Letters to the Editor

Debate continues on AVMA stand on antimicrobials

The January 1, 2004 *JAVMA* (pp 34–36) contains an exchange of letters between Drs. Tabor and Vogel on the impact of the use of antimicrobials in food animals on antimicrobial resistance in humans. It is indeed unfortunate that Dr. Tabor sees the veterinary community as being at odds with the public health community. I do not see it that way. To follow are some views that reflect my perspective as a practicing poultry veterinarian.

- Use of enrofloxacin in poultry is truly a political smoking gun, but a review of facts shows it is not a technical smoking gun at all.
- 2002 National Antimicrobial Resistance Monitoring System (NARMS) data show no resistance to enrofloxacin in *Salmonella* isolates collected from chickens and turkeys.[1]
- *Salmonella* isolates from chickens submitted to diagnostic laboratories have consistently shown zero percent resistance to ciproflox-acin from 1997 through 2002.
- Fluoroquinolone-resistant *Campylobacter* spp have been found in chickens and people in Iceland, but the drug has not been used in poultry in that country, suggesting another reservoir for such resistance.[2] Resistance is just more complicated than simple use or nonuse of an antimicrobial.
- Evaluation of NARMS data on antimicrobial-resistant *Campylobacter* spp is indeed difficult, but the numbers for 1998 through 2003 reveal a cyclic variation that can, and has, elicited numerous opinions and debates.

Use of virginiamycin in food animal medicine is another political smoking gun. Virginiamycin has been used in cattle, swine, chickens, and turkeys for over 25 years without controversy until 1997. That concern arose because of the introduction of quinupristin into human medicine for the treatment of vancomycin-resistant enterococci. Questions: Don't you think the company that developed quinupristin conducted susceptibility and resistance testing of vancomycin-resistant enterococci? In addition, don't you think results must have indicated a high degree of susceptibility or else quinupristin would never have been developed or introduced?

The political smoking guns are the real damaging aspects of the antimicrobial-resistance issue, not the facts of the issue. These smoking guns include statements such as "many intensive animal agricultural production systems create unhealthy environments for food animals," which was included in Dr. Tabor's letter. In food animal medicine, the goal is disease prevention. Unfortunately, this is not always possible; thus, we need the option of safe and effective antimicrobials. Economics are reality, not just of food animal production, but also of consumer purchasing. Today's food animal production programs provide nutritious, tasty meat for American and international consumers at a reasonable cost. By the way, this meat is also safe thanks to the professionals who work in this arena.

In my opinion, if veterinarians and other professionals examine this issue, realistic solutions to minimize antimicrobial resistance will continue to be developed. My recommendation is to continue the prudent usage campaign as championed by many scientific and food animal production associations. Specifically, I believe that all antimicrobials should be available only on the written order of a licensed, qualified veterinarian.

Spangler Klopp, DVM, DACPV
Georgetown, Del

1. United States Department of Agriculture-National Antimicrobial Resistance Monitoring System. Annual veterinary isolates data. Available at: www.arru.saa.ars.usda.gov/frames/narms/franarmsavid.htm. Accessed Nov 17, 2003.
2. Fedorka-Cray PJ, Hiett KL, Stern NJ, et al. Phenotypic and genotypic relationship of *Campylobacter* isolated in Iceland from August-October, 1999. Washington, DC: American Society of Microbiology, 1999;1.

Drs. Tabor and Walters respond:

We'd like to thank Drs. Klopp and Vogel for individually commenting on our concerns about the AVMA's present policy stance on antimicrobial additives. Their comments represent different aspects of this critical issue. First, we believe Dr. Klopp is under the misimpression that efforts to curtail enrofloxacin use in poultry were based on concerns about fluoroquinolone resistance in *Salmonella* spp (enrofloxacin is a

Instructions for Writing a Letter to the Editor

Readers are invited to submit letters to the editor. Letters may not exceed 500 words and 6 references. Not all letters are published; all letters accepted for publication are subject to editing. Those pertaining to anything published in the *JAVMA* should be received within one month of the date of publication. Submission via e-mail (*JournalLetters@avma.org*) or fax (847-925-9329) is encouraged; authors should give their full contact information including address, daytime telephone number, fax number, and e-mail address.

Letters containing defamatory, libelous, or malicious statements will not be published, nor will letters representing attacks on or attempts to demean veterinary societies, their committees or agencies. Viewpoints expressed in published letters are those of the letter writers and do not necessarily represent the opinions or policies of the AVMA.

fluoroquinolone). To the contrary, the proposed FDA ban in October 2000 was based on dramatic increases seen in fluoroquinolone resistance in *Campylobacter* spp following enrofloxacin approval in 1995.[1] Nor, as Dr. Klopp asserts, do National Antimicrobial Resistance Monitoring System (NARMS) data on *Campylobacter* resistance show "cyclic variation;" rather, resistance levels have increased steadily, save for a single year.[2] Moreover, Dr. Klopp's focus on whether prior use of virginiamycin has already caused widespread resistance to quinupristin, the analogous new human antimicrobial, obscures the real question: whether continued use of virginiamycin will accelerate development of resistance to quinupristin.

With respect to Dr. Vogel's comments on behalf of the AVMA (*JAVMA*, January 1, 2004, pp 35–36), he incorrectly implies that the public health community does not support legislation to end the routine use of medically important antimicrobials as feed additives. In fact, numerous health organizations, including the American Medical Association (AMA)[a] and the American Public Health Association (APHA),[b] have formally endorsed the bipartisan Preservation of Antibiotics for Medical Treatment Act. That bill would automatically phase out such uses two years after enactment unless the FDA first finds that their continuation would not contribute to resistance affecting humans.

Although Dr. Vogel notes that the AVMA supports the FDA's new guidance #152[3] regarding food animal antimicrobials, he neglects to mention that applying the guidance's criteria to the drugs covered by the legislation shows that the majority of those drugs (other than bacitracin) are presumptively unacceptable for use as routine feed additives for swine, chicken, and beef cattle—just as the legislation provides. And just as the guidance allows the FDA to consider additional information, so too does the bill.

Moreover, the guidance provides for a qualitative risk assessment, as opposed to the quantitative approach Dr. Vogel suggests. Existing quantitative approaches ignore key aspects of the problem, including the well-known ability of bacteria to share resistance genes with unrelated bacteria. What's more, risk assessments performed to date focus solely on contamination of food by traditional food-borne pathogens, ignoring nonfood pathways, such as workers and the environment, by which resistance genes also spread.

Why, in light of the new guidance, is legislation needed? The answer, in a word, is timeliness. The FDA has failed to establish any schedule for initiating—much less completing—reviews of existing agricultural antimicrobials. Even more important, the cumbersome regulatory process for withdrawing drugs from the market typically takes six to 20 years to complete after the FDA has determined that a particular drug or drug class should be withdrawn.[c]

Another half-century of antimicrobials-as-usual is unacceptable given that the National Centers for Disease Control and Prevention has already identified antimicrobial resistance among its "top concerns."[4] The AVMA should join the AMA, APHA, and others in supporting antimicrobial policy reform.

Gary M. Tabor, VMD, MEM
Bozeman, Mont
Mark Jerome Walters, DVM
St. Petersburg, Fla

[a]Maves MD, American Medical Association, Chicago, Ill: Personal communication, 2003.

[b]Hopert D, American Public Health Association, Washington, DC: Personal communication, 2004.

[c]Sundlof SF, Food and Drug Administration Center for Veterinary Medicine, Washington, DC: Personal communication, 2001.

1. Food and Drug Administration. Summary of notice of opportunity for hearing on withdrawal of enrofloxacin for poultry. Available at: www.fda.gov/cvm/antimicrobial/FQWithdrawal.html. Accessed Jan 28, 2004.

2. Centers for Disease Control and Prevention. National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS): 2001 annual report. Available at: www.cdc.gov/narms/annual/2001/2001.pdf. Accessed Jan 28, 2004.

3. Food and Drug Administration. Guidance for industry #152, evaluating the safety of antimicrobial new animal drugs with regard to their microbiological effects on bacteria of human health concern. Available at: www.fda.gov/cvm/guidance/fguide152.pdf. Accessed Jan 28, 2004.

4. Centers for Disease Control and Prevention. Background on antibiotic resistance. Available at www.cdc.gov/drugresistance/community. Accessed Jan 28, 2004.

Dr. Vogel responds for the AVMA:

In their original letter (*JAVMA*, January 1, 2004, pp 34–36), Drs. Tabor and Walters state a belief that "ideal AVMA policy setting should be forward looking and provide a vision for all veterinarians to aspire for a better animal health future that also safeguards public health, environmental health, and animal welfare." In the response (*JAVMA*, January 1, 2004, pp 35–36), I summarized several AVMA policies that support science- and risk-based decisions to safeguard public health while promoting animal health and welfare. The AVMA believes that the FDA's process for approval and removal of previously approved drugs is a progressive, science- and risk-based process that safeguards public health, albeit with a potential risk to animal health and welfare. The AVMA does not support passage of S. 1460/H.R. 2932 because the bills will ban antimicrobials that do not create a public health risk and will create a risk to animal health and welfare. The ban goes beyond the European ban on antimicrobial growth promotants to also ban uses for disease prevention and other undefined routine uses. Could other routine uses include uses as a feed additive for treatment of disease? In my January 1, 2004, response, I did not comment on whether the American Medical Association (AMA) supports the bills. Instead, I demonstrated the similarity of AVMA policies with the published policies of the AMA and World Health Organization.

Drs. Tabor and Walters state that the FDA guidance provides for a qualitative risk assessment, as opposed to the quantitative approach reportedly suggested in my response. The FDA guidance outlines a qualitative risk assessment approach, but it also permits sponsors to use alternative

processes, including quantitative risk assessments, to characterize the microbial food safety of the drug. The AVMA policies do not recommend one type of assessment as more advantageous than another.

The letter from Drs. Tabor and Walters alleges that the FDA process to withdraw drugs from the market "typically takes six to 20 years." The two examples provided in the reference (diethylstilbestrol and nitrofurans) are the exception, not the norm. In those instances, the scientific evidence regarding the public health risk was conflicting. When the scientific evidence of a public health risk is strong, then the process can be very short. The FDA has the authority to immediately withdraw an approval when an imminent public health risk exists.[1]

The use of antimicrobials in animals has not created an imminent risk requiring precipitous action. There is time to perform scientific assessments. Available scientific information provides evidence of declines in foodborne antimicrobial resistance as well as some increases. For example, the percentage of *Salmonella* isolates resistant to two or more antimicrobials decreased from 31% in 1996 to 22% in 2001, an improvement of 9% and a relative improvement of 29%.[2] Also, between 1996 and 2002, the estimated incidence of human infection with *Salmonella* Typhimurium decreased 31% and infection with *Campylobacter* spp decreased 24%.[3]

Lyle P. Vogel, DVM, MPH, DACVPM
Director, Scientific Activities Division
American Veterinary Medical Association
Schaumburg, Ill

1. United States Code, Title 21, Chapter 9, Subchapter V, Part A, Section 360b(e).

2. Centers for Disease Control and Prevention. National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS): 2001 annual report. Available at: www.cdc.gov/narms/annual/2001/2001.pdf. Accessed Feb 11, 2004.

3. Centers for Disease Control and Prevention. Preliminary FoodNet data on the incidence of foodborne illness—selected sites, United States, 2002. *MMWR Morb Mortal Wkly Rep* 2003;52:340–343.

Thoughts on rabies vaccination enforcement

Summers during veterinary school, I worked in Illinois for the Cook County Animal and Rabies Control going door-to-door verifying current rabies vaccinations for dogs and cats. The data obtained by my on-the-job research 25 years ago showed that about two of five owners had pets that were past due for rabies boosters (which agrees with more recent studies[1]). It was my job to create a compliance desire in the pet owner by way of a ten-day notice and threatened legal action if the needed boosters were not obtained promptly. The county vigorously prosecuted scofflaws. It was this level of enforcement, vigilance, and dedication that kept the public safe where triennial rabies boosters were allowed.

I contend that rabies vaccination compliance will likely be lower where triennial boosters are newly allowed, placing both the animal and human populations at increased risk. Triennial rabies vaccinations (and, to a lesser extent, annual rabies vaccinations) in areas where there is no centralized agency responsible for tracking compliance and enforcing appropriate vaccination laws are a betrayal of the public trust and interest and a potential tragedy in the making. Local city animal control departments are simply not able to provide this service, despite their best efforts.

Relying on guidance and assistance from federal or state governments may not be wholly prudent. The state where I practice has, until very recently, mandated annual rabies vaccination of all dogs and cats with a three-year licensed rabies vaccine. Later, the requirement became annual rabies vaccinations for dogs with a three-year licensed rabies vaccine and annual rabies vaccinations for cats with either a one-year or a three-year licensed rabies vaccine. Currently, dogs and cats may be vaccinated either annually with a one-year rabies vaccine or every three years with a three-year rabies vaccine. This puzzling decrease in governmental concern over rabies occurred despite the need for development of an oral rabies vaccine for

wildlife and despite the steady increase in cases of rabies in the United States between 1990 and 2001, with a 25% increase in rabies cases in Texas alone in 2001.[2]

In my opinion, relaxing rabies vaccination requirements at this time seems to be ill advised. But those who advocate general acceptance of the triennial rabies vaccine must also insist on accurate monitoring and effective enforcement of owner compliance.

Michael A. McLaughlin, DVM
Plano, Tex

1. American Animal Hospital Association. *The path to high quality care: practical tips to improving compliance.* Denver, Colo: American Animal Hospital Association, 2003.
2. Krebs JW, Noll HR, Rupprecht CE, et al. Rabies surveillance in the United States during 2001. *J Am Vet Med Assoc* 2002;221:1690–1701.

Requests more information on cat and dog vaccinations

The *JAVMA* printed three excellent articles on vaccination of dogs and cats in 2002, the duration of serologic response studies by Mouzin et al in the January 1, 2004 (pp 55–66) issue, and the thoughtful Commentary "A perspective on vaccine guidelines and titer test for dogs" by Drs. Moore and Glickman in the January 15, 2004 (pp 200–203) issue.

The possibility of a connection between vaccination and autoimmune diseases was included in most of the articles printed, lectures delivered, and Web materials posted. However, the only article citing a documented relationship between these two events was by Duval and Giger,[1] which was published over seven years ago! The more time that goes by without additional documentation of immune-mediated diseases occurring as a result of vaccination of dogs and cats, the less credible this association seems. Within months of the first report of a possible association between vaccination and the development of sarcomas at the injection sites in cats, there was a flood of additional case reports, epizootiologic analyses, and research studies. This has not occurred with vaccinations and autoimmune disease.

I can appreciate the basis for such concerns, and I applaud pursuing the subject through research and discussion. I am afraid, however, that the amount of smoke generated on this subject has obscured whatever actual fire may be present.

Kenneth M. Kornheiser, DVM
Plainwell, Mich

1. Duval D, Giger U. Vaccine-associated immune mediated hemolytic anemia in the dog. *J Vet Intern Med* 1996;10:290–295.

International call for communication about BSE

As many people are well aware, the report from the United Kingdom on the evidence of bovine spongiform encephalitis (BSE) as a cause of a variant form of Creutzfeldt-Jakob disease (vCJD) threatened the world terribly.[1] In response to this announcement, huge financial resources have been spent on prevention, control, and research for both BSE and vCJD.[2]

With regard to BSE and the political decision-making process, there was an interesting discussion conducted at the 10th International Symposium for Veterinary Epidemiology and Economics held November 17–21, 2003, in Chile. Some veterinary epidemiologists and economists seemed to be critical about the unbalanced use of financial resources for controlling BSE, considering the small possibility of acquiring vCJD by meat consumption. The same may be true for Japan, where we detected only nine BSE cases up to November 2003, conducting BSE testing and removing specific risk materials from all slaughtered cattle. One comment in an e-mail group even said "The risk of acquiring vCJD by consuming meat in Japan is almost equal to the chance of having breakfast with Saddam Hussein in a cafeteria in New York City." This statement may not be scientific or risk-analytic enough, but it could be a good example of comprehensive expression from an intelligent group of people. The opposite type of unbalanced epidemiologic evidence and unjustified political decision-making has also been observed in medical epidemiology. For example, there is well-known epidemiologic evidence that cigarette smoking causes many human diseases, but this information does not seem to be reflected in political decisions related to reducing cigarette consumption in Japan. In this case, the risk-reduction process has not been properly selected although sufficient epidemiologic evidence for risk of cigarette smoking does exist.

Epidemiologists, economists, and risk analysts are requested to work on qualitative and quantitative evaluation of human and animal-related evidence. In addition, we are also responsible for informing appropriate political agencies to ensure proper (or better) political decision-making. The media needs to gather the true evidence and report responsibly to enable the society to move in the proper direction. To facilitate this process, epidemiologists need to open the door to communication with people in other sectors, such as politics and the media, to provide them with appropriate information more quickly because financial resources need to be spent efficiently (and properly) for the sake of better human welfare.

Itsuro Yamane, DVM, PhD
Akiko Nishiguchi
Kannondai, Tsukuba-shi,
Ibaraki, JAPAN

1. Carr K. BSE: the questions that need answers. *Nature* 1996;380:273–274.
2. Howie I. Spending on BSE research. *Nature* 1996;383:211.