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## UNDERSTANDING FLUOROQUINOLONES AND THE CONTINUING DEBATE ON THE IMPACT OF VETERINARY USE OF ANTIMICROBIALS ON HUMAN HEALTH

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The Food and Drug Administration is currently reevaluating whether to rescind approval of the fluoroquinolones for treatment of air sacculitis and colibacillosis in poultry in the U.S. At issue is whether usage of either antibiotic in poultry will affect *Campylobacter's* susceptibility to related fluoroquinolones in humans which are often used for treating human campylobacteriosis.

### How do fluoroquinolones work and how do bacteria become resistant to this class of antibiotics?

The quinolones and fluoroquinolones are broad-spectrum, bacteriocidal antibiotics. These drugs interfere with the normal function of DNA gyrases and topoisomerases, enzymes required for the proliferation and viability of bacteria. Veterinary and human medicine has counted on these antibiotics as the last line of defense against multi-drug

Broiler Performance Data (Region) Live Production Cost					
	SW	Midwest	Southeast	Mid-Atlantic	S-Central
Feed cost/ton w/o color (\$)	135.29	123.09	1137.66	137.70	140.39
Feed cost/lb meat (¢)	12.63	11.75	13.03	13.43	13.19
Days to 4.6 lbs	45	45	45	45	44
Med. cost/ton (¢)	NA	NA	NA	NA	NA
Chick cost/lb (¢)	4.13	3.98	4.11	3.71	4.00
Vac-Med cost/lb (¢)	0.06	0.04	0.10	0.06	0.15
WB & 1/2 parts condemn. cost/lb	0.28	0.25	0.26	0.30	0.23
% mortality	6.03	4.35	5.53	5.82	4.37
Sq. Ft. @ placement	0.76	0.75	0.80	0.76	0.77
Lbs./Sq. Ft.	6.47	6.97	6.67	7.29	6.62
Down time (days)	16	16	15	17	17

Data for week ending 3/10/01

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resistant pathogens. *Controlling colibacillosis and air sacculitis has become difficult due to Escherichia coli's resistance to a multitude of antibiotics.* Eighty-six percent of clinical *E. coli* isolated at our diagnostic laboratory are resistant to tetracycline and chlortetracycline. These isolates are also recalcitrant to treatment with other antibiotics including streptomycin and the sulfa drugs (Bass et al., 1999). However, multi-drug resistant *E. coli* proved to be quite susceptible to the fluoroquinolones.

*Regardless of microorganism, emergence of fluoroquinolone resistance is generally attributed to point mutations in DNA gyrase and topoisomerase genes.* These point mutations result in amino acid changes in these proteins that ultimately affect the enzyme's ability to bind the antibiotic. Depending on the antibiotic, single or double point mutations are necessary for an organism to become resistant to a fluoroquinolone. The probability for any gene, human or bacterial, to mutate is quite low. You have a better chance at winning the Georgia lottery than for a gene to mutate. In bacteria, spontaneous mutation rate is  $10^{-7}$  to  $10^{-8}$ , which means that one bacterium in 10 million to 100 million cells have mutated. What is therefore the probability that *E. coli*, or for that matter *Campylobacter*, present in the gut or poultry litter has mutated towards fluoroquinolone resistance? We know that coliforms are generally present in poultry at about 10,000 to one million in a single gram of either poultry litter or fecal matter. Probability is quite low for that gram of sample for selecting fluoroquinolone resistant *E. coli*. However a poultry farm deals with thousands of birds and tons of poultry litter each year, therefore there is always the probability that a resistant bug exists, only waiting for selection pressure, antibiotic use, to make it the dominant organism on the farm. Resistance to some of the fluoroquinolones among *E. coli* isolates on a poultry farm may take only a single point mutation. While other newer fluoroquinolones resistance is less probable since double mutation is necessary for resistance to occur with a mutation rate of  $10^{-14}$  or one bacterium in 100 trillion (Medders et al., 1999; White et al., 2000).

### Emergence of fluoroquinolone resistance in avian *E. coli*.

Fluoroquinolones are given to poultry orally, usually through the administration of the antibiotic in the bird's drinking water. Because of this oral regimen, the antibiotic not only affects viability of *E. coli* but other microorganisms that reside in the gut including *Campylobacter*. Low dosages or repeated use of a particular fluoroquinolone product can affect the probable emergence of fluoroquinolone resistance on the farm (Medders et al., 1998). Since the approval of fluoroquinolones for poultry use, we have observed steady increase in fluoroquinolone resistance in *E. coli* isolated from necropsy submissions to the Poultry Diagnostic and Research Center (PDRC) (White et al, 2000). By 1999, thirty percent of avian *E. coli* isolates were resistant to both veterinary fluoroquinolones approved for use in the U.S. **This level of drug resistance may not naturally reflect the true incidence of resistance in the field, since diagnostic submissions generally reflect worse case scenarios tackled at PDRC.** Fluoroquinolone resistance was attributed to double mutations in the DNA gyrase. *Once the antibiotic has been used on the farm, what are the chances that fluoroquinolone/quinolone resistant bacteria persist within poultry litter?*

**Broiler Performance Data (Company)  
Live Production Cost**

	Average Co.	Top 25%	Top 5 Cos.
Feed cost/ton w/o color (\$)	137.10	131.20	130.36
Feed cost/lb meat (¢)	12.95	12.35	12.22
Days to 4.6 lbs	45	45	45
Med. cost/ton (¢)	NA	NA	NA
Chick cost/lb (¢)	4.11	3.61	2.83
Vac-Med cost/lb (¢)	0.09	0.04	0.03
WB & 1/2 parts condemn. cost/lb	0.28	0.24	0.21
% mortality	5.36	4.68	2.99
Sq. Ft. @ placement	0.77	0.76	0.77
Lbs./Sq. Ft.	6.66	6.91	6.68
Down time (days)	16	16	15

Data for week ending 3/10/01

**Broiler Whole Bird Condemnation (Region)**

	SW	Mid-West	S. East	Mid-Atlantic	S. Central
% Septox	0.388	0.466	0.284	0.386	0.159
% Airsac	0.164	0.092	0.164	0.256	0.267
% I.P.	0.059	0.032	0.127	0.089	0.067
% Leukosis	0.004	0.003	0.011	0.028	0.001
% Bruise	0.008	0.008	0.011	0.013	0.013
% Other	0.030	0.007	0.015	0.020	0.017
% Total	0.652	0.608	0.613	0.792	0.525
% 1/2 parts condemnations	0.482	0.465	0.416	0.442	0.415

Data for week ending 3/10/01

In the broiler chickens, 7 of 91 farms with a history of fluoroquinolone usage contained coliforms resistant to the quinolone naladixic acid. Naladixic acid-resistant bacteria were also resistant to other fluoroquinolones including enrofloxacin and sarafloxacin. Of 24 farms examined, we also identified quinolone resistant coliforms from the poultry litter of three farms with NO history of fluoroquinolone resistance. The number of resistant bugs in the litter exceeded the level expected from selection of spontaneous mutations to quinolone resistance (Hofacre et al., 2000). Medders *et al.* also observed similar discrepancy in their in vitro and in vivo results (1998). *What accounts for this discrepancy in mutation frequency between results observed in the laboratory and in the field?*

### **Campylobacter jejuni, ciprofloxacin resistance and the paper that launched the current FDA inquiry concerning veterinary use of fluoroquinolones.**

*In assessing the impact of veterinary use of antibiotics on human health, it is important to determine if the drug-resistant microbe in humans MATCH with isolate(s) from animals, and where it is applicable identify any common transmissible drug resistance gene(s) in both human and animal isolates. The latter point is not applicable with regards to fluoroquinolone resistance since we are dealing with spontaneous mutation in resident genes found in all bacteria. The current controversy surrounding fluoroquinolones in poultry medicine was precipitated by 1999 publication in the New England Journal of Medicine on emergence of quinolone resistance in Campylobacter jejuni (Smith et al., 1999). In this study, researchers noted an increase in naladixic acid resistant C. jejuni from 1.3 % in 1992 to 10.2 percent in 1998. Subtracting out those cases associated with foreign travel, there was a significant increase in quinolone-resistant C. jejuni from human cases of campylobacteriosis. Twenty percent of retail poultry were contaminated with quinolone-resistant C. jejuni. Through DNA fingerprinting, MATCHES were observed between C. jejuni from humans with isolates taken from retail poultry. Seasonality was also observed in incidence of quinolone resistant C. jejuni during the winter, early spring months, the time of the year one would expect the greatest medication to control colibacillosis and air sacculitis. However, the peak incidence of campylobacteriosis like other foodborne diseases in the United States is during the summer, implying resistant campylobacter, selected during drug usage on the farms during the winter months, remains on the farm to contaminate the birds during spring and summer placements. If poultry use of fluoroquinolones is responsible for emergence of ciprofloxacin resistance in C. jejuni, then one should observe: 1) seasonality in quinolone-resistant campylobacter on retail chicken correlates with seasonality of colibacillosis and air sacculitis and the necessity to medicate birds; 2) regional differences in isolation of quinolone-resistant C. jejuni from processed birds reflect similar regional differences associated with the poultry disease; 3) waxing and waning of resistance in campylobacters isolated from retail chicken mirrors disease and medication patterns in the US; and 4) differences in incidence of quinolone resistant campylobacters between retail meats from chickens and other food animals NOT currently prescribed fluoroquinolones. Is there data available to support this?*

There are many questions to be answered and a lot of data to be collected. At stake is not only the welfare of the consumer, but the health and vitality of the poultry industry. *What will be the economic consequences to the poultry industry if fluoroquinolones are pulled from the market tomorrow?* The food animal industry is sensitive to the impact of agricultural usage of antibiotics on human health and the need to prevent emergence of harmful, drug-resistant pathogens from entering the food supply. Hopefully, whatever regulatory decisions are made are based on fact and not the emotions and rhetoric that has often accompanied this debate.

### **Literature Cited**

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**Georgia Veterinary Medical Association  
Poultry Program  
June 8-9, 2001  
Jekyll Island, Georgia**

The GVMA Program is Featured on the Next Page  
*Be sure to make your room reservations early.*

Clarion Resort Buccaneer Hotel.....	(912) 635-2261
Jekyll Inn Resort .....	(800) 736-1046
Jekyll Island Club .....	(800) 535-9547
Holiday Inn .....	(800) 7-JEKYLL
Seafarer Inn & Suites.....	(912) 635-2202
Villas by the Sea .....	(800) 841-6262

**REMINDER**

All previous issues of the Poultry Informed Professional are archived on our website [www.avian.uga.edu](http://www.avian.uga.edu) under the Online Documents and The Poultry Informed Professional links.

**Broiler Whole Bird Condemnation (Company)**

	Average Co.	Top 25%	Top 5 Co.'s
% Septox	0.320	0.327	0.332
% Airsac	0.190	0.171	0.258
% I.P.	0.086	0.052	0.059
% Leukosis	0.018	0.006	0.013
% Bruise	0.011	0.012	0.015
% Other	0.020	0.005	0.009
% Total	0.645	0.572	0.687
% 1/2 parts condemnations	0.487	0.454	0.282

Data for week ending 3/10/01



The University of Georgia is committed to the principle of affirmative action and shall not discriminate against otherwise qualified persons on the basis of race, color, religion, national origin, sex, age, physical or mental handicap, disability, or veteran's status in its recruitment, admissions, employment, facility and program accessibility, or services.

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# GVMA 2001 Poultry Program

## Friday, June 8

Moderator - Dr. John Glisson

9:00 - 9:45	MG Epidemiology in North Carolina	Dr. Algis Martinez <i>(North Carolina State University)</i>
9:45 - 10:15	Current Research on Infectious Laryngotracheitis	Dr. Maricarmen Garcia <i>(University of Georgia)</i>
10:15 - 10:45	Break	
10:45 - 11:45	Advances in Transgenic Research in Chickens	Dr. Mike McDonell <i>(AviGenics, Inc.)</i>
11:45 - 12:15	Review of Respiratory Disease for 2000-2001	Dr. Louise Dufour-Zavala <i>(Georgia Poultry Laboratories)</i>

## Saturday, June 9

Moderator - Dr. Stan Kleven

8:30 - 9:30	Clinical Presentation of Exotic Diseases Velogenic Newcastle Disease	Dr. Bill Hewat <i>(Tyson Foods, Inc.)</i>
	Avian Pneumovirus	Dr. Dave Halvorson <i>(University of Minnesota)</i>
9:30 - 10:00	Antibiotic Resistance Issues	Dr. Chuck Hofacre <i>(University of Georgia)</i>
10:00 - 10:30	Break	
10:30 - 11:15	Management of Broiler Breeder Males	Dr. Leonard Fussell <i>(Cobb Vantress, Inc.)</i>
11:15 - 12:15	Inactivated Autogenous IBDV Vaccines	Dr. John Donahoe <i>(Lohmann Animal Health)</i> Dr. John Smith <i>(Fielddale Farms, Inc.)</i> Dr. Marshall Putnam <i>(Wayne Poultry)</i>

## Excerpts from the latest USDA National Agricultural Statistics Service (NASS) "Broiler Hatchery," "Chicken and Eggs" and "Turkey Hatchery" Reports

meat production during the week ending March 3, 2001. Placements were up 2 percent from the comparable week in 2000. Cumulative placements from December 31, 2000 through March 3, 2001 were 1.29 billion, down 1 percent from the same period a year earlier.

### January Egg Production Up 1 Percent

U.S. egg production totaled 7.21 billion during January 2001, up 1 percent from last year. Production included 6.11 billion table eggs and 1.10 billion hatching eggs, of which 1.03 billion were broiler-type and 67.0 million were egg-type. The total number of layers during January 2001 averaged 333 million, up 1 percent from the total average number of layers during January 2000. January egg production per 100 layers was 2,164 eggs, down 1 percent from 2,178 eggs in January 2000.

All layers in the U.S. on February 1, 2001, totaled 335 million, up 2 percent from a year ago. The 335 million layers consisted of 276 million layers producing table or commercial type eggs, 56.2 million layers producing broiler-type hatching eggs, and 2.81 million layers producing egg-type hatching eggs. Rate of lay per day on February 1, 2001, averaged 69.1 eggs per 100 layers, down slightly from the 69.4 eggs a year ago.

Laying flocks in the 30 major egg producing States produced 6.75 billion eggs during January 2001, up slightly from January 2000. The average number of layers during January, at 312 million, was up 1 percent from a year earlier.

### Egg-Type Chicks Hatched Up 11 Percent

Egg-type chicks hatched during January totaled 38 million, up 11 percent from January 2000. Eggs in incubators totaled 35.4 million on February 1, 2001, up 8 percent from a year ago.

Domestic placements of egg-type pullet chicks for future hatchery supply flocks by leading breeders totaled 381,000 during January 2001, up 80 percent from January 2000.

### Broiler Hatch Down 2 Percent

The January 2000 hatch of broiler-type chicks, at 734 million, was down 2 percent from January of the previous year. There were 613 million eggs in incubators on February 1, 2001, down 1 percent from a year earlier.

Leading breeders placed 6.69 million broiler-type pullet chicks for future domestic hatchery supply flocks during January 2001, down 3 percent from January 2000.

### Turkey Eggs in Incubators on February 1 Up 3 Percent From Last Year

Turkey eggs in incubators on February 1, 2001, in the United States totaled 31.8 million, up 3 percent from February 1 a year ago. Eggs in incubators were up 1 percent from the January 1 total of 31.7 million. Regional changes from the previous year were: East North Central, up 1 percent; West North Central, up 8 percent; North and South Atlantic, up 3 percent; South Central, down 12 percent; and West, up 8 percent.

### Poults Placed During January Up 3 Percent From Last Year

The 25.5 million poults placed during January 2001 in the United States were up 3 percent from the number placed during the same month a year ago. Placements were up 9 percent from the December 2000 total of 23.3 million. Regional changes from the previous year were: East North Central, up 3 percent; West North Central, up 6 percent; North and South Atlantic, up 5 percent; South Central, down 11 percent; and West, up 5 percent.

### Broiler Eggs Set In 15 Selected States Up Slightly

According to the most recent National Agricultural Statistics Service (NASS) report, commercial hatcheries in the 15-State weekly program set 185 million eggs in incubators during the week ending March 3, 2001. This was up slightly from the eggs set the corresponding week a year earlier. Average hatchability for chicks hatched during the week was 82 percent. Average hatchability is calculated by dividing chicks hatched during the week by eggs set three weeks earlier.

### Broiler Chicks Placed Up 2 Percent

Broiler growers in the 15-State weekly program placed 144 million chicks for

# Meetings, Seminars and Conventions

## 2001 April

**April 11-13: Poultry Industry Conference & Exhibition**, Western Fairgrounds, London, Ontario, Canada. Contact: WesternFair Association, P.O. box 7550, London ON N5Y 5PA. Phone 519-438-7203 x 222. Fax: 519-679-3124. E-mail: info@westernfair.com <http://www.westernfair.com>

**April 17-18: Health & Management Seminar**, Airport Clarion Hotel, Roanoke, VA. Contact: Rockingham Poultry Serviceman's Committee, Virginia Poultry Federation Inc., 333 Neff Ave., Suite C, Harrisonburg, VA 22801. Phone: 540-433-2451.

**April 24-26: Victam Europe 2001 "The Global Event Supplying the Feed & Food Chain" Utrecht Trade Fair**, Utrecht, The Netherlands. Contact:

Phone: +31 33 246 4404; Fax: +31 33246 4706 or Email [expo@victam.com](mailto:expo@victam.com)

**April 24-26: Agro-Foodtech China 2001 International Exhibition for Agriculture, Animal Breeding and Food-Processing Industries in China**, Contact: Florence Mouscadet. Phone: +33 149 685677; Fax: +33 149 685299.

**April 25-27: 24th Technical Turkey Conference**, Shrigley Hall Hotel near Macclesfield, UK. Contact: Fax: +44 1969 6637644 or

Email: [Turkeys@Compuserve.com](mailto:Turkeys@Compuserve.com)

**April 26-29: GPF Spring Meeting**, Callaway Gardens, GA. Contact: Georgia Poultry Federation, P.O. Box 763, Gainesville, GA 30503. Phone 770-532-0473.

## 2001 May

**May 3-4: National Breeders Roundtable**, St. Louis, MO. Contact: U.S. Poultry & Egg Association, 1530 Cooleage Road, Tucker, GA 30084-7303. Phone: 770-493-9401.

**May 7-11: Pepa Annual Convention**, Double Tree Hotel, Monterey, Calif. Contact: Pacific Egg & Poultry Association, 1521 I St., Sacramento, Calif. 95814. Phone: 916-441-0801.

**May 14-15: World Mycotoxin Forum**, Grand Hotel Huis ter Duin, Noordwijk, the Netherlands. Contact: Conference Secretariat, Bastiaanse Communication, P.O. Box 179, NL-3720 AD Bilthoven, the Netherlands. Phone: 31-30-2294247.

**May 19: GPF Night of Knights**, Cobb Galleria, Atlanta, GA Contact: Georgia

Poultry Federation, P.O. Box 763, Gainesville, GA 30503. Phone 770-532-0473.

## 2001 June

**June 1-3: AP&EA Conv.**, Birmingham-Jefferson Convention Complex, Birmingham, AL. Contact: Alabama Poultry & Egg Association, P.O. Box 240, Montgomery, AL 36101. Phone: 334-265-2732.

**June 7-10: Georgia Veterinary Medical Association Annual Meeting**, Jekyll Island, GA. Contact: GVMA, 3050 Holcomb Bridge Rd., Norcross, GA 30071-1362. Phone: 770-416-1633; Fax: 770-416-9095.

**June 8-9: APF Poultry Festival**, Arlington Hotel, Hot Springs, Ark. Contact: Judy Kimbrell, Poultry Federation, P.O. Box 1446, Little Rock, Ark. 72203. Phone: 501-375-8131.

## 2001 July

**July 14-18: AVMA-AAAP Meeting**, Boston, MA. Hotel Reservations: Internet (online reservations) [www.avma.org](http://www.avma.org) Registration for meeting: AVMA, 1931 North Meacham Rd., Suite 100, Schaumburg, IL 60173-4360. Fax: 312-705-2561.

## 2001 August

**Aug. 24: through March 2002 - International Course on Poultry Husbandry**. Contact: IPC Livestock Barneveld College, P.O. box 64, 3770 AB Barneveld, The Netherlands. Phone: +31 342 414881; Fax: +31 342 492813; E-mail: [io@ipcdiar.hacom.nl](mailto:io@ipcdiar.hacom.nl)

## 2001 September

**Sept. 1-4: 6th European Symposium on Poultry Welfare**, Zollikofen, Switzerland. Contact: Alois Mettler, WPSA Symposium 2001, Burgerweg 24, CH-3052 Zollikofen, Switzerland. Fax: +41 31 911 64 60.

**Sept. 9-12: IX European Symposium on the Quality of Eggs and Egg Products & XV European Symposium on the Quality of Poultry Meat**, Contact: Dr. S. Yalcin, Secretary of WPSA Turkish Branch, Ege

University, Faculty of Agriculture, Dept. of Animal Science, 35100 Izmir-Turkey. Phone +90 232 388 4000/1449 (ext.); Fax: +90 232 388 1864.

E-mail: [yalcin@ziraat.ege.edu.tr](mailto:yalcin@ziraat.ege.edu.tr)

**Sept. 12-14: 2nd Poultry Genetics Symposium**, Organised by the Institute for Small Animals Research, Godollo, Hungary and WPSA Working Group 3 'Breeding and Genetics'. Contact: Dr. Hidas Andras. Institute for Small Animals Research. H-2100 Godollo, Isaszegi ut, (P.O. Box 147). Phone: +36 28 420 387; Fax: +36 28 430 184; Email: [hidas@katki.hu](mailto:hidas@katki.hu)

**Sept. 17-21: World Veterinary Poultry Association XII International Congress**, Current developments and prospects for poultry disease prevention and control, Cairo, Egypt. contact: Cairo International Conference Centre, Prof. Dr. A.A. Sami Ahmed, President, Organising Committee, PO Box 2399, Cairo, Egypt. Phone: +202 2442587; Fax: +202 2474955; E-mail: [mipco@thewayout.net](mailto:mipco@thewayout.net)

**Sept. 30-Oct. 4: 13th European Symposium on Poultry Nutrition**, Floreal Club, Koning Albertlaan 59, 8370 Blankenberge, Belgium. contact: Semico-Seminar and Congress Organisation Office, Korte Meer, 16.

## 2001 October

**Oct. 9-12: XVII Latin American Poultry Congress**, Guatemala City, Guatemala. Contact: Anavi, Avenida De La Reforma 8-60, Zona 9, Edificio Galerias Reforma, Torre II, 9° Nivel, Oficina 904, Guatemala City, Guatemala. Phone: (502) 331 1381; Fax: (502) 339 2338; Email: [latino@terra.com.gt](mailto:latino@terra.com.gt);

Internet: [www.XVIII-latinoavicola.org.gt](http://www.XVIII-latinoavicola.org.gt)

**Oct. 17-19: National Meeting on Poultry Health and Processing**, Sheraton, Ocean City, Maryland. Contact: Sharon Webb, Delmarva Poultry Industry, Inc. at [dpi@ce.net](mailto:dpi@ce.net) or Fax: 302-856-1845.

## 2001 November

**Nov. 6-9: VIV Europe**, 2001, Royal Dutch Jaarbeurs Exhibition Center, Utrecht. contact: RoyalDutch Jaarbeurs, P.O. box 8500, NL 3503 RM, Utrecht, The Netherlands, Phone: + 31 (0) 30 295 5662; Fax: + 31 (0) 30 295 57 09.