The adjusted analysis of different confounding factors in the study was conducted separately. This is consistent with the results of Kaye et al. who showed that the effect of resistance was higher for *S. aureus* (odds ratio [OR] 3.4) than for *E. faecium* (OR 2.5) by using separate analyses to show death rates (9). Furthermore, these researchers found different confounding factors in the adjusted analysis of *S. aureus* than in the adjusted analysis of *E. faecium*. Because of the need to conduct separate analyses, which reduced our statistical power, our study was ultimately unable to show a difference in death rates if it existed.

In summary, future studies measuring the impact of antimicrobial resistance on death rates should be restricted to a specific type of infection cause by a single organism in a uniform setting using a validated system to predict mortality in that setting. As such, future studies should involve multiple study sites.

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Antimicrobial Resistance in *Campylobacter*

To the Editor: Iovine and Blaser (1) write, “This therapeutic use [of enrofloxacin] was withdrawn (2) but is now under appeal” and “Despite the restrictions on enrofloxacin use, emergence of fluoroquinolone-resistant *Campylobacter* species, with poultry as an important source, has been documented in the United States... Therefore, our conclusion remains: use of enrofloxacin in poultry materially contributed to increase in human infection by fluoroquinolone-resistant *Campylobacter* species.”

These claims propagate the following important errors. First, the therapeutic use of enrofloxacin was not withdrawn. Judge Davidson’s order to withdraw the approval was an initial decision, to which exceptions were filed in 2004. A final decision rests with the US Food and Drug Administration Commissioner.

Second, poultry has not been identified as an important source of fluoroquinolone resistance in human *Campylobacter* isolates. The raw data of the cited Smith et al. article (3) indicate a nonsignificant negative association between chicken consumption and fluoroquinolone resistance in human isolates. Substantial resistance levels in Northern Hemisphere countries with and without enrofloxacin use, which occurred well before fluoroquinolones were ever used in animals (3–5), also suggest that attribution of such resistance to enrofloxacin is simplistic.

Finally, rational decision-making is based on probable future consequences of a decision, not past history or causes of the current situation. Iovine and Blaser’s claim, “Thus the decision to withdraw therapeutic use of enrofloxacin (3) was warranted,” is not implied, even if enrofloxacin use...
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caused the emergence of fluoroquinolone resistance. If withdrawing enrofloxacin increases campylobacteriosis from airsacculitis-positive chickens, withdrawal may greatly harm human health. A rational withdrawal decision cannot be justified. In summary, Iovine and Blaser’s view that enrofloxacin should be banned is not supported by the data that they have cited or by principles of sound risk management and decision-making.

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In Reply: Cox and colleagues raised 3 major points. For the first point, we stated (1) “This therapeutic use was withdrawn but is now under appeal.” The actual language of US Federal Drug Administration Judge Davidson’s ruling is “Enrofloxacin found not shown to be safe under the conditions of use upon the basis of which the application was approved as required under § 512(e)(1)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 360 b(e)(1)(B)]. Approval of NADA1 for enrofloxacin ordered withdrawn” (1). The drug manufacturer now is appealing the ruling.

For the second point, the authors state that poultry has not been identified as an important source of fluoroquinolone resistance in human Campylobacter isolates. In both Denmark and Spain, introduction of fluoroquinolones into poultry led to a rapid rise in resistance to Campylobacter in both poultry and human isolates (2–5), and banning their use in Denmark led to a rapid fall in resistance (6). Cox and colleagues may maintain that there is no “proof of a causal relationship,” but the relationship is sufficiently strong, temporally restricted, biologically plausible, and coherent to convince disinterested observers, including Judge Davidson and ourselves, otherwise.

For the third point, that decisions must consider probable consequences, we agree. However, Cox et al. appear to use “possible” as their standard. In fact, nearly everything is possible, including the reasoning that they offer. However, in our opinion, based on experience as scientists and microbiologists, we deem the possible consequences described by Cox et al. as insubstantial compared to the clear and present danger to human health of continuing fluoroquinolone use in poultry. Obfuscation and delay have been effective tactics used to maintain profitability even when the facts indicate a different course of action. We hope that the FDA Commissioner will carefully weigh the actual evidence of the risk to human health imposed by the use of fluoroquinolones in poultry.

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