibiotic residues in food and issued a guidance document in January 1996 entitled "Microbiological Testing of Antimicrobial Drug Residues in Food", which indicates that additional microbiological testing will be necessary for microbiologically active residues present in food at levels higher than 1 ppm (1.5 mg/person/day). This threshold acceptable daily intake (ADI) was believed to produce no adverse effects on the human intestinal microflora of the consumer. The CVM is validating both *in vitro* and *in vivo* model systems that could be used to study how antimicrobials perturb the human gastrointestinal (GI) microflora. After reviewing the data, the FDA recently concluded that the threshold it had set is not appropriate for all classes of antimicrobials. Microbiological endpoints that could be of public health concern are affected to different degrees by different classes of antimicrobials. The FDA needs methods that are standardized and validated as useful tools to scientifically determine the levels of antibiotic residues that would cause no adverse effect on the human intestinal microflora.

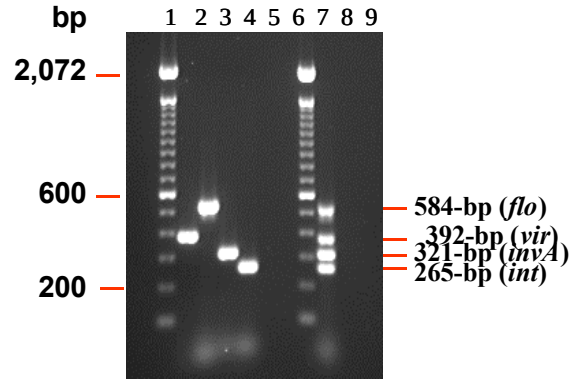

Figure 3. Analysis of *vir*, *flo*, *int* and *inv* genes from *S. typhimurium* DT18 strain by individual and multiplex PCR methods (22). Lanes 1 and 8, 100 bp DNA ladder; 2-5, individually amplified PCR products of *vir*, *flo*, *int* and *inv* genes, respectively; 9, multiplex PCR products of *vir*, *flo*, *int* and *inv* genes.

Animal waste is another route of human exposure to antimicrobials used in food producing animals (Figure 1). Public health concerns associated with antimicrobial resistance are directly and indirectly affected by microbial interactions in farm wastes containing resistant bacteria (pathogens and non-pathogens) and veterinary drug residues (19-21). Farm wastes containing bioactive veterinary drug residues and bacteria resistant to these antimicrobials are routinely fed to animals intended for food and may accumulate in manure. Major portions of these drugs are excreted either unchanged or as modified metabolites. Farm wastes applied to the land are susceptible to runoff into bodies of water (21-23), where they may be a potential reservoir for drug-resistant bacteria (8). The use of farm waste as a fertilizer, feed supplement, or bedding supplement may result in the transfer of pathogenic bacteria in the environment and may be hazardous to the health of animals and humans. It is important to

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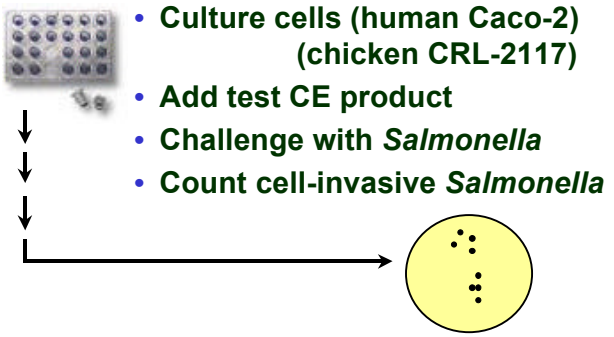

Figure 4. *In vitro* competitive exclusion assay procedure.

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determine the ability of environmental microorganisms either to degrade antimicrobial drugs to harmless metabolites or else to transform them to metabolites that have reduced antibacterial activity. Appropriate treatment of animal wastes could enhance the biodegradation of animal wastes containing antibiotics.

How Research in the Division of Microbiology at the National Center for Toxicological Research (NCTR) is Addressing These Issues

The Division of Microbiology research scientists are committed to providing valuable information to FDA regulatory scientists to evaluate the specific key regulatory issues outlined above. Development of surveillance techniques, unambiguous diagnostic techniques, and critical analysis of data may help limit the spread of drug resistance. Cooperation among public health agencies, research centers within the agencies, and private research facilities is important to monitor, characterize, and report the prevalence of drug resistance.

As a part of the Food Safety Initiative (FSI), the NCTR Division of Microbiology has established collaborative research agreements with several scientists at the CVM/FDA, Arkansas Poultry and Livestock Commission, and the Department of Poultry Sciences, University of Arkansas, Fayetteville, AR (Table 1). In addition, the division has also established collaborative agreements with chicken and turkey growers. Drs. Mohamed Nawaz and Ashraf Khan have collected litter, feed, and water samples from these farms to isolate drug-resistant bacteria. These scientists also have sampled poultry products sold at local grocery stores. Their research indicates that poultry meat sold in supermarkets, especially the liver, could act as a reservoir of fluoroquinolone-resistant *Campylobacter* spp. A low percentage of campylobacters were resistant to fluoroquinolones, and most of these strains were resistant to multiple antibiotics. These isolates have been divided into six different subgroups based on the restriction fragment length polymorphism (RFLP) patterns of the *flaA* gene amplicon digested by the endonuclease, *DdeI* (Figure 2).

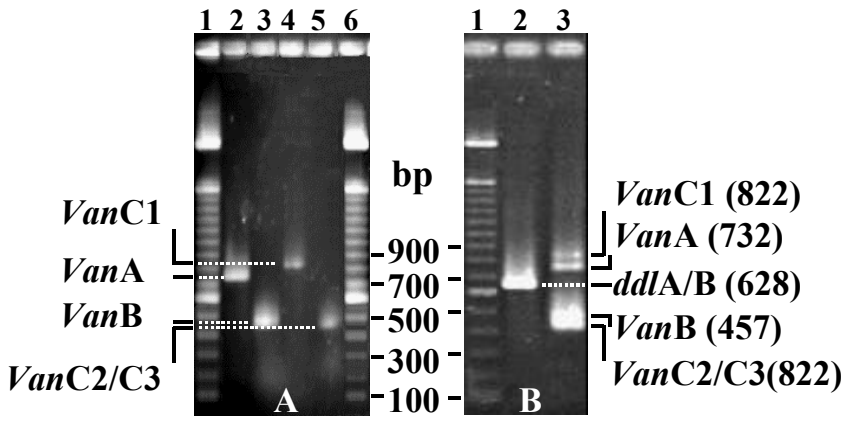

Fig. 5. Analysis of vancomycin resistance determinant genes *Van*A, *Van*B, *Van*C1, *Van*C2/C3 and *Ddl*A/B by individual (A) and multiplex (B) PCR methods. A. lanes 1 and 6, 100 bp ladder; 2, *Van*A; 3, *Van*B; 4, *Van*C1; and 5, *Van*C2/C3. B. lane 1, 100 bp DNA ladder; 2, *Ddl*A/B; and 3, *Van*A, *Van*B, *Van*C1, and *Van*C2/C3 genes PCR products.

Investigations of the drug resistance profiles of *Salmonella* spp. indicate that most strains of these pathogenic bacteria are resistant to multiple antibiotics, such as ampicillin, chloramphenicol, florfenicol, streptomycin, sulfonamides and tetracycline (ACSSuT-type). No simple, rapid, sensitive detection technique to identify pathogenic, drug-resistant strains was available. To fill this void, Dr. Ashraf Khan developed a multiplex polymerase chain reaction (PCR) method that is both rapid and sensitive for the detection of *Salmonella typhimurium* DT104 (ACCSSuT-type) from clinical, food, and environmental samples (24). Currently, this method is used by the field labs (Office of Regulatory Affairs, ORA) to detect *S. typhimurium* DT104 in food samples (Figure 3). Drs. Nawaz and Ashraf Khan, with technical support from Mr. Donald Paine, Mr. Roger Steele, and Ms. Christine Summage-West, are also investigating the possibility of establishing a baseline for the occurrence of fluoroquinolone-resistant *Campylobacter* spp., *Salmonella* spp., and *E. coli* in poultry products. By establishing a baseline, the FDA can accurately monitor the spread of fluoroquinolone resistance in pathogenic strains over time and assist in managing their spread.

Competitive exclusion products fall under the jurisdiction of the FDA when they are linked to claims of treatment of infectious diseases (i.e., salmonellosis and campylobacteriosis). As new animal drugs, competitive exclusion products must adhere to the FDA regulations that indicate that the bacterial mixtures must be well-defined. The data submitted for approval of the competitive exclusion product by the manufacturer report that the product contains 29 well-defined isolates of facultatively and obligately anaerobic bacteria (25). However, investigations by Dr. Doug Wagner (Division of Microbiology) indicate several discrepancies between our conventional identification and the list of components reported to be in one such product. The comparison of conventional phenotypic identification techniques with genotypic techniques also revealed numerous discrepancies. Our results indicate that FDA will need to standardize which types of

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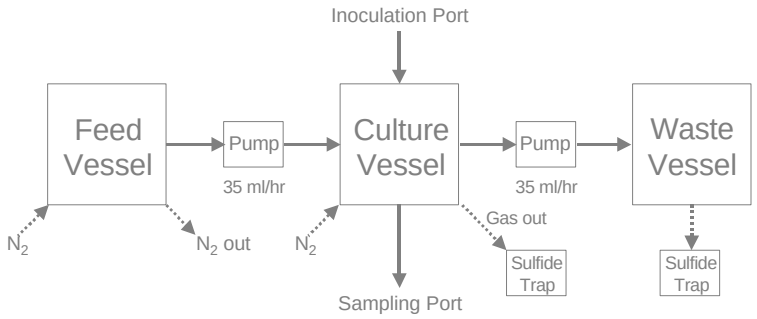

Figure 6A. This figure shows a flowchart for the chemostat system used to mimic the human colon. Pre-reduced medium is pumped from the feed vessel to the culture vessel at 35 ml/hr. The culture is pumped out to the waste vessel at the same rate to provide the environment for establishing a steady-state culture. The culture vessel has additional ports for inoculation, gas in, gas out, and sampling. During operation, the entire system is kept in an anaerobic state, similar to natural conditions in the colon.

Figure 6B. A photograph of the chemostat in operation. The large vessel on the left is the feed vessel. The small spin-flask with multiple ports is the culture vessel, and contains 500 ml of a steady-state culture of colonic bacteria. The waste vessel is located behind the culture vessel and peristaltic pump.

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identification techniques will be used to characterize the components of competitive exclusion products. Dr. Wagner, with assistance from Mr. Mike Holland, has also standardized a quick and accurate assay for determining the efficacy of potential competitive exclusion products (Figure 4). In addition, Dr. Saeed Khan has determined that all lactobacilli in the competitive exclusion product are resistant to vancomycin and contain a vancomycin-resistance (*DdlA/B*) gene. He has developed a multiplex polymerase chain reaction (PCR) that can simultaneously amplify all the multiple markers for vancomycin resistance (*Van*A, *Van*B, *Van*C1, *Van*C2, and *DdlA/B*) in any bacterial strain (Figure 5).

The Veterinary International Cooperation on Harmonization (VICH) Microbial Safety Task Force is evaluating *in vitro* and *in vivo* methods for determining "no observed effect levels" (NOELs) for antibiotic residues in food. In collaboration with the CVM, the Division of Microbiology has been performing pre-validation studies on an *in vitro* system that examines the effect of low-level antibiotic residues on the human intestinal microflora by using a chemostat to model the human intestinal tract (Figure 6A, 6B). The effect of the antibiotic residues is determined by (a) changes in cell numbers of target intestinal microflora species, (b) changes in the metabolic activity of the fecal flora, (c) development of bacterial strains resistant to the test antibiotic, and (d) disruption of the resistance to colonization by pathogenic microorganisms (barrier effect).

Using this *in vitro* system, three different concentrations of the fluoroquinolone antibiotic ciprofloxacin were tested by Dr. Bruce Erickson and Ms. Latriana Robertson for their effect on the intestinal microflora. Results show that many types of bacteria are unaffected by the tested levels of antibiotic in the growth medium, but some bacteria, such as *E. coli*, demonstrate an increase in ciprofloxacin resistance. Our study clearly indicates that the *in vitro* culture system can be a valuable tool to evaluate the effects on the human intestinal microflora of low levels of antimicrobial agents in food.

The microbiological risk associated with residues of antimicrobial agents used in food has also been evaluated by international organizations, such as the Food and Agriculture Organization/World Health Organization (FAO/WHO) Joint Expert Committee on Food Additives (JECFA). Dr. Carl E. Cerniglia meets at least once a year as an expert advisor to JECFA on the safety assessment of veterinary drugs in foods. After consulting various scientists from animal health industries, contract laboratories, regulatory authorities, and universities, Dr. Cerniglia prepared a systematic approach to assessing the safety of antimicrobial drug residues for the human intestinal microflora (18,26). This new approach is currently being used by JECFA and is proposed for adoption by the FDA in the review of antimicrobials used in the food animal production.

Another essential study, conducted

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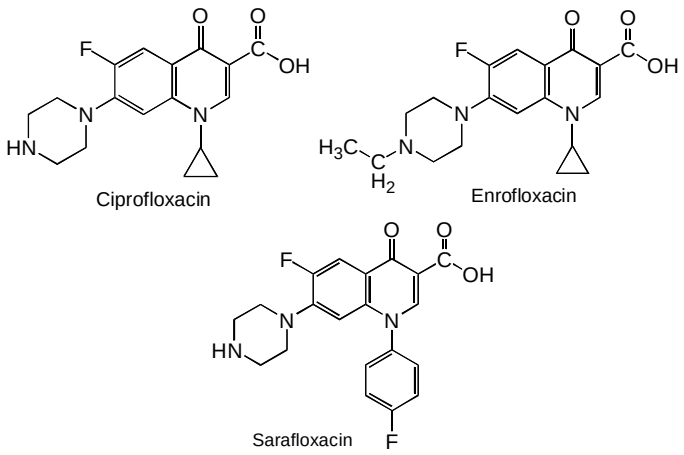

Figure 7. Structures of the fluoroquinolones ciprofloxacin, enrofloxacin, and sarafloxacin

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by Dr. Fatemeh Rafii and Ms. Rebecca Wynne, is the elucidation of the mechanism of resistance to antimicrobial agents among bacteria from the human GI tract, the majority of which are anaerobes. Some of these bacteria cause serious infections, especially in debilitated hosts. Some antimicrobial agents, like fluoroquinolones, have low activity against anaerobic bacteria. The susceptibility spectrum of clinical anaerobes is changing, and some commercially available quinolones are now inactive or only marginally active against these bacteria. Different surveys report MICs of various quinolones that range from 0.8 to >400 µg/ml (27). It is important to determine if the low rates of susceptibility are a consequence of poor drug penetrability, low affinity of the drugs for the target, activity of a multi-drug efflux pump, mutation in DNA or another mechanism. It is imperative to understand the variation in resistance in anaerobic bacteria and relate this variation to the mechanism of resistance.

Figure 8. Flow-through Microcosm Test System.

Development of resistant strains of bacteria has concerned microbiologists tremendously, because the dissemination of resistance genes may result in the spread of diseases that cannot be treated with known antimicrobial agents. The presence of resistant bacteria in the GI tract are of particular concern, because not only do they act as a reservoir for antimicrobial resistance genes, but also if they get out of place and establish themselves in other parts of the body, they can cause diseases that cannot be treated. The increased threat of antimicrobial resistance necessitates the development of new antimicrobial agents, and elucidation of the molecular mechanisms of resistance is important for the design of effective new drugs.

The environmental fate of veterinary drugs and the factors that influence the persistence and biodegradation of antibiotics used in farm animals are not yet well understood. Metabolites resulting from the biotransformation of these drugs may have either enhanced or reduced biological activity compared to the parent compound, and may affect the soil microbial ecology. The environmental fate of fluoroquinolone compounds has been investigated in the Division of Microbiology. Dr. John Sutherland, Dr. Igor Parshikov, and Ms. Anna Williams screened several fungi for the ability to biotransform ciprofloxacin, enrofloxacin and sarafloxacin (Figure 7). A common saprobic fungus, *Mucor ramannianus*, was found to transform ciprofloxacin to *N*-acetylciprofloxacin; enrofloxacin to enrofloxacin *N*-oxide, *N*-acetylciprofloxacin and desethylene-enrofloxacin; and sarafloxacin to *N*-acetylsarafloxacin and desethylene-*N*-acetylsarafloxacin (28-30). These compounds were also analyzed by Ms. Joanna Moody of the Microbiology Division and by the Mass Spectrometry Laboratory at NCTR. These studies indicate the potential of fungi to play a role in the detoxification and removal of veterinary fluoroquinolones from animal waste and contaminated sites.

Dr. Jairaj Pothuluri and co-workers have investigated the fate of erythromycin, a macrolide drug used in both fish farming and clinical medicine. New analytical methods and bioassay procedures to detect erythromycin in aquaculture sediments and water samples were developed (31-33). Microbial and chemical degradation of erythromycin in aquaculture sediment samples were determined using the NCTR microcosm test system (Figure 8). These studies, performed by Drs. Pothuluri, Kyungran Pak and Yong-Hak Kim, indicate that erythromycin is mineralized exponentially after a 120-day lag phase. The successful completion of these investigations has resulted in further collaborations with scientists from CVM and USDA/ARS on the environmental impact of two other aquaculture drugs, oxytetracycline and sulfadimethoxine-ormetoprim (Romet-30).

Summary

The spread, transfer, and preva-

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lence of antibiotic-resistant pathogenic microbes may have a major public health impact. The cost of treatment for these infections in patients with higher susceptibility to foodborne pathogenic bacteria could strain the public health-care system. Monitoring the prevalence of drug-resistant pathogenic bacteria is important to assess the magnitude of the problem and to guide prudent therapeutic recommendations. Public health surveillance to identify the reservoirs of drug resistance genes, curtailment of farm practices that aid and abet the spread of resistance genes, and development of new technologies for the rapid and sensitive detection of pathogenic microbes that have these genes, and elucidation of the mechanism of resistance development could be useful to control this problem. We, at the Division of Microbiology, NCTR, are equipped to find scientific solutions to this emerging public health issue. The findings of our investigations are provided to the FDA to assist in formulating regulations to help contain the spread of drug-resistant microorganisms and protect the efficacy of the miracle drugs for future use.

Acknowledgements

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